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Effects of d-Amphetamine on Free-Operant Response Acquisition with Immediate and Delayed Reinforcement

Mark G. LeSage
Western Michigan University

EFFECTS OF *d*-AMPHETAMINE ON FREE-OPERANT RESPONSE ACQUISITION WITH IMMEDIATE AND DELAYED REINFORCEMENT

by

Mark G. LeSage

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EFFECTS OF *d*-AMPHETAMINE ON FREE-OPERANT 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 by rats exposed to procedures in which water delivery was delayed by 0, 8, or 16 seconds relative to the response that produced it. Although neither shaping nor autoshaping occurred, substantial levels of operative-lever responding developed whenever responses produced water. Rats that did not receive water and yoked-control rats that received response-independent water emitted relatively few responses.

The lowest dose (1.0 mg/kg) of *d*-amphetamine either had no effect on or enhanced rates of 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 drug, stimulus control of responding by the operative lever developed rapidly when reinforcement was immediate. Stimulus control also developed under both 8-s nonresetting- and resetting-delay procedures, albeit less rapidly under the resetting delay. In contrast, stimulus control did not develop with a 16-second delay under either

nonresetting- or resetting-delay procedures. *d*-Amphetamine did not affect the development of stimulus control 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 acheived.

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Most importantly, I thank my parents John and Dorothy, my sister Lisa, and my grandmother Dora, for their continuing love and support. Above all, my deepest thanks go to my wife Rhonda for her unending love and support over the past several years. It has been a very long haul for both of us. Because my family is responsible for shaping those parts of my repertoire that one would tact collectively as "determination," I dedicate this dissertation to them.

Mark G. LeSage

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CHAPTER I

INTRODUCTION

Response Acquisition With Delayed Reinforcement

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 (1977) asserted that the dearth of research is due likely 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.

In early studies of response acquisition with delayed reinforcement (e.g., Harker, 1956; Logan, 1952; Seward & Weldon, 1953; Skinner, 1938), either an immediate consequence for responding confounded the effects of the delay or critical procedural details were lacking, which precluded unambiguous conclusions as to whether response acquisition could occur with delayed reinforcement. For example, Harker (1956) reported acquisition of lever-pressing in rats when reinforcement was delayed by 10 s. However, responses were primed by holding a food pellet above the lever if no response occurred

within 30 s from the previous food delivery. Thus, some responses were immediately reinforced with this procedure. Logan (1957) and Seward and Weldon (1953) also reported lever-press acquisition with delayed reinforcement. However, lever presses produced retraction of the lever and then, 10 s later, food delivery. Thus, lever retraction was perfectly correlated with food deliveries, and this correlation could have established lever retraction as an immediate conditioned reinforcer for lever pressing. Interestingly, further investigation of free-operant response acquisition with delayed reinforcement did not begin until recently.

The problems with prior studies mentioned above were not evident in a study by Lattal and Gleeson (1990). In their study, rats and pigeons were exposed 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 unsignalled 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 exposed to control procedures (e.g., no food delivery or response-independent food delivery).

Since the study reported by Lattal and Gleeson (1990), a number of investigators have pursued answers to several important questions reqarding the variables that influence response acquisition, including

(a) to what extent does the value of the delay and type of delay procedure influence the speed and degree of acquisition, (b) to what extent do the immediate consequences of reponding facilitate response acquisition with delayed reinforcement, (c) are chains of behavior acquired that mediate delays to reinforcement, and (d) can species other than rats and pigeons acquire an operant response with delayed reinforcement? The purpose of the present section is to review the findings of studies that have addressed these questions.

Delay Value and Type of Delay Procedure

As Wilkenfield, Nickel, Blakely, and Poling (1992) noted, "there is no single procedure that provides an uncontaminated assay of the effects of delayed reinforcement on the acquisition of discrete responses in a free-operant arrangement" (p. 432). Consider a nonresetting delay procedure. Under this procedure, the first response initiates a delay interval that terminates with reinforcement. Responses during the delay have no programmed consequences and occur closer in time to reinforcement, resulting in delays to reinforcement that are shorter than the nominal delay. Consequently, obtained delays can vary substantially across responses, and the mean delay tends to be shorter than the nominal delay. A resetting-delay procedure solves this problem. Under this procedure, responses during the delay interval reset the delay, thus ensuring that obtained and nominal delays are equal. However, both the nonresetting- and resetting-delay procedures differ from an FR 1 schedule with immediate reinforcement by failing to

ensure a direct relation between rate of responding and rate of reinforcement. A third delay procedure, termed a "stacked-delay" procedure by Wilkenfield et al., can be used to address this problem. Under this procedure, each response initiates a delay interval that terminates with reinforcement, even if the response occurs during the delay interval initiated by a previous response. However, as with the nonresetting delay procedure, response-reinforcer contiguity can vary substantially across responses, resulting in mean obtained delays that are shorter than nominal delays.

Wilkenfield et al. (1992) compared response acquisition under each of the aforementioned delay procedures across a wide range of delay values (from 0 to 32 s). Response acquisition was obtained under every procedure at every delay value. However, comparision of the speed and degree of acquisition under each of the procedures revealed that, although acquisition occurred, overall rates of responding generally were lower and cumulative records of responding were less negatively accelerated under the resetting-delay procedure than under the other two procedures. In addition, the speed of acquisition during the first 100 min of the session increased as the delay increased (from 4 to 16 s) under the nonresetting-delay procedure, while speed decreased as delay increased under the other two procedures.

Dickinson et al. (1992) used procedures similar to the stacked-delay procedure employed by Wilkenfield et al. (1992), but examined a delay of 64 s, in addition to shorter delays (from 0 to 32 s). As in the Wilkenfield et al. study, rats exposed to delays between 0 and 32 s emitted

significantly more responses than yoked rats exposed to noncontingent food deliveries. Moreover, as the delay increased, the rate of acquisition decreased. Rats exposed to a 64-s delay failed to respond any more than yoked controls, unless they were exposed to the chamber in the absence of reinforcement and the lever prior to training.

Facilitative Effects of Programmed Immediate Consequences

As mentioned above, one of the problems of interpreting some early studies of response acquisition with delayed reinforcement was that procedures arranged immediate consequences for responding that were perfectly correlated with reinforcement. Consequently, one could argue that such immediate consequences enhanced responding by virtue of their conditioned reinforcing properties, thus confounding conclusions regarding response acquisition strictly in terms of delayed reinforcement.

Although no immediate consequences for responding were programmed in the aforementioned study by Lattal and Gleeson (1990), Critchfield and Lattal (1993) noted that movement of the operandum produced immediate auditory (and perhaps other) stimulus changes directly correlated with food deliveries. To determine whether such immediate stimulus changes facilitate response acquisition with delayed reinforcement, they controlled auditory stimulus changes by examining the acquisition of a spatially-defined operant (breaking of a photobeam near the ceiling at the back of the chamber), rather than a lever press. For one group of rats, a 30-s resetting-delay procedure was

arranged, under which each break of the photobeam initiated an unsignalled delay interval that terminated with food delivery. For another group, the same resetting-delay procedure was arranged, but each break of the photobeam that initiated the delay interval produced a brief tone. Under these procedures, significant rates of photobeam breaking developed regardless of whether the response initiating the delay interval produced a tone or not. However, the tone did facilitate acquisition and resulted in more efficient patterns of responding.

Schlinger and Blakely (1994) also examined effects of a response-produced auditory stimulus on response acquisition with delayed reinforcement. Their pocedures were very similar to those used by Critchfield and Lattal (1993), in that the same spatially-defined operant was examined in rats performing under a resetting-delay procedure, with and without a response-produced auditory stimulus. However, two delays, 4 and 10 s, were arranged. Consistent with the findings of Critchfield and Lattal, response acquisition was facilitated when responses that initiated the delay produced the auditory stimulus. Moreover, acquisition was facilitated with the shorter delays. These findings suggest that although immediate external stimulus changes may facilitate response acquisition with delayed reinforcement, such changes are not necessary for acquisition to occur.

Behavioral Chains

Because all of the studies of response acquisiton with delayed reinforcement have employed fixed delay intervals, van Haaren (1992)

asserted that each response that initiates the delay interval could be the first link in a chain of behavior, the completion of which is immediately reinforced. Thus, when fixed delays are employed, it is unclear as to whether discrete responses or behavioral chains are acquired. Such behavioral chains may mediate the delay to reinforcement and facilitate acquisition. This analysis is supported by observations of the development of "superstitious" chains of behavior under response-independent schedules of food delivery (e.g., FT, Staddon & Simmelhag, 1971). As van Haaren states: "This raises the question whether or not the operant would also have been acquired had the delay not been fixed, but of variable duration, as it would have been less likely for behavioral chains to develop under those circumstances" (pp. 767-768).

