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Scopolamine Impairs Learning Performance of Rats in a 14-Unit T-Maze

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SPANGLER, E. L., P. RIGBY AND D. K. INGRAM. *Scopolamine impairs learning performance of rats in a 14-unit T-maze.* PHARMACOL BIOCHEM BEHAV **25**(3) 673–679, 1986.—To assess involvement of muscarinic cholinergic systems in performance of a shock-motivated 14-unit T-maze task, 3-month old Fischer-344 rats were given an IP injection of scopolamine (0.1, 0.3, 1.0 or 3.0 mg/kg), methylscopolamine (1.0 mg/kg), or saline 30 min prior to maze training on 2 consecutive days. Scopolamine, but not methylscopolamine, impaired all components of acquisition performance. Measures of error performance, run time, shock duration, and number of shocks received were significantly increased but only at the 1.0 and 3.0 mg/kg scopolamine doses. The cognitive component of the task, measured by error performance, appeared most affected. Cognitive performance deficits observed following scopolamine administration in the present study resembled age-related impairments in rats and mice previously observed in this task. The cholinergic hypothesis of geriatric memory dysfunction appears to be implicated by these findings; however, the degree to which memory systems are involved remains unclear. Other performance variables such as discriminative control of stimuli or mechanisms of attention are implicated and discussed.

Maze learning Memory Scopolamine Avoidance conditioning Cholinergic system Aging

THE cholinergic system has been reported to modulate performance in a variety of behavioral tasks involving learning and memory processes [7, 9, 30, 35]. In rats, scopolamine, an anticholinergic compound which blocks both central and peripheral muscarinic receptors, impairs acquisition and retention in the radial arm maze [11, 20, 36], reduces spontaneous alternation to chance levels [27] and interferes with passive avoidance behavior [26]. Scopolamine does not appear to interfere with simple active avoidance procedures, such as pole climbing, but does interfere with more complex avoidance schedules such as Sidman avoidance [7].

Impaired neurotransmission at central cholinergic synapses has been suggested as a mechanism responsible for age-related deficits in short-term memory [3]. Deficits in short-term memory have been reported following scopolamine administration in monkeys [5] and in humans [10]. The possibility remains, however, that the deficits are due to a loss of stimulus control [13] and/or altered states of attention [8].

Scopolamine was utilized in the present investigation to assess muscarinic cholinergic effects on performance in a shock-motivated 14-unit T-maze task [21]. In this task rats are required to make a series of successive position discriminations, presumably without the benefit of extramaze cues [21]. In a wide range of studies of mice and rats in our laboratory [14–16, 21, 22] and other laboratories [1,28], age-related impairments in this task have been observed. Our interest was thus motivated by previous observations relating the effects of aging on performance of rats in this task [14, 15, 21]. Bartus *et al.* [3] have proposed a cholinergic hypothesis of geriatric memory dysfunction to explain the considerable evidence linking age-related decline in central cholinergic neurotransmission to parallel deficits in learning and memory observed in humans and other mammalian species. Observations of age-related declines in other central neurotransmitter systems (e.g., adrenergic) which may also affect learning and memory have prompted investigators to utilize cholinergic blockade in young animals to assess the effects of alteration of central muscarinic cholinergic mechanisms on learning and memory performance [21]. Consistent with research interest in the cholinergic hypothesis [3], the objective was to assess cholinergic involvement in this task in young rats in order to consider whether alterations in this neurotransmitter system might underlie the impaired performance of aged rodents previously observed [21]. Bartus *et al.* [4] have identified this approach as a Class C model.

METHOD

Subjects

Forty male Fischer-344 rats obtained from Charles River Breeding Laboratories (Wilmington, MA) served as subjects. Upon arrival they were 90 days old and weighed approximately 250 g. The animals were housed doubly in sus-

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pended, metal cages (Wahmann) in a vivarium maintained at 22°C and on a 12-hr light/12-hr dark photocycle (lights on at 06:00). Food (NIH-07 formula) and water were provided ad lib. The rats were permitted about 3 weeks acclimation to the vivarium prior to testing.

