Pharmacology Biochemistry & Behavior, Vol. 3, pp. 993–1002.

Scopolamine Effects on Delayed Spatial Alternation in the Rat[1]

GEORGE A. HEISE,[2] BARBARA HRABRICH, NELL L. LILIE AND RICHARD A. MARTIN

Indiana University, Bloomington IN 47401

(Received 2 July 1973)

HEISE, G. A., B. HRABRICH, N. L. LILIE AND R. A. MARTIN. *Scopolamine effects on delayed spatial alternation in the rat.* PHARMAC. BIOCHEM. BEHAV. 3(6) 993–1002, 1975. – Rats were trained to press two levers in alternation on discrete trials spaced 10 sec apart. During the final sessions of alternation training, error responses per opportunity on the trials that followed reinforced trials (initial trials) did not differ from error responses per opportunity on repetitive (correction) trials (Experiment 1). Scopolamine did not increase the rats' tendency to perseverate: drug treatment did not cause the error responses per opportunity to increase over runs of consecutive error responses (Experiment 2). Scopolamine did not impair performance when alternation was controlled by visual stimuli present in the external environment at the time of the response (Experiment 3). The disruption in delayed alternation performance produced by scopolamine was attributed to effects on stimulus discrimination, resulting in impairment of control of responding by stimuli not present in the environment at the time of the response.

Delayed spatial alternation Perseveration Cholinergic blockers Scopolamine d-Amphetamine

SCOPOLAMINE is a potent blocker of central and peripheral acetylcholine activity; precise characterization of its behavioral action can contribute to an understanding of the behavioral role of central and peripheral cholinergic transmitter systems. This paper examines effects of scopolamine on sequential behavior in two-lever discrete trial delayed spatial alternation, and is particularly concerned with evaluating perseveration as a description or explanation of the effects of the drug.

Scopolamine decreases the orderliness of both spontaneous alternation (e.g., [4, 11, 14]) and learned alternation in rats. Hearst [5] showed that rats trained to alternate responses on 2 levers made many more errors after scopolamine treatment. Hearst's [5] results were confirmed by Carlton [1], who has proposed a theoretical interpretation of the disruptive effects of scopolamine in terms of recovery under the drug of previously extinguished responses [2]. Learned alternation was selected for the present analysis of scopolamine action because of its susceptibility to interference by cholinergic blocking drugs, and because the sequential dependencies between successive responses could be measured repeatedly in the same animal and compared under control and drug conditions.

Experiment 1 of this study investigated sequential dependencies in acquisition and maintenance of delayed alternation under non-drug conditions, focussing on relationships between performance on the trials that followed reinforced trials (initial trials) and performance on the correction trials that followed non-reinforced trials (repetitive trials). The effects of scopolamine, atropine, and d-amphetamine on baseline delayed alternation performance were explored in Experiment 2, and the runs of consecutive error responses produced by scopolamine were analyzed for evidence of perseveration. Experiment 3 measured the effect of scopolamine on alternation behavior which was controlled by discriminative stimuli present at the time of the response rather than (as in delayed alternation) by stimuli from the preceding trial, and demonstrated that the effect of the drug depends critically on the time of occurrence of the stimuli that control alternation performance.

GENERAL METHOD

Animals

The animals for Experiments 1 and 2 were 20 male Sprague-Dawley derived rats from Hormone Assay Laboratories, Chicago; the 9 rats used in Experiment 3, also Sprague-Dawley derived, were obtained from Murphy Farms, Plainfield, Indiana. All rats were 90–120 days old at the start of the experimentation. The animals were maintained on an approximately 23 hr water deprivation schedule. On experimental days they received 9 percent sugar solution as reinforcement in the experimental chambers and 10 to 15 min access to water following the experimental sessions. On nonexperimental days they were given water in their home cages. Food was always present in the home cages.

[1] This investigation was supported by grant No. MH14658 from NIMH. We acknowledge with thanks the contributions of Robert Conner, Suzanne Hull, Katharine Milar, Judy Tower, and Susan White to this research.

[2] Requests for reprints should be sent to George A. Heise, Department of Psychology, Indiana University, Bloomington IN 47401.

Apparatus

All training and testing except for initial lever press training took place in two-lever chambers, 25 x 24 x 20 cm. Two Gerbrands levers, requiring between 25 and 30 g force for activation, were mounted side-by-side on an end panel of the chamber. Each was 10 cm above the grid floor and displaced 6.5 cm horizontally from the center line. Also mounted 15 cm above the floor on the end panel were 3 white 6 W panel lights, 1 over each lever and 1 on the center line. A spigot for dispensing drops (ca. 0.1 cc/drop) of sugar water was placed 5.5 cm above the floor on the center line of the panel. The experimental chamber also contained a speaker for presenting a 1000 Hz, 80 DB trial stimulus.

Experiments were controlled automatically by a system of electromechanical circuitry in the room adjoining the experimental chambers. Response measures were cumulated on counters and a trial-by-trial record was maintained with an Esterline-Angus event recorder.

Procedure

A discrete-trial procedure was used in which a single lever press during a trial (a trial response) terminated the trial, producing reinforcement when the response was correct, and only trial termination when the response was incorrect.

Alternation trials were signalled by the combined presentation of the tone and illumination of the center panel light. A correct alternation response on a trial (i.e., pressing the lever not pressed on the immediately preceding trial response) terminated the trial and produced reinforcement; on the next trial reinforcement was programmed for pressing the other lever. After an incorrect trial response (i.e., pressing the same lever as that pressed on the immediately preceding trial response), the trials were repeated (repetitive trials) until a correct trial response was made. The trial was also repeated if the rat failed to respond on a trial. The trial sequence is presented schematically in Fig. 1.

