Pergamon

Pharmacology Biochemistry and Behavior, Vol. 51, Nos. 2/3, pp. 271-277, 1995

0091-3057/95 $9.50 + .00

0091-3057(94)00376-9

The Effects of Scopolamine on Memory for Time in Rats and Pigeons

ANGELO SANTI[1] AND LORRAINE WEISE

Department of Psychology, Wilfrid Laurier University, Waterloo, Ontario, Canada N2L 3C5

Received 27 June 1994

SANTI, A. AND L. WEISE. *The effects of scopolamine on memory for time in rats and pigeons.* PHARMACOL BIOCHEM BEHAV 51(2/3) 271-277, 1995.—In Experiment 1, pigeons were trained to match short (2 s) and long (8 s) sample durations to red and green comparison stimuli and red and green samples to vertical and horizontal line comparisons. They received injections of scopolamine hydrobromide (0.02 mg/kg), scopolamine methylbromide (0.02 mg/kg), or saline, and the delay interval was manipulated (0, 1, 3, and 9 s). In Experiment 2, rats were trained to discriminate short (2 s) or long (12 s) durations of house-light illumination using a choice procedure. During the test phase of each trial, the left and right levers were presented with the cue light on above one of them (cued lever) while the other was off (uncued lever). For half of the rats, the correct response following the short sample was to press the cued lever, whereas following the long sample, it was to press the uncued lever. This was reversed for the remaining rats. The rats received injections of scopolamine hydrobromide (0.15 mg/kg), scopolamine methylbromide (0.15 mg/kg), or saline, and the delay interval was manipulated (0, 1, 3, and 9 s). In pigeons, scopolamine equivalently disrupted both temporal and nontemporal memory. Memory for time, in both rats and pigeons, was significantly poorer following scopolamine injections than following methylscopolamine or saline injections. No choose-short effect was observed in either rats or pigeons during saline test sessions. The data indicate that central cholinergic blockade in both pigeons and rats disrupts the accuracy of delayed temporal discriminations. However, scopolamine does not appear to accelerate the rate at which memory for temporal events is foreshortened.

Scopolamine Delayed matching-to-sample Rats Pigeons Temporal memory Time Working memory Anticholinergic

THE EFFECTS of anticholinergic drugs on memory has been assessed in a variety of species (humans, monkeys, chimpanzees, rats, mice, and pigeons) with a variety of tasks (passive and active avoidance, spontaneous alternation, radial arm maze, delayed matching-to-sample, and various discrimination learning tasks). This research has demonstrated that tasks requiring working memory rather than reference memory are more susceptible to the effects of central cholinergic blockade (1,3,19,27,29,30,33,44,46,48). Reference memory is viewed as a relatively stable knowledge base concerning which response to make for particular stimulus sequences, which outcomes follow certain responses, and so on. Working memory is regarded as maintaining a limited amount of trial-specific information, such as the color of a sample stimulus, over relatively brief time periods. Despite the frequently reported enhanced sensitivity of working memory to cholinergic blockade, there have been a few reports of equivalent anticholinergic effects on reference memory (13,22), especially when higher doses of anticholinergics are used (3,33) or when animals are trained to a high learning criterion (20).

The enhanced sensitivity of working memory processes to cholinergic blockade would lead one to expect that these effects should be delay dependent. That is, the effect of a particular anticholinergic agent, or of increasing doses of the agent, should be greater at long than at short delay intervals. However, in pigeons tested on delayed matching-to-sample (DMTS), the effects of scopolamine have uniformly been delay independent (29,30,33,35,43). Similarly, when rats are tested on a variety of delayed response tasks, most frequently anticholinergics such as scopolamine produce a generalized disruption of performance that is equivalent across short and long delays (6,7,10,14–18,36,45). The pervasive finding of delay independence suggests either that the notion of cholinergic blockade specifically affecting working memory processes is wrong or incomplete, or that the tasks used in these studies are not sensitive enough to detect delay-dependent effects.

In almost all of the tasks used to examine the effects of anticholinergics on animal memory, the events to be remembered have been particular types of visual stimuli, auditory stimuli, olfactory stimuli, or spatial locations. The nature of

[1] To whom requests for reprints should be addressed. E-mail: asanti@mach1.wlu.ca

the memory representation for these stimuli may be different from those for other stimuli, such as event durations. That is, whereas the memory code for various visual, auditory, and spatial stimuli may be categoric in nature, the memory code for event durations appears to be analogic. Support for this idea comes from recent research on pigeons' memory for event duration. When variable-length delay intervals (DIs) are presented following temporal samples, pigeons show an increasing tendency to peck the comparison stimulus corresponding to the short-duration sample (37,38,41). Similar results have also been obtained when rats' memory for durations of house light is examined (34). This "choose-short" response bias suggests that there is an isomorphism between the temporal properties of the sample and the working memory code for that sample. That is, temporal samples appear to be represented in working memory as the number of pulses generated by the internal clock during presentation of the sample. The number of pulses generated does not appear to be coded into working memory as categoric information on some dimension other than time (e.g., "Sample Type A vs. Sample Type B" or "Peck Red vs. Peck Green). The analogically coded event duration stored in working memory shortens as a function of time since termination of the sample. The subjective shortening of the analogically coded duration is presumably responsible for the choose-short effect (40,47).