Apparatus

Pretraining for one-way active avoidance was conducted in a clear Plexiglas, straight runway (199.5 cm long, 16.2 cm wide, and 16.7 cm high) with a diagonally-placed stainless steel grid which served as the floor of the runway. The grid floor was wired in series to a Coulbourn Instruments (Model E13-08) grid floor shocker which provided scrambled shock (constant current). A guillotine door served as the back wall of the start area of the runway. A black Plexiglas box (24.8 cm long, 15 cm high, and 15 cm wide) with a guillotine door served as a goal box which could be placed into the opposite end of the runway (172.3 cm from the back wall) onto the grid floor. The back wall of the black box was movable and could be pushed forward by means of a steel rod fastened to the center of the back wall. A hand-held switch was wired to a mechanical timer that initiated a shock contingency and to a clock that measured the duration of shock and the run time from the start area to the goal box. A speaker from a white noise generator (40 dB when activated) was located near the start area.

A clear Plexiglas, automated 14-unit T-maze with a diagonally-placed stainless steel grid floor was used for acquisition training in a complex task. The configuration of this maze has been described previously [14]. The diagonally-placed grid was wired in series to a Coulbourn Instruments (Model E13-08) grid floor shocker which provided scrambled shock (constant current) to the floor of the maze. Shock contingencies were operated by electromechanical clocks with the number of shock episodes and the duration of shock recorded on electromechanical counters. The maze was separated into five distinct segments of approximately equal area by guillotine doors. A black Plexiglas box similar to ones used in pretraining could be placed onto the grid floor in the goal area of the maze. Infrared photocells were located about half-way down each alley or about one-third way down each cul-de-sac of the maze and were wired in series to a microprocessor. The sequence of infrared beam interruptions and the time between interruptions were recorded onto computer PROMS (Hamilton Avnet) by the microprocessor. A Fortran program on a VAX 11/780 computer was subsequently used to score the errors from the correct path and run time according to procedures previously described [14].

The entire maze was surrounded by four wooden walls painted flat gray. Two speakers connected to a white noise generator (40 dB when activated) were located diagonally beneath the maze to provide white noise to mask possible external auditory cues.

Both mazes were located in a large room with overhead fluorescent lighting, which provided little shadow to the maze. The maze room was maintained at a temperature of 22°C.

Procedure

Pretraining. Prior to maze training, the rats received pretraining in one-way active avoidance to a criterion in the straight runway. Each rat was removed from the vivarium and transported in its home cage to the maze room where it was allowed to acclimate for 45 min. On the first trial the animal was placed in the runway by lifting the guillotine door at the rear of the runway and gently placing the animal onto the grid floor. A timer was started, and the animal had 10 sec to avoid footshock by running into the black goal box at the opposite end of the runway. Animals failing to avoid shock received a 1.0 mA scrambled shock until they escaped to the goal box or until 60 sec had elapsed, at which time they were removed and placed into the black goal box. After entering the goal box, the guillotine door was lowered. After 30 sec, the box was removed to a holding area until the next trial, and an identical black box was placed into the goal area. Subsequent trials were identical except that the rat was gently pushed from the black box into the start area of the runway. This was accomplished by placing the black box adjacent to the start area and removing both guillotine doors simultaneously. When both doors had been removed, the movable back wall of the black box was pushed forward by means of the steel rod; and the animal was forced into the start area. Once the rat was in the start area, the guillotine door to the runway was reinserted and the timer started.

Training consisted of 10 massed practice trials with a 2-min intertrial interval (ITI) on each of 3 consecutive days (Mon, Tues, Wed) between 13:00–17:00 hr. Criteria for mastery of this task was 8 out of 10 successful avoidances on the final day of training. All animals met this criterion and began testing in the complex maze 24 hours later.