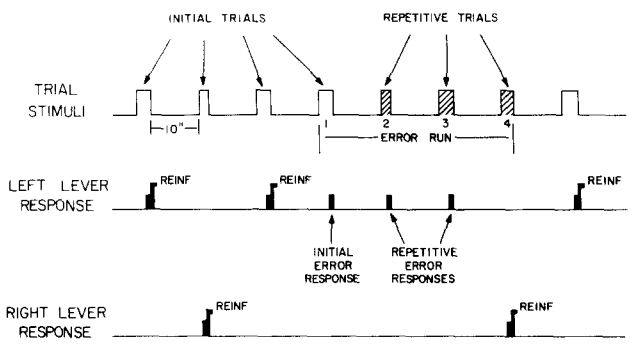

FIG. 1. Simulated segment of a spatial alternation session in which the trial responses were reinforced in the sequence: Left, Right, Left, Right, Left. Note the specification of initial trials, repetitive trials, and error responses, the occurrence of a run of error responses, and the numbering of error run position.

The inter-trial interval (ITI) was set at 10 sec, except for a single 40 sec ITI group. Lever pressing during the ITI was reduced by the pretrial delay that immediately preceded each trial. Whenever the rat pressed the lever during the pretrial delay interval, onset of the next trial was postponed for the duration of the pretrial delay. The pretrial delay was 5 sec during the early part of training and then, in some experiments, subsequently reduced to 1 sec.

Alternation and discrimination performance is conveniently described in terms of error responses, i.e., trial responses in which the rat pressed the incorrect lever. Those trials on which the rat did not respond (response failures) were not included in the measures of trial performance. Thus the usual measure of trial performance was error responses/trial responses: the conditional probability of an incorrect response on those trials on which the animal responded.

The rat's first trial response following a correct (reinforced) trial was called an initial trial response. An error response on the initial trial was called an initial error response; similarly, error responses on the repetitive trials that followed an initial error response were termed repetitive error responses. Each initial error response began an error run, a run of consecutive error responses that ended with a correct trial response (see Fig. 1). The initial trial response was assigned error run position 1 and subsequent repetitive trial responses in the run were assigned error run positions 2, 3, and so on.

Drug testing began when alternation or discrimination acquisition sessions had been completed and the ratio of error responses/trial responses was less than 0.15 when the ITI was 10 sec, and less than 0.30 when ITI was 40 sec (cf. Table 1). The animals received daily experimental sessions, 5 days per week, and drugs were administered intraperitoneally (IP) at weekly intervals 5–10 min before the experimental session.

Sessions immediately preceding drug sessions were designated control sessions; the performance of a rat on drug sessions was evaluated in relation to its performance on these control sessions. Placebo injections were not given on control sessions since previous studies in our laboratory have demonstrated repeatedly that (except perhaps for a rat's initial injection) placebo injections did not affect the performance measures.

EXPERIMENT 1

Experiment 1 provided baseline data for subsequent investigations of drug effects on sequential performance. In Experiment 1 acquisition and maintenance of delayed spatial alternation was studied in individual animals under control (non drug) conditions. The conditional probability of errors on initial trials was specifically compared to the conditional probability of errors on repetitive trials. The effects of scopolamine and d-amphetamine on these conditional probabilities was studied in Experiment 2.

METHOD

Animals

The animals were 10 rats divided into 2 subgroups that received somewhat different preliminary training: a Barrier Training group of 6 rats and a Light Training group of 4 rats.

Procedure

The acquisition procedure consisted of two parts: preliminary training sessions, in which all rats learned to

