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Alteration of Response Patterning by d-Amphetamine on Repeated Acquisition in Rats

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SCHROT, J. AND J. R. THOMAS. *Alteration of response patterning by d-amphetamine on repeated acquisition in rats.* PHARMACOL BIOCHEM BEHAV **18**(4) 529–534, 1983.—The acute effects of d-amphetamine on response patterning in a repeated acquisition baseline were investigated with rats. Each session the animals acquired a different four-member response sequence on three levers. Each sequence (trial) completion produced a food pellet. Errors produced a brief timeout that was reset by responses made during the timeout. Acute doses of d-amphetamine (0.5–4.0 mg/kg) and saline were administered 30 min presession. The response patterns analyzed were perseverative responses to a single lever (runs), and a response to each lever in either a left-to-right or right-to-left direction (traverses). The trial position, frequency, and lever location of error and timeout responses that occurred in the context of runs and traverses were studied. In contrast to control sessions, higher doses of d-amphetamine produced increases in the number of error and timeout responses emitted. The majority of these responses occurred as runs; traverse responding did not exceed control levels. Furthermore, the run error and timeout responding tended to occur early in the session and on a single response lever. The results are consistent with the view that d-amphetamine disrupts stimulus control and produces perseverative responding which may account for previous reports of disruption in repeated acquisition tasks following d-amphetamine administration.

Repeated acquisition d-Amphetamine Patterning Perseveration Rats

THE environmental contingencies influencing behavior in transition have been investigated with the procedure of repeated acquisition [1,6]. This procedure requires a subject to learn a new sequence or chain of multiple responses during each session. Evidence that "learning," or acquisition, occurs within a session is reflected by a decline in the frequency of incorrect responding as the session progresses [12]. Within-session acquisition was originally observed in monkeys [1], and later extended to pigeons [12]. With rats it was initially maintained by shock postponement [6,7] and later by food presentation [5, 8, 9, 10]. The behavior maintained with this procedure has proven to be sensitive for assessing the effects of a range of environmental insults [9,16].

Within the realm of pharmacological assessment, the repeated acquisition procedure has been used with a variety of substances [16]. Generally, effective doses of pharmacological compounds increase incorrect responding and alter the normal pattern of within session acquisition [16], which is characterized by a decreasing frequency of error responding as the session progresses. Evidence for alterations in response patterning is often presented in the form of cumulative records [16] or response totals during progressive blocks of trial completions [12,14]. Although this approach provides a summary of the distribution of inappropriate responses during the progression of a session, it does not provide detailed information concerning the patterning of responding by trial or manipulanda position.

Recently Schrot *et al.* [10] presented evidence that two types of response patterns identified as runs and traverses accounted for 50–70% of all error responses and 80–100% of all timeout (TO) responses in a repeated acquisition procedure using rats. Response runs were defined as perseverative responses to a single response lever and traverses were defined as a single response to each of three levers in either a left-to-right or right-to-left direction. That analysis required the identification and collection of each response class (i.e., correct, error, TO) by lever position (i.e., left, center, or right) and was instrumented with a microcomputer data collection and analysis system.

The present study employed a repeated acquisition procedure in conjunction with a data collection system which permitted a trial-by-trial analysis of response patterning. d-Amphetamine was chosen because of its demonstrated ability to alter session acquisition patterns of rats [7], pigeons [16], and primates [16].

METHOD

Animals

The subjects were two male Sprague-Dawley rats (Nmri:0[SD]CV) approximately 1 year old when drug administration began. They weighed 275±10 g and were maintained at approximately 80% of their free-feeding weights. Water was available continuously in the home cage. The animals were individually housed in a temperature-

controlled room with a 12-hr light-dark cycle beginning at 0600.

Apparatus

A standard two-lever rat chamber was modified with the addition of an omnidirectional pole lever, mounted from the ceiling and centered 4 cm from the intelligence panel. This additional lever extended to a height of 10 cm above the grid floor and was designated the center (C) lever. The other two levers were designated left (L), and right (R). The rat chamber was enclosed in a ventilated sound-attenuating enclosure.