Drug Treatment and Maze Training

The animals were taken to the testing room 45-min prior to testing. The order of testing and assignment to one of six drug groups were randomized. Thirty minutes prior to maze training, each rat received an intraperitoneal (IP) injection of either saline (n=6), scopolamine (0.1, 0.3, 1.0 or 3.0 mg; n=7, scopolamine hydrochloride/kg body weight; Sigma Chemical Co., St. Louis, MO), or methylscopolamine (1.0 mg scopolamine methylnitrate/kg body weight; Sigma Chemical Co., St. Louis, MO, n=6). Methylscopolamine, a principally peripherally acting muscarinic antagonist, was used to test specificity of central drug effects. The drugs were prepared fresh weekly in normal saline so that each dose was administered as a volume of 1 ml/kg. The experimenter was blind as to which treatment the animal received.

As in pretraining, on the first trial the rat was placed into the maze by hand, and a timer started. The timer initiated a contingency which allowed the animal 10 sec to traverse the initial section of the maze and to negotiate the first door before a 1.0 mA shock was activated. The shock remained activated until the animal escaped through the door. Once the animal negotiated the door, the door was closed, and the contingency reset. The contingency was reset four times as the animal progressed through four remaining doors corresponding to the four remaining segments of the maze. Thus, shock could be avoided by quickly traversing the maze. Errors were not explicitly punished. The animal had to pass through a sixth door and enter the black goal box to avoid the shock contingency in the final segment. Once the animal entered the black box, a guillotine door was lowered. After 30 sec, the black box was removed to a holding area until the next trial, and an identical black goal box was placed into the goal area. On subsequent trials the animal was pushed from the black goal box into the start area of the maze in a manner identical to that used during pretraining.

Animals received 10 massed practice trials with a 2-min ITI on each of 2 consecutive days (Thur, Fri). During each