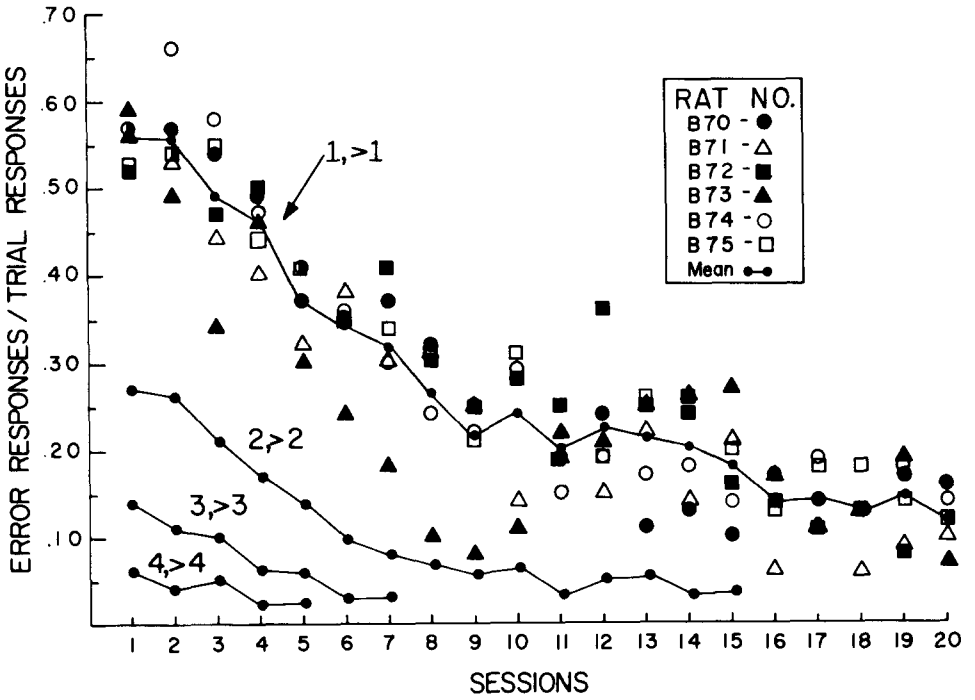

FIG. 2. Acquisition of spatial alternation performance by the 6 Barrier Training animals. Each curve shows the mean error responses summed over the error run positions indicated, and expressed as a percentage of the total trial responses. Thus the 1, > 1 curve shows the percentage of error responses over all error run positions, the 2, > 2 curve shows percentage of repetitive error responses, the 3, > 3 curve shows the percentage of error responses for error run positions 3, 4 . . . , and so on.

press both levers mainly during the discrete trials, and alternation acquisition sessions. The sessions lasted for 100 reinforced trials, the maximum trial duration was 5 sec, and the final pretrial delay was 1 sec. The rats received daily sessions, 7 days per week, during alternation acquisition.

Preliminary training of the Barrier Training group was carried out in a two-lever chamber divided into 2 equal compartments by a longitudinal floor-to-ceiling partition, such that a rat placed in one of the compartments could see 1 panel light and had access to only 1 of the levers and to the reinforcement spigot. All trial responses were reinforced. On each preliminary training session, the rats received 50 reinforcements in one compartment followed by 50 reinforcements in the other compartment. Discrete trial training sessions with the barrier in place continued until the rats had responded on more than 90 percent of the 100 trials on each of 2 consecutive sessions.

The rats in the Light Training group received their preliminary training in two-lever chambers in which the location of the illuminated panel light varied randomly from side to side on successive trials. No barrier was used. Only trial responses made on the lever under the panel light were reinforced and there were no correction trials. This light-no light simultaneous discrimination training was continued for 4 sessions of 100 reinforced trials.

Alternation training for all groups began on the first session following completion of preliminary training. The program of trial presentation during alternation acquisition was the same as in preliminary training except that the center panel light was illuminated on every trial, and the rat was required to press alternate levers on successive trials to obtain reinforcement.

RESULTS AND DISCUSSION

Figure 2 shows the acquisition of delayed alternation performance for the 6 Barrier Training rats over the first 20 alternation acquisition sessions. The total error responses declined steadily over sessions, the the 6 rats learned at similar rates. Repetitive error responses (responses at error run positions 2, >2) were about 50 percent of the total error responses during the first acquisition session but comprised only a very small percentage of the total error responses on the final acquisition sessions.

During acquisition the conditional probabilities of initial error responses (i.e., responses per opportunity: initial error responses/initial trial responses) and the conditional probabilities of repetitive error responses (repetitive error responses/repetitive trial responses) of the Barrier Training and Light Training groups are plotted in Fig. 3. A multivariate analysis of variance [12] showed that overall (Sessions 1–14) the conditional probabilities of initial and repetitive error responses differed significantly for both the Barrier and Light Training groups (respectively, $F(6,8) = 3.71$, $p<0.05$; and $F(4,10) = 23.9$, $p<0.001$). The conditional probabilities differed significantly (t for correlated measures, $p<0.05$) on Sessions 1, 2, and 4 for the Barrier Training group and on Sessions 1, 2, 3, and 4 for the Light Training group. For Sessions 5–14, on the other hand, the over-all conditional probability differences were not significant for either for Barrier Training group, $F(6,12) = 1.28$, $p>0.05$, or for the Light Training group, $F(4,14) = 3.13$, $p>0.05$.

Thus early in alternation training the conditional probability of initial error responses, i.e., the conditional probability that the same lever would be pressed on initial trials

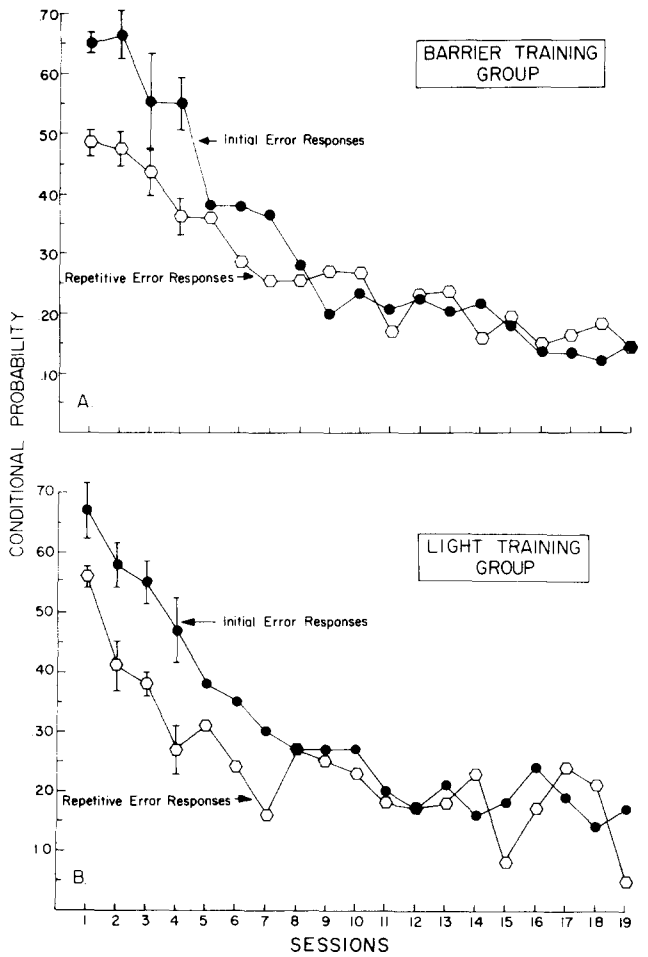

FIG. 3. Change in mean conditional probability of initial and repetitive error responses during acquisition of spatial alternation. Top (A) – Barrier Training Group. Bottom (B) – Light Training Group. Vertical lines indicate standard error of mean.

