*Pharmacology Biochemistry & Behavior*, Vol. 29, pp. 143–150. © Pergamon Journals Ltd., 1988. Printed in the U.S.A. 0091-3057/87 $3.00 + .00

# Effects of Selection Delays on Radial Maze Performance: Acquisition and Effects of Scopolamine[1]

DAVID B. PEELE

*Northrop Services, Inc., Environmental Sciences, P.O. Box 12313*
*Research Triangle Park, NC 27709*

AND

SCOTT P. BARON

*Neurotoxicology Division, Health Effects Research Laboratory*
*U.S. Environmental Protection Agency, Research Triangle Park, NC 27711*

Received 28 July 1986

PEELE, D. B. AND S. P. BARON. *Effects of selection delays on radial maze performance: Acquisition and effects of scopolamine.* PHARMACOL BIOCHEM BEHAV **29**(1) 143–150, 1988.—The effects of post-selection confinement (delays) on both the acquisition of performance and the response to the muscarinic blocker, scopolamine, were examined in an automated version of the eight arm radial maze. Long-Evans rats, exposed to post-selection delays of 0.5 sec (n=4) or 100 sec (n=4) during daily training trials did not differ in either the number of trials to acquire an accurate baseline of performance or in the amount of time required to obtain all eight food pellets. However, the pattern (delta-arm scores) of within-session arm selections demonstrated by the two groups of rats differed. Rats exposed to the 0.5-sec delay typically selected arms adjacent to arms from which they exited while rats exposed to the 100-sec delay were more likely to enter arms 2-removed from the exit arm. When scopolamine (0.03 to 1.0 mg/kg) was administered prior to testing, rats in the 100-sec delay group showed a greater reduction of accuracy and a larger increase in selection latency than rats in the 0.5-sec delay group. The differential effect of delay value on delta-arm scores was also eliminated in a dosage dependent manner with scopolamine. Scopolamine methylbromide (0.3 mg/kg) was found to have little effect on performance. In summary, the results indicate that the post-selection delay procedure is a sensitive and selective test for chemical-induced dysfunctioning of spatial memory in rats.

Radial arm maze Scopolamine Delay Acquisition Response patterning Rat

CHOICE performance in the radial arm maze has gained popularity as a general test of spatial memory in rodents [8, 18, 20]. Over the course of training, rats rapidly learn to enter each alley (arm) of the maze only once to retrieve a single food pellet placed at the distal end of the arm. Spatial memory capacity has been rapidly assessed by imposing delays following the fourth of eight choices, and determining whether the subjects enter arms that were previously visited (incorrect choice, error) or enter previously unvisited (correct choice) arms [21]. While the magnitude of the effect appears to vary considerably, rats have been reported to perform at high levels of accuracy when delays of up to 8 hr separate the fourth from the fifth arm selections ([4], but see [17]).

In contrast to the mid-session delay procedure, a novel approach to the assessment of memory in rats has recently been reported using an aversively motivated 8 arm water maze [6]. In that study, rats were initially taught to swim down each of 8 arms for a 20-sec period of escape (negative reinforcement). Following each 20-sec reinforcement period, the rats were returned to the water and required to choose a new (not previously visited) arm for an additional escape period. In the first phase of the study, delays of 40 to 1280 min were imposed following the first 4 correct selections. The 640 and 1280-min delays reduced accuracy on the final 4 selections to chance levels. When delays were introduced after each correct choice in a second phase of the experiment, accuracy of performance was reduced at much shorter delay values (i.e., 5 to 20 min). From these data, it follows that post-selection delays are much more disruptive to accurate maze performance than the imposition of a single mid-session delay, even if the total time spent in delay is equated.

[1]The research described in this article has been reviewed by the Health Effects Research Laboratory, U.S. Environmental Protection Agency and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the Agency nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

Whether similar results would be obtained from a more traditional, appetitively-motivated radial maze task is unknown. The available data indicate that brief delays (20 sec) imposed after each arm selection can alter the within-trial patterning of arm selections while leaving accuracy of performance unaffected. That is, while rats exposed to no delay choose an adjacent (1 or 2 removed) arm after exiting from an arm, rats exposed to brief post-selection delays show no consistent patterning other than avoiding the arm from which they just exited [19].

The purpose of the present study was to assess the impact of imposing 100-sec post-selection delays during acquisition and steady-state performance using an automated version of an 8 arm radial maze. The delay procedure differed from mid-session delay procedures in that the rat remained in the apparatus during the delay period rather than being removed and placed in a holding cage. Previous research utilizing mid-session delay procedures indicates that similar results are obtained whether the rat spends the delay period in the apparatus or in a home cage [4]. The impact of the delay on acquisition was assessed during each of 31 daily sessions. Following acquisition, rats were exposed to scopolamine challenges in order to assess the possible role of cholinergic mechanisms in maintaining accurate spatial memory using this novel procedure/device. Scopolamine has been shown to degrade accurate performance in the maze when mid-session delay procedures are used ([8], but see [14]), while its effects on performance maintained with post-selection delays are largely unknown. The results indicated similar effects of both scopolamine and delay on the patterning of arm selection, with a delay-dependent potentiation of scopolamine-induced disruption of accurate performance in the maze. It was concluded that the post-selection delay procedure has potential as a sensitive and selective assay for assessing spatial memory deficits in rodents exposed to potentially neurotoxic chemicals.