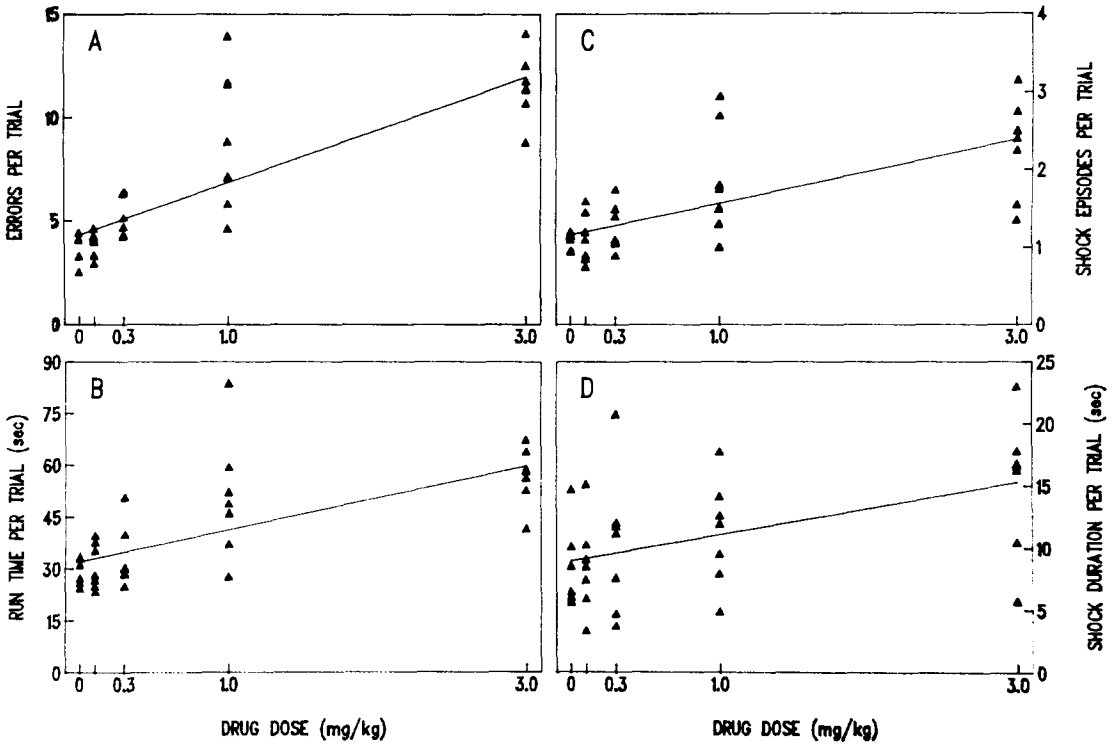

FIG. 1. Regression of scopolamine dose on performance of male Fischer-344 rats in a 14-unit T-maze: (A) Errors; (Y=4.34+2.56X; R^2=0.70); (B) Run Time; (Y=32.21+91.8X; R^2=0.48); (C) Shock Episodes; (Y=1.16+0.41X; R^2=0.49); (D) Shock Duration; (Y=8.9+2.15X; R^2=0.24).

ITI, the maze was raised by a motorized pulley, and the grid floor mopped with a 95% ethanol solution to mask possible odor cues.

Statistical analysis. Performance variables analyzed included the following: (1) number of errors (departures from the correct path) in the maze as defined previously [14] and scored by a computer program; (2) run time (sec) from the start area to the goal box as scored by the computer program; (3) number of shock episodes received; and (4) duration of shock received (sec).

To assess the magnitude of the relationship between drug dose (excluding data from the methylscopolamine group) and the performance variables, individual data from each trial were averaged across the 20 trials and submitted to a linear regression analysis. Significant correlation (Pearson product-moment) between drug dose and each performance variable was determined as $p<0.05$. An analysis of differences in the correlation coefficients was computed to determine whether the coefficients differed significantly from one another [32].

To conduct individual comparisons between the control group and each drug group, data were collapsed across four blocks of five trials and submitted to one-way analyses of variance for each variable at each block followed by a Dunnett's test. Because of the numerous comparisons to be made in the Dunnett's analysis, the criteria for statistical significance was set at $p<0.01$.

RESULTS

In a dose-dependent manner, scopolamine impaired acquisition performance in the 14-unit T-maze as assessed by all variables examined. The drug effect on performance was significant, however, only at the two highest doses.

Figure 1 presents the regression of drug dose on the performance variables. As observed, significant linear relationships were evident for all variables. However, there were notable differences in the fit of the regressions, with drug dose explaining the largest proportion of variance (R^2) in error performance (70%) and the least in shock duration (24%). According to an analysis of differences in the correlation coefficients [32], only the correlation between drug dose and error performance was significantly higher ($p<0.008$) than between drug dose and shock duration. None of the other correlations between drug dose and the performance variables differed significantly from one another (p's>0.05). Although a significant difference emerged only between the correlations for drug dose and error performance and drug dose and shock duration, the principal effect of scopolamine appeared to be on the cognitive component of the task as indicated by error performance.

It is clear in Fig. 1 that scopolamine affected performance in a dose-dependent manner. The Dunnett's analysis was designed to determine which doses produced significant effects on performance above control levels for each block of training. Mean performance at each block of trials for all variables and the individual Dunnett's comparisons are presented in Fig. 2. Although no statistical analysis to determine the effects of training blocks on the variables was performed, learning is apparent in all drug groups as evidenced by the marked decline in all variables as a function of blocks. Regarding error performance (Panel A), only the 1.0 and 3.0