as on the immediately preceding reinforced trials (win-stay responses), was substantially greater than 50 percent and greater than the conditional probability of repetitive error responses: i.e., the conditional probability that the same lever would be pressed on successive repetitive trials (lose-stay responses). This difference between win-stay and lose-stay responses evidently was not acquired in preliminary training, since the difference between initial error responses and repetitive error responses was as great for the Light Training group (which received equal win-shift and win-stay trials in preliminary training) as for the Barrier Training group (which received exclusively win-stay trials in preliminary training).

Experiment 1 showed that the conditional probabilities of error responses on initial and repetitive trials differed during the early acquisition sessions, and the relative proportions of these two types of error responses changed as acquisition proceeded. Thus the common practice in alternation or discrimination acquisition studies of combining data from initial and repetitive trials is of doubtful legitimacy, since performance on these two different kinds of trials could be affected differently by experimental manipulations. On the other hand, when alternation was well learned the conditional probabilities of initial and repetitive error responses did not differ. Therefore data from initial and repetitive trials could sometimes be combined in Experiment 2, which was concerned with drug effects on maintained alternation behavior.

EXPERIMENT 2

Experiment 2 examined the effects of scopolamine, atropine, and d-amphetamine on well-trained delayed alternation performance. Possible perservative effects of scopolamine and d-amphetamine were examined quantitatively by analyzing the conditional probabilities of error responses on consecutive trials during the runs of repetitive trials produced by these drugs.

METHOD

Animals

Drug data were obtained from 3 groups of rats that differed with respect to the ITI and trial durations of their training and testing sessions. Groups were designated by ITI (first number) and trial duration (second number). Group 10–10 consisted of 7 rats that received preliminary training with a barrier and were trained and tested with an ITI of 10 sec, a maximum trial duration of 10 sec, 5 sec pretrial delay, and 200 reinforcements per session. Group 10–5 consisted of 6 rats (the Barrier Training group from Experiment 1) that were trained and tested with an ITI of 10 sec, a maximum trial duration of 5 sec, a pretrial delay of 1 sec, and 100 reinforcements per session. Group 40–5 (4 animals) was similar to Group 10–5 except that the ITI was 40 sec, and a light training procedure (as described in Experiment 1) was used for preliminary training.

Procedure

Table 1 summarizes the various dosages of scopolamine, methscopolamine, atropine and d-amphetamine that were given to the 3 groups. Effects of drugs on sequential trial responding were determined by analyzing runs of consecutive error responses obtained when the rats in the groups designated in Table 1 received 0.5 and 1.0 mg/kg scopolamine and 1.0 mg/kg d-amphetamine, except for 4 sessions on which 3 of the rats obtained fewer than 50 percent of the allotted number of reinforcements. The number of error responses made at each error run position during each of these drug sessions was expressed as a percentage of the number of initial responses made during the session, and plotted against error run position on semi-logarithmic coordinates in Figs. 4 and 5. Similar plots were made for the error run curves obtained from each animal on its corresponding control runs.

RESULTS AND DISCUSSION

Table 1 summarizes the mean results for drugs tested with the 3 groups. Comparison of drug effects on performance of the two 10 sec ITI groups (Groups 10–5 and 10–10) indicates that measured drug effects did not depend on whether the maximum trial duration was 5 sec or 10 sec. Table 1 also indicates that a high level of alternation performance was not attained with Group 40–5, presumably because of the 40 sec gap between successive trials.

Table 1 shows that the administered doses of the 2

TABLE 1

DRUG EFFECTS ON SPATIAL ALTERNATION

Drug	Dose (mg/kg)	Group*	Number of Rats	Doses per Rat	Error Responses / Trial Responses	
					Control	Drug
Scopolamine Hydrobromide	0.5	10–5†	6	4	0.13	0.47
		10–10†	7	2	0.04	0.45
		40–5†	4	3	0.29	0.50
	1.0	10–5†	4	2	0.12	0.43
		10–10	3	2	0.06	0.55
Methscopolamine Bromide	0.5	10–10	3	3	0.03	0.10
Atropine Sulfate	5.0	10–5	5	2	0.13	0.32
		10–10	3	1	0.03	0.29
	10.0	10–10	3	2	0.04	0.39
d-Amphetamine Sulfate	0.5	10–5	5	2	0.11	0.16
		10–10	3	1	0.05	0.12
	1.0	10–5	5	2	0.12	0.19
		10–10†	3	2	0.04	0.13
		10–10	3	1	0.04	0.21

*Groups are designated by ITI (first number) and trial duration (second number) †Data used for analysis of sequential responding

cholinergic blockers, scopolamine aand atropine, substantially impaired alternation accuracy. The effect with scopolamine hydrobromide was demonstrated to be due to interference with central rather than peripheral nervous system functioning, since 0.5 mg/kg methscopolamine bromide, a quaternary compound that does not readily pass the blood brain barrier [13], affected performance significantly less than scopolamine in tertiary form ($t = 7.64$, $df = 22$, $p<0.005$). 1.0 mg/kg d-amphetamine also significantly decreased accuracy compared to control performance ($t = 8.76$, $df = 30$, $p<0.005$).