To examine this possibility, van Haaren (1992) exposed rats to fixed or variable resetting-delay procedures that arranged delays of 10 or 30 s. Other rats were exposed to an immediate-reinforcement procedure. Responding was acquired in rats exposed to variable delays of 10 or 30 s or a fixed delay of 10 s. Rats exposed to the fixed delay of 30 s emitted few responses. Response acquisition occurred most rapidly in rats exposed to the immediate reinforcement procedure. Because acquisition was observed under the variable-delay procedures, these findings do not support the notion that lever presses acquired under delayed-reinforcement procedures are the intial link in a chain of behavior that mediates the delay to reinforcement, since it is unlikely that such chains would have developed under the variable-delay procedure.

Species

All of the studies mentioned aboved employed either rats or pigeons as subjects. Thus, it is of interest whether free-operant responses in other species can be acquired with delayed reinforcement. Lattal and Metzger (1994) addressed this issue by examining response acquisition with delayed reinforcement in male Siamese fighting fish (*Beta splendens*). The response of interest was swimming through a ring in an aquarium, which broke a photobeam and intiated an unsignalled, resetting delay interval (0, 10, or 25 s) that terminated with a 15-s mirror presention. Mirror presentation elicits an aggressive display in male Siamese fighting fish and is known to serve as a positive reinforcer for them. The frequency of swimming through the ring was substantially greater in fish exposed to the delayed reinforcement procedure than in fish exposed to response-independent mirror presentations.

The findings of the studies decribed above provide strong support for the conclusion of Lattal and Metzger (1994): "[N]either explicit training procedures nor immediate reinforcement is necessary to establish operant behavior . . ." (p.35). To date, the effects of pharmacological variables on free-operant response acquisition with delayed reinforcement have not been examined. Because, in essence, the studies of response acquisition noted above examined learning, the assays used in those studies may be of interest to behavioral pharmacologists and toxicologists concerned with the effects of drugs on learning. Indeed, behavioral pharmacologists have indicated the need

to develop procedures to assess the effects of drugs on the acquisition of new behavior (Evans & Wenger, 1992).

Free-Operant Assays of Drug Effects on Learning

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 determining drug effects on the acquisition of free-operant behavior. It is the purpose of the present section to briefly describe these procedures.

Repeated Acquisition of Behavioral Chains

One free-operant procedure that is often used is the repeated-acquisition-of-response-chains. Initially developed by Boren (see Boren and Devine, 1968), this procedure requires subjects to learn a different chain of responses during each experimental session. With extended training under this procedure, the number of errors per session in mastering a new chain becomes relatively stable, with errors decreasing and completed chains increasing as the session progresses. Such steady-state performance provides a baseline of learning against which drug effects can be determined. A substantial number of studies have revealed that the repeated acquisition procedure is useful in analyzing drug effects on learning in both humans and nonhumans (e.g., Pontecorvo & Clissold, 1993; Thompson & Moerschbaecher, 1979).

For example, acute administration of moderate to high doses of stimulants (e.g., amphetamine) interferes with learning (i.e., increases

errors) in nonhumans tested under the repeated acquisition procedure (Thompson, 1974). Other studies employing the repeated acquisition procedure have obtained similar results with other drugs, including, chlordiazepoxide, pentobarbital, cocaine, chlorpromazine, imipramine, and methylphenidate. In contrast, fenfluramine, at doses tested so far, has not been shown to increase errors above baseline in either learning or performance conditions (Thompson, 1978).

Transition in Schedule Performance

Another free-operant assay of learning involves the acquisition of schedule performance. This assay has been used recently in behavioral toxicology to study the long-term effects of prenatal or neonatal exposure to drugs and toxicants on learning (for a review, see Gentry & Middaugh, 1994). The procedure involves shaping a response (e.g., lever press) that is subsequently maintained under an FR 1 schedule of reinforcement until some criterion of responding is reached (e.g., 100 responses during a 30-min session, Newland, Ng, Baggs, Gentry, Weiss, & Miller, 1986). Then, a series of abrupt increases in the ratio requirement is implemented (e.g., FR 1 to FR 25 to FR 75). The primary dependent variable is the rate of responding. Analysis is focused on how rates are affected by the changing schedule requirements and how those effects differ between subjects exposed to drugs or toxicants and subjects not so exposed. For example, Newland et al. (1986) observed substantial increases in response rates during the transition from an FR 25 to an FR 75 schedule in rats exposed neonatally to 3.0 mg/kg cadmium. A

significant decrease in rates was observed in rats exposed to 6.0 mg/kg. Moreover, consistent patterns of behavior developed in control animals after five days under the FR 75 schedule, while erratic patterns of behavior persisted in animals exposed to 6.0 mg/kg cadmium. The development of FR schedule control has been shown to be sensitive to a range of drugs, including phenobarbital, methadone, and ethanol (Gentry & Middaugh, 1994).

Lever-Press Acquisition

Another approach to studying drug effects on free-operant response acquisition was employed by Robbins (1978). In his study, drug effects on response acquisition with conditioned reinforcement were of interest. Water-deprived rats were first trained to drink water from a dipper. Water deliveries were arranged according to a variable-time (VT) 30-s schedule and preceded by a light flash 0.5-s in duration, the putative conditioned reinforcer (CR). Two levers were present in the chamber during dipper training, but responses on either lever had no programmed consequences. After dipper training, responding on one lever produced the CR (CR lever) according to a variable-ratio 2 schedule, while responses on the other lever (NCR lever) had no programmed consequences. During these acquisition sessions, water was never delivered. Robbins compared the effects of pipradrol, methylphenidate, *d*-amphetamine, and nomifensine on response rate on each lever. Pipradrol produced a dose-dependent increase in responding on the CR lever, but a dose-dependent decrease in

responding on the NCR lever. Methylphenidate also increased CR-lever responding, while *d*-amphetamine had no clear effect and nomifensine reduced CR-lever responding.

A study by Stolerman (1971a) examined the effects of chlorpromazine and chlordiazepoxide on response acquisition through the use of procedures similar to those used by Robbins (1978), with the exception that an unconditioned reinforcer (food delivery) was used. In his study, rats were given one 30-min habituation session during which they could explore the test chamber. During the next session, rats were magazine trained. "Accidental" responses on a lever that occurred in these sessions were recorded, but had no programmed consequences. After magazine training, the subjects were given two sessions of lever-press training. During these sessions, 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, which ended after 36 food deliveries. No shaping procedures were employed during training sessions. Subjects that received chlorpromazine or chlordiazepoxide prior to the training sessions acquired responding more slowly than subjects that received saline. Moreover, both drugs reduced the total number of responses per session relative to saline. Stolerman asserted that his procedure could be useful for studying drug effects on learning. Yet, to the present author's knowledge, only one other study has been conducted using those procedures, and that study was conducted by Stolerman (1971b), again with chlorpromazine.

Purposes of the Present Study

The free-operant procedures discussed above have proven useful in identifying drugs that affect learning and have provided insight into the potential behavioral mechanisms through which those drugs produce their effects. With the exception of those used by Robbins (1978) and Stolerman (1971a, b), such procedures are preceded by periods of shaping or other training to establish the operant to be analyzed. Thus, the type of learning that is examined with those procedures involves the acquisition of stimulus control or schedule control over an operant response already well established in the organism's repertoire. Those procedures do not directly address drug effects on the provenance of free-operant behavior, that is, the time during which reinforcement acts upon phylogenically-determined minimal units of reflexive and instinctive movements (e.g., exploratory behavior, Segal, 1972).

Because the studies of response acquisition with delayed reinforcement and studies of drug effects on lever-press acquisition with immediate reinforcement mentioned above address directly the provenance of free-operant behavior, the purpose of the present experiment was to examine further the utility of the procedures used in such studies (e.g., Stolerman, 1971a, b; Wilkenfield et al., 1992) for studying drug effects on learning. Because nothing is known about drug effects on learning under conditions where behavior is acquired with delayed consequences, a second purpose of the present study was to extend the work of Stolerman by examining a different drug, *d*-amphetamine, and its effects on response acquisition with both

immediate and delayed reinforcement.

CHAPTER II

METHODS

Subjects

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

Apparatus

Eight operant conditioning chambers, measuring 21 cm high, 21 cm wide, and 28 cm long, were used (MED Associates, St. Albans, VT; model ENV-007). 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 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 centrally located on the front wall 2 cm from 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 were programmed and data

recording was accomplished using an IBM-compatible personal computer and software (MED-PC version 2.9) and interfacing from MED Associates (St. Albans, VT).

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 house light was illuminated and a 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. Rats were given 30 min of free access to water in their home cages immediately following the dipper training session. Twenty-four hours later, they were 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, and (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, another group of 32 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. Under the nonresetting-delay procedure just described, obtained delays tend to be shorter than programmed delays. Therefore, a resetting-delay procedure also was employed; it ensured obtained and programmed delays were equivalent.