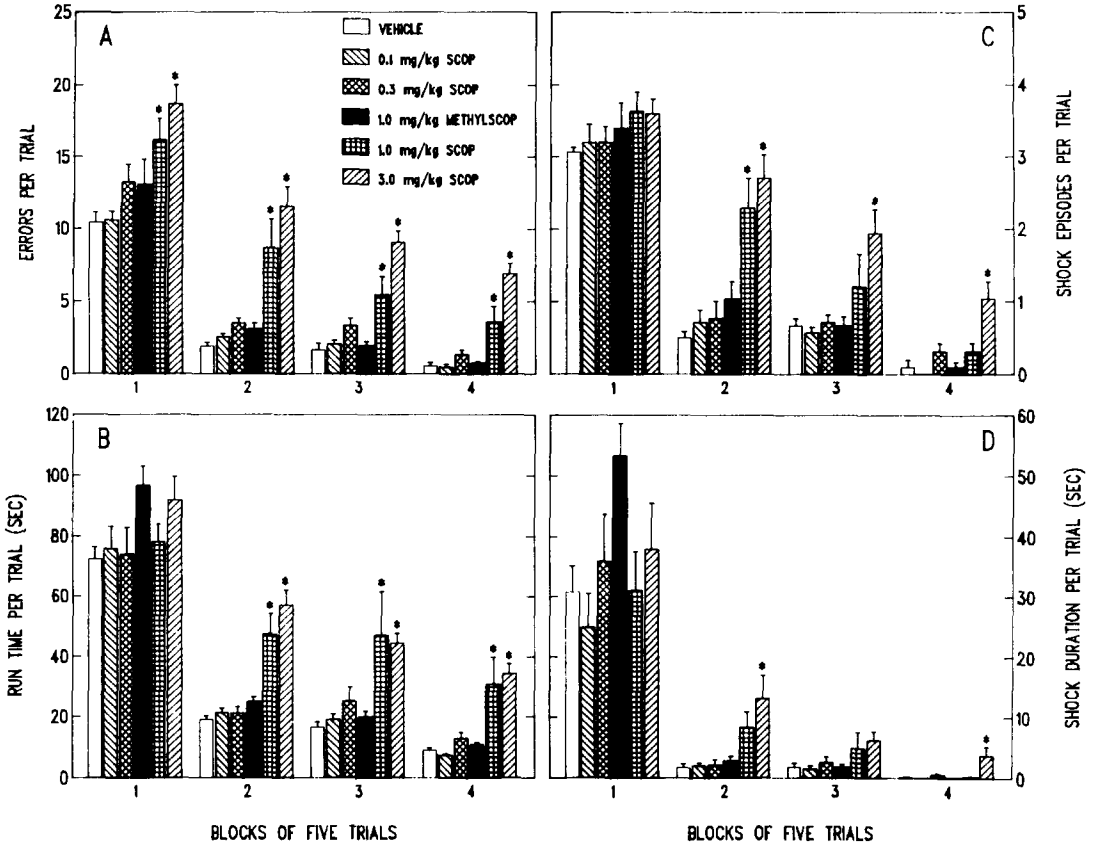

FIG. 2. Performance of male Fischer-344 rats in 14-unit T-maze as a function of drug dose, training block (4 blocks of 5 trials), and performance variable: (A) Errors; (B) Run Time; (C) Shock Episodes; (D) Shock Duration. *Significantly different from vehicle control group according to Dunnett's test, $p<0.01$.

mg/kg groups produced significantly impaired performance compared to control levels, and this effect was evident across all training blocks. Regarding run time (Panel B), again only the 1.0 and 3.0 mg/kg groups produced significantly impaired performance, but a significant drug effect was not evident during the first training block when there had been a significant drug effect on error performance. Regarding the number of shock episodes (Panel C), again the two highest doses of 1.0 and 3.0 mg/kg produced significant effects, but the effects of the 1.0 mg/kg dose were much more limited. This dose significantly increased the number of shocks received only during the second block, while the 3.0 mg/kg dose significantly increased the number of shock episodes for all training blocks except the first. Finally, regarding the duration of shock received, only the highest dose of 3.0 mg/kg produced significant effects above the control level and then only during the second and fourth blocks. In summary, the two lowest doses of scopolamine and the 1.0 mg/kg dose of methylscopolamine did not produce significant effects on performance according to this analysis.

To assess the effect of scopolamine on retention, as measured by error scores across the two training days, the data from trial 10 and trial 11 were submitted to a 5 (dose) × 2 (trial) repeated measures ANOVA. Data for the methylscopolamine group were not included. According to this analysis, the main effect of dose was significant, $F(1,29)=14.06$, $p<0.01$. However, neither the repeated measure, trial, nor the interaction of dose and trial were significant, $F(1,29)<1.0$ and $F(4,29)<1.0$, $ps>0.05$, respectively. Although scopolamine affected error performance in a dose-dependent manner, treatment prior to trial 11 did not disrupt retention. Specifically, the drug did not appear to disrupt retrieval from memory as measured by error performance. As observed in Fig. 2, other performance variables appeared equally unaffected when block 2 and block 3 data are compared.

