Pharmacology Biochemistry & Behavior, Vol. 37, pp. 587–592. © Pergamon Press plc, 1990. Printed in the U.S.A. 0091-3057/90 $3.00 + .00

A Comparison of the Effects of Diazepam and Scopolamine in Two Positively Reinforced Learning Tasks

SANDRA E. FILE, P. S. MABBUTT AND ELISABETTA TOTH

Psychopharmacology Research Unit, UMDS Division of Pharmacology, Guy's Hospital, London SE1 9RT

Received 11 June 1990

FILE, S. E., P. S. MABBUTT AND E. TOTH. *A comparison of the effects of diazepam and scopolamine in two positively reinforced learning tasks.* PHARMACOL BIOCHEM BEHAV **37**(4) 587–592, 1990.—In a helical maze scopolamine (0.5 and 1 mg/kg) significantly impaired the ability of rats to acquire a spatial learning task using reference memory. In contrast, diazepam (0.5–2 mg/kg) did not impair acquisition of this task and the only effect of diazepam (4 mg/kg) was likely to be secondary to sedative effects. Diazepam (0.5–4 mg/kg) did not impair 8-day retention of the helical maze. In a test of working and reference memory in which spatial processing was minimised, scopolamine (0.5 and 1 mg/kg) significantly impaired acquisition and increased the number of reference memory errors. Diazepam (1 and 4 mg/kg) did not impair acquisition of this task, but when a delay was interposed in the middle of a trial the diazepam-treated rats were slower to complete the task than the controls and made more errors of both working and reference memory. In contrast, when the rats were tested with a change of context, the diazepam-treated rats completed the task more quickly than the controls and made fewer errors of both working and reference memory.

Benzodiazepine Scopolamine Spatial learning Working memory Reference memory

THERE is considerable evidence from human and animal studies that benzodiazepines can impair learning and memory, but it is still a matter of some controversy whether they do so by direct, rather than indirect, means. Benzodiazepines have marked anxiolytic and sedative effects and both of these could indirectly impair performance in learning tasks. Benzodiazepines impair acquisition of negatively motivated tasks (5) and it is difficult to exclude the possibility that at least some of the impairment is due to their anxiolytic action. The most marked and consistent impairments have been found in passive avoidance tasks and this could also arise from a failure of behavioural inhibition. Impairments of response inhibition have been found in the "no-go" component of "go/no-go" tasks (5) and in tasks where the animal has to tolerate a delay in reward (18). The sedative effects of benzodiazepines will also contribute to poor performance in test situations where the animal has a high time constraint on responding or in which learning is assessed purely in the time taken to complete a task. The hippocampus is an important site of action of anxiolytic drugs and hippocampal lesions result in deficits in spatial tasks. Because of the similarity of their effects in several tasks, Gray has suggested that the effects of anxiolytic drug treatment are functionally similar to hippocampal lesions (9). If this hypothesis were correct one would expect to find benzodiazepine-induced deficits in tasks that require processing of spatial information.

Impairments in radial arm maze performance have been reported after treatment with benzodiazepines (11,20), but these have not been universally reported (10,14) and it is difficult to determine whether they should be attributed to impairments of working memory or of processing spatial information. There are two reports of impaired acquisition in spatial learning tasks in which the demands on working memory were minimal (13,20). However, since performance was also impaired by chlordiazepoxide in a cued test condition in an eight-choice arena (20), either nonspecific or reference memory impairments are a possibility.

The purpose of Experiment 1 was to examine the effects of diazepam in the acquisition of a spatial learning task that relies heavily on reference memory. The helical maze was chosen (6) in which rats have to ascend a certain number of floors of a helical maze in order to find a food reward, and in which there are no extra- or intramaze cues. In Experiment 2 a task was chosen in which it is possible to measure errors of both working and reference memory, but in which spatial processing is minimised. In this task there are 9 holes in the front wall of the test box and three of these are rewarded; the task of finding rewarded holes is one of pattern recognition, since there are no extra- or intramaze cues (7). In both these tasks the effects of diazepam during acquisition were compared with those of scopolamine, since this has been shown to impair the acquisition of spatial learning in tasks relying on reference memory (3, 13, 20). The scopolamine-induced deficits in radial arm maze acquisition are primarily restricted to situations in which spatial strategies have to be used (16,19) and its effects on working and reference memory in a nonspatial task have not been studied.