The systematic errors that occur when memory-for-event durations are tested may be particularly sensitive indices for assessing amnesic drug effects. Indirect support for this hypothesis comes from studies examining the neural mechanisms mediating resetting of the internal clock (21,23). Rats with fimbria-fornix lesions were unable to remember the amount of time that had elapsed before the introduction of a gap in a signal they were timing. This suggests that working memory for the duration of signal before a gap is disrupted by hippocampal lesions. Given the demonstrated importance of the septohippocampal cholinergic system generally for delayed matching tasks in a variety of animals (2,6,8,24,28), it is reasonable to expect that an examination of cholinergic manipulations on temporal working memory would be informative. Recently, when the effect of scopolamine on pigeons' memory for time was examined, it was found that overall accuracy was reduced and a significant choose-short bias was observed under scopolamine at delays as brief as 3 s, but not under saline (31). These results suggest that anticholinergic blockade may accelerate the rate at which memory for temporal events is foreshortened in working memory. However, the absence of a choose-short bias under saline creates difficulties for this interpretation. In addition, the form of scopolamine used had both central and peripheral effects, so the results observed may not have been due to the central effects of the drug. Further research is needed to determine whether scopolamine does accelerate subjective shortening, and whether the effect is centrally mediated.

The purpose of the present research was to examine the effects of scopolamine on pigeons' and rats' memory for time. In Experiment 1, pigeons were trained to match short (2-s) and long (8-s) sample durations to red and green comparison stimuli and red and green samples to vertical and horizontal line comparisons. This permitted an examination of drug effects on both temporal and nontemporal memory in pigeons. Pigeons received injections of scopolamine hydrobromide (0.02 mg/kg), scopolamine methylbromide (0.02 mg/kg), or saline during sessions in which the DI was varied. In Experiment 2, rats were trained to discriminate short (2-s) or long (12-s) durations of house-light illumination using a similar choice procedure. During sessions in which the DI was varied, rats received injections of scopolamine hydrobromide (0.15 mg/kg), scopolamine methylbromide (0.15 mg/kg), or saline. Scopolamine methylbromide is a quaternary anticholinergic that does not enter the CNS. It was used as a control agent to assess whether the effect of scopolamine hydrobromide was due to its central or peripheral nervous system effects. The study was designed to provide data on the following issues: a) Does central cholinergic blockade in both pigeons and rats disrupt the accuracy of delayed temporal discriminations? b) Does scopolamine accelerate the rate at which memory for temporal events is foreshortened in both pigeons and rats?

EXPERIMENT 1

Method

Subjects. Eight adult male White Carneaux pigeons, maintained at approximately 80% of their ad lib weight and housed individually with constant access to grit and water, served as subjects. Fluorescent lights were illuminated on a 12 L : 12 D cycle in the colony room. All birds had extensive experience with delayed matching tasks including memory for event duration.

Apparatus. Four Coulbourn modular operant test cages (Model E10-10) housed individually in isolation cubicles (Model E10-20) were used. Each cubicle was equipped with a ventilation fan and baffled air intake and exhaust system. Each test cage was equipped with three horizontally aligned, clear plastic keys behind which projectors could display stimuli (red or green field, a white vertical, a white horizontal, or white crossed diagonal lines on a black background, or a black dot on a white background) onto a frosted rear projection screen (Model E21-18; Coulbourn). Directly below the center key was a 5.7 × 5 cm opening that provided access to a hopper filled with mixed grain (Model E14-10; Coulbourn). A house light was located 6.5 cm above the center key and installed such that the light was directed upward to reflect from the top of the cage (Model E11-01 with bulb SL1819X; Coulbourn). All experimental events and response measures were arranged and recorded by a microcomputer system located in an adjacent room.