Resetting-Delay Procedure

Two groups of 32 rats were exposed to a tandem FR 1 not-responding-greater-than t (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 delays

values were arranged. One group of 32 rats was exposed to an 8-s delay, the other group to a 16-s delay.

Control Procedures

Three control procedures were arranged. To determine the extent to which stimulants increase lever pressing independently of reinforcement contingencies, drug effects were determined in a group of 32 rats 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 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 exposed to a VT schedule of response-independent water delivery. The frequency and distribution of water deliveries for each of these rats was yoked to one 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 it was earned by a master rat.

Pharmacological Procedure

Each group of 32 rats was divided into four squads of eight. Squad one received an injection of saline solution (vehicle), while squads two,

three, and four received 1.0, 5.6, and 10.0 mg/kg *d*-amphetamine (Sigma Chemical Co., St. Louis, MO), respectively. All injections were given intraperitoneally 10 minutes 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).

CHAPTER III

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 eight rats under each experimental procedure. Each of Figures 2 to 8 depicts cumulative operative-lever responses of individual subjects and mean cumulative operative- and inoperative-lever responses for each squad of eight rats under one experimental procedure. The thick solid lines in Figure 1 and the panels labeled "Vehicle" in Figures 2 to 8 depict acquisition in the absence of drug (i.e., during sessions preceded by vehicle injections).

Aquisition in the Absence of Drug

Cumulative Operative-Lever Pressing

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 5-10 min) and was sustained at a moderate to high rate for a substantial period, regardless of whether

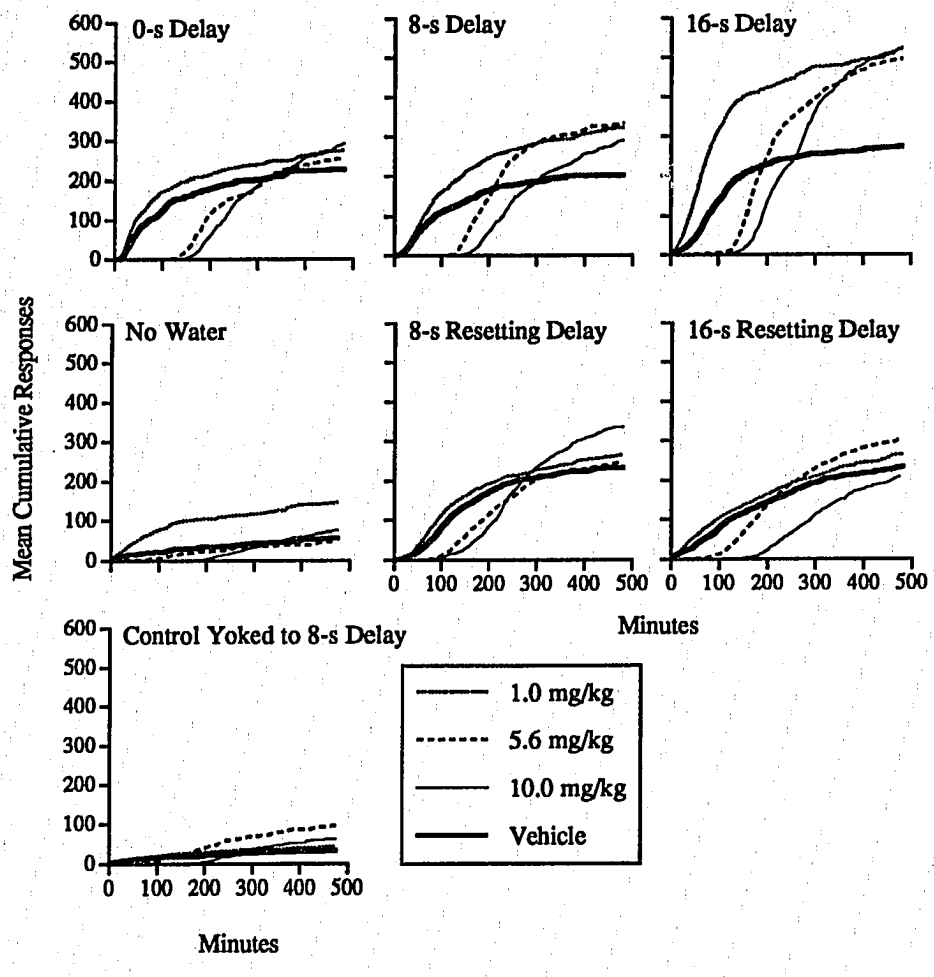

Figure 1. Mean Cumulative Responses on the Operative-Lever Across the Entire 480-min Session Under Each Experimental Procedure.

Each line represents the mean operative-lever responding of eight rats exposed to the indicated dose of *d*-amphetamine. Data were collected in 5-min bins.

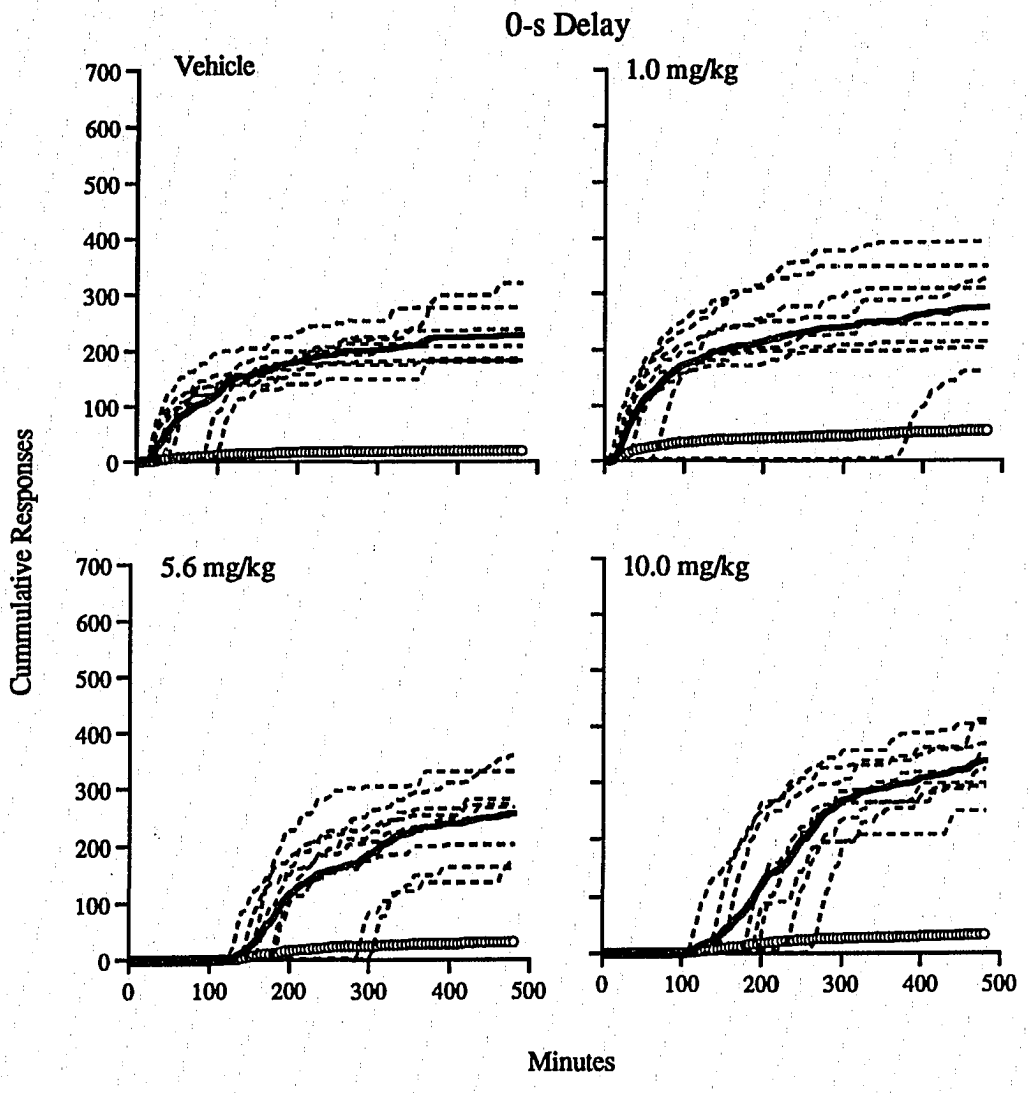

Figure 2. Cumulative Responses on the Operative Lever Across the Entire 480-min Session Under the Immediate-Reinforcement (0-s Delay) Procedure.

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.