Figure 4 shows all the error run curves obtained for individual animals from all sessions in which the groups designated in Table 1 received scopolamine. The error-run curves obtained from the animals in Group 10–10 on their sessions with 1.0 mg/kg d-amphetamine are presented in Figure 5.

The error run curves as plotted in Figs. 4 and 5 make possible a direct comparison of the conditional probabilities of the error responses (error responses per opportunity) made by the different animals at the various error run positions on their individual expermental sessions. Thus for the initial error responses on a session the conditional probability of an initial error response (error responses at error run position 1/initial responses) is indicated directly in Figs. 4 and 5 by the ordinate corresponding to error run position 1. The number of errors at error run position 2, also divided by the number of initial responses, appears at error run position 2. Hence the conditional probability of an error response at error run position 2 is given by the ratio between the ordinate at position 2 and the ordinate at position 1 (i.e., errors at position 2/errors at position 1) since each occurrence of an error at position 1 is an opportunity for an error response. Similarly, the conditional probability of an error at position 3 is indicated in Figs. 4 and 5 by the ratio between the ordinate at position 3 and the ordinate at position 2, since the errors at position 2 were the opportunities for errors at position 3, and so on.

The error run curves in Figs. 4 and 5 would be straight lines (i.e., their slopes would be constant) if the conditional probability of an error response were constant over the error run (that is, if the ratio of the number of error responses at any error position n to the number of error responses at error run position n–1 were constant). For each unit change in error run position on the linear abscissa, there would be a constant change in the corresponding