Procedure. All birds had received extensive prior delayed-matching training with color (red and green fields) and temporal (2- or 8-s illumination of crossed diagonal lines) samples. Color sample stimuli were followed by line-tilt comparison stimuli (vertical and horizontal lines), and temporal sample stimuli were followed by color comparison stimuli (red and green fields). The position of the comparison stimuli was counterbalanced over trials. Each trial began with the warning stimulus (black dot on a white background) presented on the center key. A single peck to it resulted in presentation of one of four sample stimuli on the center key. The color samples were presented for 4 s, because this is an approximate estimate of the point of subjective equality between 2- and 8-s temporal samples for pigeons (41). Immediately following the offset of the sample stimulus, the comparison stimuli were presented. For all birds, a response to the red comparison was correct following a 2-s sample, and a peck to the green comparison was correct following an 8-s sample. For five birds, a peck to the vertical line comparison following a red sample and a peck to the horizontal line comparison following a green sample was correct. For the remaining three birds, the relationship between the color sample and the correct line comparison stimulus was reversed. A single peck to the comparison stimuli turned them off and, if correct, permitted 3-s access to mixed

grain. Incorrect responses to the comparison stimuli produced a 3-s blackout followed immediately by representation of the same sample stimulus and comparison stimulus configuration. A correct response on a correction trial produced 3-s access to mixed grain, although only the choice response on the initial (noncorrection) trial was used to calculate matching accuracy. When necessary, supplementary feedings of Purina Pigeon Chow occurred after the experimental sessions.

Within each block of eight trials, all combinations of the four sample stimuli with the various comparison stimuli on the left and right keys occurred once. The order of presentation was randomized individually for each bird. All birds received 72 trials per session. Intertrial intervals were a constant 20 s in length. Prior to drug testing, the performance of all birds was at 80% or better on both color and temporal sample trials.

On each session of drug testing, the birds received one of the following injections: 0.09% saline, 0.02 mg/kg scopolamine hydrobromide; or 0.02 mg/kg scopolamine methylbromide. A 0.02-mg/kg dose was used because in our previous work it has produced reliable and selective effects on working memory (29,30,33). Larger doses disrupt both reference memory and working memory, as well as interfere with key-pecking behavior generally. The drug was purchased from Sigma Chemical Co. (St. Louis, MO). All injections were made into the pectoral muscle 10 min before each test session in a volume of 1.0 ml/kg body wt. Two different random orders of the drug treatments were generated: One of the orders was assigned to one group of four birds, and the other to the remaining four birds. Each of the drug treatments was administered once before the same injection was repeated. A total of 21 test sessions (seven saline, seven scopolamine, seven methylscopolamine) were administered. Each drug test session consisted of 96 trials, within which 18 trials for each sample occurred at the 0-s delay and two trials for each sample occurred at each of the other delays (1, 3, and 9 s). This distribution of delays was used so that the reference memory of durations of temporal samples and their associations with the comparison stimuli established during 0-s delay training would remain relatively stable during testing (41). There was no illumination in the test chamber during the delay intervals. All other parameters were the same as those described previously, but without a correction procedure.

Results and Discussion

Figure 1 shows the mean percentage correct matching performance during drug testing sessions at the four delay intervals for both temporal and color samples. Overall accuracy was significantly lower with scopolamine (66.1%) than with either saline (76.5%) or methylscopolamine (77.0%) [$F(2, 14) = 26.40$, $p < 0.01$], and it declined with increases in delay interval [$F(3, 21) = 56.38$, $p < 0.01$]. Accuracy was also significantly higher on trials with color samples (77.7%) than on trials with temporal samples (69.1%) [$F(1, 7) = 11.27$, $p < 0.05$]. The analysis also revealed significant interactions of drugs by delay interval [$F(6, 42) = 3.53$, $p < 0.05$] and sample dimension by delay interval [$F(3, 21) = 3.48$, $p < 0.05$]. There was a significant effect of drug treatments at all delays [$F(2, 14) = 25.92$, 16.67, and 9.40, except at the 9-s delay, $F(2, 14) = 2.10$, where the birds performed poorly under all conditions]. Similarly, accuracy was significantly higher on color-sample trials than on temporal-sample trials at all delays [each $F(1, 7) = 58.91$, 8.02, and 16.42, except at the 9-s delay, $F(1, 7) < 1$]. Scopolamine appears to disrupt

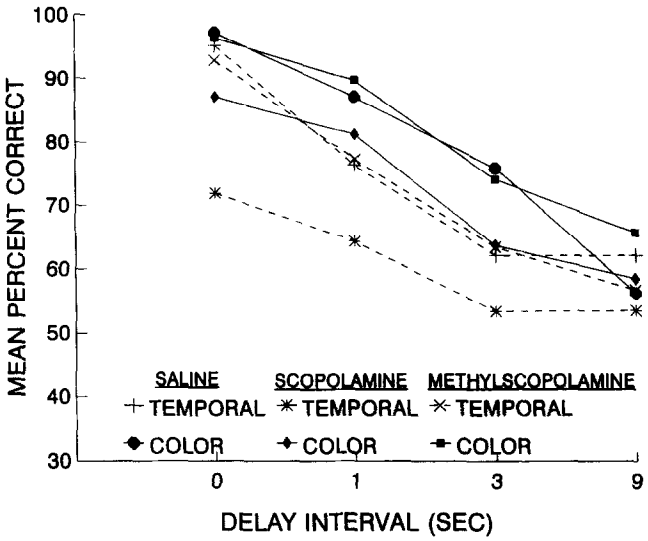

FIG. 1. Mean percent of correct matching responses of pigeons as a function of saline, scopolamine (0.02 mg/kg), or methylscopolamine (0.02 mg/kg) on temporal and color sample trials during testing at delays of 0, 1, 3, and 9 s.

both temporal and nontemporal delayed discriminations equivalently in pigeons. This effect is due to central cholinergic blockade and not the peripheral effects of scopolamine, because retention functions under scopolamine methylbromide and saline were equivalent.

