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EFFECTS OF SCOPOLAMINE ON REPEATED ACQUISITION OF RADIAL-ARM MAZE PERFORMANCE BY RATS

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Rats repeatedly acquired the performance of selecting only the four baited arms in an automated eight-arm radial maze, with the arms containing food pellets randomly assigned prior to each session. During each 14-trial (trial: obtain all four pellets) daily session, the number of errors (selecting nonbaited arms or repeating arm selections) showed a within-session decline, and choice accuracy for the first four arm selections showed a positive acceleration across trials for all rats. An index-of-curvature statistic, calculated for total errors, was used to quantify both the within- and between-session improvement of performance. Scopolamine (0.03 to 0.3 mg/kg, ip), but not methylscopolamine (0.3 mg/kg), reduced the accuracy of the first four selections of each trial and increased total within-session errors for all rats. Session times also were increased by scopolamine. An examination of within-session accuracy showed only slight signs of improvement at the higher dosages of scopolamine. The results indicate that behavior in transition states maintained by reinforcement contingencies in the radial maze is similar to that maintained by extended chained schedules, despite the fact that some of the stimuli controlling behavior in the maze are absent at the moment behavior is emitted.

Key words: repeated acquisition, stimulus control, radial-arm maze, scopolamine hydrobromide, scopolamine methylbromide, discrimination, behavioral toxicology, rat

Deficits in learning and remembering are commonly reported symptoms of human exposure to a diverse range of industrial and agricultural chemicals (Anger & Johnson, 1985; Tilson & Mitchell, 1984). Because of the vast number of chemicals existing in the environment that have not been assessed for potential neurotoxic properties, a need exists for tests of chemical effects on the acquisition of behavioral control in laboratory animals.

One test that has met with success in assessing chemical-induced disruption of learning is the repeated acquisition baseline. In studies first reported by Boren, monkeys acquired a unique food-reinforced sequence of responses each day, thus allowing acquisition to be studied recurrently in a single organism (Boren, 1963; Boren & Devine, 1968). Following these initial studies, the repeated acquisition baseline was adapted for assessment of drug-induced alterations in the acquisition of behavioral control in a number of species, including pigeons (e.g., Harting & McMillan, 1976; Thompson, 1976), rats (e.g., Calhoun & Jones, 1974; Handley & Calhoun, 1978; Pollard, McBennett, Rohrbach, & Howard, 1981; Schrot, Boren, & Moerschbaecher, 1976), dogs (Thomas & Schrot, unpublished, cited in Thompson & Moerschbaecher, 1979), the great apes (Pieper, 1976), and humans (Desjardins, Moerschbaecher, Thompson, & Thomas, 1982; Fischman, 1978). As pointed out by Thompson, the within-subject approach to the study of acquisition avoids many of the problems seen in group designs resulting from individual differences in the rate or speed of learning (Thompson, 1978, p. 190).

Although the advantages of the repeated acquisition technique for assessing drug effects have been aptly demonstrated, the use of such a baseline has been limited, partly due to the amount of time required to train animals on the task. Thompson (1973) has indicated that more than 60 daily sessions are required to produce stable baselines for pigeons repeatedly acquiring a four-member response chain. Using similar testing procedures, rats may require even more training. Howard and Pollard

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(1983) report that from 126 to over 300 daily sessions were required for their subjects to reach stable levels of performance with a four-member response chain. Schrot and collegues found that rats attained stable performance under a three-member aversively maintained acquisition baseline after 60 sessions (Schrot, Boren, Moerschbaecher, & Simoes Fontes, 1978), whereas performance maintained by a four-member food-reinforced baseline required more than 80 sessions to reach stability (Schrot, Thomas, & Banvard, 1980). Because rodents predominate as the subject of choice in behavioral toxicology, techniques that hasten the training for a repeated acquisition task will make such a task much more useful. In fact, cursory examination of the behavioral toxicology literature reveals very few instances in which this approach to the study of learning has been applied, with notable exceptions being two investigations with pigeons (Dietz, McMillan, & Mushak, 1979; Leander, McMillan, & Barlow, 1977), three with monkeys (Anger & Setzer, 1979; Galloway, 1975; Knepton & de Lorge, 1983), and three with rats (Paule & McMillan, 1986; Schrot et al., 1980; Schrot, Thomas, & Robertson, 1984). Clearly the protracted time course for establishing stable baselines of performance contributes to the scarcity of toxicological experiments utilizing repeated acquisition procedures.

Apart from practical issues concerning the amount of time required for establishing behavioral control with traditional repeated acquisition baselines, questions remain concerning the generality and validity of conclusions derived from a single approach to the study of behavior in transition states. In traditional repeated acquisition baselines, the acquisition of stimulus control typically involves stimuli present at the moment the performance is emitted (but see Moerschbaecher & Thompson, 1980). For instance, in the extended-chain procedure described by Thompson (1973), pecks at one of three keys were under the control of keylight stimuli present during the various components of the chain; by altering reinforcement contingencies, new conditional discriminations were established within each session. Whether similar conditional discriminations could be established using qualitatively different stimuli is unclear. Responding maintained by delayed matching-to-sample, delayed alternation, and radial-arm maze paradigms are all examples of performances controlled by stimuli no longer present at the time behavior is emitted. However, these procedures usually have been used to study steady-state performance rather than performance in transition. Behavior maintained by these procedures is often described as reflecting the operation of memory, because the stimuli directing behavior are no longer present at the time behavior is emitted. A more fruitful approach to the analysis of the behavioral control by these stimuli would be to determine the function that these prior stimuli have in the acquisition of stimulus control over performance in a repeated acquisition paradigm (i.e., delayed conditional discriminations). By doing so, it would be possible to compare the transition states involved in establishing stimulus control by these stimuli with the simultaneous conditional discriminations of more traditional repeated acquisition paradigms.

The present experiment describes a novel procedure designed to bring the performance of arm selection in the radial-arm maze under the control of contingencies that varied from session to session. Rats were placed in an eight-arm maze, with food pellets available in only four of the arms. Each day, the arms with food available were altered. The performance of selecting only those arms where food was available was then examined repeatedly over a number of trials within a single session. Once performance had become stable, it was challenged with the central muscarinic blocker, scopolamine. The choice of scopolamine was based on earlier reports describing the influence of cholinergic manipulations on delayed stimulus control in rodents (see Spencer & Lal, 1985).

METHOD

Subjects

Four adult male Long-Evans hooded rats, approximately 120 days of age at the start of the experiment, served as subjects. The rats were housed in individual acrylic top-hanging cages with indirect bedding in a colony room with controlled ambient temperature (21 ± 2°C) and humidity (55 ± 20%) and with a 12-hr photoperiod. The rats were placed on a restricted feeding schedule that maintained

their presession body weights at 350 g and were allowed unlimited access to water except during behavioral testing. Prior to the present experiment, the rats were trained on a standard procedure in which all arms contained food in each session (Olton & Samuelson, 1976). They each received 21 sessions of exposure to these conditions and were thus well trained at making accurate selections in the automated maze.

