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EFFECTS OF D-*AMPHETAMINE ON RESPONSE ACQUISITION WITH IMMEDIATE AND DELAYED REINFORCEMENT*

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The present study examined in 8-hour sessions the effects of *d*-amphetamine (1.0, 5.6, and 10 mg/kg) on the acquisition of lever-press responding in rats that were exposed to procedures in which water delivery was delayed by 0, 8, or 16 seconds relative to the response that produced it. Both nonresetting- and resetting-delay conditions were studied. Although neither shaping nor autoshaping occurred, substantial levels of operative-lever responding developed under all conditions in which responses produced water. The lowest dose (1.0 mg/kg) of *d*-amphetamine either had no effect on or increased operative-lever pressing, whereas higher doses typically produced an initial reduction in lever pressing. Nonetheless, overall rates of operative-lever pressing at these doses were as high as, or higher than, those observed with vehicle. Thus, response acquisition was observed under all reinforcement procedures at all drug doses. In the absence of the drug, most responding occurred on the operative lever when reinforcement was immediate. Such differential responding also developed under both nonresetting- and resetting-delay procedures when the delay was 8 seconds, but not when it was 16 seconds. *d*-Amphetamine did not affect the development of differential responding under any procedure. Thus, consistent with *d*-amphetamine's effects under repeated acquisition procedures, the drug had no detrimental effect on learning until doses that produced general behavioral disruption were administered.

Key words: delayed reinforcement, *d*-amphetamine, acquisition, tandem schedules, water, lever press, rats

There is a noteworthy paucity of research on the variables that influence free-operant response acquisition, as several behavior analysts have pointed out (e.g., Branch, 1977; Commons, Woodford, Boitano, Ducheney, & Peck, 1982; Dickinson, Watt, & Griffiths, 1992; Lattal & Gleeson, 1990). Branch asserted that the dearth of research is likely due to the fact that acquisition is an irreversible phenomenon that does not lend itself well to the steady-state methodology advocated by Sidman (1960). Recently, however, there has been an upsurge of interest in response acquisition, specifically in the effects of delayed reinforcement on the acquisition of free-operant responses.

Lattal and Gleeson (1990) exposed rats and pigeons to different tandem schedules of food delivery (e.g., tandem fixed-ratio [FR] 1 fixed-time [FT] 30 s), under which discrete responses (lever presses by rats and key pecks by pigeons) initiated unsignaled delay intervals that terminated with food delivery. Prior to such exposure, subjects learned to approach and eat from the food source, but no shaping or other procedures were implemented to train the responses. Despite the absence of shaping, both rats and pigeons acquired responding under the tandem schedules. Acquisition was not evident in subjects that were exposed to control procedures (e.g., no food delivery or response-independent food delivery).

Response acquisition with delayed reinforcement has been replicated in studies that employed different delay intervals (Dickinson et al., 1992; Schlinger & Blakely, 1994; Wilkenfield, Nickel, Blakely, & Poling, 1992), different delay procedures (van Haaren, 1992; Wilkenfield et al., 1992), different response topographies (Critchfield & Lattal, 1993; Schlinger & Blakely, 1994), and different species (e.g., Lattal & Metzger, 1994). The findings of these studies provide strong support for the conclusion of Lattal and Metzger: "neither explicit training procedures nor immediate reinforcement is necessary to establish operant behavior" (1994, p. 35).

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Drug effects on free-operant response acquisition with delayed reinforcement have not been reported but may be of interest to behavioral pharmacologists who have called for the development of new procedures for studying drug effects on the acquisition of new behavior (e.g., Evans & Wenger, 1992). Historically, studies of drug effects on learning have most often employed discrete-trials procedures (e.g., maze learning, signaled avoidance). In contrast, few procedures have been developed for the determination of drug effects on the acquisition of free-operant behavior. Those procedures that have been developed include the repeated acquisition of behavioral chains (e.g., Picker & Negus, 1993; Thompson & Moerschbaecher, 1979), acquisition of FR schedule performance (e.g., Gentry & Middaugh, 1994), and lever-press acquisition (Stolerman, 1971a, 1971b).

In the studies by Stolerman (1971a, 1971b), the effects of chlorpromazine and chlordiazepoxide on the acquisition of lever pressing by rats were examined. Subjects were given one 30-min habituation session during which they could explore the test chamber; then they were magazine trained. After magazine training, the rats were simply placed in the chamber, and lever presses produced food deliveries according to an FR 1 schedule that was in effect for the entire session. During FR 1 sessions, subjects that received chlorpromazine or chlordiazepoxide acquired responding more slowly than subjects that received saline. Moreover, both drugs reduced the total number of responses per session relative to saline-control levels.

The purpose of the present experiment was to examine further the utility of procedures similar to those used by Stolerman (1971a, 1971b) for studying drug effects on learning by examining the effects of a different drug, *d*-amphetamine. In addition, the present study extended the work of Stolerman by incorporating some of the procedures used to demonstrate response acquisition with delayed reinforcement (e.g., Wilkenfield et al., 1992).

METHOD

Subjects

Two hundred twenty-four experimentally naive male Sprague-Dawley rats, 70 to 80 days old at the beginning of the experiment, were housed in groups of 4 with unlimited access to food in a colony area with controlled lighting (12 hr light, 12 hr dark), temperature (22 to 24 °C), and humidity (60% to 70%). The rats weighed 260 to 340 g and were water deprived for 24 hr prior to each experimental session.

Apparatus

Eight operant conditioning chambers (MED Associates Model ENV-007), measuring 21 cm high, 21 cm wide, and 28 cm long, were used. Each chamber was equipped with two response levers, approximately 8.5 cm apart and 7 cm above the floor, and an automatic liquid dipper that delivered 0.1 ml of water through an aperture that was centrally located 2 cm above the chamber floor. A force of 0.14 N was required to operate the levers. Constant ambient illumination was provided by a 7-W white light that was centrally located on the front wall 2 cm below the ceiling. Each chamber was housed in a sound-attenuating cubicle. A fan mounted on the cubicle provided constant ventilation and masking noise. Experimental events and data recording were accomplished using an IBM®-compatible computer and software (MED-PC Version 2.9) and interfacing from MED Associates.

Behavioral Procedure

Dipper training. Procedures for the present experiment were similar to those used by Wilkenfield et al. (1992). All rats were exposed to one 90-min session of dipper training. Initially, each rat was placed in the chamber with the response levers removed. Then, the houselight was illuminated and a variable-time (VT) 60-s schedule of water delivery was implemented. Under this schedule, 4-s water deliveries occurred aperiodically on average every 60 s, regardless of the subject's behavior. Removal of the levers during dipper training prevented water deliveries from strengthening lever pressing. The rats were given 30 min of free access to water in their home cages immediately following the dipper training session. The rats were next water deprived for 24 hr and were then exposed to one of four behavioral procedures, described below.

The following conditions were in effect under all of the procedures: (a) Two response

levers were present, and the locus of the lever that produced water (operative lever) was counterbalanced across subjects. (b) The other lever (inoperative lever) remained inoperative for the entire session (i.e., presses on this lever never had programmed consequences). (c) The chamber remained illuminated throughout the session. (d) The session duration was 8 hr (480 min). (e) The assignment of subjects to procedures was random.

Nonresetting-delay procedure. Two groups of 32 rats were exposed to a tandem FR 1 FT *n*-s schedule of water delivery. Under this procedure, the first press of the operative lever and each subsequent first press of the operative lever after water delivery produced, after an FT interval (delay) of *n* s, 4-s access to the water-filled dipper. Presses during the delay had no programmed consequences. Two delay values were arranged. One group of 32 rats was exposed to an 8-s delay, and another group of 32 was exposed to a 16-s delay.

Because no single delay procedure provides an uncontaminated assay of the effects of delayed reinforcement on the acquisition of free-operant behavior (Wilkenfield et al., 1992), two different delay procedures were employed in the present study. The nonresetting-delay procedure just described permits responses to occur closer in time to food delivery than the programmed delay, resulting in obtained delays that are shorter than programmed delays. Therefore, a resetting-delay procedure was also employed; it ensured that obtained and programmed delays were equivalent.

Resetting-delay procedure. Two groups of 32 rats were exposed to a tandem FR 1 not-responding-longer-than-*t* ($\bar{R} > t$) schedule of water delivery. Under this procedure, the first press on the operative lever produced, after a *t*-s delay, 4-s access to the water-filled dipper. Subsequent presses on the operative lever during the delay reset the delay interval. Two delay values were arranged. One group of 32 rats was exposed to an 8-s delay, and the other group was exposed to a 16-s delay.

Control procedures. Three control procedures were arranged. To determine the extent to which stimulants increase the rate of lever pressing independently of reinforcement contingencies, drug effects were determined in a group of 32 rats that were exposed to conditions under which water was never delivered.

To evaluate the *relative* sensitivity to drug effects of responding acquired by exposure to delayed reinforcement, drug effects were determined in a group of 32 rats that were exposed to an FR 1 schedule of water delivery. Under this procedure, each press of the operative lever immediately produced 4-s access to water.

To determine the relative sensitivity to drug effects of responding under conditions of response-dependent versus response-independent water delivery, drug effects were determined in a group of 16 rats that were exposed to a VT schedule of response-independent water delivery. The frequency and distribution of water deliveries for each of these rats were yoked to 1 of 16 master rats responding under the tandem FR 1 FT 8-s schedule of water delivery described above. That is, each yoked-control rat received water when water was delivered to a master rat.