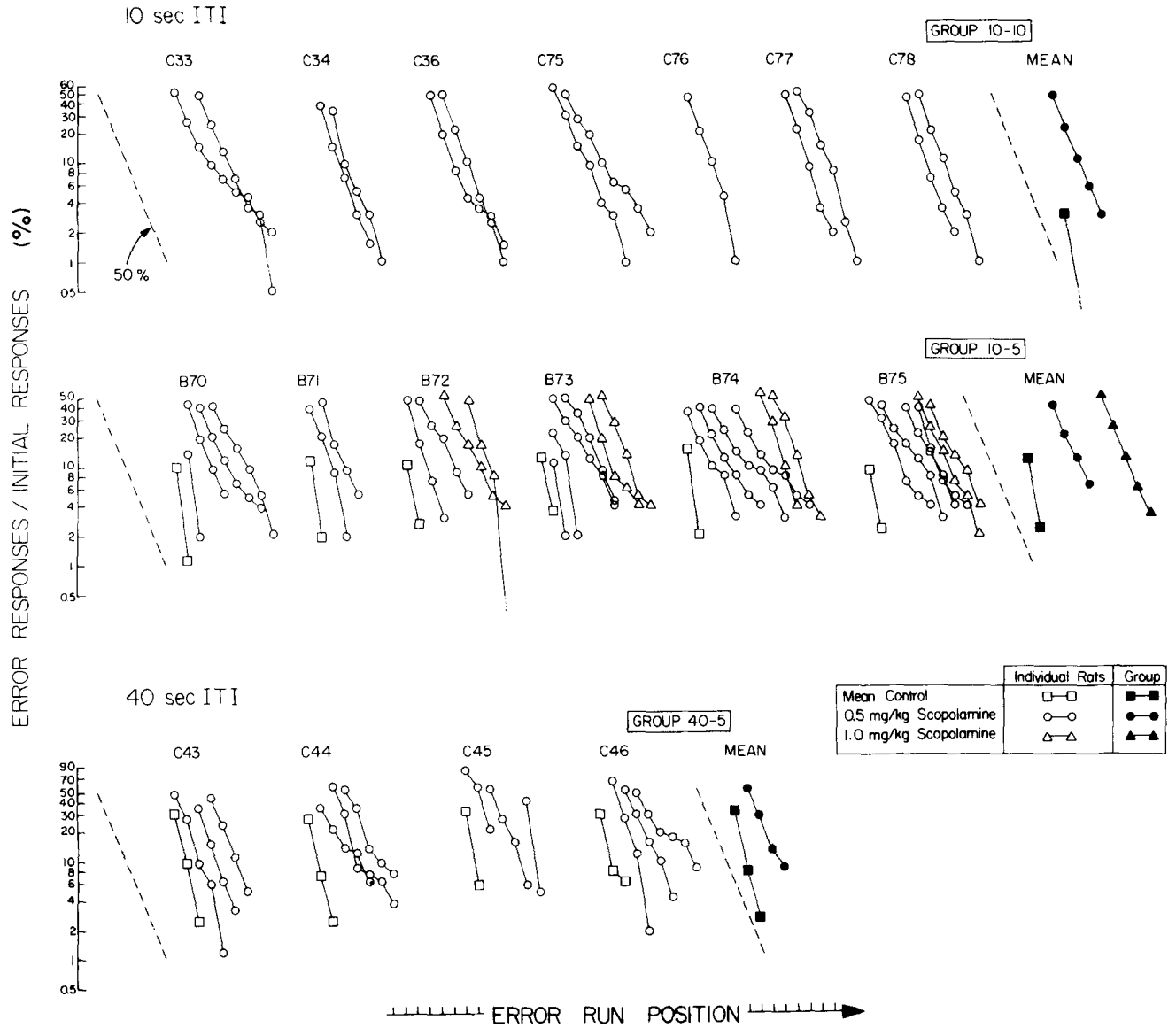

FIG. 4. Error responses (expressed as a percentage of initial trial responses) at each error run position for sessions in which the rats received 0.5 or 1.0 mg/kg scopolamine. Each curve designated by a letter-number combination shows the performance of a rat on one drug session. The highest point on each curve shows the percentage of error responses at error run position 1, the second point on each curve shows the percentage of error responses at error run position 2, and so on. Mean control and drug performance for each group of rats (obtained by averaging separately the error responses at error run positions 1, 2, 3 . . . etc. for each group) are presented at the right of the individual curves. The dashed lines are the hypothetical error run curves that would have been obtained if the conditional probability of error responses had been 0.50 at all error run positions. Experimental sessions are not shown if the rat responded on less than half of the trials during a session. Individual curves were terminated when the number of error responses at an error run position fell below 5.

value of the logarithmic ordinate (since logarithms of equal ratios are equal) and consequently the slope of the error run curve would also be constant.

The individual animal data obtained from Fig. 4 are summarized in Fig. 6, in which the mean conditional probabilities of error responses for the scopolamine sessions and for the corresponding controls are plotted for each group as a function of error run position.

The mean conditional probability of an error response increased as error run position increased for one group (10–5) treated with 0.5 mg/kg scopolamine; $F(4,91)$ between error run positions = 5.11, $p<0.001$), and was not significant for the other three groups at scopolamine doses represented in Fig. 6. The conditional probability of an error response also increased significantly with error run position for the control sessions with groups 10–10 and 10–5; $F(1,35)$ between error run positions = 6.69, $p<0.014$, and $F(2,68) = 8.17$, $p<0.001$.

Analogous results were obtained for administration of 1.0 mg/kg d-amphetamine to Group 10–10. The conditional probability of an error response increased with error run position on the drug sessions, $F(2,21) = 6.61$, $p<0.006$, as well as on the control sessions of this group.

The question of whether or not these results are

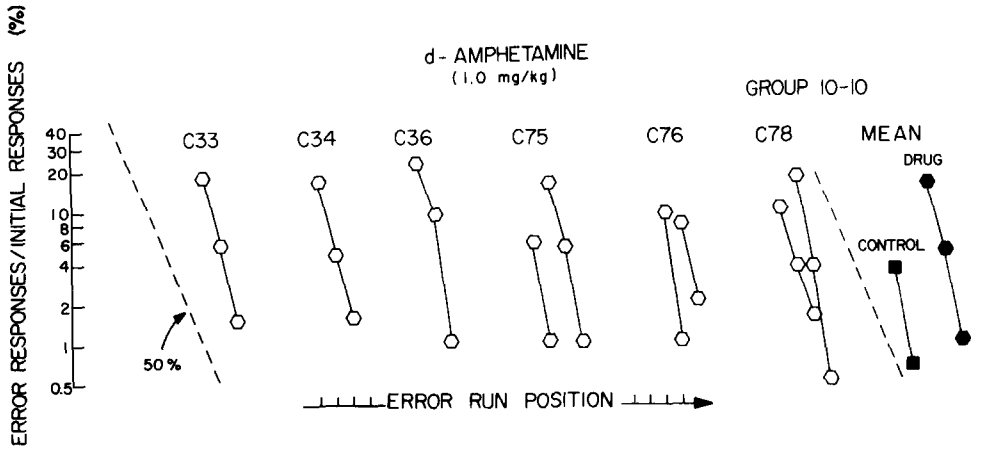

FIG. 5. Individual curves relating error responses (expressed as a percentage of initial trial responses) to error run position for rats given 1.0 mg/kg d-amphetamine. Legend as in Fig. 4.

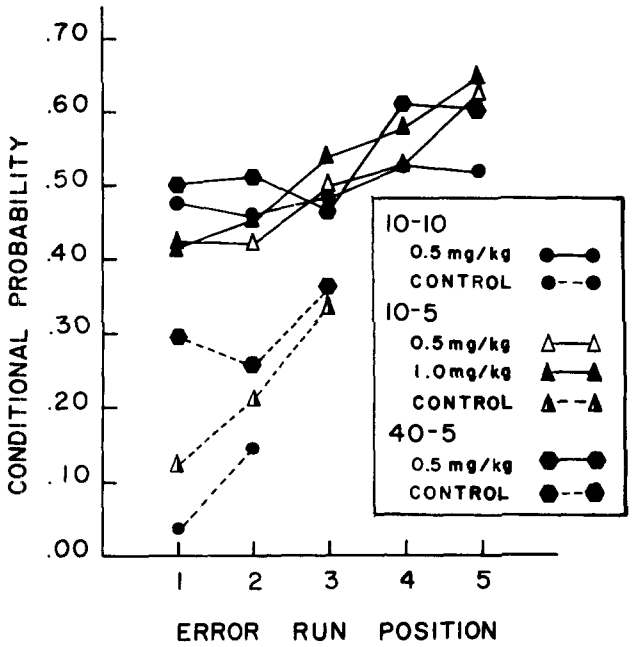

FIG. 6. Relation between mean conditional probability of an error response and error run position for control and scopolamine sessions. Data are the same as in Fig. 4; however this figure shows conditional probabilities directly.

appropriately described as perseveration is deferred for the General Discussion.