Apparatus

Behavioral testing took place in an automated version of the radial-arm maze (see Peele & Baron, in press). Each of the eight Plexiglas (floor) and sheet-metal (sides) arms measured 26 by 10.5 by 9.5 cm wide and radiated at equal angles from a 32.5-cm octagonal central arena, also constructed of Plexiglas. A Gerbrands pellet dispenser (Model G5110) was located at the distal end of each arm and could dispense 45-mg food pellets into Plexiglas cups that were centered 5 cm above the arm floor. Located at the entrance of each arm were pneumatically operated sheet-metal guillotine doors that controlled access to the arms. Photodiode pairs located at the entrance and midpoint of each arm and across the food cup orifice detected the position of a rat in the maze. The entire maze was covered in Plexiglas and located in a 110-sq ft room rich in extramaze stimuli. All stimulus conditions and data collection were arranged by a minicomputer (PDP-8A®, Digital Equipment Company) and SuperSked® software (Snapper, Kadden, & Inglis, 1982).

Procedure

On its first day of training on the repeated acquisition task, each rat was placed in the central arena of the maze with the doors to the arms closed. Following a brief (30 s) acclimation period, the doors were raised and the rat was allowed to enter each of the eight arms. An arm selection was defined as the first nose-poke into the food cup that occurred after a rat entered the arm; a repeat arm selection required that the rat exit the arm, reenter, and emit a nose-poke into the food cup. Only four of the eight arms were baited during any one session. That is, food-pellet acquisition was contingent upon the first nose-poke into the food cup of each of four arms on each trial; similar responses in the other arms or repeat responses during a trial had no scheduled consequences. A trial terminated after a rat obtained all four available pellets or after 900 s elapsed, whichever occurred first. At the termination of a trial, the rat was confined in the central arena for approximately 10 s (intertrial interval: ITI). The ITI began when a rat exited from the arm in which the last pellet was obtained, at which point all doors were closed, confining the rat in the central arena. After the ITI, another trial was initiated by opening all arm doors and allowing arm selections. Within each session, the same four arms were baited on all trials. The actual baited arms were selected randomly (without replacement) at the beginning of each session. Throughout the experiment, sessions were conducted 5 days per week (Monday through Friday) at approximately the same time of day.

Sessions initially consisted of 10 trials (Sessions 1 to 19) with all rats exposed to the same unique set of baited arms chosen prior to each daily session. Beginning with Session 20 and continuing throughout the experiment, each session consisted of 14 trials. During Sessions 15 to 25, there appeared to be a confound in the procedure that resulted in the following observation: on the first trial of each session, rats exposed to the apparatus first (S1, S3) were consistently less accurate than those rats exposed later in the day (S4, S6). To compensate for potential interactions between order of testing and the resulting accuracy scores, the baiting procedure was altered on Session 27 so that each rat was exposed to a unique set of baited arms in each session (i.e., the baited set of arms changed across sessions and across subjects). These conditions continued for the remainder of the experiment. During each session, the following data were collected:

1. Accuracy: percentage of the first four arm selections that produced food.
2. Total errors: number of nonreinforced arm selections during each trial, defined as the initial nose-poke occurring after a rat entered an arm.
3. Latency: seconds required to obtain all four food pellets during a single trial.
4. Session time: seconds, exclusive of ITI, required to complete all trials during a single session.

The analysis of errors included a classification of error type according to whether rats chose the same arm on two occasions within

a trial (Type B, repeat selections of a baited arm; Type NBC, repeat selections of an unbaited arm), or whether an error resulted from an initial visit to an unbaited arm (Type NB). To determine the decline of within-session errors, an index-of-curvature statistic (Fry, Kelleher, & Cook, 1960) was computed for selected baseline and drug sessions: values approaching −1.0 indicate a decline in within-session errors, whereas values approaching zero indicate a constant error rate across trials. In those instances in which trials were not completed due to latencies exceeding 900 s, the index-of-curvature statistic was not computed. At the conclusion of sessions for each rat, the maze arms were checked for any pellets that remained (this did not occur) and the floor of the maze was cleaned with paper towels saturated with a 20% ethyl alcohol solution.

Scopolamine Treatment

Following selected sessions (Sessions 39, 42, and 44), rats were exposed to injections (ip) of isotonic saline in order to acclimate them to the injection procedure. Beginning in Session 47 and continuing through Session 79, injections were of the isotonic saline vehicle or of scopolamine hydrobromide (Sigma Chemical Co.; 0.030, 0.056, 0.100, 0.177, or 0.300 mg/kg body weight, ip, expressed as the salt). Each rat received each dosage in a semirandom order on two occasions 20 min prior to the Tuesday and Friday sessions. In addition, each rat received a single ip injection of scopolamine methylbromide (methylscopolamine; Sigma Chemical Co.). Only a single dosage (0.3 mg/kg) of this compound was administrated because of previous reports that dosages of 0.17 and 1.00 mg/kg had no effect either on accuracy in the standard eight-arm maze or on time to consume 50 45-mg pellets by rats (Eckerman, Gordon, Edwards, MacPhail, & Gage, 1980). All compounds were administered in a volume of 1 mL/kg body weight.

To determine the statistical significance of scopolamine effects on performance, total errors, index of curvature, and session times were each subjected to the nonparametric Kruskal-Wallis test. The alpha level for main effects was set at .05. If a statistically reliable main effect was determined, group comparisons were assessed using orthogonal contrasts (Marascuilo & McSweeney, 1977).

RESULTS

Rats exposed to the repeated acquisition procedure rapidly acquired accurate performance within each session. As shown in the upper left panel of Figure 1, performance during the first three sessions was characterized by accuracy scores that increased across trials for all subjects. During the first three sessions, rats accurately selected baited arms on approximately 50% of their selections during the initial trials, with average choice accuracy increasing to approximately 75% to 80% by Trial 10. As training progressed, performance showed two important trends: First, accuracy began to shift upwards on initial trials (e.g., M = 75% on Trial 1, Sessions 17 to 19, not shown in figure), and second, accuracy began to show higher asymptotic levels (e.g., M = 90% by Sessions 17 to 19). When the number of within-session trials was increased from 10 to 14 beginning in Session 20, accuracy of performance on the repeated acquisition task continued unchanged from that under the 10-trial procedure.

When baited arms were selected independently for each rat beginning with Session 27, performance began to exhibit more consistency both across subjects and across sessions. As shown in the middle and lower panels of Figure 1, the accuracy of performance by all subjects on the final procedure began to display a consistent tendency to begin at levels between 40% and 50% and reached an asymptote of approximately 95%. This trend in the accuracy of arm selections during the 14-trial procedure persisted roughly unchanged throughout the remainder of the experiment.