Pharmacological Procedure

Each group of 32 rats was divided into four squads of 8. Squad 1 received an injection of saline solution (vehicle), and Squads 2, 3, and 4 received 1.0, 5.6, and 10.0 mg/kg *d*-amphetamine sulfate (Sigma), respectively. All injections were given intraperitoneally 10 min prior to the start of the experimental session. The drug was dissolved in a 0.85% isotonic saline solution to a constant injection volume of 1 ml/kg. Doses were selected on the basis of prior studies of the effects of *d*-amphetamine on schedule-controlled behavior (McKearny & Barrett, 1978).

RESULTS

Cumulative responses on the operative and inoperative levers were recorded for each subject in 5-min bins across the entire session. Figure 1 shows mean cumulative operative-lever responses for each of the four squads of 8 rats under each experimental procedure. Figures 2 through 8 depict cumulative operative-lever responses of individual subjects and mean cumulative operative- and inoperative-lever responses for each squad of 8 rats under one experimental procedure.

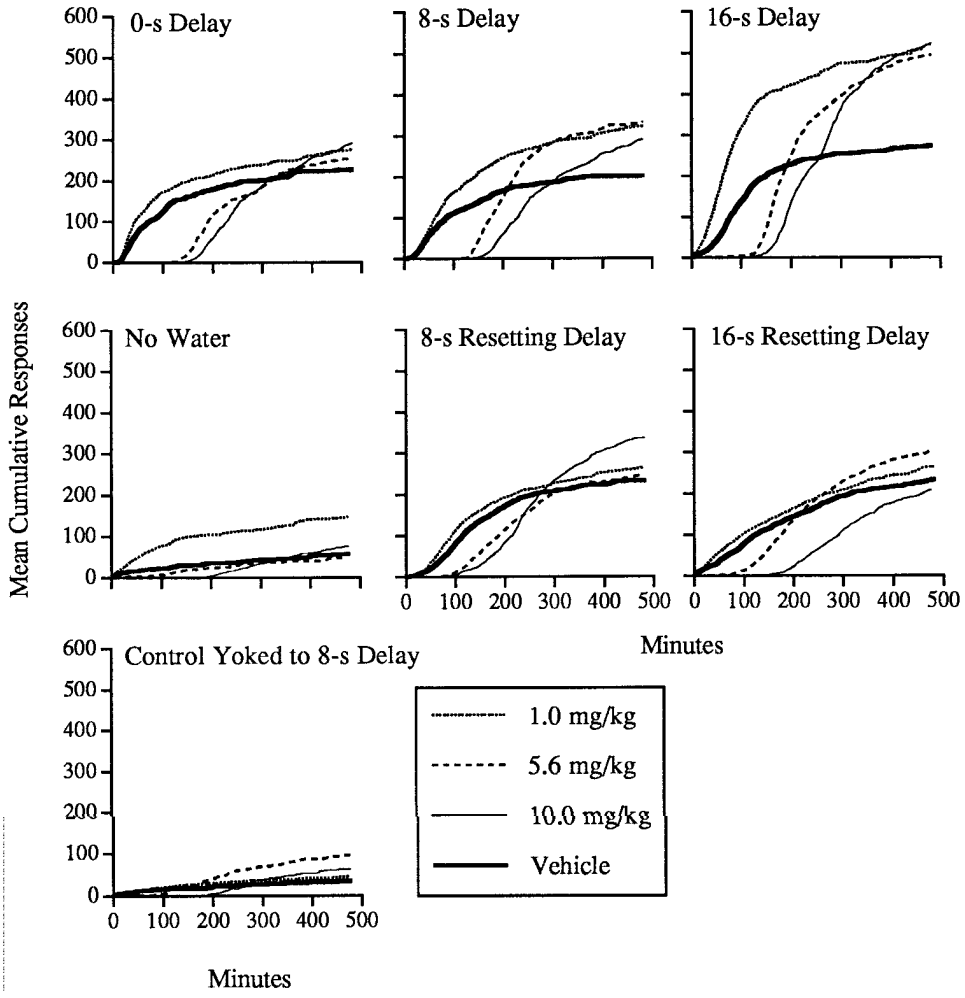

Fig. 1. Mean cumulative responses on the operative lever during the entire 480-min session under each experimental procedure. Each line represents the mean operative-lever responding of 8 rats exposed to the indicated dose of *d*-amphetamine. The thick solid lines depict acquisition in the absence of drug (i.e., during sessions preceded by vehicle injections). Data were collected in 5-min bins.

Drug Effects on Cumulative and Overall Responding

Responding in the absence of drug. Figures 1 to 8 show that, in the absence of drug, substantial operative-lever pressing occurred in all rats exposed to procedures that arranged response-dependent water delivery, but not in those exposed to procedures that either did not arrange water delivery or arranged response-independent water delivery. In most cases, lever pressing began early in the session (within the first 5 to 10 min) and was sustained at a moderate to high rate for a substantial period, regardless of whether responding produced immediate or delayed reinforcement. The majority of responses by rats under the no-water procedure and by the yoked rats under the yoked-control procedure were emitted early in the session, but persistent responding was not observed in these subjects. Although substantial between-subject variability is evident with respect to total responses per session, the mean cumulative records appear to be reasonably representative of the course of acquisition for individual subjects. With immediate reinforcement and both nonresetting delays, an abrupt increase in response rate typically occurred and was sustained for several minutes,

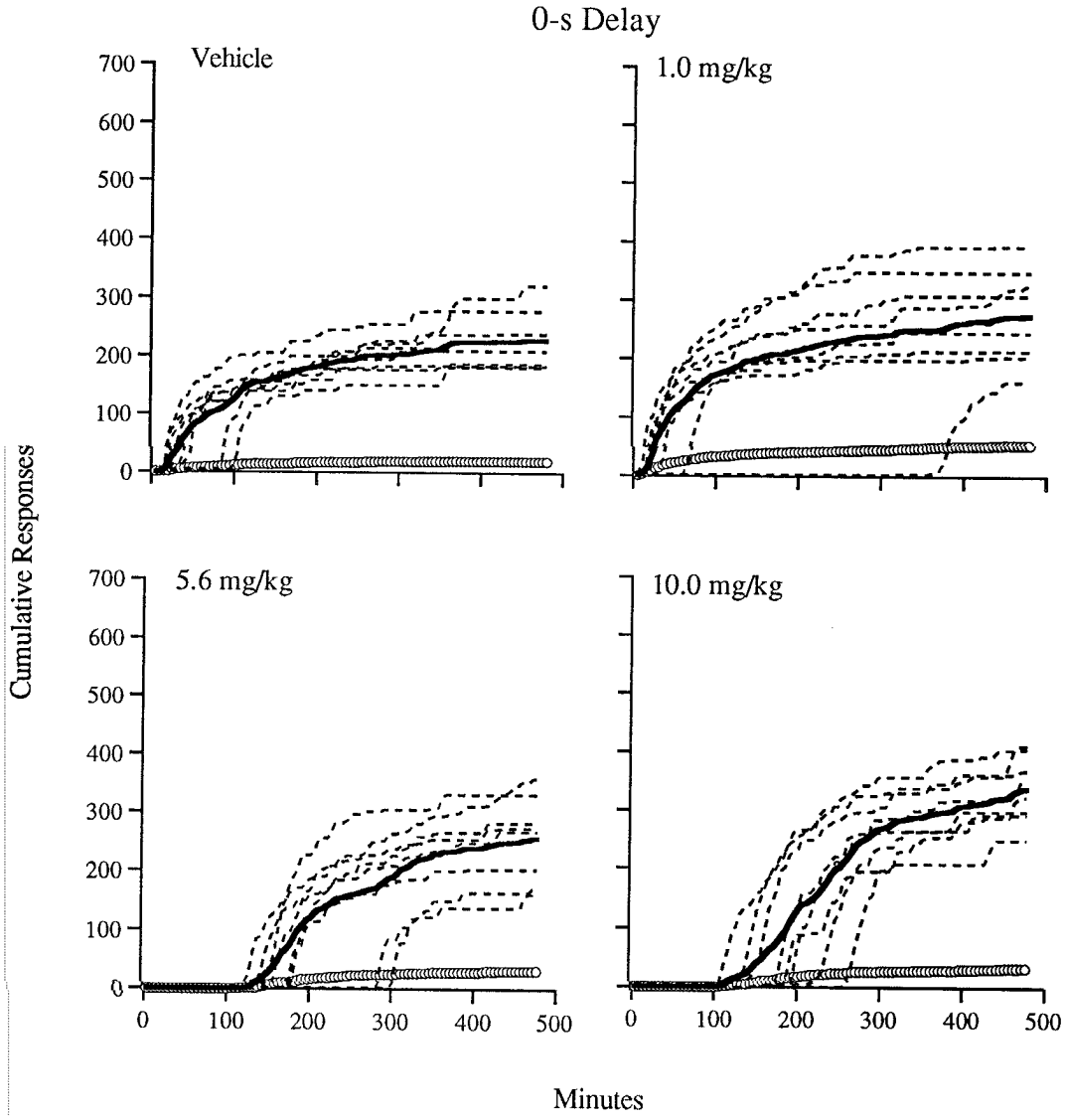

Fig. 2. Cumulative responses on the operative lever during the entire 480-min session under the immediate-reinforcement (0-s delay) procedure. Each dotted line represents data from 1 of 8 individual rats exposed to the indicated dose of *d*-amphetamine. Solid lines represent the group mean. Lines of open circles represent mean cumulative responding on the inoperative lever. The panel labeled "Vehicle" depicts acquisition in the absence of drug (i.e., during sessions preceded by vehicle injections).

followed by a rapid decline in rate. Under the resetting-delay procedures, increases in response rate were usually less abrupt, and cumulative records of operative-lever responding were not as negatively accelerated as they were with immediate reinforcement and nonresetting delays.