EXPERIMENT 3

Experiment 2 demonstrated that scopolamine disrupted delayed spatial alternation performance. Experiment 3 was designed to separate possible drug effects on (1) the control of delayed alternation behavior (e.g., effects such as perseveration, disinhibition, amnesia, etc.) from effects on (2) responding per se, i.e., on performance of the sequence of motor responses involved in pressing the two levers in alternation on successive trials. Drug effects on responding were evaluated in Experiment 3 with rats trained to perform an alternating discrimination, in which alternation was controlled by a light that was on alternately over the two levers on successive trials. Thus, in Experiment 3 the rats performed essentially the same sequence of lever presses as in Experiment 2, but the alternation behavior in Experiment 3 was controlled by stimuli present at the time of the response rather than (as in Experiment 2) by events and stimuli from the preceding trial.

White [17] reported that scopolamine did not appreciably alter performance of a simultaneous light-no light discrimination similar to that employed in Experiment 3. Therefore, if scopolamine were to disrupt performance of the light-cued alternating discrimination of Experiment 3, the result could be attributed to an effect on alternation responding rather than on discrimination of the light. If, on the other hand, scopolamine does not alter performance on the alternating discrimination, it can be concluded that the drug affects neither discrimination of the light nor alternation responding.

METHOD

Animals and Procedure

Nine rats were trained according to the Light Training procedure, as described under Experiment 1. The correct lever switched randomly from side to side on successive trials; a panel light was illuminated over the correct lever during each trial. Trials were repeated if the animal either pressed the incorrect lever, or did not press the lever. The maximum trial duration was 5 sec, ITI was 10 sec, and pretrial delay was 1 sec. There were 100 reinforced trials per session.

Training on this random discrimination was continued until each rat had completed 2 successive sessions in which it responded correctly on over 85 percent of the trials in the session. All rats then received preliminary injections of 0.5 and 1.0 mg/kg scopolamine. (Results of these preliminary injections are not reported here.)

Upon completion of the preliminary injections, each rat received the following sequence of experimental sessions: alternating discrimination – 2 sessions; random discrimination – 3 sessions; and alternating discrimination – 1 session. All 3 alternating discrimination sessions were test

TABLE 2

EFFECT OF SCOPOLAMINE ON LIGHT–ON, LIGHT–OFF GO/GO ALTERNATING DISCRIMINATION (N = 9)

	Saline Control	Scopolamine	
		0.5 mg/kg	1.0 mg/kg
Percent Responses			
Mean	78	50	39
Median	84	63	68
(Range)	(44–98)	(20–100)	(3–98)
Percent Correct			
Mean	98	95	96
Median	97	96	99
(Range)	(94–100)	(76–99)	(90–100)

sessions: a saline injection was administered on the first alternating discrimination session, and scopolamine (0.5 and 1.0 mg/kg) was given on the other two alternating discrimination sessions.

Experimental sessions with the alternating discrimination were held to the absolute minimum needed for testing in order to minimize the possibility that the alternation behavior could be controlled by stimuli from preceding trials (as in delayed alternation) rather than by the discriminative stimuli (light on over the correct lever) present on the trial.

RESULTS AND DISCUSSION

Table 2 shows the effects of saline and 0.5 and 1.0 mg/kg scopolamine on performance on the alternating discrimination. (Table 2 shows both mean and median performance because discrepant results were obtained with several rats.) Even though both doses of scopolamine were sufficient to reduce substantially the proportion of trials on which the rats responded, neither dose affected the accuracy of the alternation lever pressing. On those trials on which the rats did respond, the mean (and median) percentage of correct responses was always 95 percent or higher.

Thus, doses of scopolamine which profoundly disrupted the accuracy of delayed alternation behavior in Experiment 2 did not affect accuracy of performance on the alternating discriminations in Experiment 3. Since the sequence of motor responses was essentially the same in delayed alternation as in the alternating discrimination it is unlikely that the drug appreciably affected performance of the alternation lever pressing response. Instead, the much greater effect of scopolamine on delayed alternation must be attributed to the difference in the stimulus control in the 2 experiments: in delayed alternation responding was controlled by stimuli or events no longer present in the environment when the response was made, whereas in the alternating discrimination the stimulus that controlled alternation was present in the environment at the time of the response.

GENERAL DISCUSSION

Cholinergic blockers and d-amphetamine increased the conditional probability of error responses by rats performing on a baseline of discrete trial delayed spatial alternation. Scopolamine, in particular, increased the conditional probability of error responses to nearly 0.50. The effects of scopolamine on alternation behavior will be examined in terms of 3 possible descriptions or interpretations of the behavioral effects of the drug: perseveration, disinhibition, and discrimination deficit.

Perseveration

Perseveration has been so casually and variously used to describe repetitive behavior that any definition of the term must be unavoidably arbitrary. Perseveration as a drug effect implies an increased tendency to repeat the same response on successive trials; in spatial alternation all such repetitions are error responses. However, the general increase in error responses observed in spatial alternation does not by itself warrant a special designation perseveration, since all alternation errors consist of pressing the same lever on successive trials. Therefore, in this discussion the term perseveration will be reserved for an increase in response repetition on the trial that follows the occurrence of an error response. Specifically, perseveration will be said to occur when the conditional probability of error responses (error responses per opportunity, or conditional probability of an error response given an error response) increases over the error run.

Experiment 2 showed that the conditional probability of an error response tended to increase with error run position for the animals treated with scopolamine. However this

increase was statistically significant for only one group and scopolamine dosage (Group 10–5 and 0.5 mg/kg). Furthermore, the conditional probability of an error response also increased significantly on the non-drug (control) sessions for both Groups 10–5 and 10–10. Thus it is doubtful that drug treatment caused an increase in the repetition of error responses during the error run.