The effects of scopolamine on temporal memory were examined in more detail by including sample duration (short or long) as a factor. These data are displayed in Fig. 2. Overall accuracy was significantly lower with scopolamine (60.8%) than with either saline (73.9%) or methylscopolamine (72.6%) [$F(2, 14) = 22.31$, $p < 0.01$], and it declined with increases

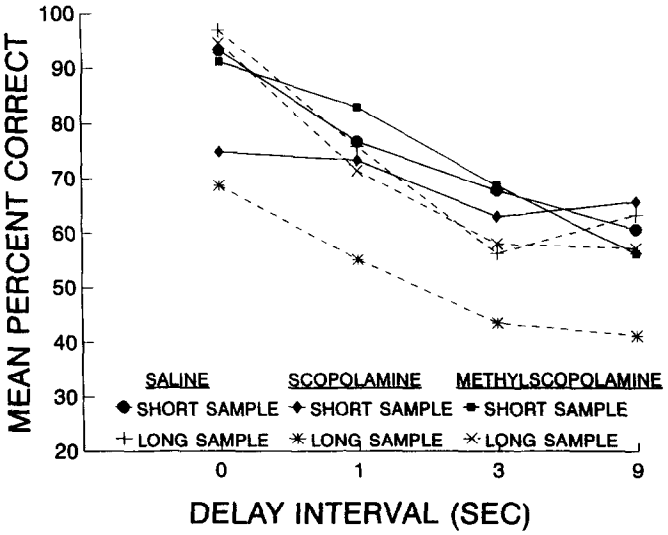

FIG. 2. Mean percent of correct matching responses of pigeons as a function of saline, scopolamine (0.02 mg/kg), or methylscopolamine (0.02 mg/kg) on short and long sample trials during testing at delays of 0, 1, 3, and 9 s.

in delay interval [$F(3, 21) = 40.32$, $p < 0.01$]. The analysis also revealed a significant drug × delay interval interaction [$F(6, 42) = 3.28$, $p < 0.05$]. The effect of drug treatments was significant at the 0-s and 1-s delays [$F(2, 14) = 65.65$ and 6.71] but not at the 3-s and 9-s delays [$F(2, 14) = 2.75$ and 3.23]. For scopolamine sessions, accuracy on short-sample trials appeared to be greater than on long-sample trials. However, neither the effect of sample duration nor any interactions involving sample duration were statistically significant. The overall pattern of these results are similar to those previously reported by Santi and Bridson (31) in that there was a trend for a choose-short effect to occur under scopolamine but no evidence of such an effect under saline. The replicable absence of a choose-short effect under saline is somewhat surprising because it is normally quite robust (11,12,37-41,47). Numerous studies indicate that choose-short effects appear to result from the subjective shortening of an analogic code (12,40,41, 47); however, the failure to observe a statistically significant choose-short effect under scopolamine in the present research is inconsistent with the hypothesis that scopolamine accelerates the rate at which event durations are subjectively shortened in working memory.

EXPERIMENT 2

Method

Subjects. Eight male Sprague-Dawley rats maintained at approximately 80% of their ad lib weights served as subjects. They were housed in individual stainless-steel cages in a room maintained on a 12 L : 12 D schedule. The rats had free access to water at all times in the colony room. All rats had previous experience with the current DMTS task in which ITI and DI manipulations had been investigated. Five had also served, 3 mo previously, in a study examining the effects of amphetamine on temporal memory.

Apparatus. Four Coulbourn modular operant test cages (Model E10-10) housed individually in isolation cubicles (Model E10-20) were used. The cubicles were equipped with a ventilation fan and baffled air intake exhaust systems. Each test cage was equipped with a 45-mg pellet feeder (Model E14-06), which was mounted in the centre of the front wall. Two retractable levers (Model E23-07) were mounted 2.5 cm above the grid floor on either side of the pellet feeder. A 7.5-W opaque white jewel lamp was mounted directly above each retractable lever. A house light was located 6.5 cm above the pellet feeder and installed such that the light was directed upward to reflect from the top of the cage (Model E11-01 with bulb SL1819X; Coulbourn). All experimental events and response measures were controlled by a microcomputer located in an adjacent room.