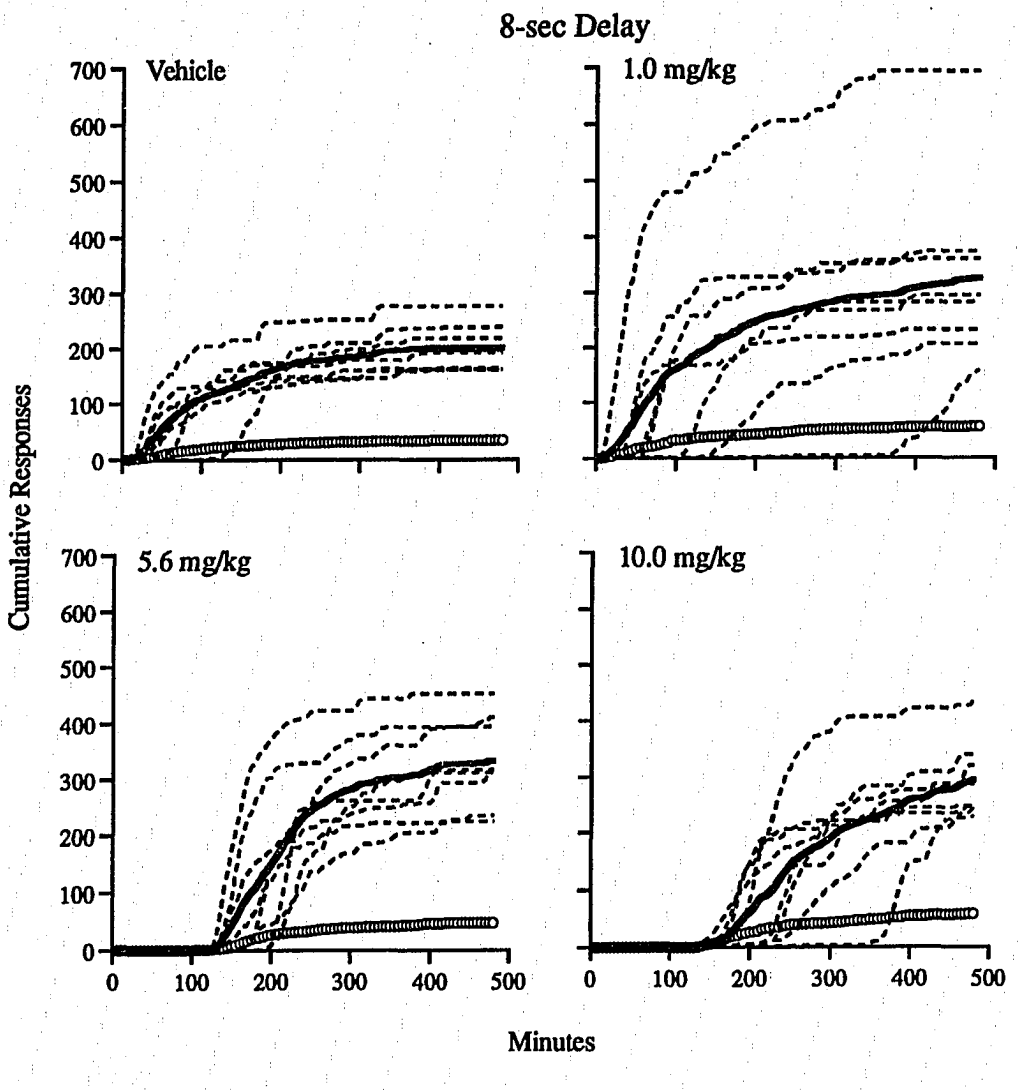

Figure 3. Cumulative Responses on the Operative Lever Across the Entire 480-min Session Under the 8-s Nonresetting-Delay Procedure.

See Figure 1 caption for further information.

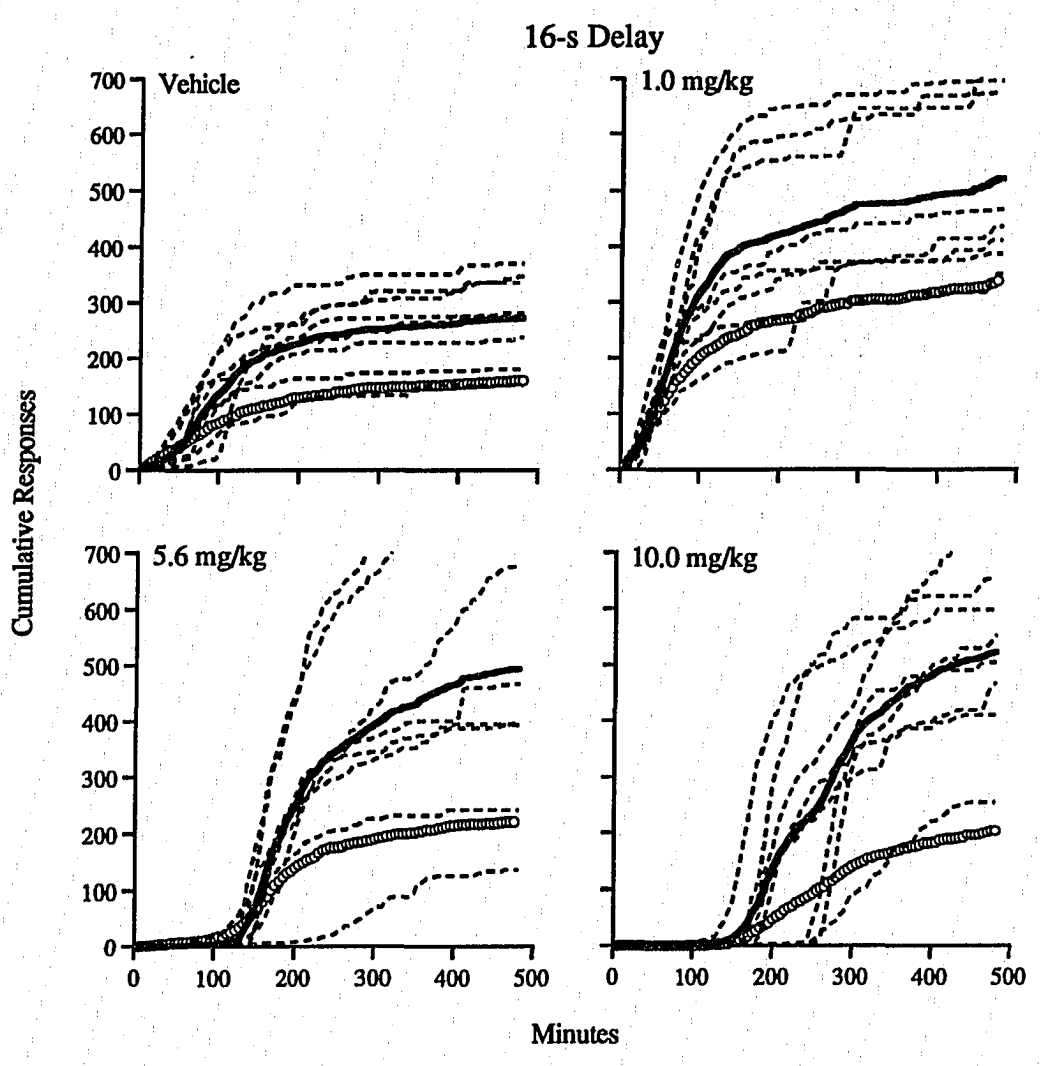

Figure 4. Cumulative Responses on the Operative Lever Across the Entire 480-min Session Under the 16-s Nonresetting-Delay Procedure.

See Figure 1 caption for further information.