TABLE 1

MEAN (±SEM) RATIO OF ALTERNATION ERRORS TO FREQUENCY OF OPPORTUNITIES TO MAKE ALTERNATION ERRORS IN A 14-UNIT T-MAZE

	Drug Dose (mg/kg)				
Training Block	Vehicle	0.1	0.3	1.0	3.0
Block 1*	0.45 (0.038)	0.52 (0.054)	0.50 (0.048)	0.57 (0.037)	0.65 (0.061)
All Blocks*	0.21 (0.017)	0.23 (0.024)	0.27 (0.024)	0.42 (0.046)	0.57 (0.057)

*Five trials per block.

A separate analysis was conducted to determine if an alternation strategy was being used by the rats to negotiate this maze as indicated previously [21] and whether scopolamine affected the use of this strategy. A computer program was written to score only forward-going sequences of responses (of at least 3 turns in the maze) that resulted in an error and to count errors that occurred when the opportunity for demonstrating an alternation pattern of responding (left (L): right (R)) was presented, e.g., LRL or RLR. Thus, an alternation error was defined as an error that would have occurred if the rat were following an alternation strategy during forward-going position discriminations in the maze.

Table 1 presents the ratio of alternation errors to the frequency of opportunities to make alternation errors. When examining performance across all blocks, it is clear that the proportional frequency of alternation errors was relatively low (21–57%) compared to total opportunities, but this assessment is confounded in part by the reduced frequency of errors as a function of training. More appropriately then would be an examination of alternation error rate during the first training block. As observed in Table 1, the percentage of alternation errors was higher (45–65%). A relationship of this parameter with scopolamine dose is evident when one examines either the first or all blocks of training. The correlations between scopolamine dose and alternation errors were significant when examined in the first block, $r(31)=0.47$, $p=0.003$, and for all blocks, $r(31)=0.81$, $p<0.001$. These correlations, however, are partially confounded by the correlation between alternation errors and error performance in general, $r(31)=0.39$, $p=0.012$, and $r(31)=0.89$, $p<0.001$, for the first and all blocks, respectively. A statistical control for this potential confounding was implemented by examining the partial correlation between scopolamine dose and alternation errors with total errors as a covariate. The results of this analysis indicated that when the rate of all errors was statistically controlled, there was a reduced correlation between drug dose and alternation errors, but this relationship remained significant for the first block, $R(30)=0.30$, $p=0.045$, but not significant for all blocks, $R(30)=0.29$, $p=0.052$, although the coefficients were virtually identical. It appeared then that scopolamine dose accounted for about 9% (R^2) of that variance in error performance which indicated an alternation strategy was utilized.

DISCUSSION

Previous reports from our laboratory [14–16, 21, 22] and others [1,28] have documented marked age-related impairments in rats and mice during acquisition training in the 14-unit T-maze used in the present study. The current objective was to assess possible involvement of central cholinergic systems in the ability of rats to learn this task. Such involvement would implicate the cholinergic hypothesis of geriatric memory dysfunction [3] regarding age-related declines observed in maze performance. The present results appear to support this hypothesis in that treatment of young rats with a muscarinic antagonist impaired maze acquisition. Scopolamine treatment 30 min prior to maze training affected performance in all components of the task in a dose-dependent manner. The cognitive component of the task, measured by error performance, appeared most influenced by administration of scopolamine. Run time, shock duration, and number of shocks were also affected but these performance parameters were not as highly correlated with drug dose as was error performance. Moreover, compared to vehicle-injected controls, the 1.0 mg/kg dose of scopolamine increased error performance during all training blocks, but did not significantly increase shock episodes or shock duration during the last two blocks. Run time was significantly increased by this dose during all blocks except the first when there were significantly more errors. Methylscopolamine, a primarily peripheral-acting muscarinic antagonist, did not interfere with any performance measure. Thus, blockade of central muscarinic receptors by scopolamine administration in young rats disrupts cognitive performance and appears to mimic age-related impairments in acquisition previously observed in this task [14–16, 21, 22].