METHOD

Animals

Male hooded Lister rats (Olac Ltd., Bicester) approximately

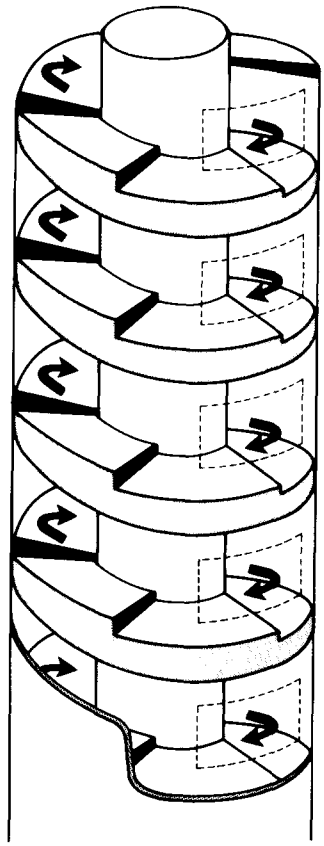

FIG. 1. Diagrammatic representation of the helical maze. The rectangles shown by broken lines represent sliding doors to permit entry or removal of the rat at the start and finish of the trial. The maze is entirely enclosed by the walls of each story and there is a roof over the top floor.

200 g at the start of the study were housed in groups of five with food and water freely available. They were housed in a room with lights on from 0600 to 1700 h.

Apparatus

The helical maze (see Fig. 1) was wooden and consisted of 10 identical circular floors, 49 cm in diameter and 11 cm in height, connected by a helical staircase with 6 steps between each floor. The maze was unlit and totally enclosed by the walls of each story and with a roof over the top floor. The floors were thoroughly cleaned and shuffled after each day's trial in order to minimise any intramaze cues to the floor that was rewarded. The interruption of infrared photobeams on each floor provided automatic measures of the latency to reach each floor, the time spent on each floor and the direction of movement.

The hole-box used to measure working and reference memory has been previously described by Caan (4). Briefly, it is a wooden box $40 \times 40 \times 30$ cm, with one transparent perspex wall in which there are 9 equally spaced 1.5 cm diameter holes in a horizontal line. There is no roof on the box, but the apparatus was placed in a dimly lit room (<30 scotopic lux). The holes in the front wall allow the rat to reach through to a small ledge on which sugar puffs (honey and brown sugar coated wheat puffs from Quaker Oats) were placed. In this experiment holes 1, 4 and 7 were baited with one sugar puff each. For the context change experiment the test box was identical except the holes were covered on the outside with a round cap.

Drugs

Diazepam (kindly donated by Roche Products Ltd.) was suspended in distilled water with a drop of Tween-20 and maintained in an ultrasonic water bath until immediately before injection. Scopolamine hydrobromide (Sigma) was dissolved in distilled water. The drugs were made up to various concentrations to give a constant injection volume of 2 ml/kg. Rats in the control groups received equi-volume injections of water/Tween or water, as appropriate. All injections were IP 30 min before testing.

Procedure

For 3 days before training the rats were given daily dietary supplements of sugar puffs in their home cages, since these were to serve as rewards in the learning tasks. This is a highly favoured food and undeprived rats will work for this reward. Because of the anticholinergic action of scopolamine to cause a 'dry mouth' for the scopolamine groups and their controls, the sugar puffs were dipped in milk when they were used as rewards in the learning tasks. In the helical maze rats were randomly allocated 10 to each of the following groups: control (water/Tween); diazepam (0.5, 1, 2 and 4 mg/kg); control (water); scopolamine (0.5 and 1 mg/kg). In the working and reference memory task rats were randomly allocated 10 to each of the following groups: control (water/Tween); diazepam (1 and 4 mg/kg); control (water); scopolamine (0.5 and 1 mg/kg). In both tasks rats were tested in an order randomised for drug treatment, but the same test order was maintained for each trial. Boluses were removed and the apparatus was wiped after each trial.