Mean cumulative inoperative-lever responding was substantially lower than cumulative operative-lever responding under all reinforcement procedures except the 16-s resetting delay. In general, mean levels of inoperative-lever responding were higher with delayed reinforcement than with immediate reinforcement. Mean inoperative-lever rates were higher under 16-s delays than under 8-s delays and were higher under resetting delays than under nonresetting delays. Under the

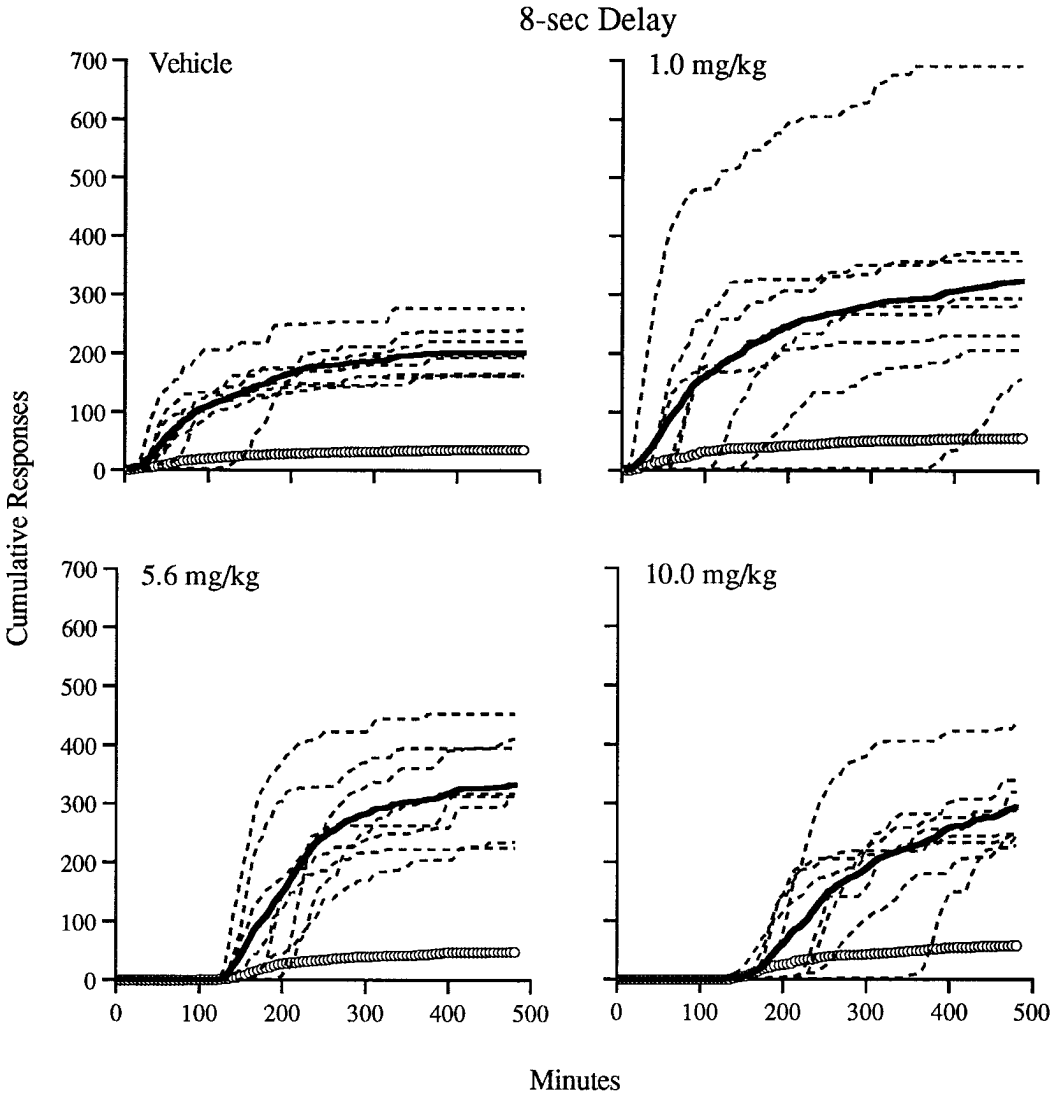

Fig. 3. Cumulative responses on the operative lever during the entire 480-min session under the 8-s nonresetting-delay procedure. For details see Figure 2.

16-s resetting delay, rates of operative-lever and inoperative-lever responding were essentially equal throughout the session, indicating an absence of differential responding on the operative lever.

The point at which mean cumulative records of operative and inoperative responding began to separate (i.e., the point at which differential responding began to develop) was a function of delay length and delay type. That is, separation in the mean cumulative records occurred later in the session with 16-s delays than with 0-s or 8-s delays and occurred later with resetting delays than with nonresetting delays. Further analysis of inoperative-lever responding is provided below.

To facilitate interpretation of the cumulative records, overall response-rate measures were calculated and analyzed both visually and statistically. Figure 9 depicts mean overall response rates on the operative and inoperative levers under each procedure. The data for the no-water procedure represent the average of the rates on both levers, because neither lever was operative and no substantial bias for either lever was evident. This figure

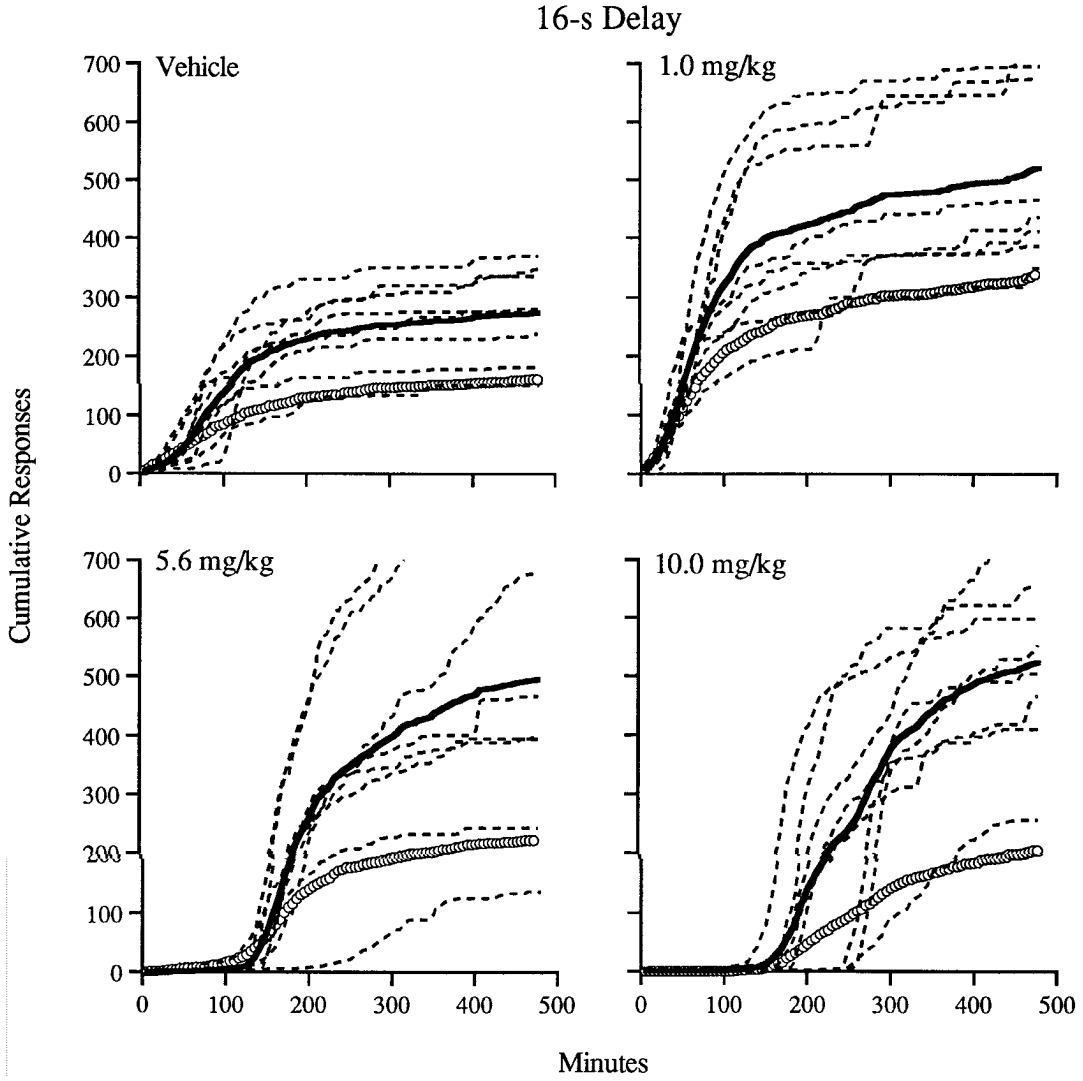

Fig. 4. Cumulative responses on the operative lever during the entire 480-min session under the 16-s nonresetting-delay procedure. Cumulative records that end before 480 min represent cumulative responding that extended beyond the vertical axis and were 803 and 839 responses for 2 rats exposed to 5.6 mg/kg *d*-amphetamine and 747 for 1 rat exposed to 10.0 mg/kg *d*-amphetamine. For details see Figure 2.

shows that mean overall rates of operative-lever responding were higher with immediate reinforcement and both values of the nonresetting and resetting delays than under the no-water procedure. Analysis of variance was conducted on operative-lever rates and revealed a significant overall effect of the reinforcement procedures ($F = 18.14$, $p = .001$). Multiple comparison tests (Fisher's PLSD) revealed that overall rates under each reinforcement procedure were significantly higher than rates under the no-water procedure ($p < .05$). Such differential levels of responding confirm that response acquisition was obtained with both immediate and delayed reinforcement. Overall rates under delayed reinforcement were not significantly different from rates with immediate reinforcement ($p > .05$), suggesting that reinforcement delay did not attenuate acquisition in terms of overall levels of responding.