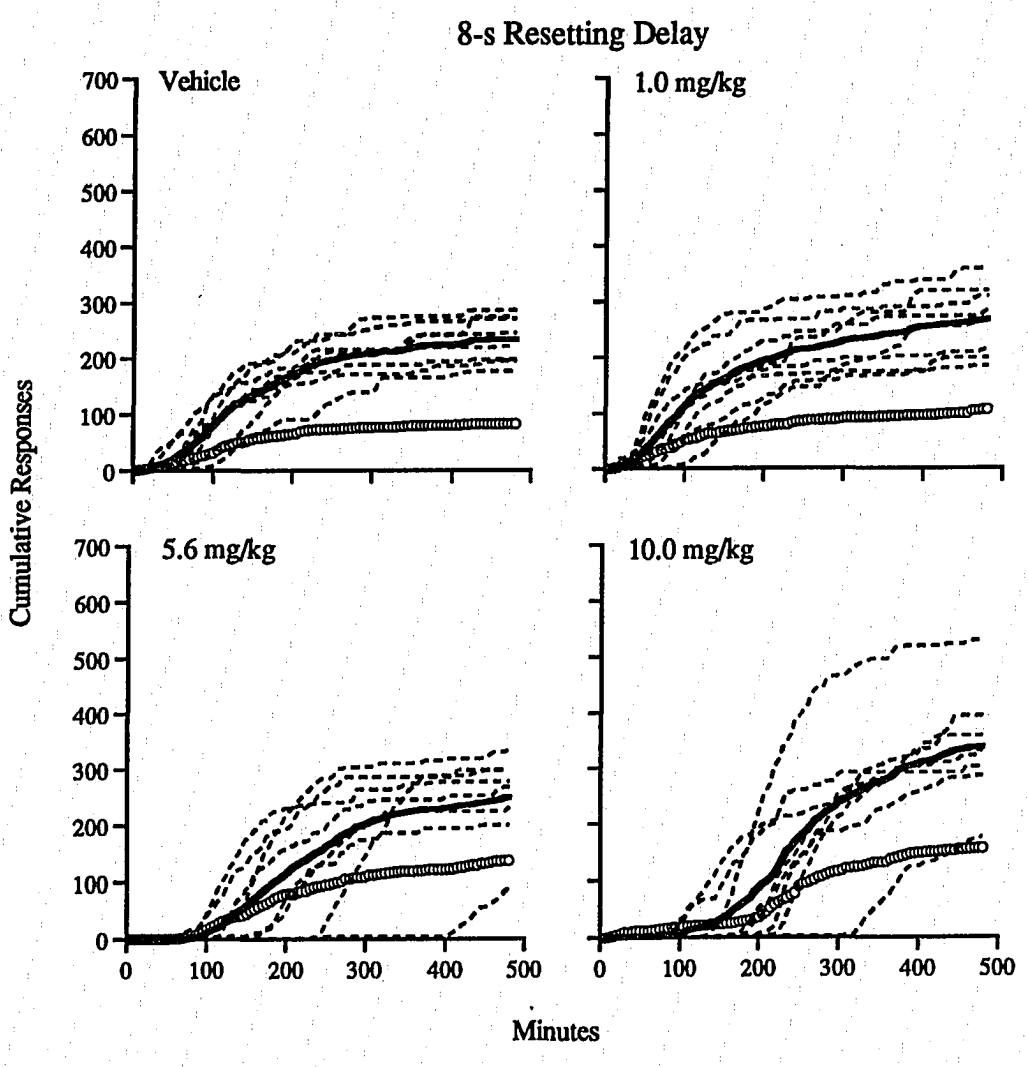

Figure 5. Cumulative Responses on the Operative Lever Across the Entire 480-min Session Under the 8-s Resetting-Delay Procedure.

See Figure 1 caption for further information.

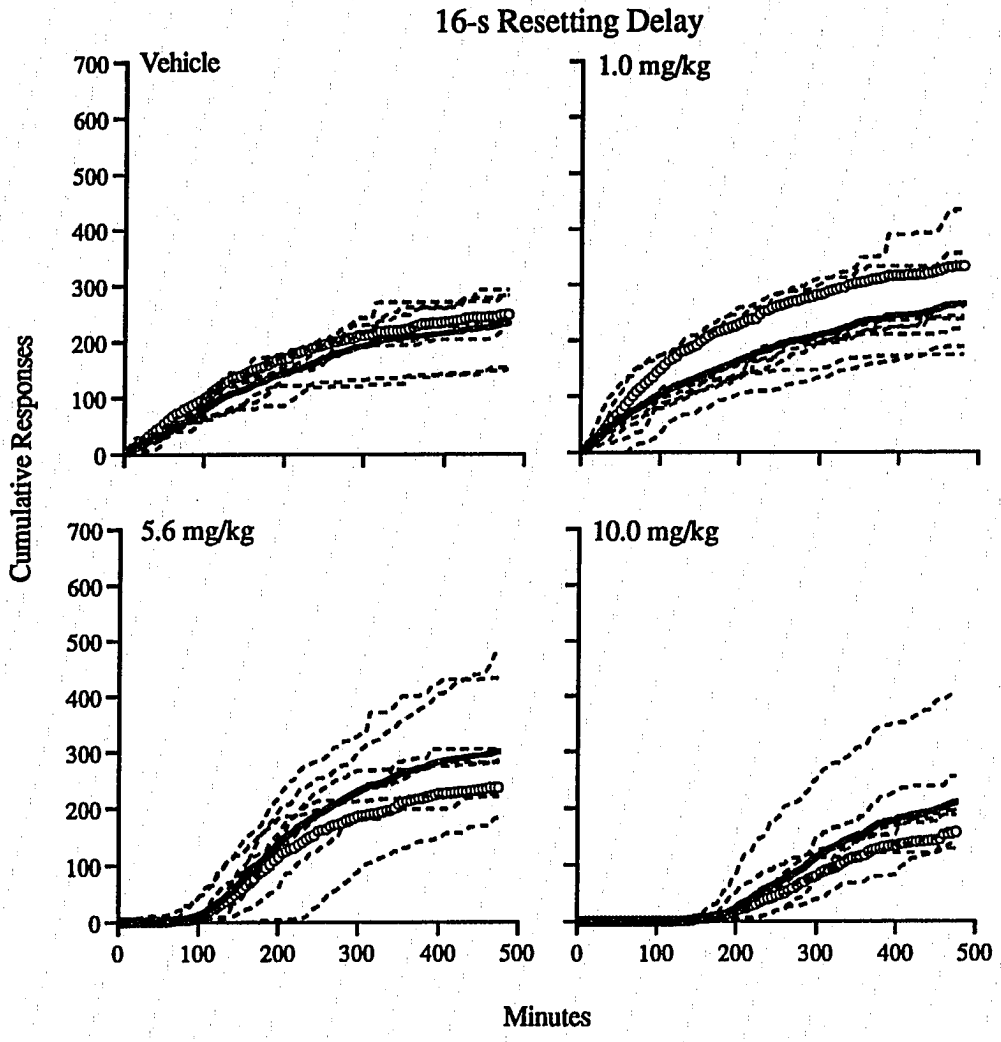

Figure 6. Cumulative Responses on the Operative Lever Across the Entire 480-min Session Under the 16-s Resetting-Delay Procedure.

See Figure 1 caption for further information.

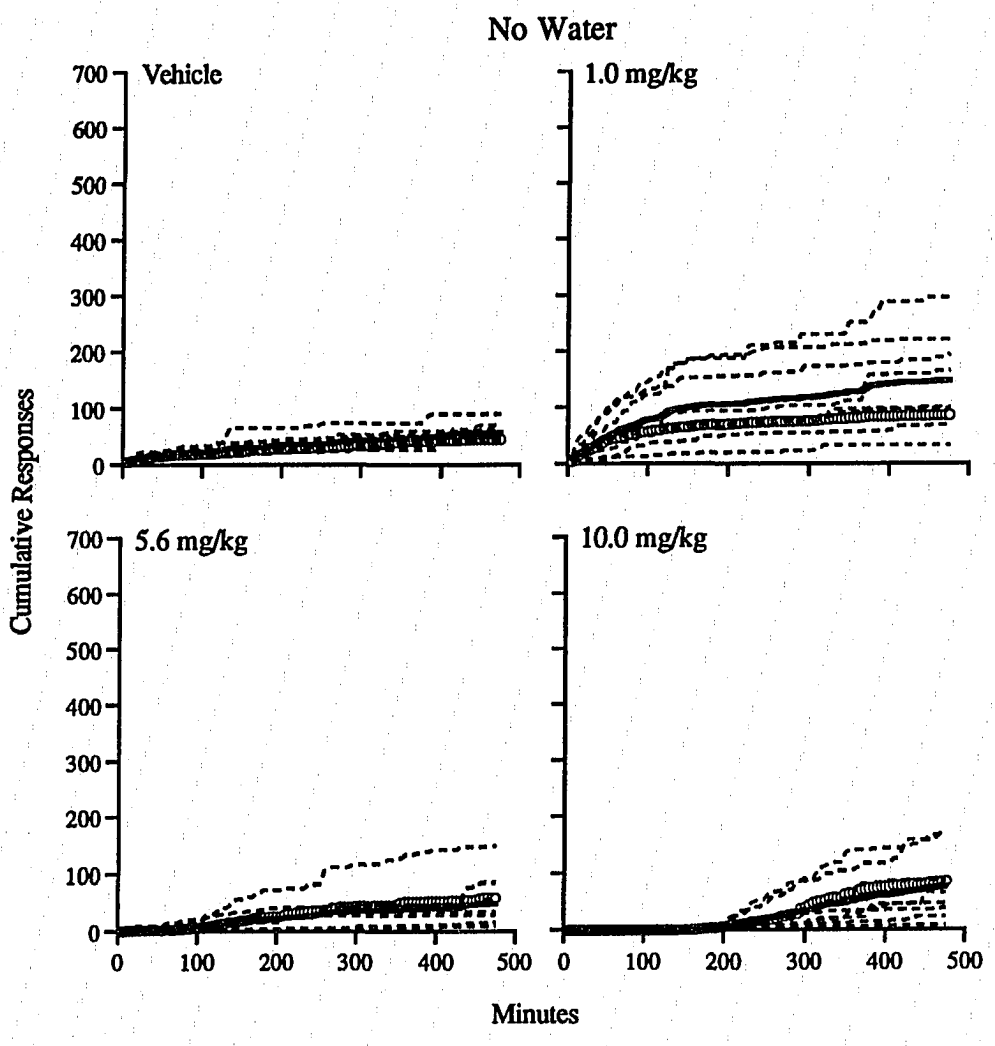

Figure 7. Cumulative Responses on the Operative Lever Across the Entire 480-min Session Under the No-water Procedure.