Helical Maze

The rats were given five days of familiarisation with the maze before training and drug administration began; this is because diazepam alters the initial exploration of the maze (8). On the first four days groups of five rats were placed in the maze on the bottom floor (floor zero) and allowed 15 min free exploration. On day 1 all the floors were baited with 5 sugar puffs; on day 2 there were 5 puffs on floors 5–7 and 2 puffs on floors 1–4; on day 3 there were 5 puffs on floors 6 and 7 and 2 puffs on floors 1–5; on day 4 there were 5 puffs on floor 7 and 2 puffs on floors 1–6. On day 5 each rat was placed singly in the maze on the bottom floor and allowed 5 min free exploration, with one sugar puff on each of floors 4–7. From day 6 onwards the rats were injected with their appropriate drug and placed singly into the maze at floor 4 and a single reward was placed on the first step of floor 7. The trial lasted 5 min or until the rat reached floor 7 and took the reward. Training continued with one trial per day for 15 trials or until the rat reached the composite criterion of obtaining the reward on 3 successive trials and on the last trial of doing so in <1 min, without making a backwards turn. When the rats reached this composite criterion they were left in their home cages (but daily injections were continued) until a retention test 8 days later.

Working and Reference Memory Hole-Box

Each rat was placed singly into the box, facing away from the perspex wall, and allowed 10 min or until it had taken all three puffs; the time to do this was recorded. Trials were given at 48-h intervals until a criterion of taking all 3 puffs in <60 s, with no more than one error, was reached. The rats were not injected on

TABLE 1

MEDIAN TRIALS TO REACH VARIOUS CRITERIA IN THE HELICAL MAZE

	1st Reward	3 Rewards	<60 s	No Back Turns	Combination
Control	1	4	3	3	9
Scopolamine					
0.5 mg/kg	1	7	9	15*	15*
1 mg/kg	1	5.5	6.5*	10*	15*
Control	2.5	6	4.5	7	8.5
Diazepam					
0.5 mg	4	7.5	7	7	10.5
1 mg/kg	3.5	7.5	6.5	7	8
2 mg/kg	4.5	8	7.5	7	10.5
4 mg/kg	6	8	10*	8	12*

*$p<0.05$ compared with control group, Mann-Whitney U-tests.

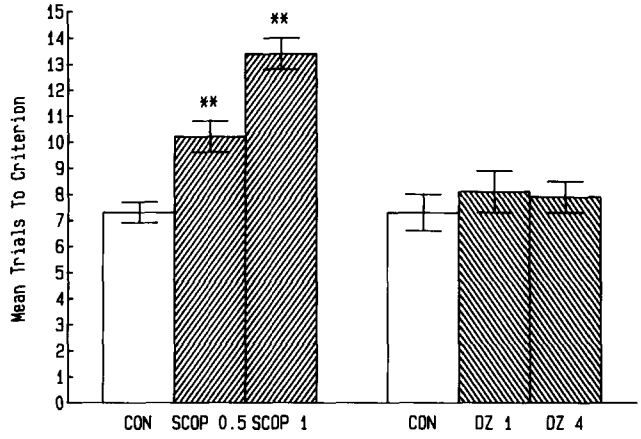

FIG. 2. Mean (±sem) trials to reach criterion in the working and reference memory task by control groups (CON) and those injected with scopolamine (SCOP 0.5 and 1 mg/kg) or diazepam (DZ 1 and 4 mg/kg). **$p<0.01$ compared with control group.

the days on which they were not tested. When the control and diazepam (1 and 4 mg/kg) groups reached criterion they were tested the following day in the task with a 2.5-min delay interposed after the first reward was taken. The rats were placed in a small holding cage in the same room for the delay. After this delay test the rats were retrained, if necessary, to again reach criterion in the normal test condition. They were then tested in the different context condition. This meant testing them in a box that was identical except the holes were covered on the outside of the ledge, so that they were dark and not light.

The holes visited were recorded and thus the following classes of error could be calculated: Reference Memory errors (visiting holes that were never baited); Working Memory errors (returning to a hole from which the puff had already been taken); Reward Failures (visiting a rewarded hole, but failing to take the sugar puff).

Statistics

The number of trials to reach various criteria (to first reach a reward; to reach the reward on 3 successive trials; to reach the reward in <60 s; to reach the reward without making a backwards turn; and the final, composite criterion) in the helical maze were scored and analysed by Kruskall-Wallis H-tests. The errors in the working and reference memory task were analysed by Kruskall-Wallis and Mann-Whitney U-tests. The trials to reach criterion in the working and reference memory task were analysed by a single factor analysis of variance and the latency to complete the task was analysed by a two-way split-plot analysis of variance.