## METHOD

### *Animals*

Eight adult male Long-Evans hooded rats (Charles River Breeding Laboratories, Wilmington, MA) were used. Rats were housed individually in plastic ceiling-suspended cages (45×24×20 cm) in a colony room with temperature (21.0±2.0°C) and relative humidity (55±5%) held constant and a 12-hr/12-hr light/dark cycle (lights on at 0600 hr). Rats were maintained at 350 g body weight by restricting their daily ration of food; water was available ad lib.

### *Apparatus*

All behavioral testing took place in an automated version of the radial arm maze originally described by Walsh *et al.* [25]. The maze consisted of eight alleys (26 cm long, 10.5 cm wide and 9.5 cm high) constructed of sheet metal (sides) and Plexiglas (floor) radiating equidistantly from an octagonal central arena (32.5 cm diameter). A Gerbrands pellet dispenser (Model G5110) was located at the distal end of each alley and could dispense 45-mg food pellets (BioServe Corp, Frenchtown, NJ) into a Plexiglas food cup centered 5 cm from the floor on the end wall of each alley. Access to the arms was controlled by eight pneumatically-operated sheet metal guillotine doors. A rat's location in the maze was determined from photo emitter/detector pairs located at the entrance and mid-point of each arm (2.5 cm from the center arena and 5 cm above the floor) as well as in the food cups.

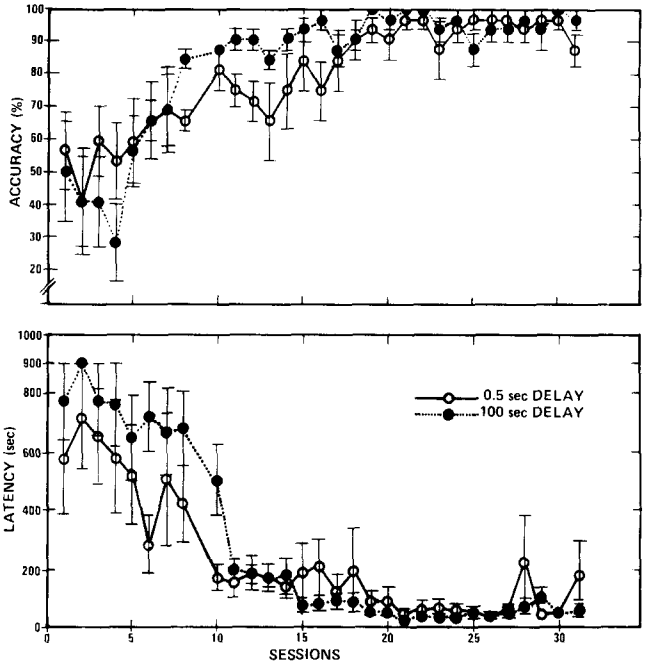


FIG. 1. Acquisition of performance in the automated radial arm maze for rats trained with either 0.5-sec (○) or 100-sec (●) post-selection delays. Accuracy of performance, the percentage of new arms selected during the first eight selections, is shown in the upper panel. Mean latency of performance during acquisition, the amount of time (sec) to obtain all eight pellets, is shown in the lower panel. Each point represents the mean (±SE) for 4 rats during each of 31 daily sessions.

The maze was raised 70 cm from the floor, covered with Plexiglas, and located in a 110-sq ft test room rich in extra-maze cues. Stimulus conditions and data collection were arranged by a minicomputer (PDP 8/a) and SuperSKED software [21].

### *Procedure*

Behavioral training took place in two stages. In the first stage rats were individually confined in one of the arms of the maze with several food pellets placed in and around the food hopper. In addition, food pellets were dispensed for each nose-poke into the food hopper. The session ended after 25 pellets were delivered. On the second day of pre-training, rats were placed in the center arena with all doors closed for 180 seconds after which all doors were opened to allow the rats access to the arms where pellets were placed in each of the hoppers. During this stage, nose-pokes also produced pellets (one per arm), with the session ending after 8 pellets were delivered.

Throughout the course of the experiment, the following performance measures were computed for each subject: accuracy—the percentage of 'new' (not previously chosen) alley selections made during the first 8 alley selections; latency—the amount of time taken to obtain all 8 pellets, excluding delay time (upper limit of 900 sec); delta-arm score—frequency distribution describing the arm selection distance (to the left or right) relative to the arm from which a rat exits (i.e., 0 removed is returning to the same arm, 1 removed is entering an adjacent arm, etc.). The effects of scopolamine (see below) on accuracy and latency were as-