An analysis of absolute numbers of errors that occurred during repeated acquisition training revealed a within-session decline that was most prominent late in training. As shown in the left panel of Figure 2, this within-session decline of errors was essentially absent during Sessions 1 to 3. With the designation of baited arms for each rat individually at the beginning of each session (beginning with Session 27), there was an increase in the total number of errors that occurred during the initial two to three trials of each session. The increase was most evident in the performance of Rats S4 and S6. As shown in the right panel of Figure 2, a mean of 6.75 errors occurred on the first trial of Sessions 33 to 35. This trend remained

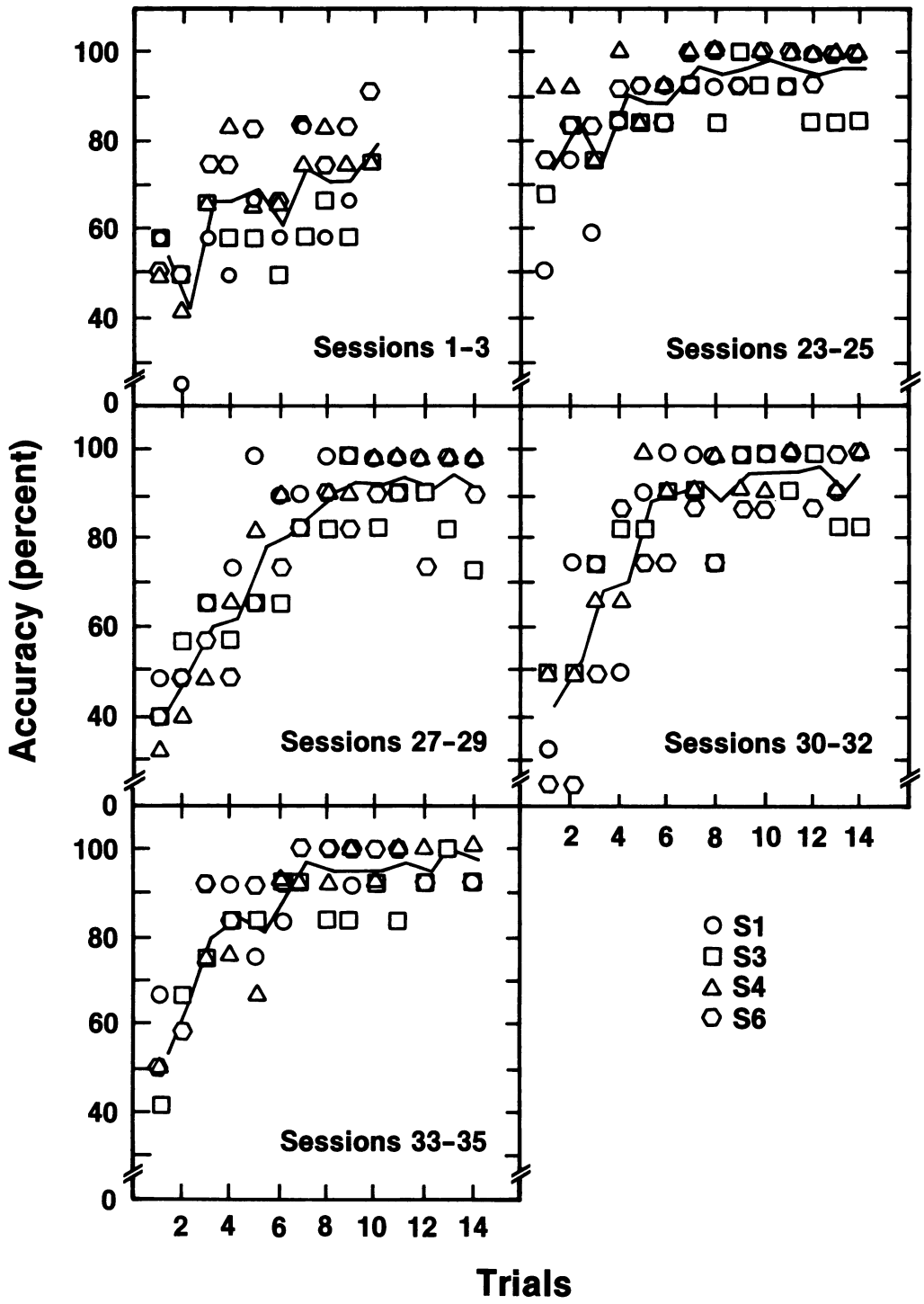

Fig. 1. The accuracy (% correct) of the first four arm selections by rats on the 10- (upper left panel) and 14-trial repeated acquisition procedures. Data points for individual rats are the mean of the three daily sessions indicated in each panel of the figure. The group mean is represented by the lines.

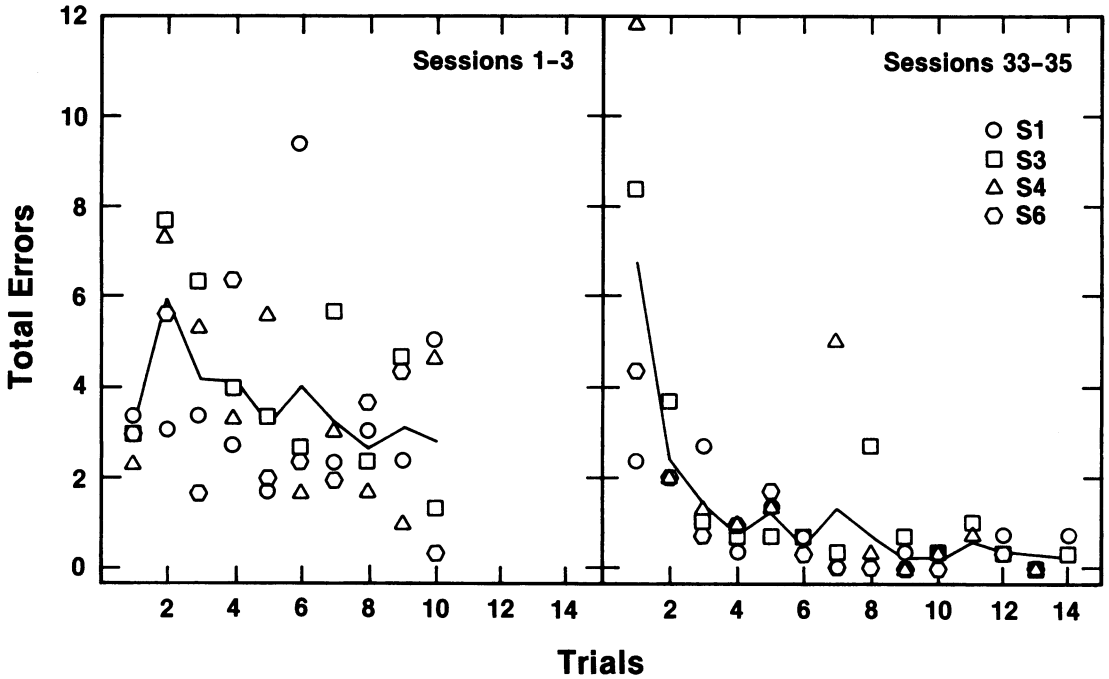

Fig. 2. Total errors on the repeated acquisition task as a function of trials on a unique set of baited arms. Left panel represents performances for each rat, maintained by the 10-trial procedure during Sessions 1 to 3, and that maintained by the 14-trial procedure (Sessions 33 to 35) is shown in the right panel. Group means are represented by the lines.

essentially unchanged during the remainder of the experiment.

The development of a within-session decline in total errors across the initial 35 sessions of the experiment was reflected in the index-of-curvature values for each subject. As shown in Figure 3, the lack of a prominent within-session decline of errors at the start of training resulted in index values of approximately zero, indicating little within-session decrease in errors. Over the course of the experiment, index values for all subjects showed a downward trend, approaching asymptotic values between −0.5 and −0.6 during Sessions 25 to 35. Values for Rat S3 were the most variable, notably during Sessions 24, 29 and 33.