RESULTS

Helical Maze

Scopolamine (0.5 and 1 mg/kg) significantly impaired the acquisition of the helical maze and only 3 rats in each group reached the composite criterion within 15 trials (see Table 1). However, there was no scopolamine impairment in the number of trials to first reach the reward, or to do so on 3 successive trials and thus it is unlikely that the scopolamine-treated rats were finding the reward less attractive. Both doses of scopolamine also impaired the number of trials the rats took before they were able to reach the rewarded floor without making a backwards turn; only the higher dose impaired their ability to reach the criterion of finding the reward in <60 s (see Table 1). Because so few of the scopolamine-treated rats reached criterion, the retention test was not conducted in these groups.

In contrast, diazepam (0.5–2 mg/kg) did not significantly increase the trials to reach any of the criterion points. The rats treated with diazepam (4 mg/kg) took significantly longer to reach the criterion of reaching the rewarded floor in <60 s, which is likely to be a result of the very sedative effects of this dose. As a consequence, this group also took longer to reach the final criterion (see Table 1). There was no significant difference between the groups in the latency to reach the reward on the 8 day retention test ($H=2.0$) and all the rats reached the reward in <60 s [control mean = 31.4 s, diazepam (4 mg/kg) mean = 40.5 s]. There was no significant difference between the groups in the number of errors (backward turns) made to reach the reward on the retention trial [$H<1.0$; control mean = 1.5, diazepam (4 mg/kg) mean = 1.3].

Working and Reference Memory

Scopolamine significantly impaired acquisition in the working and reference memory task, as shown by the trials to reach criterion, $F(2,27)=34.9$, $p<0.0001$ (see Fig. 2). The times taken to complete the task were analysed for the first 6 days, before any of the rats had reached criterion. The scopolamine-treated rats were significantly slower to complete the task, $F(2,27)=13.2$, $p<0.0001$, and also showed significantly less improvement over trials [drug × trial interaction, $F(10,135)=3.1$, $p=0.001$] (see Table 2).

Scopolamine significantly increased the total errors made in reaching criterion, $F(2,27)=6.2$, $p<0.01$. Analysing each type of error separately, scopolamine significantly increased the number of reference memory errors, $F(2,27)=5.3$, $p<0.01$, but did not change working memory errors, $F(2,26)<1.0$ (see Fig. 3). Scopolamine significantly increased failures to take the reward, $F(2,27)=5.7$, $p<0.01$. Analysis of the errors days 1–6 (thereafter several of the control group reached criterion) showed that the scopolamine-treated rats made more reference memory errors on days 4–6 ($p<0.001$ on day 4, $p<0.0001$ on days 5 and 6 significantly increased by both doses). In contrast, they did not make significantly more working memory errors on any individual day.

TABLE 2

MEAN (±sem) TIME (s) TO COMPLETE THE WORKING AND REFERENCE MEMORY TASK OVER THE FIRST 6 TRIALS FOR CONTROL RATS (CON) AND FOR RATS INJECTED WITH SCOPOLAMINE (SCOP 0.5 AND 1 mg/kg) OR DIAZEPAM (DZ 1 AND 4 mg/kg)

	Trials					
	1	2	3	4	5	6
CON	521.5 ± 41	370.4 ± 81	280.9 ± 75	179.5 ± 67	60.2 ± 12	33.0 ± 8
SCOP 0.5	582.2 ± 18	533.1 ± 40	474.2 ± 66	430.5 ± 68	411.6 ± 77	214.4 ± 66
SCOP 1	592.5 ± 7	543.1 ± 47	468.4 ± 69	516.5 ± 57	488.5 ± 58	456.9 ± 73
CON	365.1 ± 54	141.3 ± 22	102.2 ± 26	60.5 ± 12		
DZ 1	574.1 ± 26	256.8 ± 27	149.9 ± 33	72.5 ± 12		
DZ 4	575.5 ± 24	313.1 ± 69	237.4 ± 67	158.5 ± 52		

Data are presented for the trials prior to any rats reaching criterion.

From trials 4–6 the scopolamine treated rats significantly more often failed to take the reward on visiting a baited hole (days 4–6, $p<0.01$ for both doses).