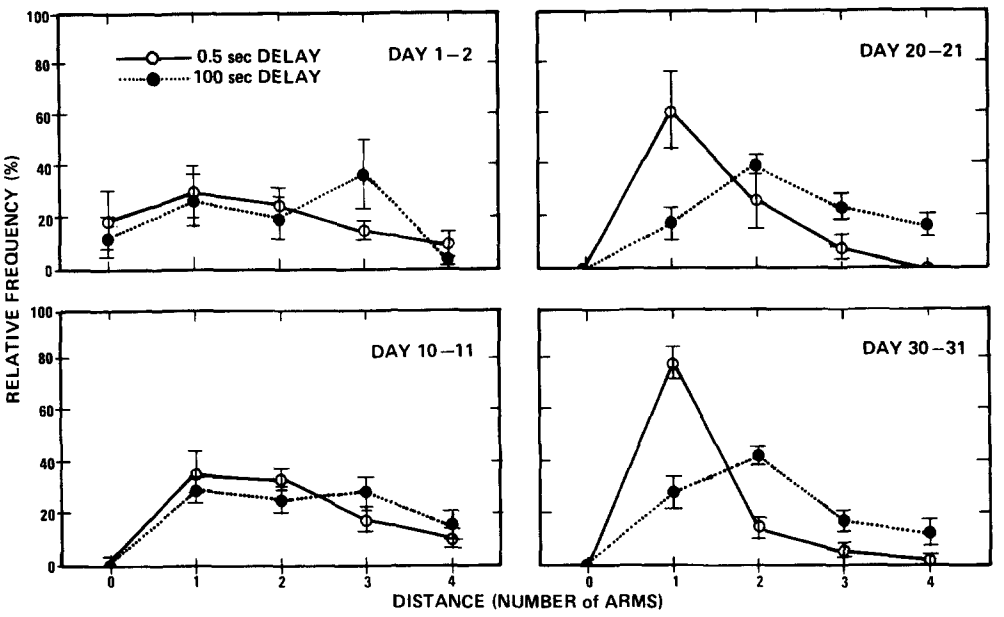


FIG. 2. Delta-arm scores for rats in either the 0.5-sec (○) or 100-sec (●) post-selection delay conditions during sessions 1 and 2, 10 and 11, 20 and 21, and 30 and 31 (session numbers represented in the upper right corner of each panel). Each point represents the mean (±SE) percentage of arm selections for two sessions as a function of the distance (number of arms) separating successive arm selections (see text for details).

sessed statistically using a 2-way analysis of variance (ANOVA), with an alpha level of 0.01. The delta-arm score distributions for the two groups were compared using a chi-square analysis, with an alpha level set at 0.001.

*Delay Training*

The final contingencies were initiated beginning on the third day of training. Performance in the maze was examined by placing each animal on the central arena of the maze with all doors closed. Following a 1-min acclimation period, all doors were simultaneously opened. Nose-pokes into the food cup located in each arm produced a food pellet only once per session, with subsequent nose pokes recorded but having no scheduled consequences. Simultaneous with each pellet delivery, the door to the chosen alley was closed, confining the rat (in the arm) for a fixed period of time: for four rats the delay period was 100 sec and for the other four it was 0.5 sec. Previous research in our lab indicated that rats exposed to post-selection delays would often 'freeze' or show signs of disruption in response to the sound of the doors closing, accompanied by somewhat retarded rates of acquisition compared to rats exposed to no delay (MacPhail, Peele and Baron, unpublished data). As a result of these findings, the present experiment included the 0.5-sec delay period to control for the confounding by this variable: any behavioral effect resulting from the opening/closing of the alley doors would be shared by the two groups of animals. An alley selection (choice) was defined as an instance where a rat entered an alley and emitted a nose-poke into the food hopper. Errors were defined as repeated alley selections. Sessions terminated after all 8 food pellets were obtained or after 900 seconds, which ever came first.

*Scopolamine Challenge*

In order to assess the potential role of cholinergic involvement in radial arm maze delay conditioning, rats were exposed to scopolamine hydrobromide (Sigma Chemical Co., St. Louis, MO: 0, 0.03, 0.1, 0.3, 0.56, 1.0 mg/kg, IP), expressed as the weight of the salt and dissolved in isotonic saline, 20 min pre-session, with each rat receiving each dosage of the compound in a semi-random order. Mid-range dosages (0.1, 0.3, 0.56 mg/kg) were administered on 2 occasions. Scopolamine was administered prior to Tuesday and Friday sessions in a volume of 1 ml/kg b.wt. In order to assess for peripheral nervous system involvement in the effects of scopolamine on performance, rats also received a single pre-session dosage of scopolamine methylbromide (Sigma Chemical Co., St. Louis, MO: 0.3 mg/kg, IP).

## RESULTS

*Acquisition*

All rats exposed to the delay training procedures acquired accurate maze performance over the course of 31 sessions, as shown in Fig. 1. As shown in the upper panel of the figure, both groups initially had equivalent accuracy scores, reflecting roughly chance levels of performance (approximately 50%), and showed asymptotic levels of accuracy (90–95%) after about 20 sessions. While the 100-sec delay group appeared to lag behind the 0.5-sec delay group during the first 4 sessions, they later equalled and even exceeded the mean level of accuracy demonstrated by the 0.5-sec delay group (see sessions 8 to 16).

The effect of post-selection delays on mean latency (time to obtain all 8 pellets) is shown in the bottom panel of Fig. 1. Initially, rats in the 100-sec delay group took longer in general to complete the task than did rats in the 0.5-sec delay group. This effect on latency was only evident during the first 10 sessions after which both groups appeared to complete the task at the same rate. In summary, rats in both the 0.5- and 100-sec delay groups acquired the task with equiv-

alent levels of accuracy and latency by the end of 31 training sessions. This equivalence of performance demonstrated by the 0.5- and 100-sec delay groups is, however, in contrast to the data for response patterning (delta-arm scores) during acquisition.