Session times during the initial 35 sessions of the experiment are shown for all subjects in Figure 4. During the first session, rats took from 350 to 460 s to complete all 10 trials and were completing the same number of trials in roughly half that amount of time by Session 10. Apart from minor fluctuations, session times remained roughly unchanged through Session 35, with a slight increase occurring when the 14-trial procedure was incorporated during Sessions 20 to 35. In general, the initial three to six trials of a session accounted for the bulk of session time; latencies for the final four to six trials during a session were generally no more than 10 to 12 s each.

Scopolamine Effects

Following the administration of scopolamine, rats showed a dosage-related decrease in the accuracy of the initial four arm selections over trials, as shown in Figure 5. Accuracy of performance following dosages of 0.03 and 0.056 mg/kg for scopolamine and 0.3 mg/kg for methylscopolamine (data not shown) was essentially unchanged from that following saline. At scopolamine dosages of 0.1 mg/kg and higher, there was a progressive impairment of accurate arm selection in all rats. At these higher dosages, several rats (Rat S4 following both determinations of the effects of 0.1, 0.177, and 0.3 mg/kg; Rat S3 after one determination of the effects of 0.177 mg/kg) stopped selecting arms after four to six trials. Scopolamine effects on accuracy of performance included both a decline in the slopes of the accuracy curves and a reduction in asymptotic accuracy levels. These effects were most prominent at the 0.3 mg/kg dosage.

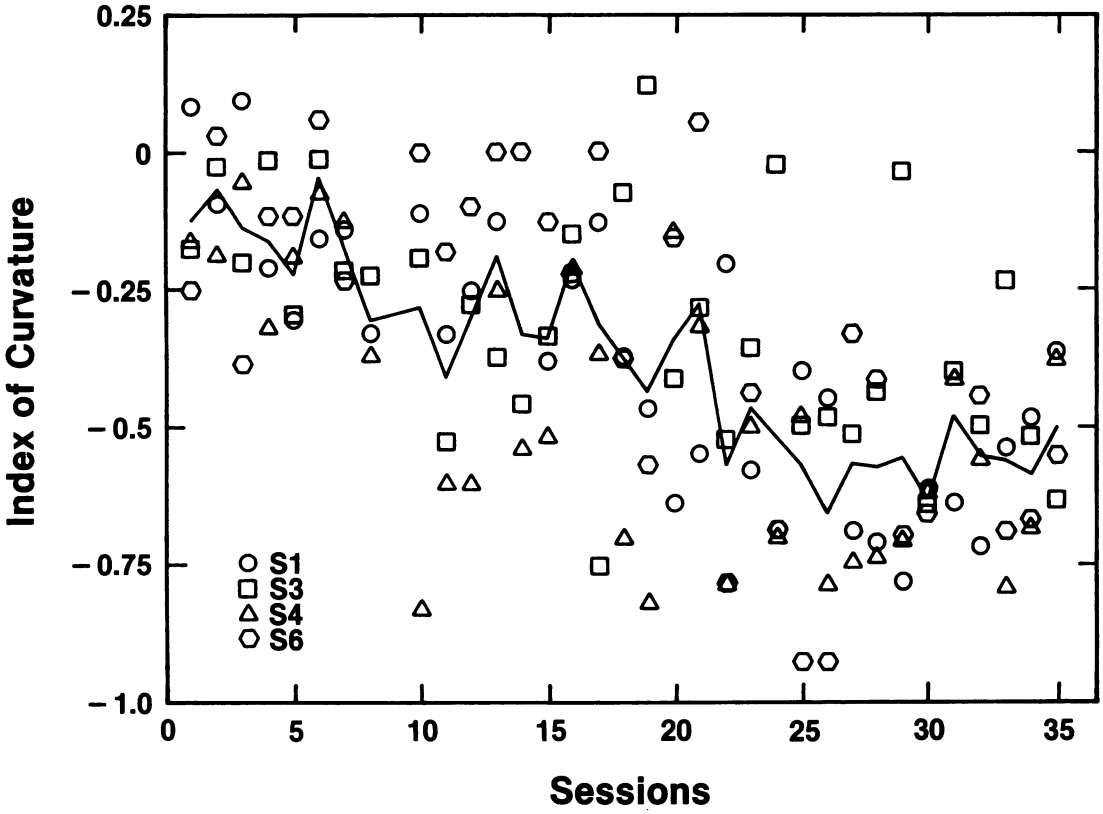

Fig. 3. Index of curvature values, computed for total within-trial errors, for each of the initial 35 sessions of exposure to the repeated acquisition procedure. The group mean is represented by the line. Values less than zero indicate a within-session reduction of errors.

For each rat, the reduction in accuracy following scopolamine administration was accompanied by a dosage-related increase in total errors, as shown in Figure 6. Following both saline and methylscopolamine administration, approximately four to five errors occurred during the first two or three trials, followed by few, if any, errors on remaining trials. At scopolamine dosages of 0.1 mg/kg and higher, however, more errors occurred not only on initial trials, but during all 14 within-session trials. After a dosage of 0.3 mg/kg, rats occasionally committed more than 20 errors in obtaining the four pellets during single trials (e.g., Rat S6 on Trial 6). Percentages of error type, shown in Table 1, revealed that most errors, under both control and drug conditions, resulted from rats entering nonbaited arms (Type NB). Repeat visits to both nonbaited (Type NBC) and baited (Type B) arms also showed dosage-related increases, with all rats exhibiting more Type-B errors. The percentage of Type-NB errors decreased as scopolamine dose increased. At a dosage of 0.3 mg/kg of scopolamine, there were roughly twice as many repeat visits to baited arms (Type B) as to unbaited (Type NBC) arms. A statistical assessment of total errors revealed a significant effect of scopolamine dosage ($H = 29.86$, $p < .001$). Orthogonal contrasts indicated that dosages of 0.1 mg/kg and higher, although not different from each other, produced a number of errors that was significantly different ($p < .05$) from dosages of 0.056 mg/kg or less.

In addition to increasing the total number of errors per session, scopolamine produced an attenuation of the typical within-session decline in error production that was observed during baseline sessions. This attenuation, reflected in the increase in index-of-curvature scores following scopolamaine administration, is shown in Figure 7.