See Figure 1 caption for further information.

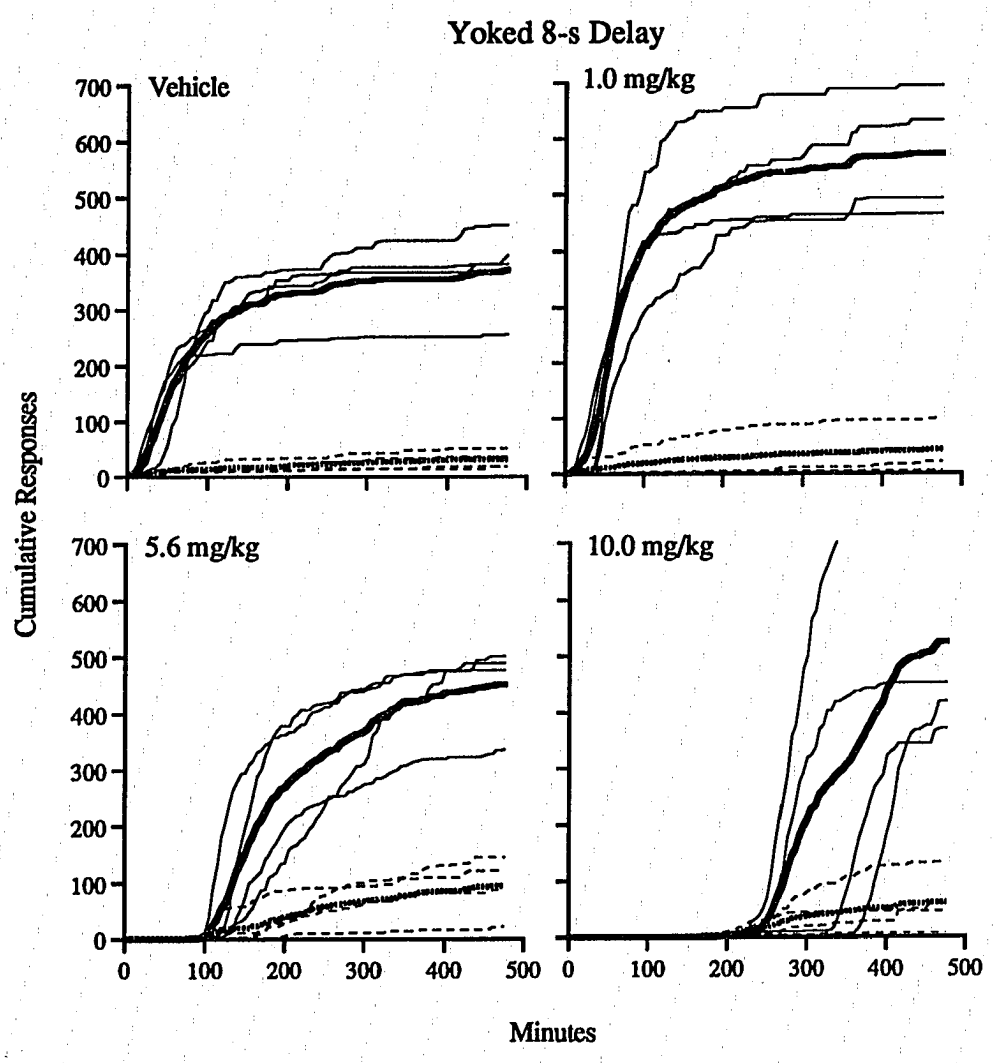

Figure 8. Cumulative Responses on the Operative Lever Across the Entire 480-min Session Under the Yoked-control Procedure.

Thin solid lines represent cumulative responses for 1 of 4 master rats exposed to the 8-s nonresetting-delay procedure under the indicated dose of *d*-amphetamine. Thick solid lines represent the mean cumulative responding of these master rats. Thin broken lines represent cumulative responding on the operative lever for 1 of 4 control rats yoked to the aforementioned master rats. Thick broken lines represent the mean cumulative responding of these control rats.

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

Cumulative Inoperative-Lever Pressing

Mean cumulative inoperative-lever responding was substantially lower than cumulative operative-lever responding under all reinforcement procedures except the 16-s resetting delay. Mean levels of inoperative-lever responding were generally higher with delayed reinforcement than with immediate reinforcement. Mean inoperative-lever rates were higher under 16-s delays than under 8-s delays, and under resetting delays than under nonresetting delays. Under the 16-s resetting delay, rates of operative-lever and inoperative-lever responding were essentially equal throughout the session, indicating an absence of

stimulus control by the lever on which responses produced water (see below).

The point at which mean cumulative records of operative and inoperative responding began to separate (i.e., the point at which stimulus control began to develop) appeared to be 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 with resetting delays than with nonresetting delays. Further analysis of inoperative responding is provided below.

Overall Rates of Operative- and Inoperative-Lever Pressing

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, since neither lever was operative and no substantial bias for either lever was evident. This figure shows that mean overall rates of operative 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 greater than rates under the no-water procedure ($p < .05$).

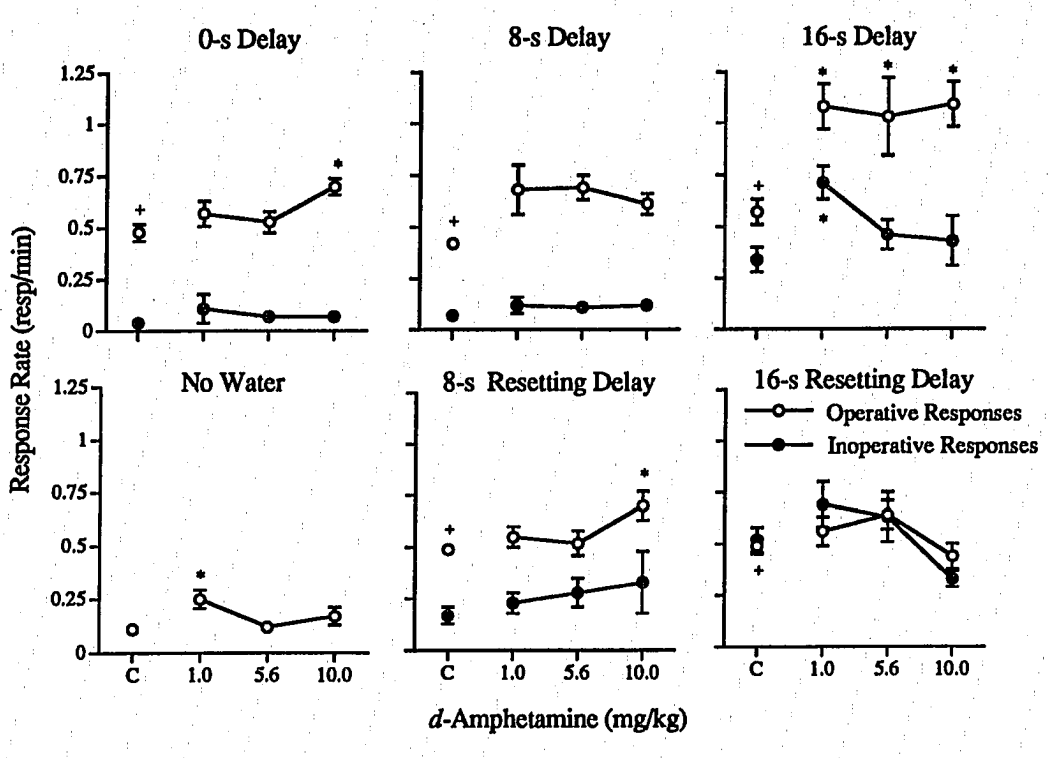

Figure 9. Mean Overall Response Rates on the Operative and Inoperative Levers Under the Indicated Experimental Procedure.

Each data point represents the mean rate for eight rats. Data points above C indicate mean rates for rats exposed to vehicle. Other data points represent mean rates for rats exposed the indicated dose of *d*-amphetamine. The data for the no-water procedure represent the average of the rates on both levers, since neither lever was operative and no substantial bias for either lever was evident. Vertical line represent standard errors of the mean. +Significantly different from the no-water vehicle mean, $p < .05$. *Significantly different from vehicle under the same procedure, $p < .05$.

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.