Procedure

The terminal response contingencies required the animal to complete correctly a four-member response chain on three levers (one lever repeating) to obtain a 45-mg food pellet. A different auditory stimulus signalled each chain member. Correct responses advanced the chain to the next member and ultimately produced reinforcement. The reinforced response initiated a 1.5-sec feeder cycle during which the auditory stimulus was off and two lights adjacent to the food hopper were on. Incorrect responses produced a 3-sec timeout signalled by turning off the houselight and auditory stimulus. A response on any lever during the timeout reset the timeout. Incorrect responses did not reset the sequence. Each auditory stimulus was present until a correct response advanced the sequence to the next member and produced the next stimulus. The ordering of stimuli was the same from session to session. The four auditory stimuli were a 900-Hz tone, 1/sec clicks, a 2000-Hz tone, and 10/sec clicks. The intensity of all auditory stimuli was set at 72 dB as measured with a sound level meter. The required correct sequence of lever presses changed from session to session, e.g., LCLR, CLRL. The restrictions that governed the composition of response sequences have been previously described [12]. Sessions terminated after 150 reinforcements or 2 hr, whichever occurred first, and were conducted five days a week.

The shaping procedure used to arrive at the terminal four-member chain was as follows. The animals were shaped to respond to each of the three levers for three sessions of 150 reinforcements each. During these sessions the three levers were active at all times, there were no incorrect responses, therefore the animals could switch between levers in any sequence and be reinforced. The auditory stimuli and TO stimulus were not presented during these sessions.

Beginning with the fourth training session, the animals were required to respond in a designated four-member sequence (i.e., LRLC) and the sequence was changed from session to session. The auditory stimuli associated with each sequence member and the TO produced by incorrect responses were introduced at this time. These reinforcement contingencies were in effect for approximately 10 sessions. Each correct response in the sequence produced a food pellet and sessions terminated after 150 reinforcements. During the next five sessions reinforcement was produced following the last three correct responses of each sequence. This was followed by five sessions in which reinforcement followed the last two correct responses of each sequence. Finally, reinforcement was contingent upon completion of the entire four member chain. Approximately 20 additional sessions were conducted before the subjects were consistently completing 150 sequences within the 2-hr time limitation. Sessions were conducted until error responding stabilized and consistent patterns of within-session acquisition emerged.

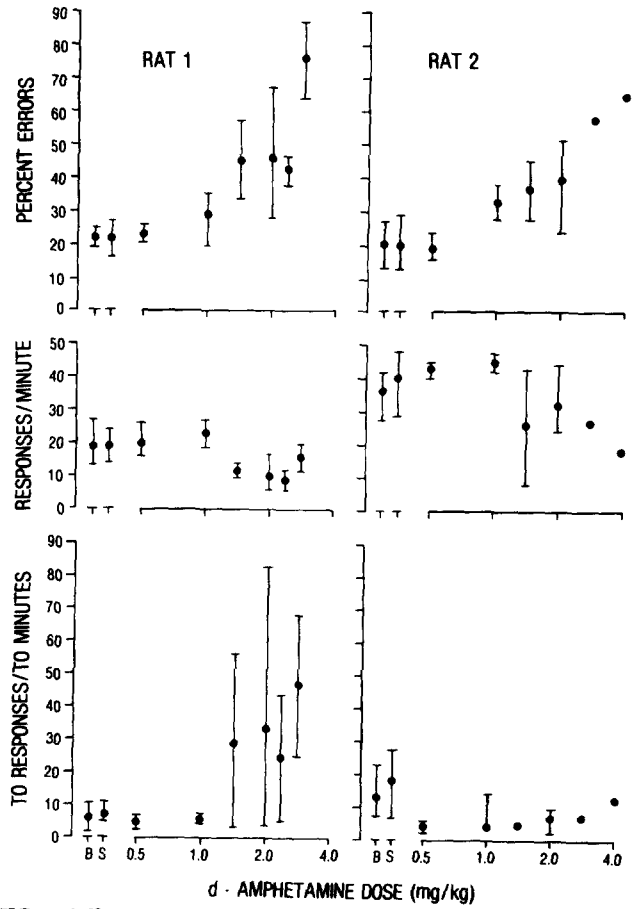

FIG. 1. Effects of d-amphetamine on percent error (errors/errors + correct) responding, response rate (errors + correct/sessions time − TO time), and TO response rate (TO responses/TO time). The points and vertical lines at S and B represent the mean and range of 7 saline and baseline sessions respectively. The points and vertical lines in the dose-effect curves represent the mean and range of at least two determinations at each point, except for the points at 3.0 and 4.0 mg/kg for Rat 2 which are single determinations.