The effect of delay value on the patterning of arm selections, as represented by the delta-arm scores, is shown in Fig. 2. During the first two sessions, the delta-arm scores for the two groups were nearly identical, with rats from each group showing no pronounced bias for choosing an arm of any fixed distance from the arm they had just exited. Of particular interest was the observation that both groups of rats returned to the same arm from which they had just exited on 10 to 20 percent of their choices. During Days 10 and 11, rats from both groups no longer re-entered arms from which they had just exited, and the delta-arm distributions from both groups appeared roughly equivalent. A chi-square analysis of the delta-arm scores for Days 1 and 2 and Days 10 and 11 indicated that the distributions at both time points were not significantly different, $\chi^2(4)=13.8$, n.s., $\chi^2(4)=6.8$, n.s., for Days 1,2 and 10,11, respectively. Between-group differences in the delta-arm scores began to emerge by Days 20 and 21, with the 0.5-sec group of rats entering an adjacent arm on approximately 60% of their alley selections. During the same sessions, the 100-sec delay rats showed delta-arm distributions that peaked at an arm distance 2-removed from the exit arm. In addition to the difference in the peak distance demonstrated by the two groups, there was a noticeable difference in the steepness of the two curves, with the 100-sec group showing a much flatter distribution than that for the 0.5-sec rats. A chi-square analysis of the two delta-arm distributions for Days 20 and 21 yielded statistical significance, $\chi^2(4)=48.3$, $p<0.0001$. The curves for each group changed very little from Days 20 and 21 to Days 30 and 31. A comparison of the delta-arm distributions for the 0.5- and 100-sec groups for Days 30 and 31 indicated a statistically significant difference between the pattern of arm selections, $\chi^2(4)=54.4$, $p<0.0001$.

*Scopolamine Challenge*

The effects of pre-session scopolamine administration on accuracy and latency are summarized in Fig. 3. As shown in the upper panel of the figure, scopolamine decreased accuracy in a dosage-dependent fashion for both groups of rats, although the scopolamine-induced decrease in accuracy was more pronounced for the 100-sec delay group. The scopolamine-induced disruption of accuracy for the 0.5-sec delay group appeared to asymptote at a dosage of 0.56 mg/kg, where accuracy was reduced to approximately 70%. On the other hand, the 100-sec delay group continued to show a decline in accuracy of performance as the dosage was increased to 1.0 mg/kg. A statistical analysis (2-way ANOVA) of the effect of scopolamine and delay on accuracy revealed a significant effect of drug dosage, $F(5,68)=12.72$, $p<0.001$, and delay value, $F(1,68)=8.93$, $p<0.004$, but not a significant interaction between the two treatments, $F(5,68)=1.33$, $p<0.26$. This delay-dependent effect of scopolamine on accuracy of performance in the maze was accompanied by a scopolamine-induced increase in latency, as shown in the lower panel of Fig. 3. During non-injection and vehicle-injection sessions, rats in both groups obtained all 8 pellets (latency) in less than 60 sec. As the dosage of scopolamine increased from 0.03 to 1.0 mg/kg, there was a dosage-related increase in latency for the 0.5- and 100-sec delay groups to 425 and 725 sec, respectively. A statistical assessment of reliability for this effect revealed a significant effect of both the drug dosage, $F(5,68)=13.96$, $p<0.001$, and the delay value, $F(1,68)=8.87$, $p<0.004$, with no significant interaction, $F(5,68)=1.46$, $p<0.22$. The effect of pre-session administration of the peripherally active scopolamine methylbromide was virtually indistinguishable from the effects of vehicle administration for both the 0.5- and 100-sec delay groups, as shown in Fig. 3. Comparisons ($t$-test) between vehicle and scopolamine methylbromide sessions showed no significant difference for either the accuracy or latency measures. During all drug sessions, rats consistently consumed all pellets obtained for nose-pokes in the maze.

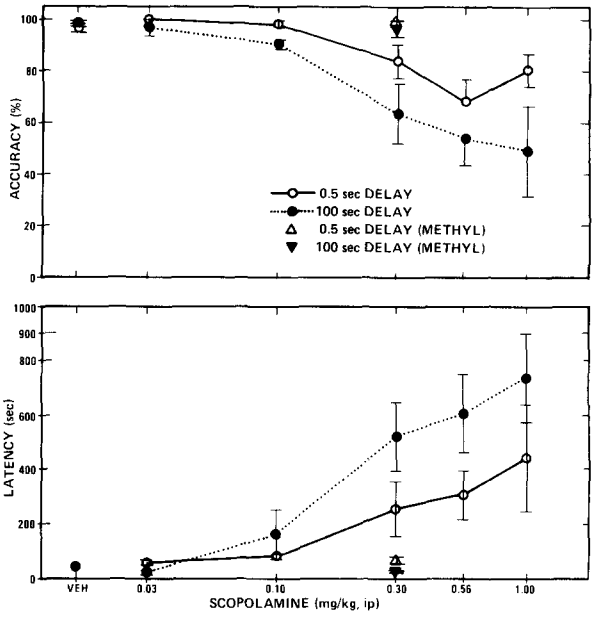


FIG. 3. The effects of scopolamine hydrobromide and scopolamine methylbromide on mean (±SE) accuracy (upper panel) and latency (lower panel) of performance for rats exposed to either 0.5-sec or 100-sec post-selection delays. The effects of dosages of scopolamine hydrobromide are represented by filled (100-sec delay) and unfilled (0.5-sec delay) circles, while the effects of scopolamine methylbromide (0.3 mg/kg) are represented by filled (100-sec delay) or unfilled (0.5-sec delay) triangles.