Following saline administration, error production showed within-session declines, as indicated by index-of-curvature values that ranged from −0.58 to −0.72. The adminis-

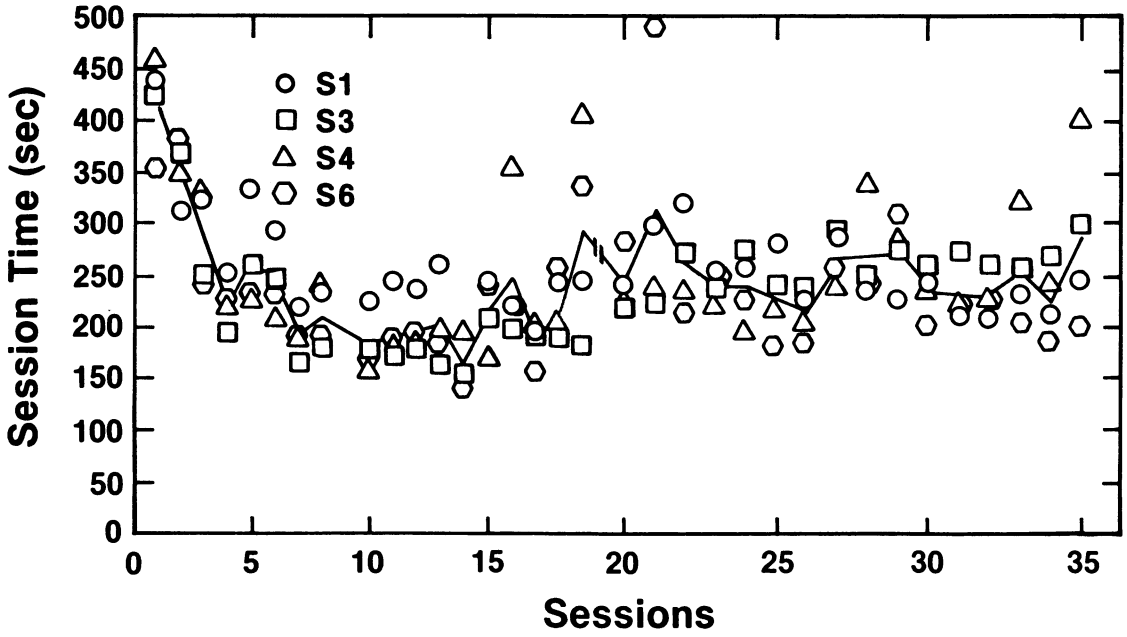

Fig. 4. Session time (seconds) for rats performing on the repeated acquisition task. Each point represents the time, exclusive of intertrial interval, required for rats to obtain all four pellets over 10 (Sessions 1 to 20) or 14 (Sessions 21 to 35) trials. An upper limit of 900 s was placed on obtaining pellets during each trial. Individual data points and the mean of those points (line) are shown for Sessions 1 to 35.

tration of methylscopolamine (filled symbols, Figure 7) produced a slight increase in within-session decline of errors, with index values falling to between −0.73 and −0.9. This trend was diminished by administration of scopolamine. As the dosage of scopolamine increased, index-of-curvature values showed an upward shift that approached zero; at dosages of 0.177 and 0.3 mg/kg, all rats showed index values that were well outside the range of baseline values. Index values were not computed for Rat S4 at dosages of 0.1 mg/kg and higher, due to trial terminations (latencies greater than 900 s). The effect of scopolamine on index of curvature was statistically significant (H = 14.26, $p < .01$). Orthogonal contrasts indicated that only the values for 0.177 and 0.3 mg/kg dosages were significantly different from saline ($p < .05$).

To illustrate the contrast in performances maintained following saline and scopolamine administration, the sequential pattern of arm selections for Rat S1 is shown in Figure 8. Arms in which food pellets were delivered during both current and prior sessions are indicated at the left of each panel of the figure. As the rat progressed from Trial 1 to 14 following saline administration, there was a reduction in the total number of selections required to obtain all pellets (filled symbols). Although there was an occasional repeated sequence of selections (see Trials 5 to 8), this showed no consistent tendency. Following scopolamine (0.177 mg/kg), the normal reduction in errors across trials was lacking, as shown in the lower panel of the figure. Although there were no Type-NBC errors committed by this rat during this session, a mean of three and six Type-NBC errors occurred during the determination of the effects of 0.1 and 0.3 mg/kg, respectively. Type-B errors, on the other hand, occurred reliably at all dosages of scopolamine administered and can be seen during Trial 6 of the scopolamine sessions illustrated in Figure 8.

The administration of scopolamine also lengthened session times for all subjects. Following the administration of saline and methylscopolamine, rats completed 14 trials in a mean of 229 and 261 s, respectively. Scopolamine dosages of 0.03 and 0.056 mg/kg did not increase session times above these levels, whereas dosages of 0.1, 0.177, and 0.3 mg/kg increased mean session time to 865, 987, and 1,472 s, respectively. A statistical assessment

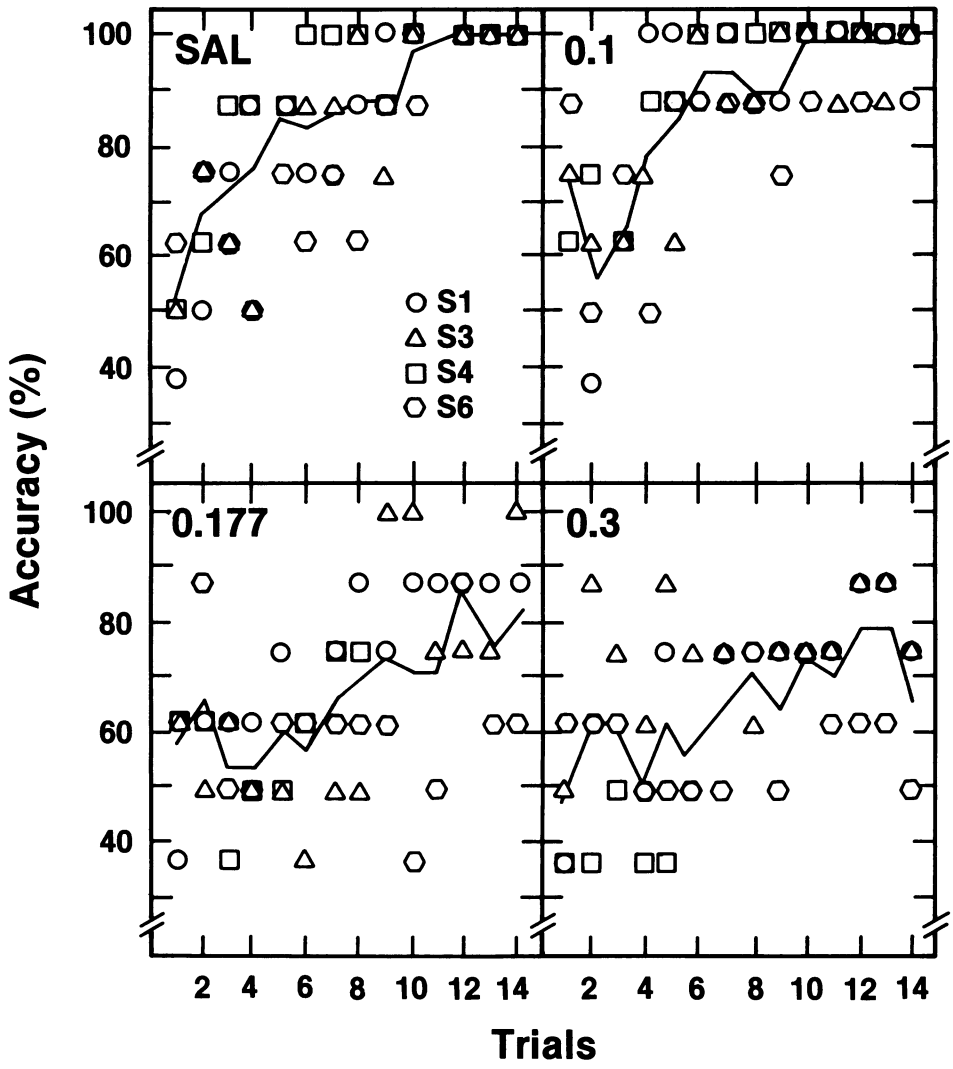

Fig. 5. The effects of selected dosages of scopolamine (0.0, 0.1, 0.177, and 0.3 mg/kg, ip) on within-session accuracy of the first four arm selections of each trial. The individual data points represent the mean of two determinations at each dosage of scopolamine hydrobromide. Group mean values are indicated by the line. Missing data points represent instances in which a trial was not completed within the upepr time limit of 900 s.