Responding in the presence of drug. Figures 1 to 8 show that 1.0 mg/kg *d*-amphetamine only slightly enhanced mean rates of opera-

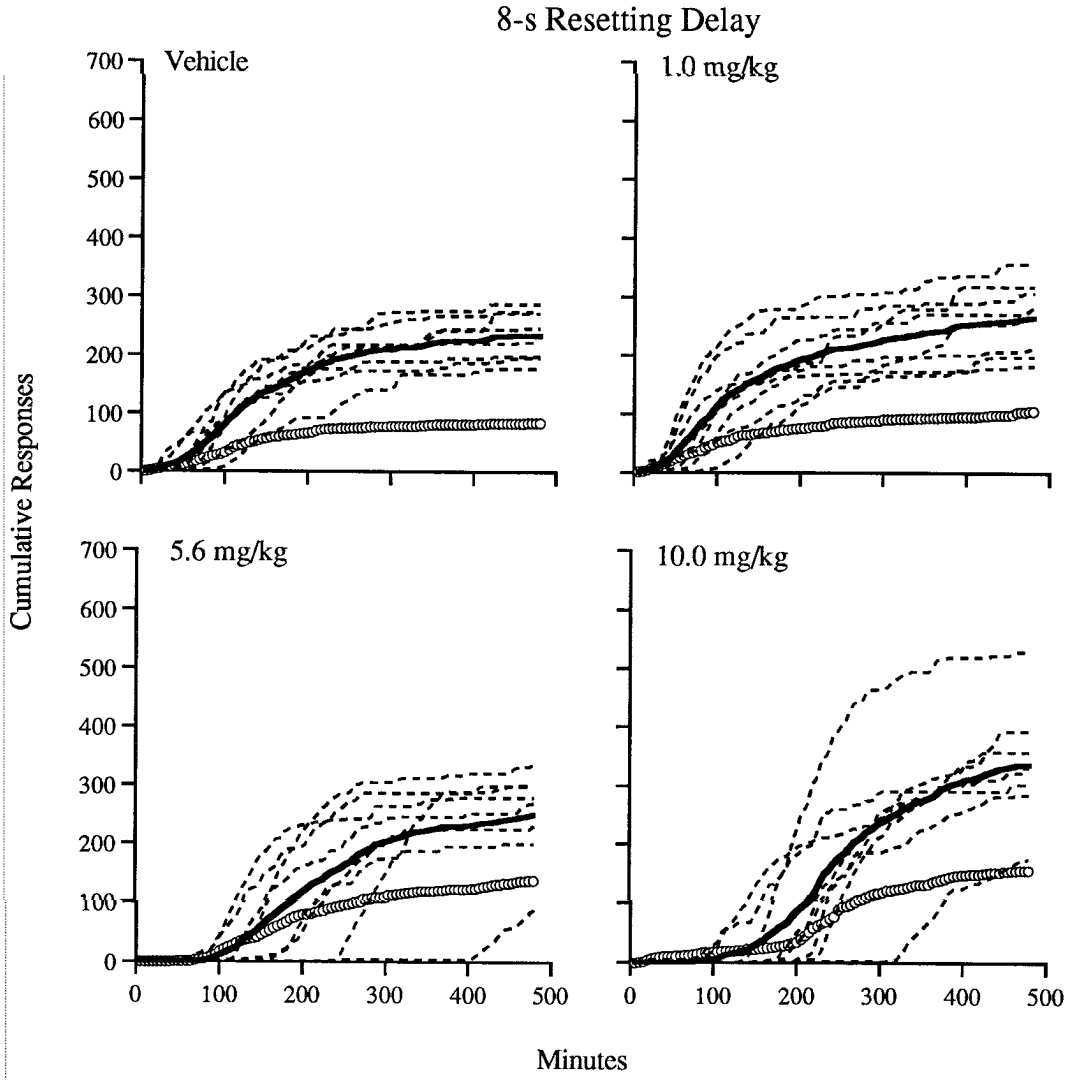

Fig. 5. Cumulative responses on the operative lever during the entire 480-min session under the 8-s resetting-delay procedure. For details see Figure 2.

tive-lever responding under the immediate-reinforcement and resetting-delay procedures but markedly enhanced mean rates of operative-lever responding under the nonresetting procedure, with the largest relative effect seen with the 16-s delay. In general, in the presence of drug, considerable between-subject variability was evident in total operative-lever responses per session and in the points in time at which substantial operative-lever responding began to occur.

The mean level of operative-lever responding was also higher under the no-water procedure for rats exposed to 1.0 mg/kg *d*-amphetamine than for rats exposed to vehicle. Like subjects exposed to vehicle, rats exposed to 1.0 mg/kg *d*-amphetamine emitted the majority of responses early in the session, but responding persisted for a longer period in the animals that received drug. The mean level of operative-lever responding did not differ between yoked-control rats exposed to 1.0 mg/kg *d*-amphetamine and those exposed to vehicle.

d-Amphetamine doses of 5.6 and 10.0 mg/kg slowed acquisition by producing a

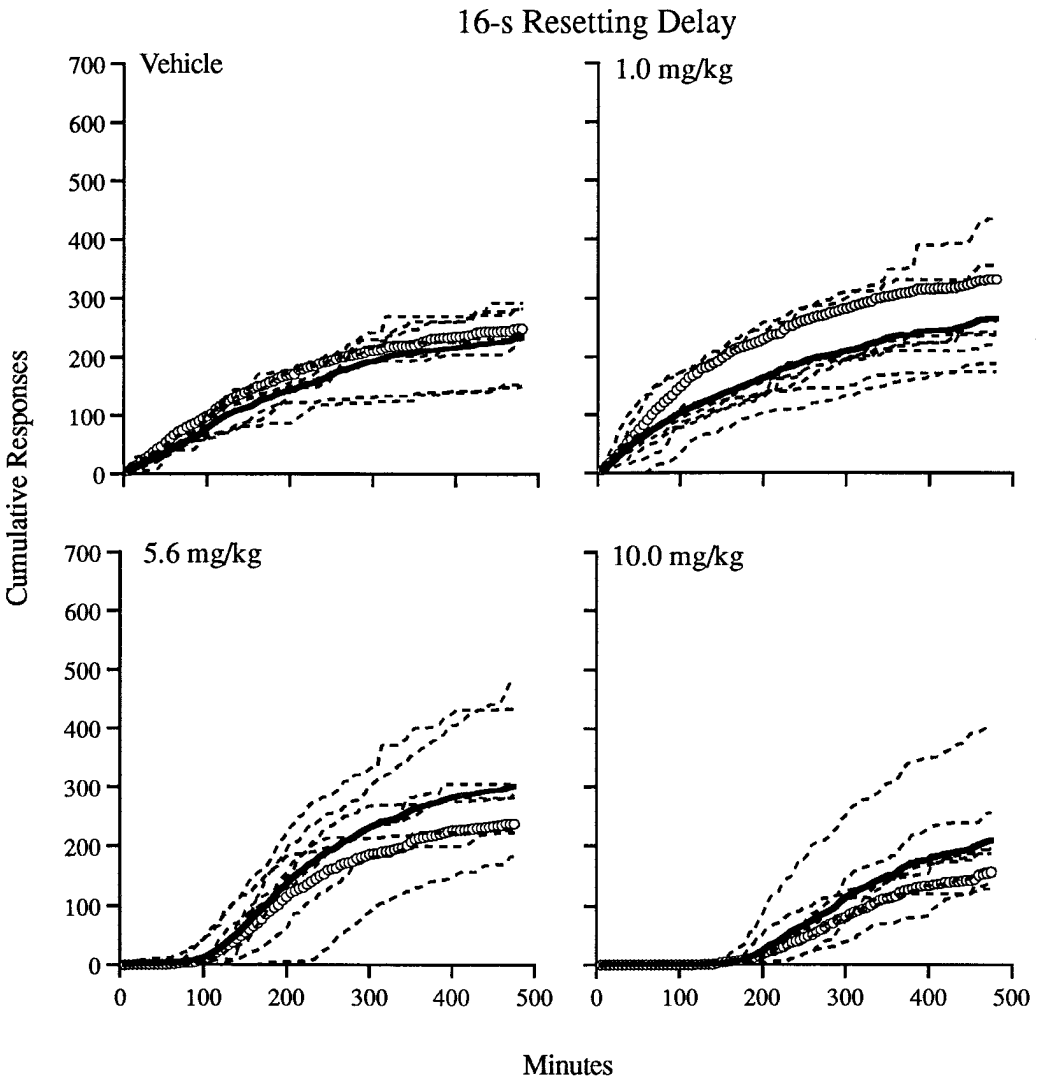

Fig. 6. Cumulative responses on the operative lever during the entire 480-min session under the 16-s resetting-delay procedure. For details see Figure 2.

general suppression of responding for the first 100 min of the session or longer. At these doses, stereotypy, predominantly involving sniffing and licking the floor of the chamber, was observed in all rats at the beginning of the session. At 5.6 and 10 mg/kg *d*-amphetamine, most rats exposed to the immediate-reinforcement or nonresetting-delay procedures began to emit operative-lever responses within the first 200 min of the session. Once responding occurred in these animals, its rate increased rapidly, in a pattern similar to that observed in rats that received lower doses or no drug. Overall, the mean number of responses emitted under the nonresetting delay was considerably greater in rats exposed to the 5.6 and 10.0 mg/kg doses than in rats exposed to vehicle.