For the diazepam study, the times taken to complete the task were analysed over the first four days, since from day 5 several of the rats had reached criterion. Diazepam (1 and 4 mg/kg) significantly increased the time taken to complete the task, $F(2,27)=7.0$, $p<0.005$. However, all the animals showed a significant decrease in time to complete the task over the first four days, $F(3,81)=94.8$, $p<0.0001$, indicating rapid acquisition (see Table 2). Diazepam did not significantly retard the rate of improvement over trials [drug × trial interaction, $F(6,81)=1.9$]. Furthermore, there was no difference between the controls and the diazepam-treated rats in the trials to reach criterion, $F(2,27)<1.0$ (see Fig. 2).

Diazepam did not increase the number of reference memory errors made by each rat in reaching criterion, $F(2,27)=2.3$, and the trend was for a decreased number made by the diazepam (4 mg/kg) group (see Fig. 3). There was no effect of diazepam on the number of working memory errors, the failures to take the reward, $F(2,27)<1.0$, in both cases, or on the total errors of all kinds, $F(2,27)=1.3$. On a day-by-day analysis of the errors for days 1–4 (thereafter several rats reached criterion) the only significant differences were a reduced total number of errors made by the diazepam (4 mg/kg) group on day 1 ($U=10$, $p<0.01$) and fewer reference memory errors made by the diazepam (4 mg/kg) group on day 2 ($U=22$, $p<0.05$).

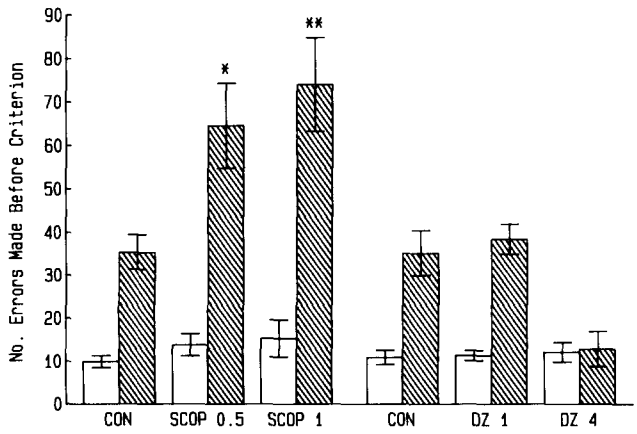

FIG. 3. Mean (±sem) number of errors of working (clear columns) and reference (hatched columns) memory made in reaching criterion by control groups (CON) and those injected with scopolamine (SCOP 0.5 and 1 mg/kg) or diazepam (DZ 1 and 4 mg/kg). *$p<0.05$, **$p<0.01$ compared with control group.

When the rats that had reached criterion were tested with a delay interposed in the middle of the trial, diazepam significantly increased the time to complete the task, $F(2,25)=4.9$, $p=0.01$, and the total number of errors made ($H=11.8$, $p<0.0001$) (see Table 3). Considering the different types of error, diazepam significantly increased both the number of working memory ($H=10.6$, $p<0.0001$) and reference memory errors ($H=10.0$, $p<0.0001$) (see Fig. 4). When the context was changed, diazepam treatment again had a significant effect, but this time it was to *reduce* the time to complete the task, $F(2,24)=3.7$, $p<0.05$, and the total number of errors made ($H=15.8$, $p<0.0001$) (see Table 3). Both the number of working memory ($H=9.2$, $p<0.001$) and reference memory ($H=11.6$, $p<0.0001$) errors were reduced (see Fig. 4).

DISCUSSION

Scopolamine significantly impaired acquisition of the helical maze, which was a reference memory task requiring processing of spatial information. This is similar to the impairments with scopolamine (0.1 and 0.2 mg/kg) in the acquisition of a Morris water maze, also using reference memory (3). Scopolamine has been reported to impair acquisition of a radial arm maze (16), but rats using nonspatial strategies were relatively unimpaired (19). However, the acquisition deficits with scopolamine do not seem

TABLE 3

MEAN (±sem) TIME AND MEDIAN TOTAL ERRORS TO COMPLETE THE TASK WHEN A DELAY OR CONTEXT CHANGE WAS INTRODUCED FOR CONTROL ANIMALS (CON) AND FOR THOSE TREATED WITH DIAZEPAM (DZ 1 AND 4 mg/kg)

	CON	DZ 1	DZ 4
Delay			
Time	15.9 ± 2.0	20.1 ± 1.7	25.1 ± 2.4†
Errors	1	4‡	5‡
Context			
Time	127.2 ± 28.8	74.3 ± 17.2	52.8 ± 6.0*
Errors	8	4*	2‡

*$p<0.05$, †$p<0.01$, ‡$p<0.005$ compared with controls.