Speed of Acquisition

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 minutes 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 group are presented as white bars in Figure 10, which shows that the slopes obtained under the reinforcement procedures were substantially greater than the slope 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 greater 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

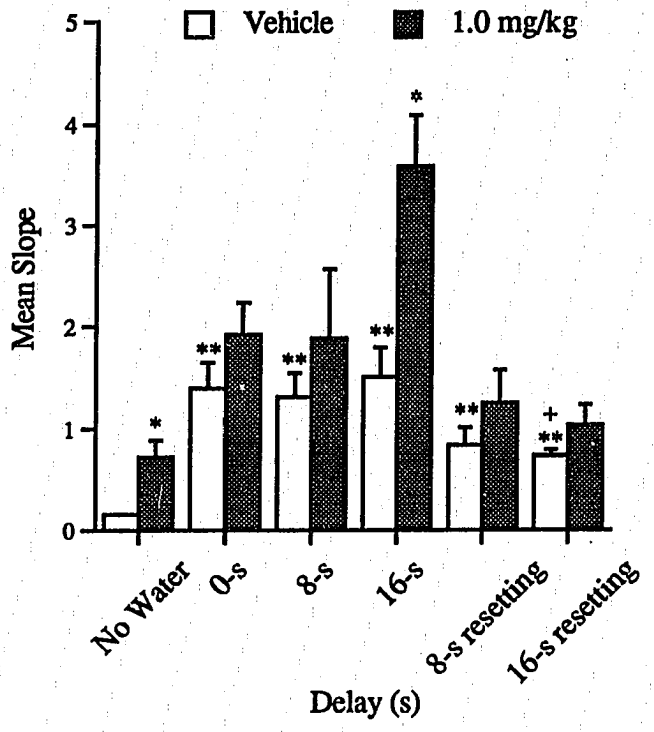

Figure 10. Mean Slope of Regression Lines Fitted to the Cumulative Records of Operative-Lever Responding Across the First 100 Min of the Session Under the Indicated Experimental Sessions.

Each bar represents the mean of individual slopes for eight rats. White bars indicate mean slopes for rats exposed to vehicle, dark bars for rats exposed to 1.0 mg/kg *d*-amphetamine. The greater the slope the faster the acqusisition in terms of total responses emitted. Vertical line 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 0-s delay vehicle, $p < .05$.

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, while the resetting-delay procedure did, albeit significantly so only with the 16-s delay.

Response Efficiency

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 also was calculated. Response efficiency is inversely related to these two measures; as the proportion of inoperative responses and responses in the delay interval increase, 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- and

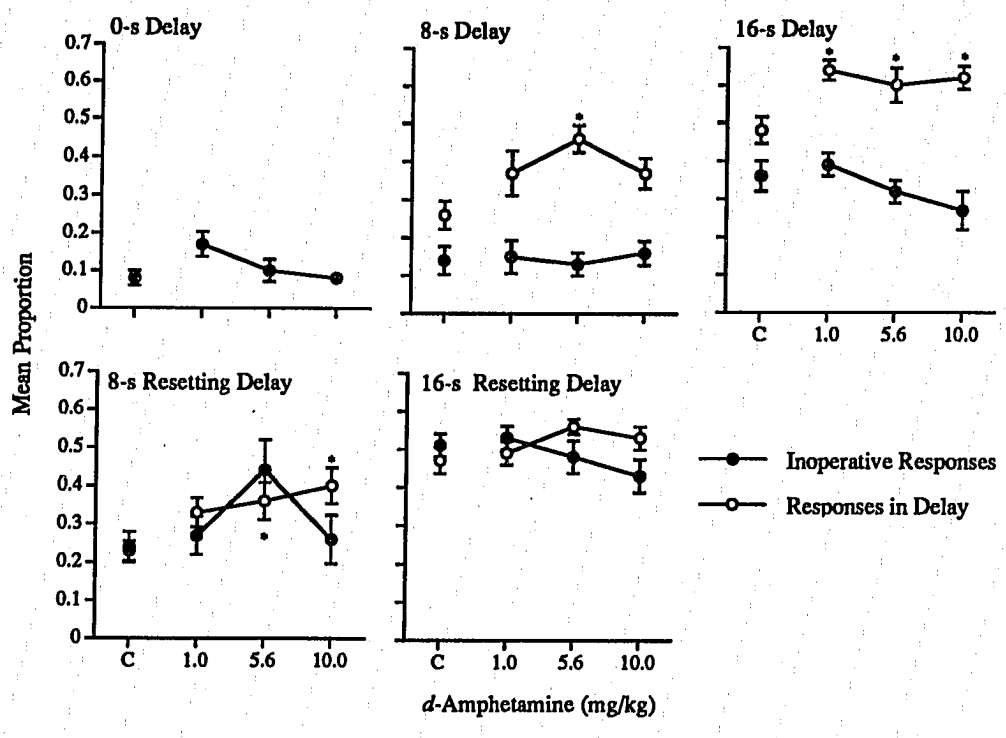

Figure 11. Mean Proportion of Inoperative Responding and Responding in the Delay Interval Under the Indicated Experimental Procedure.

Each data point represents the mean rate for eight rats. Data points above C indicate mean rates for rats exposed to vehicle, other data points for rats exposed the indicated dose of *d*-amphetamine. Vertical line represent standard errors of the mean. *Significantly different from vehicle under the same procedure, $p < .05$.

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 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 ($p > .05$).

Development of Stimulus Control

The proportion of total responses emitted on the inoperative lever provides an index of the development of stimulus control (by the operative lever), as well as an index of response efficiency. Because

substantial operative-lever responding was observed within the first 100 min of the session in the absence of drug, the mean proportion of inoperative-lever responses in each 5-min bin across the first 100 min was calculated. These proportions are depicted in Figure 12. Proportions of 0.5 indicate an absence of stimulus control (i.e., equal responding on both levers). Proportions ranging from 0.5 to 0.0 indicate increasing degrees of stimulus control (i.e., more responding on the operative lever). As this figure shows, stimulus control developed within the first 25 min of the session under the immediate-reinforcement procedure. Development of stimulus control also was evident early in the session under the 8-s nonresetting-delay procedure. Stimulus control developed slower and to a lesser degree under the 8-s nonresetting-delay procedure, but was nonetheless evident within 100 min. In contrast, clear stimulus control of 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 100 min. Thus, although response acquisition in terms of rate of operative-lever responding was evident within the first 100 min with both immediate and delayed reinforcement, stimulus control of responding was not evident within this period with nonresetting and resetting delays of 16 s.

Acquisition in the Presence of Drug

Drug Effects on Cumulative and Overall Responding

Figures 1 to 8 show that 1.0 mg/kg *d*-amphetamine produced only

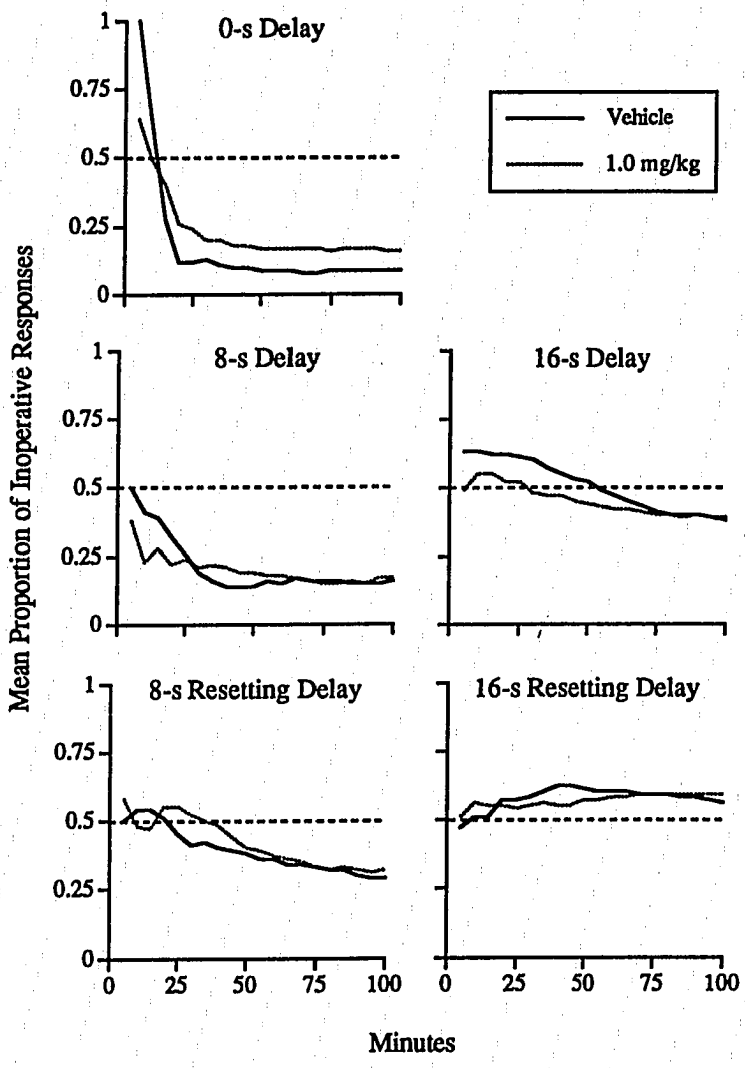

Figure 12. Mean Proportion of Inoperative Responses Across the First 100 Min of the Session Under the Indicated Experimental Procedure.