For rats exposed to 5.6 and 10.0 mg/kg doses under the resetting-delay procedure, responding was acquired relatively slowly. As with the 1.0 mg/kg dose, substantial between-subject variability was evident in total operative-lever responses per session and in the points in time at which substantial operative-lever responding began to occur. This vari-

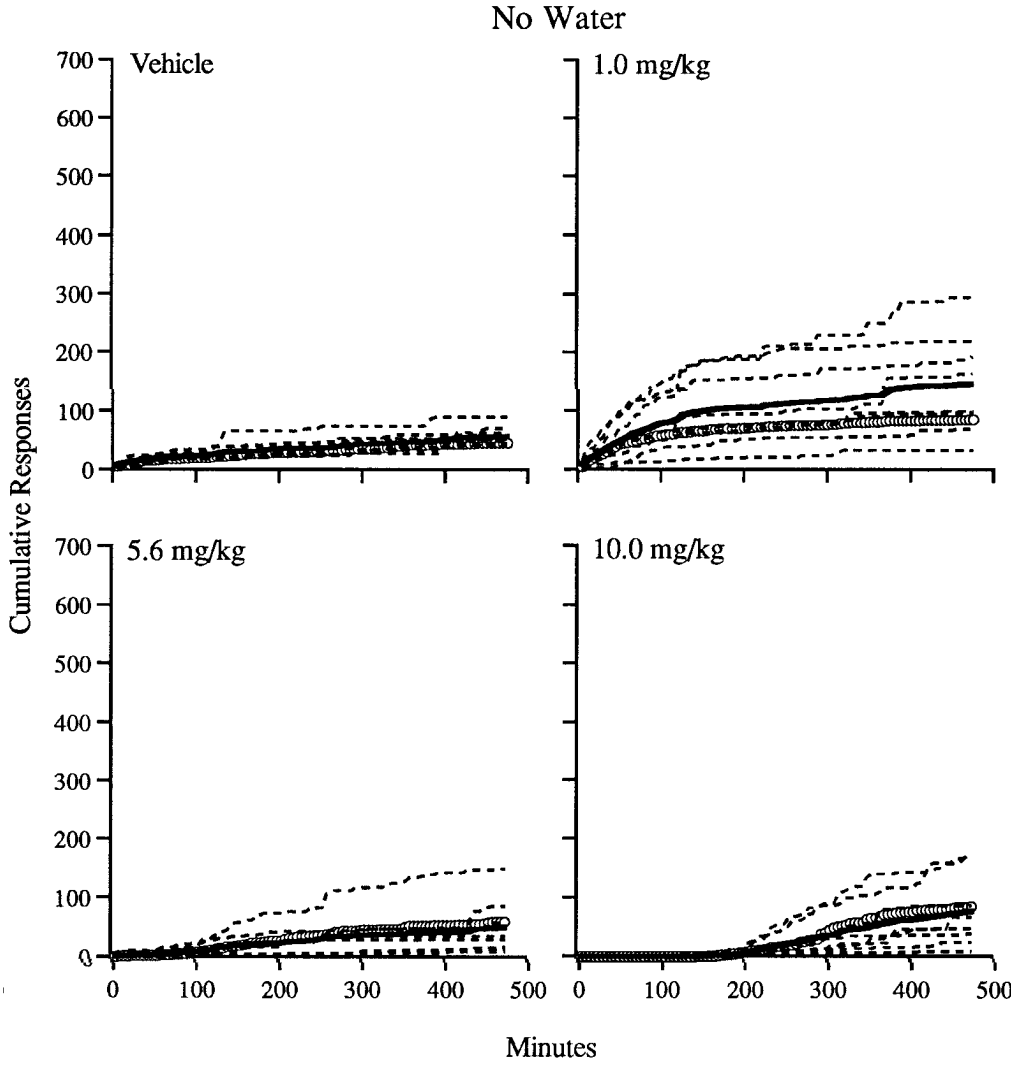

Fig. 7. Cumulative responses on the operative lever during the entire 480-min session under the no-water procedure. For details see Figure 2.

ability was somewhat greater under the nonresetting-delay procedure than under the resetting-delay procedure.

In general, *d*-amphetamine increased the rate of operative-lever responding, although not always significantly, and did not affect inoperative-lever responding (the 16-s resetting-delay condition is an exception). Figure 9 shows that overall operative-lever response rates under the immediate-reinforcement procedure were slightly higher for rats exposed to the 1.0 and 5.6 mg/kg doses than for rats exposed to vehicle. The mean operative-lever response rate under this procedure for rats exposed to the 10.0 mg/kg dose was considerably higher than for rats exposed to vehicle. Analysis of variance confirmed a significant drug effect under the immediate-reinforcement procedure ($F = 3.886$, $p = .019$). Multiple comparison tests revealed that mean operative-lever response rates were significantly above the vehicle control level at the 10.0 mg/kg dose but not at the 1.0 and 5.6 mg/kg doses.

Mean overall operative-lever rates were also higher under the nonresetting-delay procedure for rats exposed to drug. Although the mean operative-lever rate was higher under

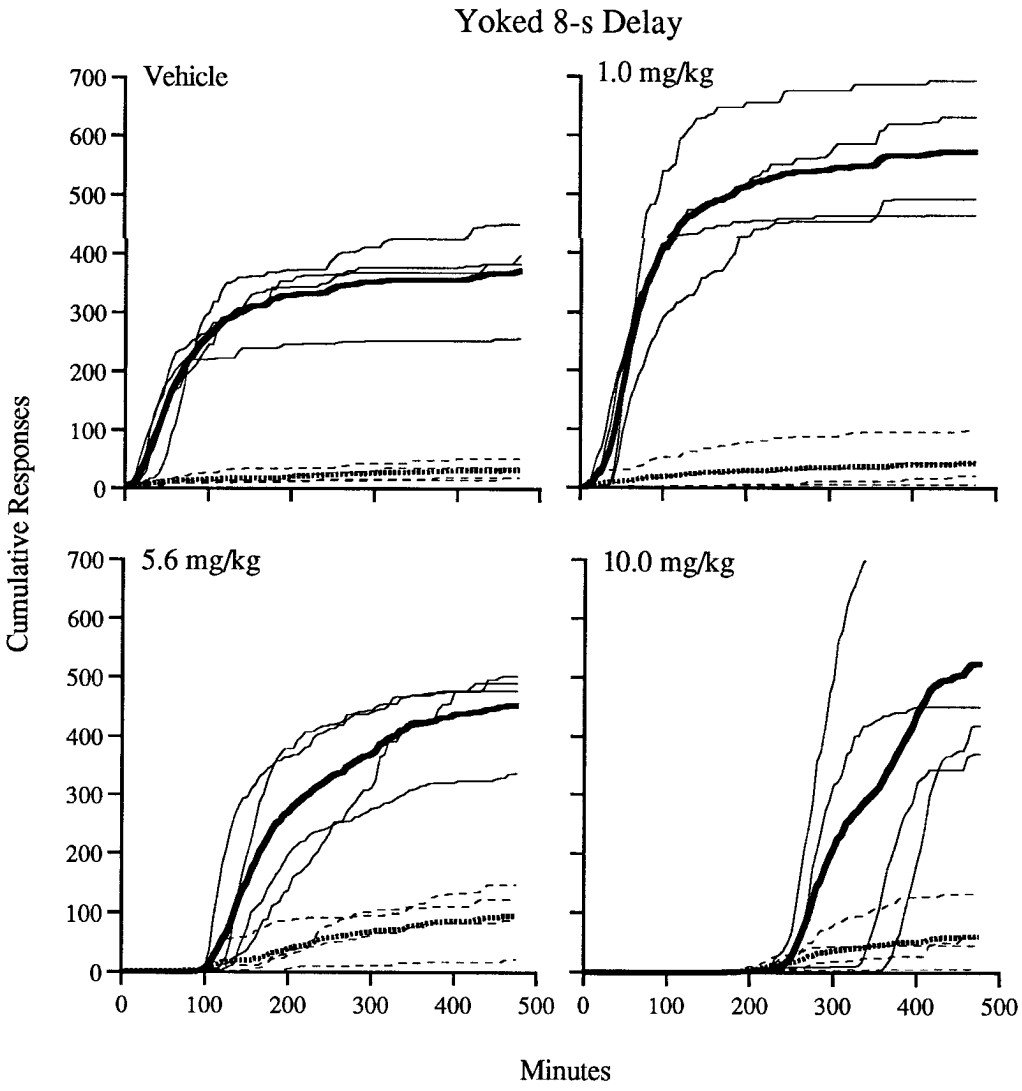

Fig. 8. Cumulative responses on the operative lever during the entire 480-min session under the yoked-control procedure. Broken lines represent cumulative responding on the operative lever for 1 of 4 control rats that were yoked to master rats responding under the 8-s nonresetting-delay procedure. Thick solid lines represent the mean cumulative responding of these control rats.

the 8-s nonresetting delay for rats exposed to each dose of drug than for rats exposed to vehicle, analysis of variance revealed that this effect approached significance only at the .05 level ($F = 2.826$, $p = .0567$). In contrast, substantially higher mean rates of operative-lever responding occurred under the 16-s nonresetting delay at every dose. Analysis of variance revealed a significant overall drug effect under this procedure ($F = 3.871$, $p = .0196$), and multiple comparisons confirmed that overall operative-lever rates at each dose of drug were significantly different from vehicle ($p < .05$).