Subsequent to a number of baseline parameter manipulations, a dose-effect function was obtained for d-amphetamine sulfate over a range of 0.5 to 4.0 mg/kg. d-Amphetamine sulfate as the salt was dissolved in saline and administered intraperitoneally 30 min prior to the test sessions. The volume of each injection was 0.1 ml/100 g of body weight. Drug injections were administered once per week. Control injections of saline in the same volume/body weight ratio were administered throughout the study.

RESULTS

d-Amphetamine increased percent error responding, slightly depressed response rates, and increased the rate of TO responding. The top two panels of Fig. 1 depict percent error responding as a function of d-amphetamine dose. Percent error responding increased as drug dose increased. The middle panels depict response rate as a function of drug dose. With increasing drug doses response rates declined to approximately 1/2 of control levels at the higher doses. The

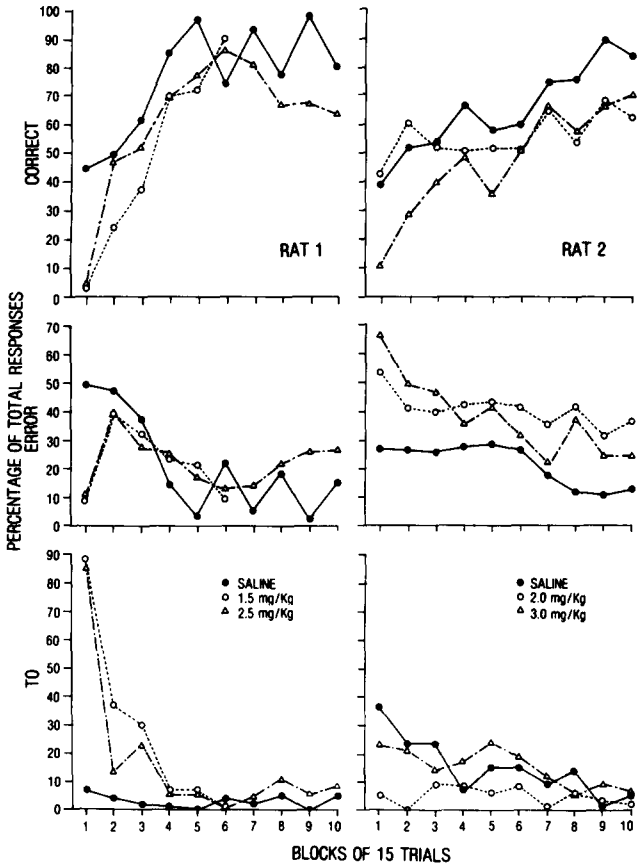

FIG. 2. Percentage of total responses according to response type for ten successive blocks of 15 trials each. The same saline and drug sessions are shown for each animal for each response type. The percentage for each response type was calculated as response type/total responses (correct + error + TO) for each block of 15 trials. The solid circle, open circle and triangle, represent individual session data for each animal. The 1.5 mg/kg session for Rat 1 was terminated after the completion of 90 trials according to the time limitation criterion.