In addition to the disruptions of accuracy and latency, scopolamine altered the patterning of arm selection in the two groups of exposed rats in a dosage dependent manner, as shown in Fig. 4. In general, the disruption took the form of a flattening of the response distribution curves. At the highest dosages, the delta-arm scores for the two groups did not differ, with the only pronounced bias being a near zero probability of entering an arm from which they had just exited. Comparison (chi-square) of delta-arm distributions from the 0.5- and 100-sec groups indicated that at dosages less than or equal to 0.3 mg/kg, the two distributions were statistically different, $\chi^2(4)=26.9$ to 151.4, $p<0.0001$, while at 0.56 mg/kg, $\chi^2(4)=17.02$, n.s., and 1.0 mg/kg, $\chi^2(4)=11.6$, n.s., the distributions were essentially equivalent. There were no observable effects of scopolamine methylbromide on the patterning of responding for either the 0.5-sec or the 100-sec groups as shown in Fig. 4.

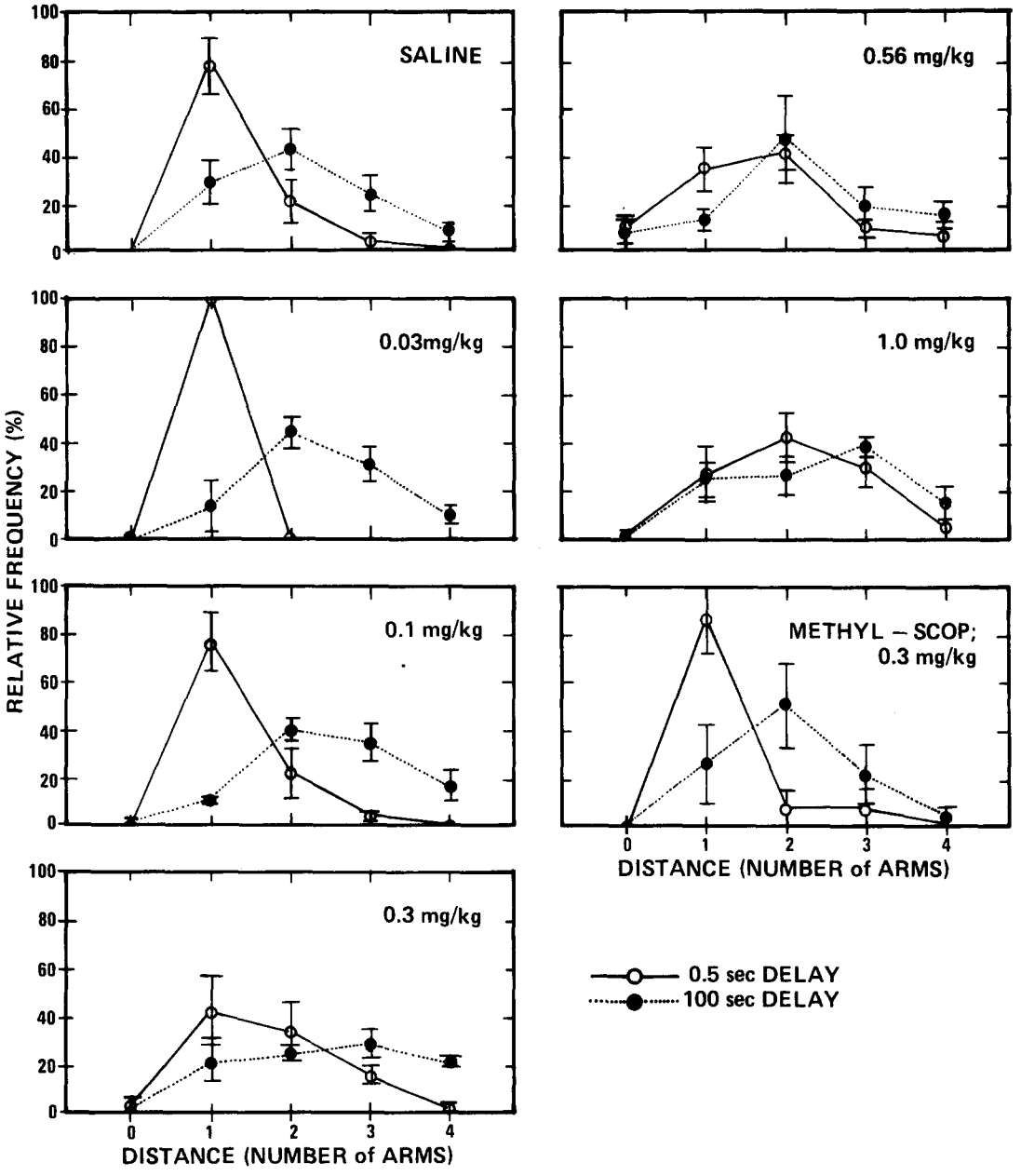


FIG. 4. The effects of scopolamine hydrobromide and scopolamine methylbromide on delta-arm scores for rats in either the 0.5-sec (○) or 100-sec (●) post-selection delay condition. Each point represents the group mean (±SE) percentage of arm selections as a function of the distance (number of arms) separating successive arm selections.

## DISCUSSION

The data from the present experiment suggest two primary effects of the post-selection confinement procedure on maze performance. In acquisition, the prominent effect of the delay value was on the patterning of arm selections (delta-arm scores), with the 0.5-sec delay rats showing a high probability of successively choosing adjacent arms from the just-exited arm—a tendency not seen in the 100-sec delay rats. The effect of the delays on choice accuracy was more subtle. Both the 0.5- and 100-sec delay groups acquired accurate performances in the maze at roughly equivalent rates and with roughly equivalent asymptotic levels. Performance differed between the groups, however, following the administration of scopolamine where the 100-sec delay rats showed a greater disruption of both accuracy and latency relative to that of the 0.5-sec delay rats.