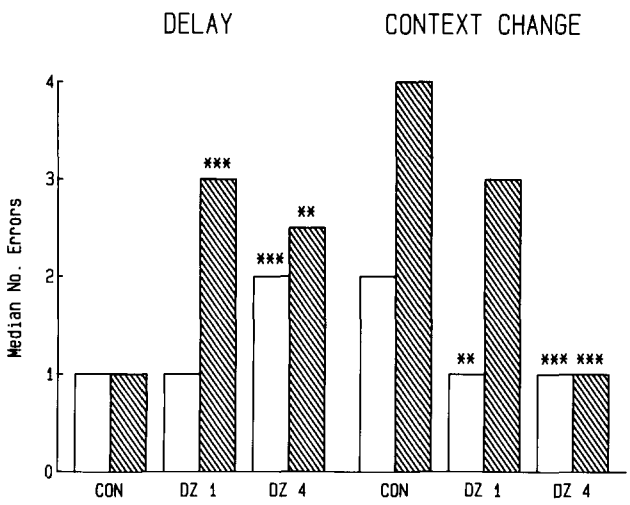

FIG. 4. Median number of errors of working (clear columns) and reference (hatched columns) memory made in the delay and context change tests by control groups (CON) and those injected with diazepam (DZ 1 and 4 mg/kg). $^{**}p<0.01$, $^{***}p<0.005$ compared with control group.

restricted to spatial tasks since we also found scopolamine to impair acquisition and increase errors of reference memory in our second task in which spatial processing was minimised.

There is less agreement on the effects of scopolamine on *performance* of radial arm maze tasks. Okaichi and Jarrard (15) found similar impairments in both place and cue learning and an equal increase in errors of working and reference memory. In overtrained rats scopolamine impaired performance of a radial arm water maze only when a delay was introduced in the middle of a trial (2,3). In rats pretrained in the radial arm maze with half the arms baited scopolamine impaired performance and increased working memory errors (1,21). However, under conditions of pretraining, reference memory errors would be less likely than working memory errors. The overall pattern of impairments are not specific to reference or working memory or even restricted to spatial learning. It therefore seems that the demands of the task determine scopolamine's effects and that it will disrupt whichever processes are the more vulnerable.

The two tasks used in the present study successfully distinguished between the actions of scopolamine and diazepam. Diazepam (0.5–2 mg/kg) produced no impairments of acquisition and the impairment seen with diazepam (4 mg/kg) in the trials taken to reach the rewarded floor in <60 s is most likely to be due to sedative effects. In an easier version of the task when rats had to descend 3 floors of the maze diazepam (1 and 4 mg/kg) was without effect on any criterion measure (8). However, diazepam did disrupt performance of the second task when a delay was introduced in the middle of the trial. Both doses (1 and 4 mg/kg) increased the errors of reference memory and the highest dose also increased working memory errors. These impairments could reflect the general inability of benzodiazepine-treated rats to tolerate delay and to inhibit responding (5,18), or they could reflect impairments in attention, secondary to sedative effects. The control animals were considerably more disrupted in their performance by the context change than they were by the delay. They took a long time to complete the task and spent considerable time investigating the novel test box. Diazepam significantly reduced errors in the changed context, both doses decreasing working memory errors and the higher dose also reducing errors of reference memory. This improvement could be the result of diazepam's anxiolytic action reducing the impact of a novel situation. There was certainly no evidence for diazepam-induced impairment of reference memory and our results would in general support Willner and Birbeck's conclusion (20) that the deficits that have been found by some in radial arm maze tasks are due to nonspecific factors. Our experiments involved repeated drug administration and performance was evaluated in the drugged state. However, although most studies have used acute administration there is surprisingly little evidence from the animal literature for a specific amnesic action of the benzodiazepines (17) and the impairments are not strongly state-dependent (17). Our failure to find any impairment of reference memory is in agreement with the finding from human studies that semantic and procedural memory is unimpaired (12). However, we found no evidence for an increase in errors of working memory which would be analogous to the impaired episodic memory found in humans (12).