Others have also failed to observe perseveration with scopolamine in alternation situations. Warburton and Heise [16] found that on discrete trial 2 lever double alternation the number of errors increased with increasing dose of scopolamine, but the proportions of switch and stay errors did not change with dosage and did not differ from each other. Similarly Leaton and Utell [9], who studied the effects of scopolamine on spontaneous alternation by rats in a T-maze, reported that high doses of scopolamine (1.2 mg/kg) significantly reduced the percentage of spontaneous alternations, but did not produce significant perseveration.

The conclusion that animals treated with scopolamine do not perseverate in various alternation situations may hold only if successive responses are separated by time intervals of several seconds. For example, Hearst [5] concluded that rats treated with scopolamine perseverated in a double discrimination task (the rats were required to press one lever when a tone was on, and to press the other lever when a clicking sound was on). In Hearst's experiment the ratio of stay to switch responses changed from approximately 1.0 under control conditions to 3.2 under drug. However, Hearst tabulated all responses – responses during the ITI's as well as responses during trials – when calculating the proportion of switch and stay responses. Thus his measured proportion of stay responses included the bursts of rapid responding on one lever that sometimes occurred during the ITI.

Disinhibition

Carlton and Markiewicz [3] define disinhibition produced by a drug as the occurrence of responses that do not normally occur in the nondrugged state. Thus Carlton [2] has proposed that errors increase following administration of cholinergic blockers in delayed alternation because extinguished error responses (stay responses) reappear that compete with alternation (switch responses). Carlton and Markiewicz [3] describe a variety of situations (e.g., extinction, habituation, passive avoidance) in which previously extinguished responses reappear following treatment with cholinergic blockers. However, these are all no go situations, in which there is a specific occasion for not responding and the disinhibited responses that intrude under the drug can be identified and measured. In delayed alternation and other choice or go/go situations, there are no no/go trials; all error responses are competing responses made on the wrong lever. Since error responses and competing responses are thus indistinguishable, the proposition that competing responses account for the error responses in delayed alternation is not directly testable in the delayed alternation situation.

Discrimination Deficit

Experiment 3 showed that scopolamine did not affect the motor expression of the alternation response, since the drug did not disrupt alternation performance controlled by visual stimuli present at the time of the response. Apparently scopolamine disrupts alternation only when (as in Experiment 2) the behavior is controlled by stimuli or events that are no longer present at the time of the response. These stimuli or events come from prior trials, and are somehow remembered over the ITI delay.

Analogous observations have been reported by Laties [7] and by Laties and Weiss [8], who compared the effects of various drugs on the performance of pigeons under various externally controlled (control by stimuli present at the time of the response) and internally controlled schedules of reinforcement. Their experiments generally confirm the proposition that "... behavior under control of external discriminative stimuli is less sensitive to modification by drugs than behavior not under such control" [7].

There are 2 principal ways in which scopolamine might interfere with control of alternation behavior by prior trial stimuli or events: by interference with the storage of the controlling stimuli over the ITI delay, or with the registration and retrieval of these stimuli. The former possibility was examined by Heise and Conner (described in [6]) who compared accuracy of delayed alternation performance under nondrug and drug conditions when ITI duration was systematically varied during the experimental session. Accuracy of alternation performance decreased with increasing ITI duration under control conditions, and was further decreased by administration of scopolamine. However the magnitude of the scopolamine effect did not increase with increasing ITI: the decrement produced by the drug was as great for short ITI durations (e.g., 2.5 sec) as for much longer ITI's. It was concluded that scopolamine did not alter a time-dependent storage process but rather affected registration and/or retrieval of the prior trial stimuli that controlled alternation. This conclusion is consistent with the results of a Theory of Signal Detection analysis of scopolamine effects on discrimination behavior reported by Warburton [15]. Warburton found that scopolamine impaired stimulus detectability (but not response bias) both when behavior was controlled by stimuli no longer present at the time of the response and when behavior was controlled by small changes in stimulus intensity at the time of the response.

The conclusion that scopolamine altered discriminability of the stimuli or events that controlled alternation must necessarily remain tentative, since we do not know precisely what these stimuli or events are. However, we do know that delayed alternation is not controlled by orienting or postural responses that fill the gap between trials, since systematic observations of rats well trained in delayed alternation showed that they did not perform a consistent or stereotyped sequence of responses throughout the ITI [10]. Although scopolamine did not interfere with a simultaneous light-no light discrimination in Experiment 3 when there was no delay between stimulus presentation and response, the drug does impair discriminations between presumably less salient stimuli such as auditory stimuli [5] or steady and flashing lights (unpublished observations). It seems reasonable to suppose that discriminations between the very similar prior trial stimuli that control the left and right alternation responses would also be susceptible to disruption by scopolamine.

In summary, the present experiments have shown that perseveration does not appropriately describe the effects of scopolamine on sequences of delayed alternation responding. The drug does not interfere with the execution of the required alternating sequence of responses when the behav-

ior is controlled by visual stimuli present at the time of the response. Although the specific effect of scopolamine on delayed alternation has not been identified, it is known that scopolamine does not alter retention or storage (as distinguished from discrimination) of the stimuli from the preceding trial that control performance on a trial. Scopolamine has been shown to impair stimulus detectability: it is postulated that the drug disrupts delayed alternation performance by impairing registration and/or retrieval of the prior trial stimuli that control the behavior.

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