The finding that 100-sec post-selection delays did not alter the accuracy of performance in the automated maze is in agreement with previous reports investigating the effects of post-selection delays on performance using the non-automated maze. Rats trained on a 17-arm non-automated maze have been reported to show no disruption of accuracy (measured during the first 17 choices) when brief delays were imposed after each selection [19]. In that study, as in the present study, rats displayed a pronounced bias in their within-session selection of arms—a tendency that was elimi-

nated by 10- to 15-sec post-selection confinement periods. Similar effects have been reported for rats with short (i.e., 10 sec) post-selection confinements during acquisition of 8-arm radial maze performance [5,23]. Previous research from our lab further indicates that the effects of delay on patterning observed in the present study are also obtained when rats were trained under no-delay conditions and later exposed to post-selection delays (MacPhail, Baron and Peele, unpublished).

Recently, Dale and Roberts [11] reported that inter-selection distance in a radial maze can be modified by motivational factors: inter-selection distance (i.e., delta-arm score) was consistently shorter with water reinforcement than with food reinforcement. Also, Markowska *et al.* [17] reported that inter-selection distances are consistently greater in a two-level radial maze than in a standard radial maze. Incidental to the design of both experiments was the resulting imposition of brief delay periods separating arm selections. In the Dale and Roberts experiment, there was a 10-fold increase in the amount of time taken to consume the water (as opposed to food) reinforcer thereby increasing the time separating arm selections. In the Markowska *et al.* study, post-selection delays were differentially introduced in the two-level maze procedure because of the physical layout of the apparatus: subjects returned to the central arena of the maze by exiting from the distal end of the arm after each selection. In these experiments, inter-selection distances increased as a function of post-selection delay. Furthermore, these results occurred in the absence of any deleterious effects on selection accuracy, thus supporting the basic findings from the present experiment.

While imposing a 100-sec post-selection delay did not reduce accuracy or latency of performance during the acquisition phase of the present experiment, it did result in a potentiation of scopolamine-induced disruption of performance. The deleterious effects of centrally active anticholinergic compounds on radial arm maze performance has been previously reported for both rats [13] and mice [16]. For rats, the disruption of maze performance by scopolamine can be reversed by co-administered physostigmine [24]. Given the wealth of data relating alterations in normal cognitive (memory) function with cholinergic manipulations (cf. [1]), it is not surprising that the disruption of performance of this task by scopolamine has, in general, been attributed to a disruption of spatial memory, or more specifically, a disruption of 'working memory' (e.g., [2, 15, 27]). One possible alternative explanation is that scopolamine altered either the ability or the motivation (i.e., performance variables) of the rats to complete the task. However, this explanation is at odds with a number of observations, including the fact that the rats in the present study consistently consumed all obtained pellets following each dosage of scopolamine. In addition, several other studies on radial maze performance have assessed the possibility of motivational alternations following scopolamine administration. Overall, these studies have indicated that at dosages of scopolamine less than 1 mg/kg scopolamine there is little if any decline in the propensity of rats to consume the food-pellet reinforcer, as shown in post-dosing tests of food consumption [13]. The use of alternative reinforcing stimuli, i.e., sucrose [2], chocolate [26], designed to circumvent motivational deficits due to scopolamine-induced dry-mouth has generally produced results that do not differ qualitatively from those of experiments using traditional food pellets as reinforcers.

Another question arising from the interpretation of scopolamine effects in the present experiment is whether the disruption is due to the central or peripheral effects of the drug. The fact that the peripherally acting scopolamine methylbromide produced none of the effects on accuracy, latency or patterning seen in the present study with scopolamine hydrobromide suggests a central site of action. Several studies have compared centrally vs. peripherally active forms of anticholinergic drugs, e.g., scopolamine hydrobromide vs. scopolamine methylbromide [13] and atropine sulfate vs. atropine methyl nitrate [16], and found that disruption only occurs with the centrally active form of the compound.

It seems appropriate to conclude that spatial memory, as measured in the present experiment, was susceptible to disruption by a centrally active anticholinergic compound. However, in an experiment using the mid-session delay paradigm, scopolamine administered in dosages up to 5 mg/kg was reported to produce no disruption of spatial memory except at dosages which produced severe behavioral debilitation in the rats [14]. The authors report that, even though modest increases in the rates of errors occurred (a significant effect of drug dose was reported, $p<0.03$), in their opinion, these effects were due to performance variables independent of any primary effect on memory. Other investigators have reported a decrement in the accuracy of performance using other procedures in the radial maze. Buresova and Bures [8] examined the performance of rats in a 12-arm maze using a procedure with and without a brief (5 min) mid-session delay; pre-session dosing with scopolamine (0.1 mg/kg), which was without effect on performance using no-delay in a 12-arm maze, produced significant disruption of performance when a delay was introduced separating correct choices six and seven. The discrepancy in the findings between the Buresova and Bures study and the Godding *et al.* study could be attributable to a number of factors, including the fact that the former study utilized a 12-arm maze as opposed to the 8-arm maze used in the later study, making it a more difficult problem to solve. Both studies used highly trained rats, large group sizes (n=12 or 17), similar tests for statistical significance, and rats in each study had experience with solving the maze with and without the delay periods. The more relevant variable appears to be the time-course for the effects that may have differed between the two studies. In the Godding *et al.* study, a 5-hr period intervened between the first and second half of trials: accordingly, they administered the drug either 3 hr prior to the trials, immediately after the first four correct choices, or 2 hours prior to the initiation of the second half of the trial. On the other hand, in the Buresova and Bures study scopolamine was administered 10 minutes prior to testing. From this we can assume that the rats in the Buresova and Bures study were at roughly the same level of scopolamine-intoxication throughout the trial while those in the Godding *et al.* study were not. While it remains unclear which, if any, of these possible explanations are correct, other data exist which support the findings reported by Buresova and Bures. In a mid-session delay (5 hour) procedure, rats administered scopolamine (0.5 mg/kg) immediately after the first four correct selections subsequently showed deficits on their selection of the four remaining baited arms [12].