of the scopolamine-induced increase in session time indicated that the effect was significant ($H = 31.02$, $p < .001$). Orthogonal contrasts indicated that dosages of 0.1, 0.177, and 0.3 mg/kg produced session times that were significantly longer ($p < .05$) than those following dosages of 0.056 mg/kg and less.

DISCUSSION

The present experiment was designed to extend the study of behavioral transition states by developing a repeated acquisition procedure for the radial-arm maze. The purpose of developing such a test was two-fold: to determine whether steps could be taken to substantially shorten the time required to establish a repeated acquisition baseline, and to determine whether the acquisition of behavioral control based on temporally distant stimuli could be established within a single experimental session. Acquisition was described by several measures including the index-of-curvature statistic. Accordingly, acquisition, or learning, was defined as the within-session decline of errors as reflected by negative index-of-cur-

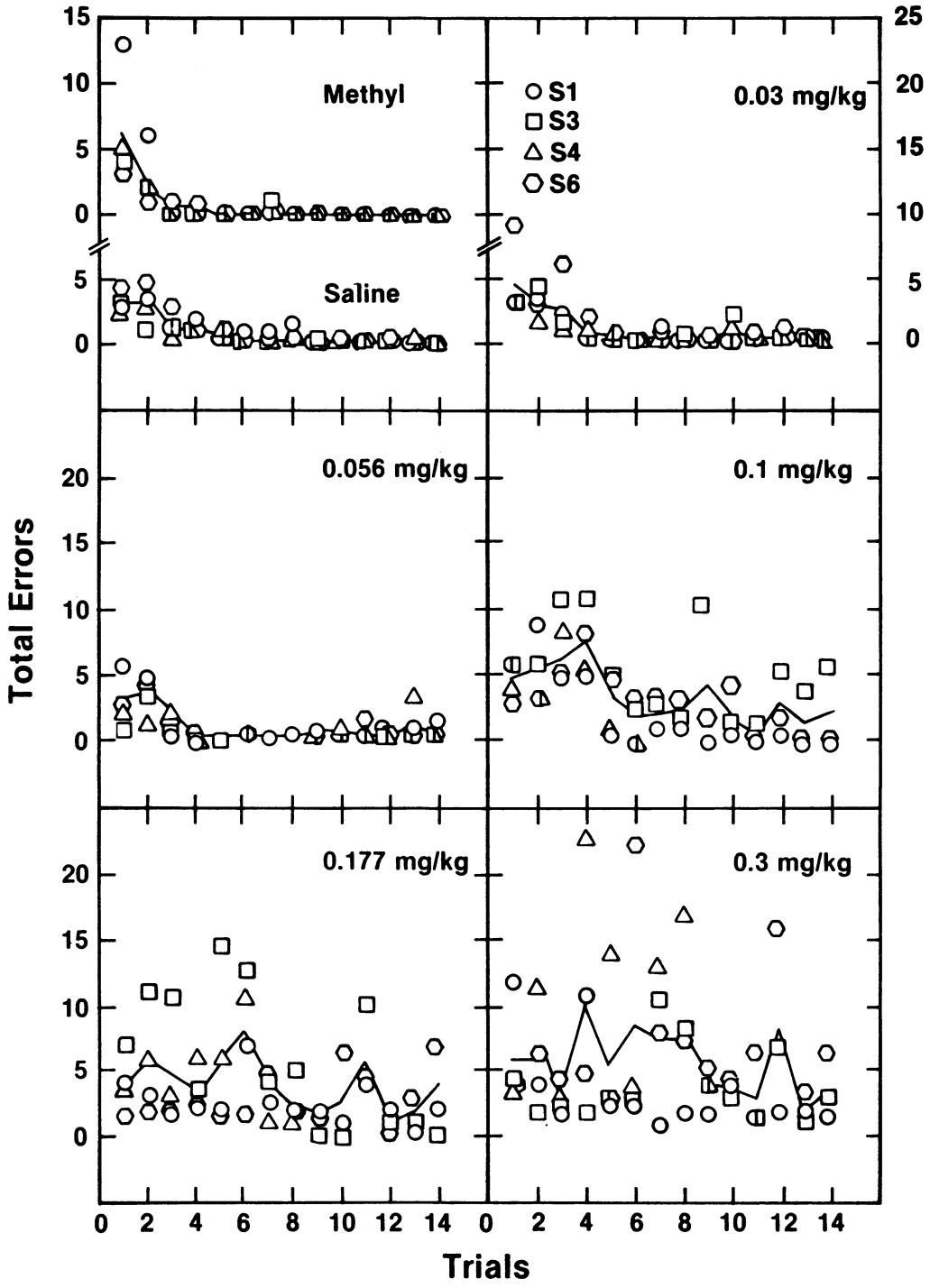

Fig. 6. The effects of scopolamine on the frequency of total within-session errors on the repeated acquisition task. The individual data points represent the mean of two determinations at each dosage of scopolamine. The upper left panel of the figure represents the effect of both saline (vehicle) and methylscopolamine on the accuracy of performance, on separate ordinate axes. Group means are represented by lines.

Table 1

Error types committed following scopolamine administration expressed as a percentage of total session errors.

Subject	Dosage of scopolamine (mg/kg)					
Error type	0 (Sal) (%)	0.03 (%)	0.056 (%)	0.1 (%)	0.177 (%)	0.3 (%)
S1						
B	16	13	26	22	27	23
NB	84	87	70	66	73	65
NBC	0	0	4	12	0	12
S3						
B	0	16	0	31	27	29
NB	100	84	100	54	57	58
NBC	0	0	0	15	16	13
S4						
B	12	7	25	34	33	40
NB	88	93	75	52	57	43
NBC	0	0	0	14	10	17
S6						
B	10	21	5	26	15	27
NB	81	68	90	69	82	59
NBC	9	11	5	5	3	14

B, repeat selections of baited arms; NB, selections of unbaited arms; NBC, repeat selections of unbaited arms.