Under the 8-s resetting-delay procedure, the mean overall operative-lever response rate in rats that received 10 mg/kg *d*-amphetamine was substantially higher than the mean rate for control rats. Rates in rats that received the 1.0 or 5.6 mg/kg dose were similar to the control mean. Analysis of variance confirmed a significant drug effect under this

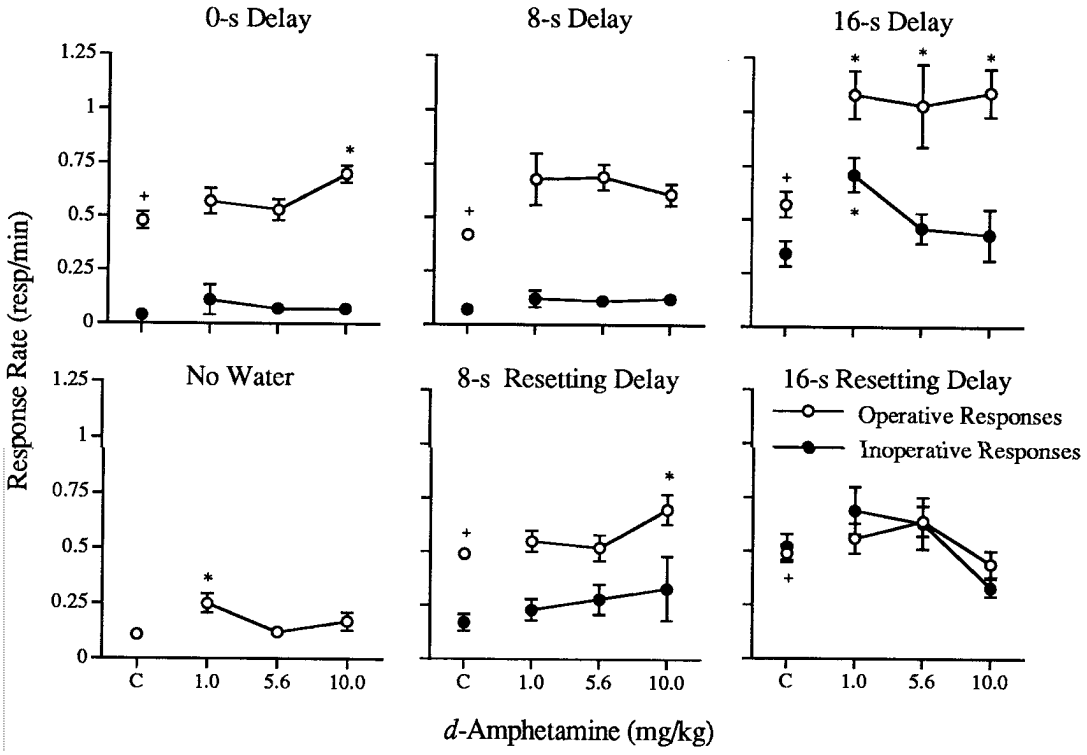

Fig. 9. Mean overall response rates on the operative and inoperative levers under the indicated experimental procedure. Each data point represents the mean rate for 8 rats. Data points above C indicate mean rates for rats exposed to vehicle. Other data points represent mean rates for rats exposed to the indicated dose of *d*-amphetamine. The data for the no-water procedure represent the average of the rates on both levers, because neither lever was operative and no substantial bias for either lever was evident. Vertical lines represent standard errors of the mean. [+]Significantly different from the no-water vehicle mean, $p < .05$. [*]Significantly different from vehicle under the same procedure, $p < .05$.

procedure ($F = 3.015$, $p = .0466$), and multiple comparisons revealed that mean operative-lever rates were significantly different from vehicle only for rats exposed to the 10.0 mg/kg dose ($p < .05$).

Mean operative-lever response rates under the 16-s resetting-delay procedure were slightly higher for rats exposed to 1.0 and 5.6 mg/kg *d*-amphetamine than for rats exposed to vehicle, whereas the rate for rats exposed to the 10.0 mg/kg dose was slightly below the control level. However, analysis of variance indicated that mean operative-lever response rates under the 16-s nonresetting delay in rats exposed to drug were not significantly different than in rats exposed to vehicle ($F = 2.179$, $p = .1128$).

Mean response rates under the no-water procedure were considerably higher than the control level for rats exposed to 1.0 mg/kg *d*-amphetamine but not for those exposed to 5.6 and 10.0 mg/kg. Analysis of variance confirmed a significant drug effect under this procedure ($F = 3.753$, $p = .022$), and multiple comparison tests indicated that response rates were significantly higher for rats exposed to 1.0 mg/kg, but not to 5.6 and 10.0 mg/kg, than for rats exposed to vehicle.

In most cases, mean overall rates of inoperative-lever responding were not appreciably affected by any dose of drug under any procedure. Slightly higher mean rates were observed in some groups exposed to drug than in control groups, but the differences were small and inconsistent across doses and procedures. An exception is the substantial difference in inoperative-lever response rates that were observed between control rats and rats that received 1.0 mg/kg *d*-amphetamine under the 16-s nonresetting-delay procedure.

Table 1

Individual and mean obtained delays for subjects exposed to the indicated dose of *d*-amphetamine and length of nonresetting delay.

	8-s delay				16-s delay			
	Dose (mg/kg)				Dose (mg/kg)			
	C	1.0	5.6	10.0	C	1.0	5.6	10.0
	7.03	3.90	4.86	5.97	9.01	8.21	11.12	8.24
	6.10	5.10	4.47	7.50	9.94	11.50	10.15	10.56
	6.26	6.36	4.45	4.98	10.27	9.61	8.08	8.42
	7.46	6.16	6.09	6.90	9.27	8.90	10.0	9.38
	6.12	7.12	6.17	4.84	12.78	11.38	7.84	11.54
	7.49	7.71	5.40	3.91	11.10	9.32	8.23	8.02
	5.79	5.90	6.18	5.33	10.57	9.73	8.87	7.16
	6.01	5.66	4.40	5.85	11.44	9.70	11.43	6.34
M	6.53	5.99	5.25	5.66	10.55	9.79	9.47	8.71
SEM	0.24	0.42	0.29	0.41	0.43	0.40	0.50	0.61

Analysis of variance of overall inoperative-lever rate data under this procedure confirmed a significant drug effect ($F = 3.493$, $p = .0286$), and multiple comparison tests confirmed that the mean rate of inoperative-lever responding was significantly higher for rats exposed to 1.0 mg/kg *d*-amphetamine, but not to 5.6 and 10.0 mg/kg, than for rats exposed to vehicle.

Drug Effects on Obtained Delays

Although the nominal reinforcement delays under the nonresetting-delay procedure were 8 and 16 s, obtained delays were consistently shorter. Table 1 presents the mean obtained delays for individual subjects under each nonresetting-delay value and dose of drug. As this table shows, in the absence of drug, obtained delays were shorter than nominal delays. Moreover, obtained delays were slightly shorter for rats exposed to drug than for rats exposed to vehicle. However, analysis of variance did not indicate a significant drug effect on obtained delays with either the 8-s ($F = 2.438$, $p = .0854$) or 16-s ($F = 2.415$, $p = .0875$) delays.

Drug Effects on the Speed of Acquisition

Speed in the absence of drug. To compare the speed of acquisition across procedures, linear regression lines were fitted to the cumulative response data of individual subjects via the method of least squares. This was accomplished by regressing cumulative responses on cumulative session time across the first 100 min of the session. Data from only the first 100 min were used because visual inspection of the cumulative records indicated that acquisition characteristically was evident within this period, after which curves began to flatten substantially. The mean slopes for each vehicle-only group are presented as white bars in Figure 10, which shows that the slopes obtained under the reinforcement procedures were substantially higher than the slopes obtained under the no-water procedure. Analysis of variance confirmed that these differences were significant ($F = 6.626$, $p = .001$). Multiple comparisons revealed that the slope under each reinforcement procedure was significantly higher than the slope under the no-water procedure ($p < .05$). Moreover, it appeared that acquisition was slower (i.e., slopes were lower) under resetting procedures than under the 0-s delay procedure. Multiple comparisons revealed that the slope obtained under the 16-s, but not the 8-s, resetting delay was significantly lower than the slope obtained under the 0-s delay ($p < .05$). Thus, the nonresetting-delay procedure did not attenuate the speed of acquisition, but the resetting-delay procedure did, albeit significantly so only with the 16-s delay.