In conclusion, while in these two learning tasks the deficits caused by scopolamine were specific to reference memory it seems that this reflects the demands of the tasks, rather than an effect of scopolamine that can be generalised to all tasks. There were no deficits in reference memory with diazepam unless a delay was introduced into the task and it is most likely that these reflected effects on nonmemorial processes. Thus, while it has been possible to clearly distinguish between the effects of scopolamine and diazepam with the two tasks we used, unfortunately there seems little to support a conclusion that either drug is having very specific effects on memory processes.

REFERENCES

1. Beatty, W. W.; Bierley, R. A. Scopolamine degrades spatial working memory but spares spatial reference memory: dissimilarity of anticholinergic effect and restriction of distal visual cues. Pharmacol. Biochem. Behav. 23:1–6; 1985.
2. Buresová, O.; Bures, J. Radial maze as a tool for assessing the effect of drugs on the working memory of rats. Psychopharmacology (Berlin) 77:268–271; 1982.
3. Buresová, O.; Bolhuis, J. J.; Bures, J. Differential effects of cholinergic blockade on performance of rats in the water tank navigation task and in a radial water maze. Behav. Neurosci. 100:476–482; 1986.
4. Caan, A. W. Chronic alcohol administration leads to persistent increase in aggression in rats, after withdrawal, in a new behavioural test. Neurosci. Lett. S32:S41; 1988.
5. Cole, S. O. Effects of benzodiazepines on acquisition and performance: A critical assessment. Neurosci. Biobehav. Rev. 10:265–272; 1986.
6. Curry, P. C.; Caan, A. W. Chronic alcohol administration leads to persistent deficit in 'internal' 3-D spatial memory in rats, after withdrawal in a new behavioural test. Neurosci. Lett. S32–S40; 1988.
7. File, S. E.; Mabbutt, P. S. Chronic ethanol and chlordiazepoxide: Contrasting effects on reward learning. Alcohol 7:307–310; 1990.
8. File, S. E.; Toth, E. Characterisation of spatial learning in a helical maze in absence of intra- and extra-maze cues. Br. J. Pharmacol. 99: 254P; 1990.
9. Gray, J. A. The neuropsychology of anxiety. Oxford: Oxford University Press; 1982.
10. Hiraga, Y.; Iwasaki, T. Effects of cholinergic and monoaminergic antagonists and tranquilizers upon spatial memory in rats. Pharmacol. Biochem. Behav. 20:205–207; 1984.
11. Hodges, H.; Green, S. Effects of chlordiazepoxide on cued radial maze performance in rats. Psychopharmacology (Berlin) 88:460–466; 1986.
12. Lister, R. G. The amnesic action of benzodiazepines in man. Neurosci. Biobehav. Rev. 9:87–94; 1985.
13. McNaughton, N.; Morris, R. G. M. Chlordiazepoxide, an anxiolytic benzodiazepine, impairs place navigation in rats. Behav. Brain Res.

24:39–46; 1987.
14. McNaughton, N.; Davis, N. M.; Brookes, S.; Rawlins, J. N. P.; Feldon, J.; Gray, J. A. Minor tranquillisers and hippocampal connections—some behavioural dissociations. In: Sinz, R.; Rosenzweig, M. R., eds. Psychophysiology 1980. Amsterdam: Elsevier, Gustav Fischer; 1983:183–189.
15. Okaichi, H.; Jarrard, L. E. Scopolamine impairs performance of a place and cue task in rats. Behav. Neural Biol. 35:319–325; 1982.
16. Stevens, R. Scopolamine impairs spatial maze performance in rats. Physiol. Behav. 27:385–386; 1981.
17. Thiébot, M-H. Some evidence for amnesic-like effects of benzodiazepines in animals. Neurosci. Biobehav. Rev. 9:95–100; 1985.
18. Thiebot, M. H.; Jobert, A.; Soubrie, P. Effets comparés du muscimol et du diazepam sur les inhibitions du comportement induites chez le rat par la nouveauté, la punition et le nonrenforcement. Psychopharmacology (Berlin) 61:85–89; 1979.
19. Watts, J.; Stevens, R.; Robinson, C. Effects of scopolamine on radial maze performance in rats. Physiol. Behav. 26:845–851; 1981.
20. Willner, P.; Birbeck, K-A. Effects of chlordiazepoxide and sodium valproate in two tests of spatial behaviour. Pharmacol. Biochem. Behav. 25:747–751; 1986.
21. 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.