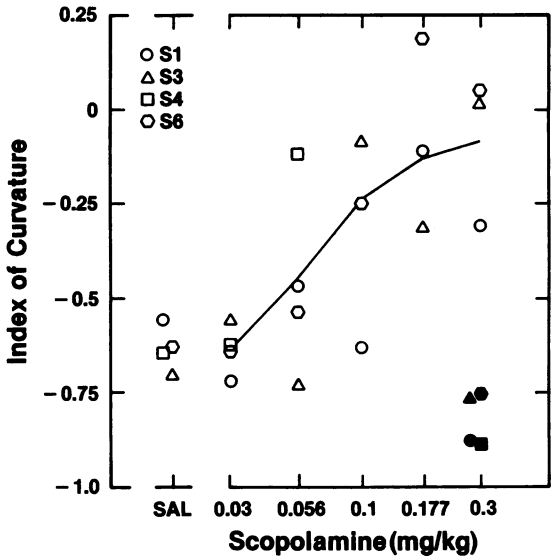

Fig. 7. The effects of scopolamine on index of curvature values computed for total within-session errors on the repeated aquisition task. Points at SAL represent the effects of the saline vehicle, whereas filled symbols located over 0.3 represent the effects of methylscopolamine. The effects of dosages of scopolamine are indicated by open symbols, with the group mean effect indicated by the line. Missing data points represent instances in which a trial was not completed within the upper time limit of 900 s.

vature values. The use of the index-of-curvature statistic seems to be quite useful in quantitative assessments of behavioral acquisition as well as treatment effects on acquisition, as suggested by Thompson (1973).

The results from the present experiment suggest that the paradigm is, in fact, well suited to serve as a simple test of acquisition. Rats began showing within-session decrements in the number of errors (i.e., acquisition) during their first three sessions. The final performance maintained by the procedure demonstrated properties similar to those seen using more traditional repeated acquisition baselines, such as a reduction of within-session errors and the development of highly accurate performance on novel sets of contingencies within each daily session. Unfortunately, we cannot conclude from the present data whether rats acquire stable baselines faster with the present techniques than with more traditional methods for studying repeated acquisition.

In the present experiment, the rats were not naive prior to starting the experiment (they had a history of training in the standard eight-arm maze procedure), and the procedure underwent refinement during the course of the experiment. Using the refined methods derived from the present experiment (i.e., contingencies present starting with Session 27), we have been successful in establishing stable behavioral baselines in 12 naive rats within a maximum of 20 daily sessions. These observations, in combination with the data reported above, are consistent with the notion that rats can be easily trained on this task in the same amount of time or less than on repeated acquisition tests using chained schedules of reinforcement (cf. Thompson & Moerschbaecher, 1979).

Several features of the present procedure distinguish it from more traditional repeated acquisition baselines, including the discrete nature of the dependent variable. Accuracy in the four-baited maze problem lies in discrete increments of 25% and must be judged against chance accuracy levels. According to the calculations of Beatty and Shavalia (1980), a rat confronted with four of eight arms baited will correctly choose, on average, 1.637 arms during the first four selections, thus placing chance levels of performance during the first four selections at 41%. At steady state, then, rats faced with the procedures described here should demonstrate selection with accuracies of approximately 40% to 50%, and (based on the

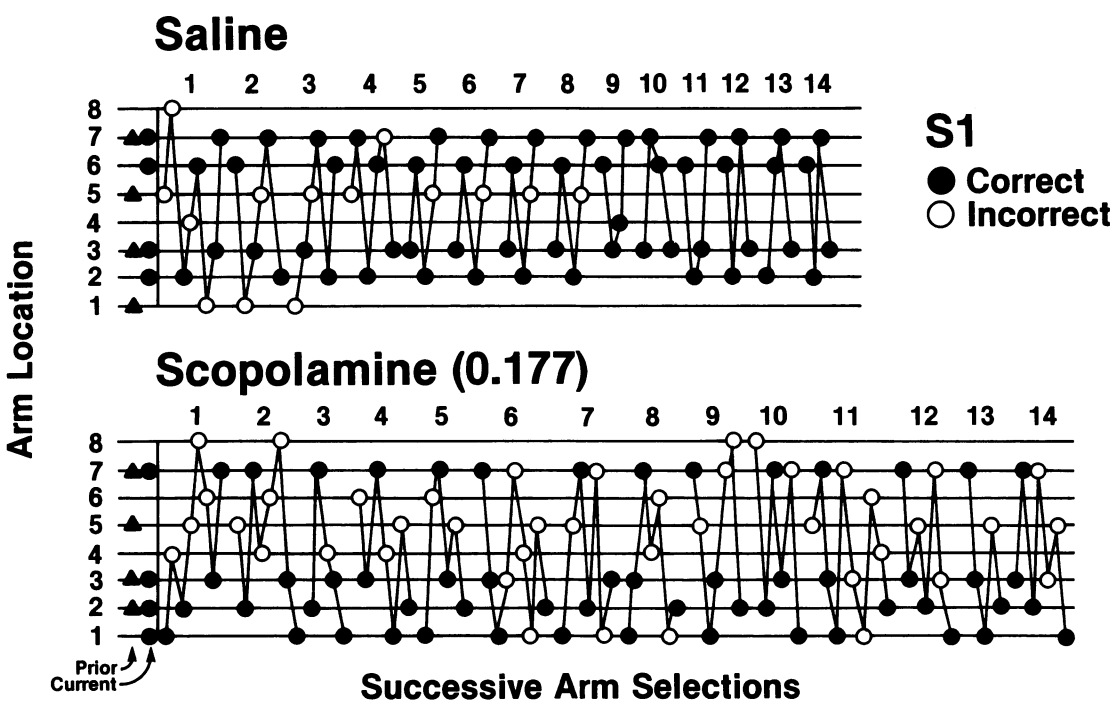

Fig. 8. Arm selections for Rat 1 during two 14-trial sessions of the radial-arm maze procedure. The upper and lower panels represent performance following saline and 0.177 mg/kg scopolamine, respectively. Each horizontal line represents one of the eight arms of the maze; the *x* axis indicates the sequential selections during the session. Trials, indicated by the numbers appearing at the top, are separated by breaks in the lines that connect points. The arms with pellets (i.e., the "baited" arms) for the current and prior sessions are indicated by the filled circles and triangles, respectively, located at the far left of each panel. Correct and incorrect arm selections are indicated by filled and unfilled circles, respectively.

present data) perform at accuracy levels approaching 100% for the final half of each session. It is interesting to note that rats performed at these levels during Sessions 27 through 29, in which novel sets of baited arms were arranged for each rat on each session. Prior to this, accuracies of 70% and greater were demonstrated by rats tested last (i.e., after other rats) during daily sessions, presumably due to the presence of odor trails (Amsel, Hug, & Surridge, 1969).

Perhaps the most salient feature distinguishing the procedures reported here from those of the more traditional approaches to studying transition states is the nature of the stimulus control involved in the maintenance of behavior. In traditional chained schedule methods, stimulus control takes the form of simultaneous conditional discriminations. Accurate responding (usually defined spatially; i.e., left, center, or right key) is conditional on key color. In the present experiment, accurate responding, also defined spatially, was conditional on (under the control of) temporally distant stimuli. That is, the location of reinforcer availability will be the same as that on prior trials. Thus, the procedure could be described as maintaining delayed conditional discriminations.