Other results supporting the findings of the present study come from data on the effects of scopolamine administered during acquisition of radial maze performance. Rats receiving scopolamine prior to each of 14 daily sessions show retarded acquisition of maze performance compared to that

shown by rats similarly treated with the saline vehicle [26]. Moreover, animals that developed a pattern of selecting adjacent arms (i.e., one-removed) were less disrupted by scopolamine administration. But more relevent to the issue of the role of temporal variables in scopolamine's effect on maze performance, the effect of scopolamine on acquisition of performance was enhanced when a short (10 sec) delay was imposed between each arm selection [23]; this finding is even more intriguing when one considers that the dosage of scopolamine used in the Watts *et al.* study (0.5 mg/kg) was greater than that used in the Stevens study (0.3 mg/kg). In addition to the effects with scopolamine, the use of brief delays imposed at various points during testing has been instrumental in detecting otherwise silent drug effects. For instance, amphetamine, which has been reported to be without effects on accuracy of performance in the maze without delays [13] produced substantial disruption in a procedure where brief delays were inserted [3]. Similar findings for vasopressin analogues have been reported [9].

One possible explanation for the delay-dependent effects on radial maze performance in the present experiment is that rats in the 100-sec delay group utilized spatial cues in obtaining food pellets in the maze while rats in the 0.5-sec group utilized response strategies in doing so. The selective disruption of the 100-sec delay group by scopolamine could then be attributed to differing sources of stimulus control: external for the 100-sec group and internal (response-produced) for the 0.5-sec group. A similar proposal has been made by Stevens [23] to account for the enhanced sensitivity to the disruption by scopolamine of maze performance in rats lacking a response strategy. The problem with such an interpretation is that the presence of a strategy must be inferred from the presence of highly patterned arm selections. Further, the direction of travel during arm selections must be considered. For instance, a rat could obtain 8 pellets in 8 selections if all selections were made in one direction (i.e., clockwise) and if successive arm selections were separated by a constant odd number of arms. In the present experiment, both the 0.5- and 100-sec delay groups demonstrated highly pattered delta-arm scores which differed only in their modal distance (1- vs. 2-removed). Only 2 rats from the 0.5-sec delay group showed a consistent trend (i.e., selected adjacent arms in a counterclockwise direction) in their direction of travel while selecting arms. These two rats were almost identical to the other rats in the 0.5-sec group, however, in both their baseline accuracy in the maze and their responsiveness to scopolamine challenge. Similar observations have been made concerning scopolamine effects on accuracy of performance by rats in a standard 8-arm radial maze procedure [13]. The delay-dependent difference in delta-arm scores observed in the present experiment cannot, then, be explained on the presence or absence of response strategies. It may simply be impossible to determine the presence or absence of a response strategy on the basis of response stereotype alone [10]. Further research utilizing forced-choice techniques (cf. [4]) in a post-selection delay procedure might provide the necessary data for determining the mechanism responsible for these differences.

Taken as a whole, the research on scopolamine effects on radial maze performance supports the findings of the present study that scopolamine's effect on performance is due to a disruption in the normal processing of spatial information. These data contribute to a growing literature supporting the notion that central muscarinic antagonism leads to disruption of short-term or 'working' memory (cf. [7,22]). Moreover, the scopolamine-induced disruption of accurate maze performance reported here was worsened by imposing delays (delayed stimulus control) separating discriminative stimuli (previously chosen arms) and the performances they occasion (selecting non-visited arms). Whether the disruption of stimulus control is more easily accomplished when delays are imposed at each component (i.e., after each correct choice) rather than simply at the mid-point of the task seems to find support not only in the data from the present experiment but also from previous experiments using aversively motivated maze performance [6]. The advantages of the automated version of the radial arm maze seem to be that it (a) removes any source of performance confounding by the presence of an experimenter, (b) it allows a wealth of information to be collected simultaneously, and (c) allows manipulations such as the imposition of selection delays and multiple-sessions without the constant vigilance of an experimenter. The ease with which these delay manipulations were accomplished using the automated maze and the reliability of effects attests to the usefulness of this device. In addition, use of the post-selection delay procedure for examining chemical effects on behavior has a potential advantage over the mid-session delay procedure since it not only appears to increase sensitivity but also (and more importantly) testing can be accomplished in a short period of time (test session duration). This feature may be increasingly important in assessing the neurotoxic (e.g., amnestic) potential of a relatively unknown compound whose time-course of effects may (a) be unknown, or (b) be so rapid that a prolonged mid-session delay procedure would be unable to detect any alteration. Further testing with other compounds is required to assess the adequacy of these proposals.

ACKNOWLEDGEMENTS

We owe special thanks to Dr. R. C. MacPhail for helpful suggestions during the course of the experiment.