Speed in the presence of drug. Because 1.0 mg/kg *d*-amphetamine increased overall rates of responding under some procedures, it was of interest to determine whether this dose increased the speed of acquisition relative to vehicle across the first 100 min of the session. To make this determination, regression lines were fitted to the cumulative response data of individual subjects exposed to

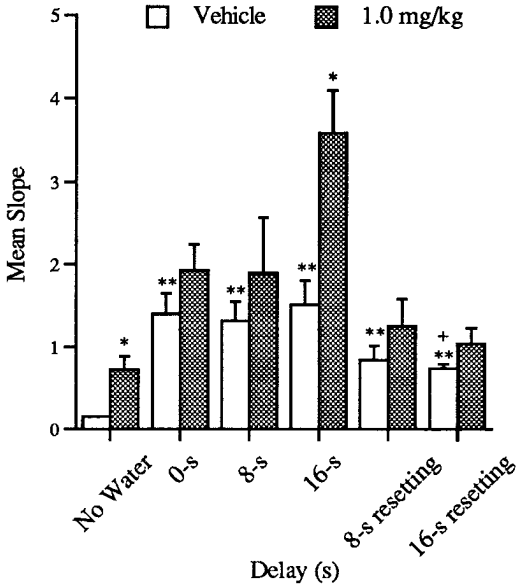

Fig. 10. Mean slope of regression lines fitted to the cumulative records of operative-lever responding during the first 100 min of the session under the indicated experimental conditions. Each bar represents the mean of individual slopes for 8 rats. White bars indicate mean slopes for rats exposed to vehicle; dark bars present mean slopes for rats exposed to 1.0 mg/kg *d*-amphetamine. The higher the slope, the faster the acquisition in terms of total responses emitted. Vertical lines represent standard errors of the mean. *Significantly different from vehicle under the same procedure, $p < .05$. **Significantly different from no-water vehicle, $p < .05$. +Significantly different from immediate-reinforcement (0-s delay) vehicle, $p < .05$.

the 1.0 mg/kg dose via the methods described previously. Almost all rats that received the 5.6 and 10.0 mg/kg doses emitted too few responses during the first 100 min to permit meaningful analysis. The mean slopes for each group are presented in Figure 10. This figure shows that the mean slope obtained under all procedures was higher for rats exposed to the 1.0 mg/kg dose than for rats exposed to vehicle. The mean slope was significantly different from vehicle only under the no-water ($F = 12.218$, $p = .0036$) and 16-s nonresetting-delay ($F = 12.882$, $p = .003$) procedures. Analysis of variance confirmed a significant effect of reinforcement procedures at 1.0 mg/kg ($F = 6.381$, $p = .002$). Multiple comparisons between slopes under the no-water and reinforcement procedures at this dose revealed that mean slopes were significantly higher under the immediate-reinforcement and nonresetting-delay procedures than under the no-water procedure ($p < .05$). Although slopes at the 1.0 mg/kg dose under the resetting-delay procedures were higher than slopes at this dose under the no-water procedure, the difference between them was not statistically significant ($p > .05$).

Drug Effects on Response Efficiency

Efficiency in the absence of drug. To examine the effect of delayed reinforcement on response efficiency, the proportion of inoperative-lever responses and the proportion of responses in the delay interval were calculated for rats exposed to the nonresetting- and resetting-delay procedures. For comparison, the proportion of inoperative-lever responses for rats exposed to the 0-s delay procedure was also calculated. Response efficiency is inversely related to these two measures; as the proportion of inoperative-lever responses and responses in the delay interval increases, response efficiency decreases (cf. Critchfield & Lattal, 1993; Schlinger & Blakely, 1994).

Mean proportions of total responses emitted on the inoperative lever and of total responses emitted during the delay are shown in Figure 11. In the absence of drug, the mean proportion of inoperative-lever responses was greater when reinforcement was delayed than when it was immediate. Analysis of variance confirmed a significant effect of the delay procedures on this measure of performance ($F = 26.83$, $p = .001$). Multiple comparisons revealed that proportions of inoperative-lever responding under the 16-s nonresetting delay and both the 8-s and 16-s resetting-delay procedures were significantly greater than proportions under the immediate reinforcement procedure ($p < .05$). The mean proportion of inoperative-lever responding with the 8-s nonresetting delay, although slightly greater, was not significantly different from the mean proportion with immediate reinforcement ($p > .05$).

Under both the resetting- and nonresetting-delay procedures, the proportion of inoperative-lever responding increased as a direct function of delay length, with significantly higher proportions obtained with the 16-s delay than with the 8-s delay ($p < .05$). The mean proportion of inoperative-lever responding also varied as a function of delay type, with

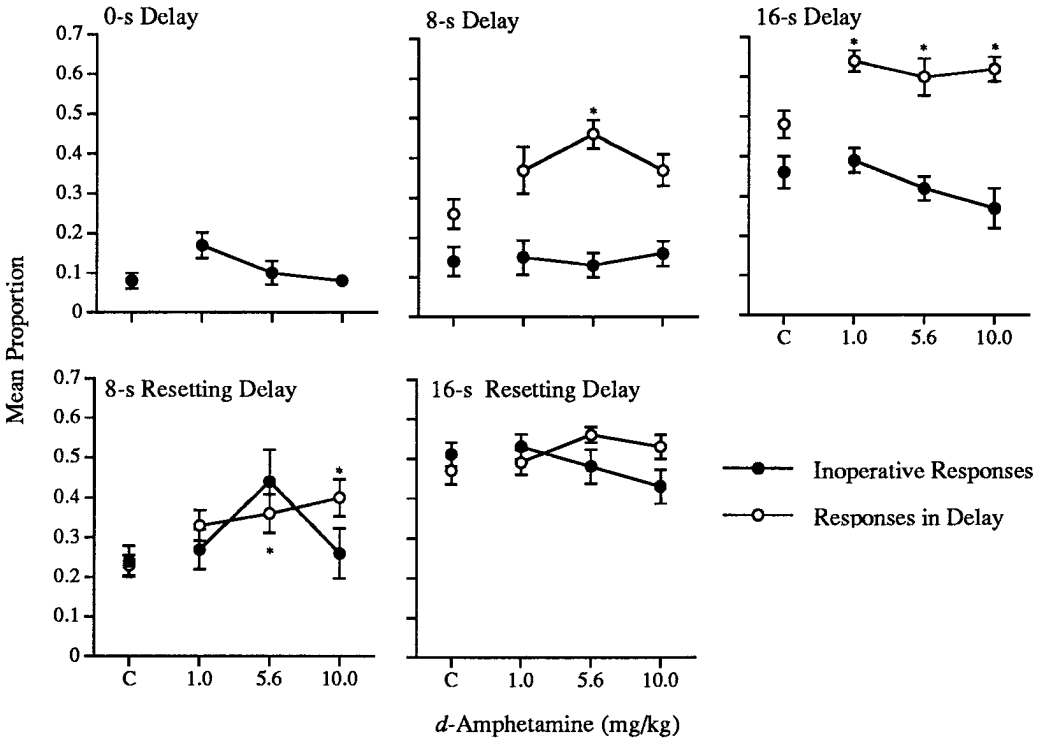

Fig. 11. Mean proportion of inoperative-lever responding (inoperative responses divided by total responses) and responding in the delay interval under the indicated experimental procedure. Each data point represents the mean response rate for 8 rats. Data points above C indicate mean proportions for rats exposed to vehicle; the other data points indicate response proportions for rats exposed to the indicated dose of *d*-amphetamine. Vertical lines represent standard errors of the mean. *Significantly different from vehicle under the same procedure, $p < .05$.

significantly higher proportions observed under the resetting procedure than under the nonresetting procedure ($p < .05$).

Figure 11 also shows that the mean proportion of responses in the delay interval was higher with the 16-s delay than with the 8-s delay for both the nonresetting- and resetting-delay procedures ($p < .05$). In contrast to the data obtained for the proportion of inoperative-lever responses, the proportion of responses in the delay did not differ as a function of whether resetting or nonresetting delays were arranged ($p > .05$).

The development of differential responding on the two levers can be considered as a measure of sensitivity to programmed consequences (learning) as well as a measure of response efficacy. Because substantial operative-lever responding was observed within the first 100 min of the session in the absence of drug, the mean proportion of responses to the inoperative lever was calculated for each 5-min bin during the first 100 min. These proportions are depicted in Figure 12. Proportions of .5 indicate an absence of differential responding (i.e., equal responding on both levers). Proportions ranging from .5 to 0 indicate increasing degrees of differential responding (i.e., more responding on the operative lever). As this figure shows, differential responding developed within the first 25 min of the session under the immediate-reinforcement procedure. Differential responding was also evident early in the session under the 8-s nonresetting-delay procedure. Differential responding developed more slowly and to a lesser degree under the 8-s nonresetting-delay procedure, but was nonetheless evident within 100 min. In contrast, clearly differential responding was not evident within 100 min under the 16-s resetting- and nonresetting-delay procedures, although it appeared to start developing with the 16-s nonresetting delay after approximately 75 min. Thus, al-