Procedure. All rats had been previously trained in a DMTS procedure to discriminate short (2-s) and long (12 s) durations of house-light illumination. Each trial was initiated by onset of the house light for 2 or 12 s. Termination of the sample was followed by a 2-s period during which the cue light above either the left or right lever was illuminated before entry of the levers into the chamber. This will be referred to as a 0-s delay condition, because the onset of the cue light immediately after sample termination provided the rat with information concerning the correct spatial location to respond to once the levers were inserted. Within each block of four trials, all combinations of the two sample durations with the two test conditions (i.e., cued left-uncued right, or uncued left-cued right) occurred once. The order of presentation was randomized individually for each rat. For three rats, responding on the cued lever was correct after the 2-s signal and responding on the uncued lever was incorrect; following a 12-s signal, the uncued lever was correct and the cued lever was incorrect. These contingencies between event duration and correct lever were reversed for the remaining five rats. A response to the correct lever turned off the cue light, retracted both levers, and resulted in delivery of a food pellet. Pellet delivery produced an audible click, and the light in the magazine was illuminated for 0.5 s. A response to the incorrect lever turned off the cue light and retracted both levers. A correction procedure was used throughout training. Following an incorrect response, a 5-s delay period occurred; this was followed immediately by representation of the same sample duration and the same cued-uncued-lever configuration. A correct response on a correction trial turned off the cue light, retracted both levers, and resulted in delivery of a food pellet. Only the choice response on the initial (noncorrection) trial was used to calculate matching accuracy. Following delivery of the reinforcer, an intertrial interval of 25-s was spent in darkness. All rats received 72 trials per session. Prior to drug testing, the performance of all rats was 80% or better.

During each session of drug testing, the rats received one of the following injections: 0.15 mg/kg scopolamine hydrobromide; 0.15 mg/kg scopolamine methylbromide; or 0.09% saline. Although this dose is higher than that typically used with pigeons, it was selected on the basis of previous scopolamine studies on memory in rats. This dose is a relatively low dose of scopolamine for rats that does not produce gross sensorimotor disturbance or loss of motivation (25). The drug was purchased from Sigma Chemical Co. (St. Louis, MO). Twenty minutes before each test session, each rat was given an IP injection in a volume of 1.0 ml/kg body wt. Two different random orders of the drug treatments were generated. Four rats received one order; those remaining received the other order. Each of the drug treatments was administered once before the same injection was repeated. A total of 15 test sessions (five saline, five scopolamine, and five methylscopolamine) was administered. Each drug test session consisted of two blocks of 36 trials. Within each block of 36 trials, there were 12 short and 12 long samples tested at the 0-s delay and two short and two long sample durations tested at each delay of 1, 3, and 9 s. This distribution of delays was used so that the reference memory of the sample durations and their associations with the correct comparison response established during 0-s delay training would remain relatively stable during testing (41). The delay intervals represented periods of darkness between sample termination and onset of the cue light for 2 s before lever entry. All other parameters were the same as in the training sessions, but without a correction procedure.

RESULTS AND DISCUSSION

Figure 3 presents the mean percentage of correct matching responses obtained during drug testing sessions. Overall accuracy was significantly lower with scopolamine (60.0%) than with either saline (64.0%) or methylscopolamine (67.8%) [$F(2, 14) = 6.06$, $p < 0.01$], and it declined with increases in delay interval [$F(3, 21) = 71.18$, $p < 0.01$]. The analysis also revealed a significant drug × delay interval interaction [$F(6, 42) = 2.48$, $p < 0.05$]. The effect of drug treatments was significant at the 0- and 1-s delays [each $F(2, 14) = 6.07$ and 5.22], but not at the 3- and 9-s delays [each $F(2, 14) = 2.66$ and 1.05]. At the 0-s delay, scopolamine reduced accuracy significantly compared to both saline and methylscopolamine. At the 1-s delay, accuracy under saline and methylscopol-

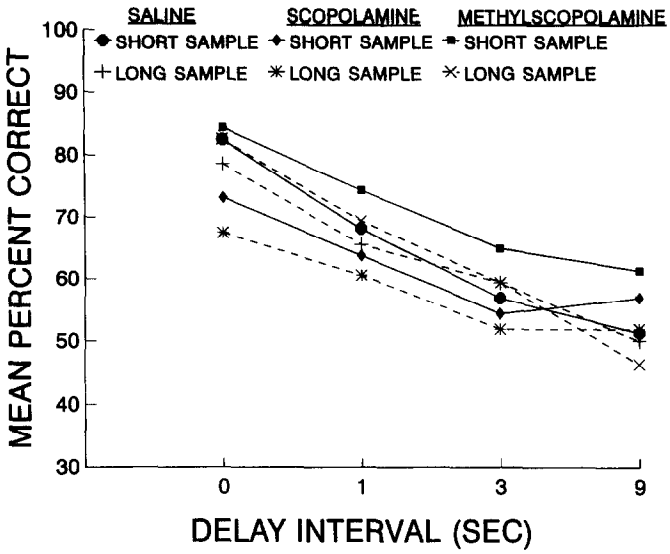

FIG. 3. Mean percent of correct matching responses of rats as a function of saline, scopolamine (0.15 mg/kg), or methylscopolamine (0.15 mg/kg) on short and long sample trials during testing at delays of 0, 1, 3, and 9 s.

amine was again equivalent, but scopolamine significantly reduced accuracy only with respect to methylscopolamine. At the longer delays, the rats performed poorly under all conditions. Neither the effect of sample duration nor any interactions involving sample duration were statistically significant. The absence of a choose-short effect under saline was unexpected because we have observed these effects in both rats and pigeons in studies not involving scopolamine (5,32,34).