## REFERENCES

1. Bartus, R. T., R. L. Dean, M. J. Pontecorvo and C. Flicker. The cholinergic hypothesis: A historic overview, current perspective and future directions. In: *Memory Dysfunctions: An Integration of Animal and Human Research From Preclinical and Clinical Perspectives*, edited by D. S. Olton, E. Gamzu and S. Corkin. *Annals of the New York Academy of Sciences*, Vol 444, 332–358, 1985.
2. Beatty, W. W. and R. A. Bierley. Scopolamine degrades spatial working memory but spares spatial reference memory: Dissimilarity of anticholinergic effects and restriction of distal visual cues. *Pharmacol Biochem Behav* **23**: 1–6, 1985.
3. Beatty, W. W., R. A. Bierley and J. Boyd. Amphetamine disrupts both working and reference memories of rats trained in a radial maze. *Behav Neural Biol* **42**: 169–176, 1984.
4. Beatty, W. W. and D. A. Shavalia. Spatial memory in rats: Time course of working memory and effects of anesthetics. *Behav Neural Biol* **28**: 454–462, 1980.
5. Bolhuis, J. J., S. Bulsma and P. Ansmink. Exponential decay of spatial memory of rats in a radial maze. *Behav Neural Biol* **46**: 115–122, 1986.
6. Bolhuis, J. J., O. Buresova and J. Bures. Persistence of working memory of rats in an aversively motivated radial maze. *Behav Brain Res* **15**: 43–49, 1985.

7. Brito, G. N. O., B. J. Davis, L. C. Stopp and M. E. Stanton. Memory and the septo-hippocampal cholinergic system in the rat. *Psychopharmacology (Berlin)* **81:** 315–320, 1983.
8. Buresova, O. and J. Bures. Radial maze as a tool for assessing the effects of drugs on the working memory of rats. *Psychopharmacology (Berlin)* **77:** 268–271, 1982.
9. Buresova, O. and J. Skopkova. Vasopressin analogues and spatial short-term memory in rats. *Peptides* **1:** 261–263, 1980.
10. Dale, R. H. I. Spatial and temporal response patterns on the eight-arm radial maze. *Physiol Behav* **36:** 787–790, 1986.
11. Dale, R. H. I. and W. A. Roberts. Variations in radial maze performance under different levels of food and water deprivation. *Anim Learn Behav* **14:** 60–64, 1986.
12. Decker, M. W. and M. Gallagher. Scopolamine-disruption of radial arm maze performance: Modification by noradrenergic depletion. *Soc Neurosci Abstr* **11:** 380, 1985.
13. Eckerman, D. A., W. A. Gordon, J. D. Edwards, R. C. MacPhail and M. I. Gage. Effects of scopolamine, pentobarbital and amphetamine on radial arm maze performance in the rat. *Pharmacol Biochem Behav* **12:** 595–602, 1980.
14. Godding, P. R., J. R. Rush and W. W. Beatty. Scopolamine does not disrupt spatial working memory in rats. *Pharmacol Biochem Behav* **16:** 919–923, 1982.
15. Honig, W. K. Studies of working memory in the pigeon. In: *Cognitive Processes in Animal Behavior,* edited by S. H. Hulse, H. Fowler and W. K. Honig. Hillsdale, NJ: Earlbaum, 1978, pp. 211–248.
16. Levy, A., P. B. Kluge and T. F. Elsmore. Radial arm maze performance of mice: Acquisition and atropine effects. *Behav Neural Biol* **39:** 229–240, 1983.
17. Markowska, A., O. Buresova and J. Bures. An attempt to account for controversial estimates of working memory persistence in the radial maze. *Behav Neural Biol* **38:** 97–112, 1983.
18. Olton, D. S. Characteristics of spatial memory. In: *Cognitive Processes in Animal Behavior,* edited by S. H. Hulse, H. Fowler and W. K. Honig. Hillsdale, NJ: Earlbaum, 1978, pp. 341–373.
19. Olton, D. S., C. Collison and M. A. Werz. Spatial memory and radial arm maze performance of rats. *Learn Motiv* **8:** 289–314, 1977.
20. Olton, D. S. and B. C. Papas. Spatial memory and hippocampal function. *Neuropsychologia* **17:** 669–682, 1979.
21. Snapper, A. G., R. M. Kadden and G. B. Inglis. State notation of behavioral procedures. *Behav Res Meth Instr* **14:** 329–342, 1982.
22. Spencer, D. G. and H. Lal. Central cholinergic involvement in learning and memory. In: *Central Cholinergic Mechanisms and Adaptive Dysfunctions,* edited by M. M. Singh, D. M. Warburton, H. Lal and B. Mason. New York: Plenum Press, 1985, pp. 141–159.
23. Stevens, R. Scopolamine impairs spatial maze performance in rats. *Physiol Behav* **27:** 385–386, 1981.
24. Vincent, G., R. Harney and E. Gamzu. The effect of physostigmine and/or scopolamine on radial arm maze performance in rats. *Soc Neurosci Abstr* **11:** 380, 1985.
25. Walsh, T. J., D. B. Miller and R. S. Dyer. Trimethyltin, a selective limbic system neurotoxicant, impairs radial-arm maze performance. *Neurobehav Toxicol Teratol* **4:** 177–183, 1982.
26. Watts, J., R. Stevens and C. Robinson. Effects of scopolamine on radial maze performance in rats. *Physiol Behav* **26:** 845–851, 1981.
27. Wirsching, B. A., R. J. Beninger, K. Jhamandas, R. J. Boegman and S. R. El-Defrawy. Differential effects of scopolamine in working and reference memory in rats in the radial maze. *Pharmacol Biochem Behav* **20:** 659–662, 1984.