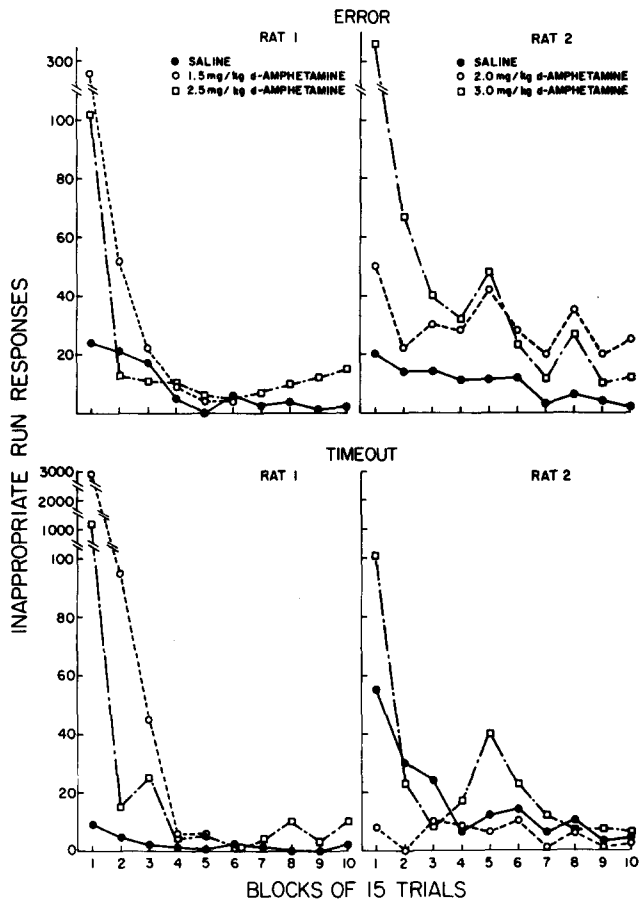

FIG. 3. Inappropriate run responses for 10 successive blocks of 15 trials each. The sessions presented are the same as those presented in Fig. 2. Run error responses are presented in the top two panels and run timeout responses are presented in the bottom panels of the figure. The solid circle, open circle, and square represent individual session data for each animal.

bottom panels of Fig. 1 depict the rate of responding during TO as a function of drug dose. For Rat 1 TO response rate increased at doses of 1.5 mg/kg or greater and the variability from session to session at these doses was also greatly increased. TO response rates for Rat 2 were either within or slightly below the control range at all drug doses.

The percentage of each response type (correct, error, or timeout) during successive 15 trial blocks is shown in Fig. 2. A saline and two drug sessions are presented for each animal. In this and succeeding figures the 1.5 mg/kg data for Rat 1 represents the first 90 trial completions of a session terminated by the 2-hr time limitation. The top two panels show percent correct responding for the two animals. During the saline sessions correct responding during the first block was under 50% and increased as the session progressed. Terminal levels of correct responding were above 80% for both animals. Error responding (middle panels) during saline sessions decreased during the course of each session. Timeout responding (lower panels) for Rat 1 was at relatively low and consistent levels during the saline session and Rat 2 showed a progressive decline from moderate to low levels of TO responding during the saline session. Drug treatment modified the relative distributions of these response types. The proportion of correct responses was generally below the control level throughout the drug sessions. The very low proportion of both correct and error responding exhibited by Rat 1 during the first block reflects this animal's tendency to respond during TO in the initial portion of drug sessions. Rat 1's error responding peaked during the second block as TO responding declined. In succeeding blocks of the session error responding declined along with TO responding. Rat 2 shows a different distribution of error and timeout responding during drug sessions. This animal's error responding (middle panel) was generally elevated throughout drug sessions, although there was evidence of a progressive decline as the sessions progressed. Timeout responding during drug sessions, however, was below or comparable to the control session.

Run error and TO response totals for 10 blocks of 15 trials each for both animals are depicted in Fig. 3. The top panels show the run error data for the two rats. During the saline session run error responses declined as the session prog-