GENERAL DISCUSSION

The present findings are consistent with the previously reported disruptive effects of scopolamine on matching of nontemporal events, in that disruption occurred at even the shortest delay interval (6,10,14–18,29,30,33,35,36,43,45). In addition to affecting nontemporal delayed discriminations, the present results indicate that scopolamine disrupts temporal delayed discriminations in a similar fashion in both rats and pigeons. The drug × delay interval interaction that was observed in both studies occurred because scopolamine disrupted accuracy at the short delays (0 and 1 s), but not at the longer delays (3 and 9 s). The longer delay intervals reduced accuracy in the control conditions sufficiently to prevent a disruptive effect of scopolamine from being detected. Consequently, the nature of the drug × delay interaction is not consistent with the hypothesis that scopolamine accelerates the rate of forgetting. The results indicate a generalized disruption of performance in which poor performance at the long delays prevented a drug effect from being detected. In both species, the effect is due to central cholinergic blockade and not the peripheral effects of scopolamine, because retention functions under scopolamine methylbromide and saline were equivalent.

Ennaceur and Meliani (9) found that low doses of scopolamine (0.25 and 0.50 mg/kg) disrupted radial-maze learning but not object recognition memory in rats. They concluded that this result was consistent with the finding that working memory tests based on nonspatial information were less sensitive to scopolamine effects. However, their conclusion may be premature. The present results indicate that the same low doses of scopolamine that disrupt radial-maze learning in rats can also disrupt working memory tests based on temporal information.

The data obtained in the present research support the hypothesis that manipulation of the neurotransmitter acetylcholine affects behavior in tasks requiring memory processes not only in mammalian species, but in an avian species as well. Although previous research with a variety of species has indicated that tasks requiring working memory rather than reference memory are more susceptible to the effects of anticholinergics (1,3,19,27,29,30,33,46,48), it has been difficult to isolate the specific cognitive processes affected. Many reasons could account for this; however, the present research attempted to determine whether the nature of the code stored in working memory is a factor in the sensitivity of delayed discrimination performance to anticholinergic effects. Behavioral research has supported the hypothesis that the working memory code for event durations is analogic rather than categoric (12,40,47), and that this analogic code is subject to foreshortening (41). Contrary to our previous finding (31), the present results do not support the hypothesis that anticholinergic blockade accelerates the rate at which memory for temporal events is foreshortened in working memory. If it did accelerate the rate at which memory for temporal events is foreshortened, we should have observed significantly larger choose-short effects under scopolamine than under saline, and these effects should have occurred at shorter delay intervals with scopolamine than with saline. Although we have not been able to replicate the finding of a choose-short effect under scopolamine, we have repeatedly found that the choose-short effect does not occur under saline conditions when scopolamine is being concurrently tested.

The reliability of the choose-short effect has been well established by the results of many different studies, but it has also been shown that the effect is strongly affected by procedural variables, such as the ITI and DI durations (41), the ITI and DI values used during training relative to those in testing (38,39), and the specific type of DMTS procedure used (5,11,12,32). The procedural variables used in the present research were consistent with those known normally to result in the choose-short effect. The absence of a choose-short effect in saline sessions is apparently due to the intervening sessions in which scopolamine was administered. In other research conducted in our laboratory with both rats and pigeons, we found a choose-short effect under saline when the drug administered in other sessions was amphetamine. In the amphetamine studies, the injections of saline and amphetamine were either blocked or alternated regularly. In our scopolamine studies, the injections of saline and scopolamine were randomized. Consequently, further research is need to determine whether the absence of a choose-short effect under saline is due to the nature of the neurochemical system being manipulated on drug sessions or to the predictability of saline and drug sessions.

Comparison of the present effects of scopolamine on temporal discriminations in pigeons and rats with those effects reported for *d*-amphetamine (26,42) and tetrahydrocannabinol (4) is complicated because of several differences in procedure. However, in both rats (26) and pigeons (4,42) at a 0-s delay, drugs such as *d*-amphetamine and tetrahydrocannabinol produced significant choose-short biases particularly as the doses of these drugs were increased. Unfortunately, in these studies the delay interval was not manipulated; there-

fore, we cannot determine whether a choose-short effect would have been observed under saline. Nevertheless, there is now considerable evidence that the accuracy of temporal discriminations in both rats and pigeons is disrupted even at a 0-s delay by drugs such as scopolamine, amphetamine, and tetrahydrocannabinol.