Despite numerous studies of the effects of scopolamine on a variety of behavioral tasks, the nature of the behavioral deficits remains unclear. Some investigators have observed that scopolamine disrupts acquisition [36] and retention [20,37] of a radial arm maze task and have attributed these deficits to a disruption of working, or short-term, memory. In these studies the memory for previous responses was observed to be impaired in that rats given the drug tended to reenter arms which they had previously entered and obtained the available food. Godding *et al.* [13] questioned this interpretation based on their failure to observe an increasing scopolamine-induced disruption of performance as a function of increasing retention interval (i.e., between the fourth and fifth choice of each session). Further evidence for this interpretation is derived from studies of spatial alternation in which the degree of disruption was not observed to be greater even though increasing delay lengths separated the opportunity to respond [18]. In addition, in a delayed nonmatching-to-sample paradigm in rats [34], scopolamine disrupted response accuracy equally at all intervals. However, in monkeys [5, 30, 31] greater deficits have been reported in delayed response studies at increasing delay intervals; therefore, a memory deficit explanation cannot be discounted.

Eckerman *et al.* [11] suggested that the disruption of performance in the radial arm maze results from a loss of discriminitive stimulus control. This loss of stimulus control results in a confusion of arm locations with the rat being unable to identify arms previously entered. Studies in the 14-unit T-maze, which utilize differing delay intervals between trials, will be required to address the issue of memory loss versus loss of discriminitive control of stimuli. The requirement for visual or auditory cues to learn accurately in the 14-unit maze has been eliminated, e.g., rats can learn the maze under dark conditions and with white noise [21], but stimulus control over performance has yet to be identified. Visual stimulus perception was not impaired by scopolamine in a previous test involving a nonmatching-to-sample operant task [34]. In addition, using a complex spatial learning task in rats, Soffie *et al.* [33] observed the ability of scopolamine-treated rats to use a visual cue accurately but not acquire a spatial orientation strategy requiring use of an additional visual cue.

A related explanation has been offered by Cheal [8], who introduced evidence that scopolamine-induced deficits may be related to a failure in mechanisms of attention. Memory of a novel stimulus in gerbils given scopolamine was observed to be intact; however, the frequency of approaching the object did not decrease while the duration per approach was shorter. These findings suggested that maintenance of attention was disrupted and would implicate cholinergic pathways as an integrator of sensory, limbic, and motor input rather than being directly involved in retention.

In our study scopolamine tended to increase errors resulting from an alternation strategy. In contrast, previous investigations have noted a disruption of spontaneous alternation in the T-maze and Y-maze [2,27] and alternation between levers in an operant paradigm for food rewards [19]. Disruption of performance in a two-choice task, such as spatial alternation or alternating during an operant task, may not be comparable to application of an alternation strategy in the 14-unit T-maze. It is possible that alternation may be a viable response strategy for the rat when such a complex task is utilized [21]. Our findings do suggest that a perseverative strategy is employed; however, the modest amount of variance (9%) accounted for by alternation performance in the scopolamine-treated animals does not provide strong evidence that the treated rats were simply using a response sequence to solve this task. Similarly, Spencer *et al.* [34] observed that the perseverative effects of scopolamine in an operant task were minimal and argued that these effects may have been due to the lack of the retrieval of a response rule. In our case, the response rule would be to not alternate at particular choice-points. Soffie *et al.* [33] suggested that scopolamine-treated animals assumed simple strategies that may be controlled in a complex spatial task by particular cues while other cues are ignored. This observation would again raise the issue of attentional deficits resulting from scopolamine treatment.