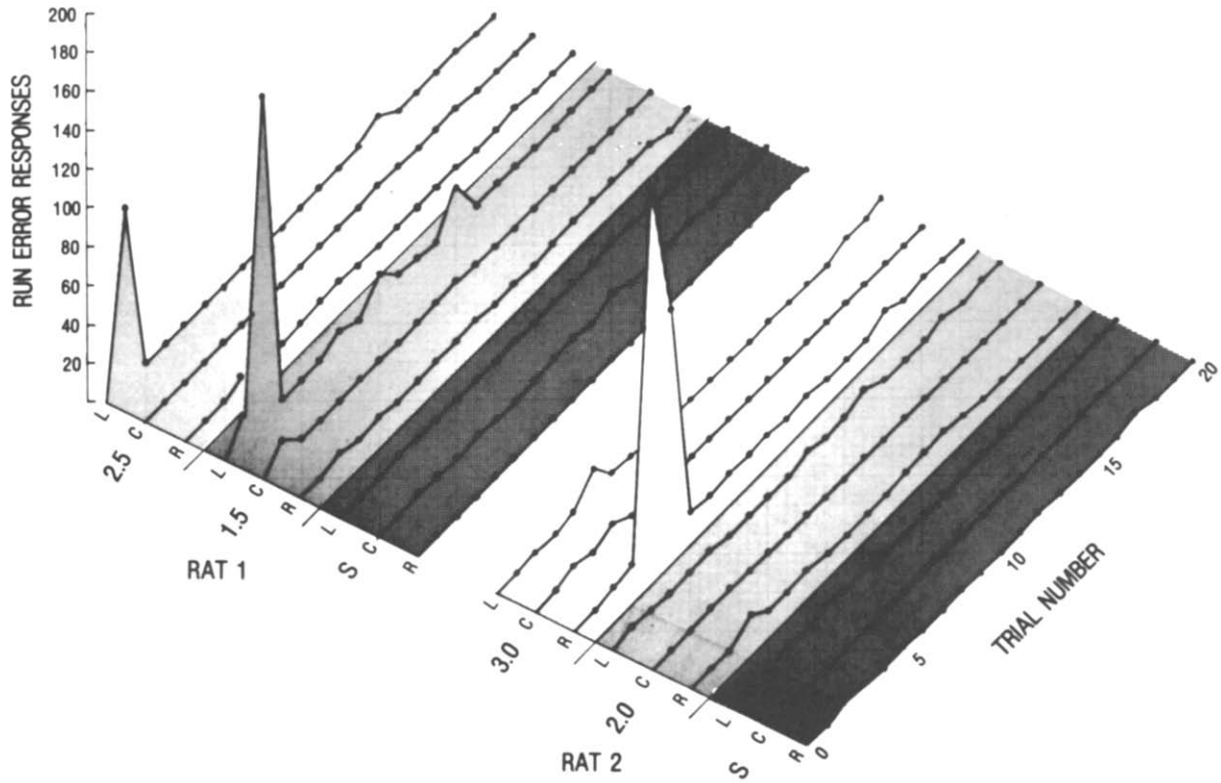

FIG. 4. Run error responses during the first 20 trials of a saline and two drug sessions for two rats. The sessions presented are the same as those presented in Figs. 2 and 3. For each condition the number of run error responses occurring on the left (L), center (C), and right (R) levers during each trial are presented. Note that the data for Rat 2 is presented in the right portion of the figure. The point at trial 4, R lever, 3.0 mg/kg dose for Rat 2 represents 190 run error responses. The points at trial 2, L lever, 1.5 mg/kg, and at trial 1, L lever, 2.5 mg/kg for Rat 1 represent 168 and 92 run error responses respectively.

ressed. This was a typical within-session distribution pattern for these rats during all control sessions. During drug sessions run error responses for both animals were elevated during the initial portion of the sessions and generally declined as the session progressed. The within-session decline exhibited by Rat 2 was less precipitous with the 2.0 mg/kg dose; however, run error levels did decline by 50% from the initial to final block of trial completions.

The bottom panels of Fig. 3 depict run TO responding for the two rats. Within session declines in TO responding occurred for both animals during the saline sessions. The decline was more pronounced for Rat 2 than for Rat 1. The primary effect of d-amphetamine on Rat 1 was to greatly increase the number of run TO responses during the initial portions of these drug sessions. Run TO responses during the first trial block were in excess of 1000 with both drug doses. Run TO responding declined precipitously after the first trial block and was within control levels by the end of the third trial block. Rat 2's run TO responses were elevated only with the 3.0 mg/kg dose during the first and fifth trial blocks.

Figure 4 shows the number of run error responses by lever position for each of the first 20 trials of the saline and drug sessions selected. During the saline sessions there was very little evidence of run error responding for either animal. When run error responding occurred during drug sessions it tended to occur early in the session, on the same lever, and during only a few trials. For example, Rat 2 emitted a total of 142 run error responses during the entire saline session depicted, representing 63% of total session error responding. During the 3.0 mg/kg session this rat emitted 307 run error responses on the right lever during trials 4 and 5, representing 37% of total session error responding, and 49% of total session run error responding. Rat 1 emitted 83 run error responses during its saline session, representing 38% of total session error responding. This animal, however, emitted 168 run error responses on the left lever during trial 2 of the 1.5 mg/kg session and 92 left lever run error responses during trial 1 of the 2.5 mg/kg session. That represented 46% of session run error responses and 33% of session error responses during the 1.5 mg/kg session and 45% of session run error responses and 26% of session error responses during the 1.5 mg/kg session.