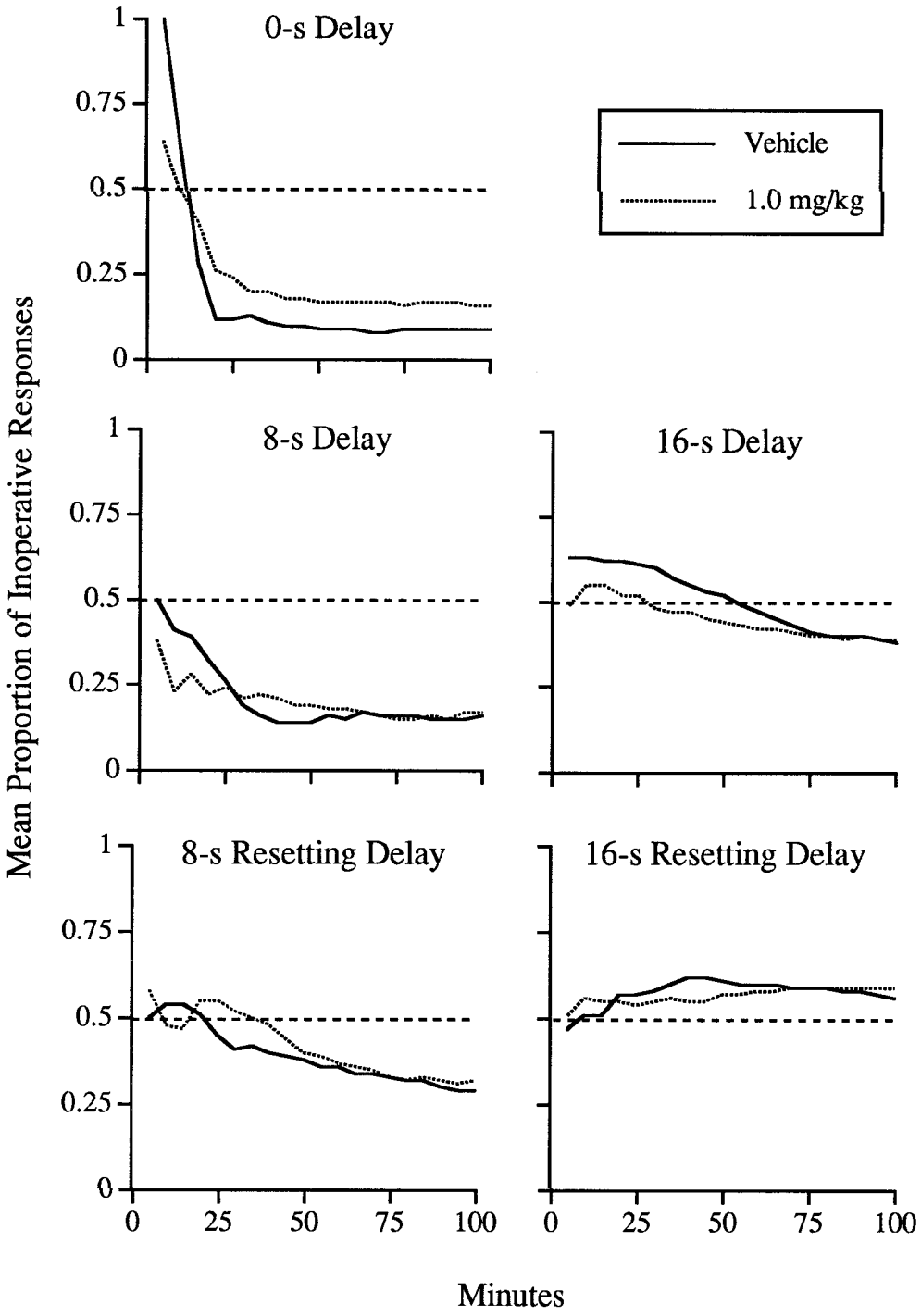

Fig. 12. Mean proportion of inoperative-lever responses (inoperative responses divided by total responses) during the first 100 min of the session under the indicated experimental procedure. Solid lines represent the mean for 8 rats exposed to vehicle; broken lines give the mean for 8 rats exposed to 1.0 mg/kg *d*-amphetamine. Horizontal broken lines represent a proportion of .50, the value at which levels of operative- and inoperative-lever responding are equal.

though response acquisition in terms of rate of operative-lever responding was evident within the first 100 min with both immediate and delayed reinforcement, differential responding was not evident within this period with nonresetting and resetting delays of 16 s.

Because rats exposed to 1.0 mg/kg *d*-amphetamine, but not to higher doses, acquired responding within the first 100 min of the session, the effect of the 1.0 mg/kg dose on the development of differential responding was examined. As Figure 12 shows, similar measures of differential responding were obtained in rats that received this dose and in rats that received vehicle injections.

Efficiency in the presence of drug. In general, *d*-amphetamine did not substantially affect the proportion of inoperative-lever responses under any of the experimental procedures (see Figure 11). For some groups, mean proportions of inoperative-lever responses were slightly higher or lower in rats exposed to drug than for rats exposed to vehicle, but none of these differences were large. Analysis of variance on proportions of inoperative-lever responses at each dose of drug under each procedure failed to detect any significant difference in this measure between rats exposed to drug and rats exposed to vehicle.

In contrast, as shown in Figure 11, mean proportions of responses in the delay under the nonresetting-delay procedure were substantially higher in rats exposed to drug than in rats exposed to vehicle. Analyses of variance on this measure at each dose of drug confirmed a significant drug effect under the 8-s ($F = 3.403$, $p = .0313$) and 16-s ($F = 4.156$, $p = .0148$) nonresetting delays. Multiple comparison tests revealed that the proportion of responses in the delay was significantly higher ($p < .05$) under the 8-s nonresetting delay for rats exposed to the 5.6 mg/kg dose , but not to the 1.0 and 10.0 mg/kg doses, than for rats exposed to vehicle. Moreover, the proportion of responses in the delay under the 16-s nonresetting delay was significantly higher ($p < .05$) for rats exposed to the 1.0, 5.6, and 10.0 mg/kg doses than for rats exposed to vehicle.

The mean proportion of responses in the delay was also higher under the 8-s resetting delay for rats exposed to drug than for rats exposed to vehicle. Analysis of variance confirmed a significant drug effect under this procedure ($F = 3.211$, $p = .0381$), and multiple comparison tests confirmed that the mean proportion of responses in the delay was significantly higher ($p < .05$) for rats exposed to the 5.6 and 10.0 mg/kg doses, but not to the 1.0 mg/kg doses, than for rats exposed to vehicle. Rats exposed to drug under the 16-s resetting delay exhibited a slightly higher mean proportion of responses in the delay than did rats exposed to vehicle, but these differences were small and analysis of variance failed to confirm that any of them were significant ($F = 1.722$, $p = .1853$).

DISCUSSION

The results of the present study concur with prior reports that free-operant responses can be acquired with immediate and delayed reinforcement in the absence of shaping or autoshaping (Critchfield & Lattal, 1993; Dickinson et al., 1992; Lattal & Gleeson, 1990; Lattal & Metzger, 1994; Schlinger & Blakely, 1994; Wilkenfield et al., 1992). They extend prior findings by demonstrating that, in the absence of drug, most responding occurred on the operative lever when reinforcement was immediate. Differential levels of responding on the operative and inoperative levers also developed under both nonresetting- and resetting-delay procedures when the delay was 8 s but not when it was 16 s.

The major way in which the current study extends prior investigations of response acquisition with delayed reinforcement is the examination of the effects of *d*-amphetamine. In the present study, the lowest dose (1.0 mg/kg) of the drug either had no effect on or enhanced rates of operative-lever pressing and, thus, acquisition. In contrast, higher doses typically produced an initial general reduction in the rates of lever pressing. Nonetheless, overall rates of operative-lever pressing at these doses were as high as, or higher than, those observed with vehicle. Thus, response acquisition was observed under all reinforcement procedures at all drug doses, insofar as overall rates of operative-lever pressing were substantially higher in the presence of drug under the reinforcement procedures than under the no-water and yoked-control procedures.

The other index of acquisition, the development of differential responding on the op-

erative lever, was not affected by 1.0 mg/kg *d*-amphetamine. Although the mean proportion of inoperative-lever responding was slightly lower at the beginning of the session under the 0-s delay and nonresetting-delay procedures, substantial intersubject variability in this measure made the effect ambiguous. Hence, it did not appear that the 1.0 mg/kg dose substantially affected the development of differential responding. The initial general disruption of lever pressing by the 5.6 and 10.0 mg/kg doses precluded any straightforward analysis of the effects of these doses on the development of differential responding.

These findings are consistent with those of prior studies of the effects of *d*-amphetamine on repeated acquisition of behavioral chains. In general, under this assay (a) low doses of *d*-amphetamine either have no effect on or slightly enhance accuracy (learning) and response rates, (b) moderate doses sometimes reduce accuracy without affecting response rates, and (c) high doses reduce both accuracy and response rates (Evans & Wenger, 1990, 1992; Harting & McMillan, 1976; Paule & McMillan, 1984; Thompson, 1974). Moreover, drug effects on the course of acquisition in the present study were similar to the effects observed under repeated acquisition procedures.

As in the present study, low doses of *d*-amphetamine have been shown to have no effect on or to increase within-session accuracy (learning) under repeated acquisition, whereas moderate to high doses decrease within-session accuracy, although acquisition still occurs (e.g., Evans & Wenger, 1992). Although 5.6 and 10.0 mg/kg *d*-amphetamine slowed response acquisition in the present study, these doses produced a general disruption of lever pressing under all procedures by increasing stereotypies that are incompatible with lever pressing, an effect of *d*-amphetamine that is well documented (Seiden, Sabol, & Ricaurte, 1993). The present results, like prior findings with the repeated acquisition procedure, provide general support for the conclusion of Evans and Wenger (1992) with regard to amphetamine and other stimulants: "There is no detrimental effect of these psychomotor stimulants on 'learning' until doses which produce a general behavioral disruption are achieved" (p. 636).

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