Like Kasckow *et al.* [24], we did not observe that administration of a muscarinic antagonist produced any gross motor impairment or impairment of general alertness that influenced run times and would justify an interpretation of the results in terms of reduced motivation. Rather, the declines in shock duration and shock episodes for the 1.0 mg/kg scopolamine group suggest that the increased run times were simply a result of increased error performance. Unlike the Kasckrow *et al.* [24], we did not use a food reinforcement which might be affected by scopolamine treatment; however, this issue has not been addressed sufficiently in the current study to completely rule out an intervening performance variable such as motivation.

The rate of acquisition for the 1.0 and 3.0 mg/kg scopolamine groups is obviously slower (Fig. 2), and their performance scores in the final block of trials, particularly for error performance, were worse. As in previous studies [2,20], methylscopolamine was not significantly disruptive to any of the performance measures. Further declines in error performance observed on the second day, following a second scopolamine treatment, suggest that scopolamine may not substantially disrupt retrieval from reference memory in this task.

In contrast to performance in the radial arm maze, error performance in the 14-unit T-maze reflects reference, or long-term memory, more heavily than working memory [21]. In the 14-unit T-maze, the rat must acquire and retain a fixed pattern of position discriminations. The correct response does not change from trial to trial as in the radial arm maze. However, during within-trial performance, flexible stimulus response associations are required in that the rat must retain instances of incorrect turns during that trial and, thus, rely on working memory [21]. Several studies in the radial arm maze have demonstrated that lesions which disrupt cholinergic innervation of the hippocampus disrupt working but not reference memory [29]. In these studies the memory for unbaited arms (e.g., reference memory) was not disrupted while memory for baited arms (e.g., working memory) was disrupted. It cannot be discerned from the present investigation which aspect of memory was disrupted during acquisition of the 14-unit T-maze. It can be noted, however, that higher doses were required to elicit deficits in rats in the 14-unit T-maze, a reference memory task, than have been reported in the radial arm maze, a working memory task [11, 36, 37]. In addition, at least one previous study of rats has reported age-related deficits in a maze task that has both working and reference memory components [25]. So it is possible that both components were disrupted by scopolamine administration in the present study. This appeared true in the Spencer *et al.* study [34] in which scopolamine impaired performance in both a delayed nonmatching-to-sample task (i.e., working memory task) and in a visual discrimination task (i.e., reference memory task). Thus, blockage of muscarinic receptors may affect performance in both components of memory.

Pharmacologic disruption of central cholinergic neurotransmission in young rats resulted in performance deficits similar to those previously observed in aged rodents in this task. Such studies are crucial for implication of the cholinergic hypothesis in age-related learning and memory deficits [3]. Age-related declines in central cholinergic systems have been reported in rodents (e.g., decreased muscarinic receptor density and binding) and in humans with senile dementia of the Alzheimer's type (e.g., decreased levels of choline acetyltransferase in frontal cortex and decreased cholinergic innervation of frontal cortex via nucleus basalis of Meynert) [3]. However, the correlation of age-related learning and memory deficits with declines in central cholinergic systems is not sufficient to implicate the cholinergic hypothesis, since age-related declines in other neurotransmitter systems, such as catecholaminergic systems, are known [38]. Further experimental studies are needed which demonstrate that cholinergic treatments can improve the performance of aged animals in this task [4].

In summary, scopolamine administration impaired normal acquisition of a 14-unit T-maze task by young rats. These findings provide further support for the cholinergic hypothesis of geriatric memory dysfunction bearing on the poor performance of aged rats in this maze task [3]. However, it remains unclear whether memory per se was impaired since other performance variables, such as a loss of discriminative control over stimuli or disruption of mechanisms of attention, remain viable explanations of impaired performance. Future investigations should focus on the effects of scopolamine on consolidation of and retrieval from memory in this task. These types of studies should provide information on the relationship between cholinergic systems and memory functions. In addition, it will provide further information regarding differences between working and reference memory. Moreover, identification of the degree of stimulus control in the 14-unit T-maze will permit assessment of the effect of scopolamine on attentional factors in this paradigm.

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