Figure 5 shows timeout run responding by lever position for each of the first 20 trials of the saline and drug sessions selected. The distribution or pattern of run timeout responding during drug sessions was similar to that observed for run error responding in that they tended to occur on a single lever during a few trials at the beginning of the session. Rat 1 emitted a total of 20 run TO responses during the saline session, representing 77% of session TO responding. However, during the 1.5 mg/kg drug session this rat emitted a total of 2705 left lever run timeout responses during five trials (1,2,6,8,12). That represented 89% of session run timeout responses, and 88% of session timeout responding. With a 2.5 mg/kg dose Rat 1 emitted 1181 timeout responses on the

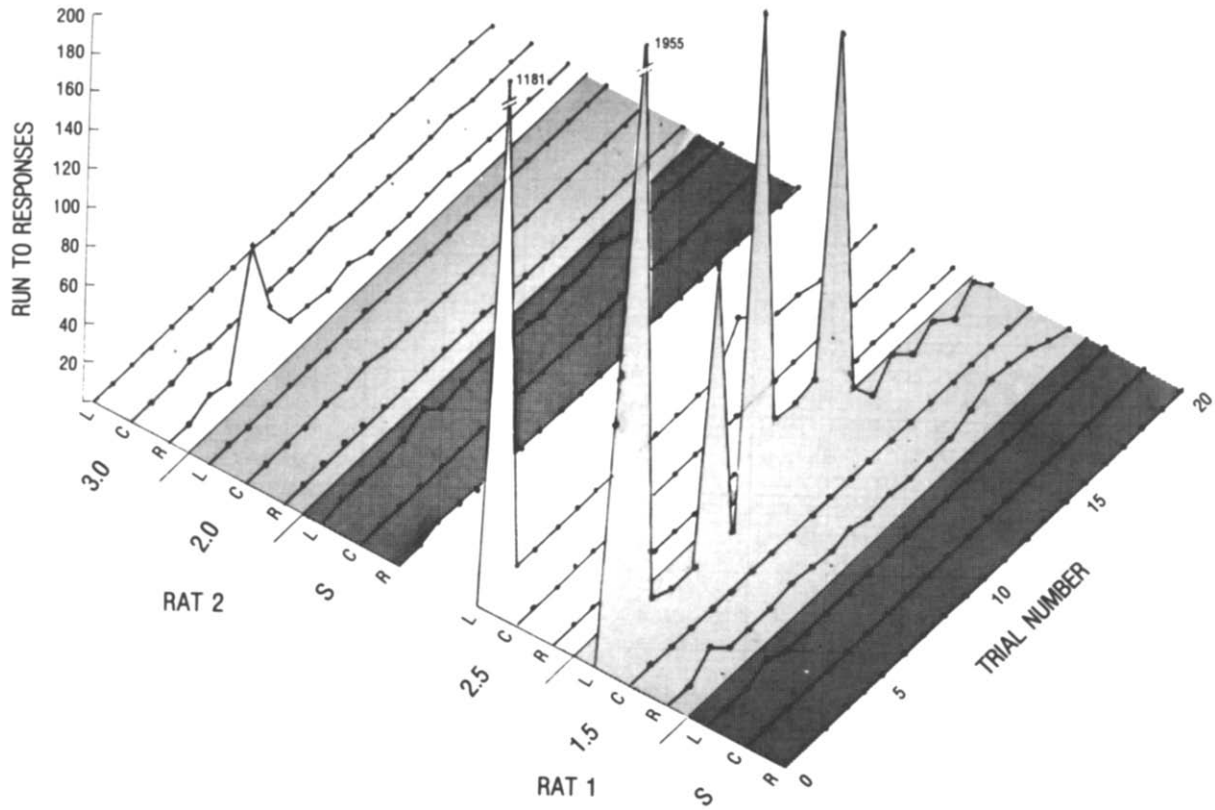

FIG. 5. Run timeout responses during the first 20 trials of a saline and two drug sessions for two rats. The sessions presented are the same as those in Figs. 2, 3, and 4. For each condition the number of run TO responses occurring on the left (L), center (C), and right (R) levers during each trial are presented. Note that the data for Rat 1 is presented in the right portion of the figure. For Rat 1 trial 2, L lever, 1.5 mg/kg depicts 290 responses at the break point, while 1955 run TO responses actually occurred. Similarly, trial 1, L lever, 2.5 mg/kg for this rat depicts 260 responses at the break point while 1181 run TO responses actually occurred.

left lever during trial 1, representing 91% of session run timeout responses and 90% of session TO responding. Rat 2 emitted a total of 161 run TO responses during the saline session, representing 88% of session TO responding. Control session TO responding never exceeded 10 responses during any one trial. Rat 2 emitted relatively few run TO responses during drug sessions, emitting a peak of 64 run TO responses on the right lever during trial four and 22 during trial 5 with a 3.0 mg/kg dose of d-amphetamine. Those two trials represented 34% of session run TO responses and 27% of session TO responses.