To assess the usefulness and sensitivity of the repeated acquisition procedure in characterizing experimentally induced learning deficits, the present experiment included a pharmacological challenge by scopolamine. Cholinergic blockers such as scopolamine and atropine alter steady-state performance in the radial-arm maze of both rats (e.g., Beatty & Bierley, 1985; Eckerman et al., 1980) and mice (Levy, Elsmore, & Hursh, 1984). More relevant to the present experiment, scopolamine in dosages of 0.3 to 0.5 mg/kg has been shown to attenuate the acquisition of performance by rats in the standard eight-arm maze (Stevens, 1981; Watts, Stevens, & Robinson, 1981). The scopolamine-induced disruption of acquisition in the present experiment, compared to that

seen in the experiments by Stevens (1981) and Watts et al. (1981), demonstrates the utility of the repeated acquisition approach. In the present experiment, scopolamine-induced disruption of acquisition was characterized by less accurate arm selection overall and, at asymptote, lengthened session times and increased total numbers of errors. More importantly, scopolamine decreased the within-session decline in selection errors. This effect was determined to be significant via an index-of-curvature statistic. The effects of scopolamine on behavior in the maze were also shown to be dependent upon drug dosage. Because the peripherally acting anticholinergic agent, methylscopolamine, failed to produce similar disruption of maze performance, it was concluded that the scopolamine-induced disruption depended on drug action in the central nervous system. In addition, it is unlikely that scopolamine produced its disruptive influence via alterations in motivational factors (e.g., dry mouth) because all rats were observed to consume all pellets delivered even at the highest dosage administered (see also Eckerman et al., 1980). The present results with scopolamine support a number of reports on the disruption of learning by manipulations designed to perturb the cholinergic nervous system of laboratory animals. For instance, Levy et al. (1984) have shown that performance (accuracy and trials to first correct sequence) on a repeated acquisition task by monkeys was impaired by atropine but not methylatropine. Using a similar repeated acquisition task with monkeys, McDonough and Penetar (1983) have demonstrated atropine-induced disruption of learning and performance that was accompanied by a dosage-dependent decrease in response rate.

One potential advantage of the repeated acquisition task in the maze is that it allows errors to be categorized. In previous attempts at categorizing maze errors, Olton has shown a functional equivalence of a number of manipulations designed to compromise normal hippocampal functioning. In those experiments, rats chose arms in a maze in which only half the arms were baited; the same arms contained food each day. Hippocampally impaired rats continue to select previously baited arms within a session (i.e., "working memory" errors) while generally avoiding the unbaited arms (i.e., "reference memory" errors; see Knowlton, McGowan, Olton, & Gamzu, 1985; Olton, Becker, & Handelmann, 1979; Olton & Papas, 1979; Olton & Wolf, 1981). Although these effects appear to be quite reliable, the contingencies maintaining behavior involved in the various error types and the role of those contingencies in the observed differential sensitivity to treatment are unknown.

Traditionally, studies utilizing radial-maze techniques have focused on explanations of behavioral control incorporating cognitive concepts and appeals to specialized, species-specific predispositions. For instance, the more rapid acquisition of a "win-shift," as compared to a "win-stay," strategy in the T maze has been attributed to genetic factors that predispose rats to seek food according to certain strategies (i.e., "win-shift" as opposed to "win-stay"; Haig, Rawlins, Olton, Mead, & Taylor, 1983; Olton, Handelmann, & Walker, 1981; Olton & Schlosberg, 1978). The observed predominance of the so-called "win-shift" strategy in foraging behavior of rats has been used to explain the rapidity with which rats acquire rapid performance in the standard radial-arm maze (Olton & Schlosberg, 1978). Following this line of reasoning for the present experiment, one might predict that Type-NBC (rather than Type-B) errors should predominate in the repeated acquisition baseline. However, during both baseline (i.e., following saline administration) and scopolamine sessions, repeat visits to arms consisted primarily of visits to previously baited arms (Type-B errors). Similar findings have been reported for the effects of scopolamine on rats performing on a "working memory" paradigm, in which the same half of the arms in a radial maze contain food each day. There, scopolamine alters the number of repeat visits to baited but not unbaited arms (Beatty & Bierley, 1985; Wirsching, Beninger, Jhamandas, Boegman, & El-Defrawy, 1984). The conclusion reached by these investigators, namely, that the differential effects of scopolamine on error type were due to differential sensitivities of hypothetical memory processes, fails to consider the relevance of stimulus factors, behavioral stability, or differential reinforcement contingencies responsible for the differential effects of scopolamine on errant selections of baited versus unbaited arms.

Perhaps a more plausible explanation for the differential sensitivity of error types to dis-

ruption by scopolamine in the present experiment is the existence of differential contingencies of reinforcement. For arms containing food (baited), contingencies changed within (but not between) a trial depending on performance, whereas for arms containing no food (unbaited), the contingencies were invariant. Therefore, within a trial, correct arm selection involved a conditional discrimination dependent on both current (the arms) and recently presented (prior selection within a trial) stimuli whereas an incorrect arm selection involved a simple discrimination dependent on a more fixed relationship between exteroceptive stimuli and availability of food. Analogous conditions also exist for the standard "working/reference memory" task reported above. The tendency for an agent such as scopolamine to increase repeat visits to previously selected correct arms might more profitably be seen to reflect not a selective alteration of a hypothetical memory process but rather a loss of behavioral control by those stimuli accompanying the completion of one and initiation of another within-session trial. Alternatively, the differential disruption may involve the relative sensitivity to disruption of behavior under the control of past versus currently present stimuli. One method of assessing this possibility is to arrange probe sessions in which stimuli accompanying the beginning and end of trials are presented at various times during a session following either saline or scopolamine injections.

In summary, the results from the present experiment demonstrate the feasibility of using a radial-arm maze for repeatedly assessing acquisition, and indicate the potential usefulness of the technique for experiments designed to evaluate the influence of chemicals on behavior in transition states. The spatial stimuli used in the maze seem to be quite saline for rats and require no special equipment for calibration. Acquisition of the task is rapid, and individual animals can be observed for long periods of time, making the procedure ideal for repeated assessment of chemical effects in individual animals. Although computer-controlled technology enhances the power of the procedure, it could easily be adapted to the nonautomated version of the eight-arm radial maze. Similar adaptations have been made with the T maze (Poschel, 1977) and the Morris water maze (Whishaw, 1985), converting those tasks into repeated acquisition tasks for rodents. In addition, there are potential modifications in the apparatus and/or procedure that would undoubtedly improve the quality of data collected during the repeated acquisition of maze performance. The potential for rats to use within-session (between-trial) odor markings for obtaining the pellets was not eliminated, and as such confounds the issue of what stimuli are controlling performance. Although the contribution of odor trails in the standard eight-arm maze procedure is reported to be negligible (Olton & Collison, 1979), similar experiments using the present procedure have not been performed. In the absence of such data, the problem could be reduced by wiping down the maze after each trial, or by employing a self-cleaning system within the maze. Also, better ventilation could be added. Another possible improvement would be to increase the number of arms, thus lowering chance levels of performance. This should decrease the slope of the acquisition curve and increase the sensitivity of the procedure for detecting the effects of chemicals or other manipulations designed to alter (attenuate or improve) the acquisition process. The present procedures for transforming the radial-arm maze task into a repeated acquisition task should be a valuable tool in screening for potential neurotoxic properties of chemicals.

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