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. Bresnahan, E. L.; Wiser, P. R.; Muth, N. J.; Ingram, D. K. Delayed matching-to-sample by rats in a new avoidance-motivated maze: Response to scopolamine and fimbria-fornix lesions. Physiol. Behav. 51:735-746; 1992.
3. Buresova, O.; Bolhuis, J. J.; Bures, J. Differential effects of cholinergic blockade on performance of rats in the water tank navigation task and in the radial water maze. Behav. Neurosci. 100:476-482; 1986.
4. Daniel, S. A.; Thompson, T. Methadone-induced attenuation of the effects of tetrahydrocannabinol on temporal discriminations in pigeons. J. Pharmacol. Exp. Ther. 213:247-253; 1980.
5. Ducharme, M. J.; Santi, A. Alterations in the memory code for temporal events induced by differential outcome expectancies in pigeons. Anim. Learn. Behav. 21:73-81; 1993.
6. Dunnett, S. B. Comparative effects of cholinergic drugs and lesions of the nucleus basalis or fimbria-fornix on delayed matching in rats. Psychopharmacology (Berlin) 87:357-363; 1985.
7. Dunnett, S. B.; Evenden, J. L.; Iversen, S. D. Delay-dependent short-term memory deficits in aged rats. Psychopharmacology (Berlin) 96:174-180; 1988.
8. Ennaceur, A.; Meliani, K. A new one-trial test for neurobiological studies of memory in rats. III. Spatial and nonspatial working memory. Behav. Brain Res. 51:83-92; 1992.
9. Ennaceur, A.; Meliani, K. Effects of physostigmine and scopolamine on rats' performances in object-recognition and radial-maze tests. Psychopharmacology (Berlin) 109:321-330; 1992.
10. Godding, P. R.; Rush, J. R.; Beatty, W. W. Scopolamine does not disrupt spatial working memory in rats. Pharmacol. Biochem. Behav. 16:919-923; 1982.
11. Grant, D. S.; Spetch, M. L. Pigeons' memory for event duration: Differences between choice and successive matching tasks. Learn. Motiv. 22:180-199; 1991.
12. Grant, D. S.; Spetch, M. L. Analogical and nonanalogical coding of samples differing in duration in a choice-matching task in pigeons. J. Exp. Psychol. Anim. Behav. Proc. 19:15-25; 1993.
13. Hagan, J. J.; Tweedie, F.; Morris, R. G. Lack of task specificity and absence of posttraining effects of atropine on learning. Behav. Neurosci. 100:483-493; 1986.
14. Heise, G. A.; Connor, R.; Martin, R. A. Effects of scopolamine on variable intertrial interval spatial alternation and memory in the rat. Psychopharmacology (Berlin) 49:131-137; 1976.
15. Heise, G. A.; Hrabrich, B.; Lilie, N. L.; Martin, R. A. Scopolamine effects on delayed spatial alternation in the rat. Pharmacol. Biochem. Behav. 3:993-1002; 1975.
16. Huston, A. E.; Aggleton, J. P. The effects of cholinergic drugs upon recognition memory in rats. Q. J. Exp. Psychol. 39B:297-314; 1987.
17. Kirk, R. C.; White, K. G.; McNaughton, N. Low dose scopolamine affects discriminability but not rate of forgetting in delayed conditional discrimination. Psychopharmacology (Berlin) 96: 541-546; 1988.
18. Ksir, C. J. Scopolamine effects on two-trial delayed response performance in the rat. Psychopharmacology (Berlin) 34:127-134; 1974.
19. Levy, A.; Kluge, P. B.; Elsmore, T. F. Radial arm maze performance of mice: Acquisition and atropine effects. Behav. Neural Biol. 39:229-240; 1983.
20. Lydon, R. G.; Nakajima, S. Differential effects of scopolamine on working and reference memory depend upon level of training. Pharmacol. Biochem. Behav. 43:645-650; 1992.
21. Meck, W. H.; Church, R. M.; Olton, D. S. Hippocampus, time and memory. Behav. Neurosci. 98:3-22; 1984.
22. Okaichi, H.; Jarrard. L. E. Scopolamine impairs performance of a place and cue task in rats. Behav. Neural Biol. 36:319-325; 1982.
23. Olton, D. S.; Meck, W. H.; Church, R. M. Separation of hippocampal and amygdaloid involvement in temporal memory dysfunctions. Brain Res. 404:180-188; 1987.
24. Olton, D. S.; Wenk, G. Animal models of the cognitive impairments produced by degeneration of the basal forebrain cholinergic system. In: Meltzer, H. Y., ed. Psychopharmacology: The third generation of progress. New York: Raven Press; 1987:941-953.
25. Pontecorvo, M. J.; Clissold, D. B.; White, M. F.; Ferkany, J. W. *N*-methyl-d-aspartate antagonists and working memory performance: Comparison with the effects of scopolamine, propranolol, diazepam, and phenylisopropyladenosine. Behav. Neurosci. 105:521-535; 1991.
26. Rapp, D. L.; Robbins, T. W. The effects of d-amphetamine on temporal discrimination in the rat. Psychopharmacology (Berlin) 51:91-100; 1976.
27. Rauch, S. L.; Raskin, L. A. Cholinergic mediation of spatial memory in the preweanling rat: Application of the radial arm maze paradigm. Behav. Neurosci. 98:35-43; 1984.
28. Ravel, N.; Elaagouby, A.; Gervais, R. Scopolamine injection into the olfactory bulb impairs short-term olfactory memory in rats. Behav. Neurosci. 108:317-324; 1994.
29. Santi, A. Pharmacological studies of working and reference memory in pigeons. In: Bond, N. W.; Siddle, D. A. T., eds. Psychobiology: Issues and applications. North Holland: Elsevier Science Publishers BV; 1989:45-61.
30. Santi, A.; Bogles, J.; Petelka, S. The effect of scopolamine and physostigmine on working and reference memory in pigeons. Behav. Neural Biol. 49:61-73; 1988.
31. Santi, A.; Bridson, S. The effects of scopolamine and cues to forget on pigeons' memory for time. Pharmacol. Biochem. Behav. 39:935-940; 1991.
32. Santi, A.; Bridson, S.; Ducharme, M. J. Memory codes for temporal and nontemporal samples in many-to-one matching by pigeons. Anim. Learn. Behav. 21:120-130; 1993.
33. Santi, A.; Hanemaayer, C.; Reason, W. The effect of scopolamine on reference and working memory in pigeons. Anim. Learn. Behav. 15:395-402; 1987.
34. Santi, A.; Weise, L.; Kuiper, D. Memory for event duration in rats. Paper presented at the Canadian Society for Brain, Behaviour, and Cognitive Science Meeting, Vancouver, BC, June 1994.
35. Savage, L. M.; Stanchfield, M. A.; Overmier, J. B. The effects of scopolamine, diazepam, and lorazepam on working memory in pigeons: An analysis of reinforcement procedures and sample problem type. Pharmacol. Biochem. Behav. 48:183-191; 1994.
36. Spencer, D. G. J.; Pontecorvo, M. J.; Heise, G. A. Central cholinergic involvement in working memory: Effects of scopolamine on continuous nonmatching and discrimination performance in the rat. Behav. Neurosci. 99:1049-1065; 1985.
37. Spetch, M. L. Systematic errors in pigeons' memory for event duration: Interaction between training and test delay. Anim. Learn. Behav. 15:1-5; 1987.
38. Spetch, M. L.; Rusak, B. Pigeons' memory for event duration: Intertrial interval and delay effects. Anim. Learn. Behav. 17:147-156; 1989.
39. Spetch, M. L.; Rusak, B. Temporal context effects in pigeons' memory for event duration. Learn. Motiv. 23:117-144; 1992.
40. Spetch, M. L.; Sinha, S. S. Proactive effects in pigeons' memory for event durations: Evidence for analogical retention. J. Exp. Psychol. Anim. Behav. Proc. 15:347-357; 1989.