The maximum number of runs for either rat that occurred during a control session was 8 by Rat 1, containing a total of 22 responses of all types on all levers. In contrast Rat 1 emitted a total of 2137 run responses in 3 runs during the second trial with a 1.5 mg/kg dose, and 1274 run responses in 4 runs during the first trial with the 2.5 mg/kg dose. The maximum number of runs and run responses for Rat 2 occurred during the fourth trial with the 3.0 mg/kg dose when 264 run responses occurred during 7 separate runs. These data indicate that active doses of d-amphetamine resulted in long runs of repetitive responding to a single lever during the initial part of drug sessions.

DISCUSSION

The response patterns normally obtained from rats responding on a repeated acquisition task were modified by d-amphetamine. The total number of inappropriate responses (error+TO) emitted during a session increased as a function of dose. Additionally, the within-session distributions of error and timeout responses changed with respect to magnitude and slope following administration of the larger doses of d-amphetamine. Analysis of response patterns identified as runs and traverses revealed no drug effect on traverse responding but substantial increases in the magnitude of both run error and TO responses at the higher d-amphetamine doses. The control levels of error and TO responding during both runs and traverses were similar to those previously reported for rats in a repeated acquisition procedure [10].

The impairment of acquisition obtained in the present study is consistent with previous reports that d-amphetamine increases error responding and disrupts response patterning in a repeated acquisition procedure [7, 12, 13, 14, 16]. For example, Thompson [12] investigated the effects of d-amphetamine on the acquisition of four-member response chains in pigeons. In that procedure a food reinforcer was delivered after every fifth chain completion and incorrect responses produced a 5-sec TO during which responses had no consequence. A dose of 4 mg/kg increased the number of errors emitted during a session as well as the session duration, owing to increased pausing. The increased error responding tended to occur during the initial portion of the session. Timeout responding, however, was within the control range.

Increases in error responding with higher doses of d-amphetamine were also observed in the present study, and the increases were greatest during the initial portion of the session. The animals also emitted an increased number of TO responses as a result of high doses of d-amphetamine. The distribution of error and TO responses by lever position and trial number, and the patterns in which they occurred revealed the following effects of d-amphetamine on the acquisition process.

The majority of error and TO responses emitted during drug sessions tended to occur on the same lever, during a few trials, and during the initial portion of the sessions. Rat 1, for instance, consistently responded on the left lever and most of its TO and error responses following d-amphetamine administration occurred during the first 10 trials of the session. Rat 2 evidenced a similar pattern on the right lever although the magnitude of the increase was considerably less. The increment in error and TO responding produced by d-amphetamine administration occurred primarily as run rather than traverse responding. In addition, the number of runs per trial relative to the number of responses emitted during the trial was small. The numerous run TO responses made by Rat 1 during the initial d-amphetamine trials occurred during four or fewer separate runs in each instance. These findings indicate that subsequent to d-amphetamine administration the animal perseverated on a single lever for extended periods of time. The observation of response perseveration on individual levers is consistent with previous findings concerning amphetamine effects [3]. The pattern that emerged during the prolonged runs contained little pausing and could be characterized as stereotypic responding. This pattern of responding may have been responsible for previously reported disruptions of repeated acquisition tasks following d-amphetamine administration [7, 12, 13, 14, 16].

The increase in run error and TO responding observed following drug administration indicate that d-amphetamine disrupted stimulus control [2, 11, 15]. During control conditions relatively few TO responses occurred and the number and length of runs was small compared to that observed with the higher drug doses. The small number of run responses during control conditions indicates that the animals were switching levers frequently; usually a change in response location occurred following a single response to a given lever. Reinforcement or a stimulus change signalling progression through the sequence never occurred following a successive response to the same lever. The initial response at a lever location, following a switch, was either correct or incorrect but a second response to the same lever was always incorrect. Switching lever location was therefore a necessary condition for sequence completion and reinforcement delivery. Presumably, changing lever location before responding came under the control of the previous response location and/or auditory stimuli. Following drug administration there was an increased frequency of responding during the TO stimulus and of responding repeatedly on the same lever. These alterations in response patterning were observed early in the sessions, prior to acquisition and the establishment of stronger stimulus control [4]. Both of these findings may indicate that the drug interfered with the control exerted by the TO stimulus and the stimuli controlling the choice of lever location.

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The experiments reported herein were conducted according to the principles set forth in the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council, DHEW, Pub. No. (NIH) 78-23.

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