41. Spetch, M. L.; Wilkie, D. M. Subjective shortening: A model of pigeons' memory for event duration. J. Exp. Psychol. Anim. Behav. Proc. 9:14–30; 1983.
42. Stubbs, D. A.; Thomas, J. R. Discrimination of stimulus duration and d-amphetamine in pigeons: A psychophysical analysis. Psychopharmacologia 36:313–322; 1974.
43. Teal, J. J.; Evans, H. L. Effects of DAVP, a vasopressin analog, on delayed matching behavior in the pigeon. Pharmacol. Biochem. Behav. 17:1123–1127; 1982.
44. Troster, A. I.; Beatty, W. W.; Staton, R. D.; Rorabaugh, A. G. Effects of scopolamine on anterograde and remote memory in humans. Psychobiology 17:12–18; 1989.
45. Weisman, R. G.; Bruce, R.; Beninger, R. J. Simple and delayed conditional discrimination in rats: The effects of delays and scopolamine. Learn. Motiv. 18:274–287; 1987.
46. Whishaw, I. Q. Cholinergic receptor blockade in the rat impairs locale but not taxon strategies for place navigation in a swimming pool. Behav. Neurosci. 99:979–1005; 1985.
47. Wilkie, D. M.; Willson, R. J. Discriminal distance analysis supports the hypothesis that pigeons retrospectively encode event duration. Anim. Learn. Behav. 18:124–132; 1990.
48. 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.