Solid lines represent the mean for eight rats exposed to vehicle, broken lines for eigth rats exposed to 1.0 mg/kg *d*-amphetamine. Lower proportions of inoperative responding indicate greater stimulus control by the operative lever. Horizontal broken lines represent a proportion of inoperative responding of 0.50, the value at which levels of operative and inoperative responding are equal.

a slight enhancement of mean rates of operative-lever responding under the immediate-reinforcement and resetting-delay procedures. At 1.0 mg/kg the drug produced a more marked increase in 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 also was higher under the no-water procedure for rats exposed to 1.0 mg/kg than for rats exposed to vehicle. Like subjects exposed to vehicle, rats exposed to 1.0 mg/kg 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 and to vehicle.

d-Amphetamine doses of 5.6 and 10.0 mg/kg slowed acquisition by producing a 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, it increased rapidly, in a pattern similar to that observed in rats that received lower doses or no drug. Overall, the mean total

responses emitted under the nonresetting delay was considerably greater in rats exposed to 5.6 and 10.0 mg/kg 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 1.0 mg/kg, 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. Such variability was somewhat greater under the nonresetting-delay procedure than under the resetting-delay procedure.

To facilitate interpretation of drug effects on overall rates of responding, the effects of *d*-amphetamine on mean overall operative-lever and inoperative-lever response rates are depicted in Figure 9. This figure shows that overall operative-lever rates under the immediate-reinforcement procedure were slightly higher for rats exposed to 1.0 and 5.6 mg/kg than for rats exposed to vehicle. The mean operative-lever response rate under this procedure for rats exposed to 10.0 mg/kg 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 *d*-amphetamine dose, but not at the 1.0 and 5.6 mg/kg doses.

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

mean operative-lever rate was higher under 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 only approached significance 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 vehicle-control rats. Rates in rats that received 1.0 or 5.6 mg/kg were similar to the vehicle-control mean. Analysis of variance confirmed a significant drug effect under this 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 10.0 mg/kg ($p < .05$).

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, while the rate for rats exposed to 10.0 mg/kg was slightly below the vehicle-control level. However, analysis of variance indicated that mean operative-lever rates under the 16-s nonresetting delay in rats exposed to drug were not significantly different from rats exposed to vehicle ($F = 2.179$, $p = .1128$).

Mean response rates under the no-water procedure were considerably higher than the vehicle-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 greater for rats exposed to 1.0 mg/kg, but not 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 vehicle-control groups, but the difference was small and inconsistent across doses and procedures. An exception is the substantial difference in inoperative-lever response rates observed between vehicle-control rats and rats that received 1.0 mg/kg *d*-amphetamine under the 16-s nonresetting-delay procedure. 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 responding was significantly higher for rats exposed to 1.0 mg/kg *d*-amphetamine, but not 5.6 and 10.0 mg/kg, than for rats exposed to vehicle.

Drug Effects on the Speed of Acquisition

Because 1.0 mg/kg *d*-amphetamine increased overall rates of responding under some procedures, it was of interest 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 1.0 mg/kg via the methods described previously. Almost all rats that received 5.6 and 10.0 mg/kg emitted too few responses during the first 100 min to allow for 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 greater for rats exposed to 1.0 mg/kg than for rats exposed to vehicle. The mean slope was only significantly different from vehicle 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 greater under the immediate-reinforcement and nonresetting-delay procedures than under the no-water procedure ($p < .05$). Although slopes at 1.0 mg/kg under the resetting delay procedures were greater 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

Drug effects on response efficiency are depicted in Figure 11. As this figure shows, in general, *d*-amphetamine did not substantially affect the proportion of inoperative-lever responses under any of the

experimental procedures. 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 differences in this measure between rats exposed to drug and rats exposed to vehicle.

In contrast, 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 nonresetting delay ($F = 4.156$, and $p = .0148$). 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 5.6 mg/kg, but not 1.0 and 10.0 mg/kg, 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 1.0, 5.6, and 10.0 mg/kg than for rats exposed to vehicle.

The mean proportion of responses in the delay also was 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 5.6 and 10.0

mg/kg, but not 1.0 mg/kg, 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 rats exposed to vehicle, but these differences were small and analysis of variance failed to confirm that any of them were significant ($F = 1.722$, $p = .1853$).

Drug Effects on the Development of Stimulus Control

Because rats exposed to 1.0 mg/kg *d*-amphetamine acquired responding within the first 100 min of the session, the effect of this dose on the development of stimulus control was compared to the development of stimulus control in the absence of drug. As mentioned above, rats that received 5.6 and 10.0 mg/kg emitted too few responses during the first 100 min to allow for meaningful analysis. The mean proportion of inoperative-lever responding across the first 100 min of the session for rats exposed to 1.0 mg/kg under each reinforcement procedure is depicted in Figure 12. As this figure shows, this dose did not substantially affect the development of stimulus control. As in rats exposed to vehicle, stimulus control developed within the first 25 min of the session under the immediate-reinforcement procedure for rats exposed to 1.0 mg/kg, although the mean proportion of inoperative-lever responses in the latter group was slightly higher after 20 min. Acquisition of stimulus control also was evident early in the session for rats exposed to 1.0 mg/kg under the 8-s nonresetting-delay procedure, while under the 8-s resetting delay procedure acquisition of stimulus control was much slower and not as complete. As with rats exposed to

vehicle under these procedure, there was no evidence of the acquisition of stimulus control within 100 min in rats exposed to 1.0 mg/kg under 16-s resetting and nonresetting delays.

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. Means and standard errors also are presented for each group at each 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.

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)			
Subject	C	1.0	5.6	10.0	C	1.0	5.6	10.0
1	7.03	3.90	4.86	5.97	9.01	8.21	11.12	8.24
2	6.10	5.10	4.47	7.50	9.94	11.50	10.15	10.56
3	6.26	6.36	4.45	4.98	10.27	9.61	8.08	8.42
4	7.46	6.16	6.09	6.90	9.27	8.90	10.0	9.38
5	6.12	7.12	6.17	4.84	12.78	11.38	7.84	11.54
6	7.49	7.71	5.40	3.91	11.10	9.32	8.23	8.02
7	5.79	5.90	6.18	5.33	10.57	9.73	8.87	7.16
8	6.01	5.66	4.40	5.85	11.44	9.70	11.43	6.34
Mean	6.53	5.99	5.25	5.66	10.55	9.79	9.47	8.71
*S.E.M.	0.24	0.42	0.29	0.41	0.43	0.40	0.50	0.61

*Standard error of the mean

CHAPTER IV

DISCUSSION

The Present Findings in Relation to Prior Studies of Response Acquisition With Delayed Reinforcement

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 also extend the findings of prior studies with respect to the type of reinforcer. The present study is the first to demonstrate response acquisition with delayed water reinforcement.

Wilkenfield et al. (1992) directly compared response acquisition under resetting- and nonresetting-delay procedures, and the patterns of acquisition observed in the present study are consistent with their findings in several ways. First, in the absence of drug, levels of operative-lever responding under all immediate- and delayed-reinforcement conditions differed significantly from levels of responding under the no-water procedure and yoked-control procedures. Second, the speed of operative-lever-response acquisition was slower under the resetting-delay procedure, in that slopes of cumulative-response records were lower and less negatively accelerated under this procedure than under the immediate-reinforcement and nonresetting-delay procedures.

Third, overall rates of operative-lever responding under the nonresetting procedures were higher under the 16-s delay than under the 8-s delay.

Finally, response efficiency, indexed in terms of the proportion of total responses emitted on the operative lever, decreased as a function of delay length and delay type. That is, response efficiency was lower with 16-s delays than with 8-s delays, and lower under the resetting-delay procedure than under the nonresetting-delay procedure. Moreover, under the nonresetting-delay procedure rates of inoperative-lever responding were often equal to or greater than rates of operative responding. As Wilkenfield et al. (1992) explained, the higher rates of inoperative-lever responding under resetting-delay procedures may be interpreted in two ways. First, inoperative-lever pressing was adventitiously reinforced by water deliveries, and delays to water delivery were generally shorter for inoperative-lever responses than operative-lever responses. Second, the R > t contingency reduced the probability of operative-lever responses in the delay interval and increased the probabitilty of other behavior, including responses on the inoperative lever.

Interestingly, however, the mean proportions of inoperative-lever responding under the resetting-delay procedure observed in the Wilkenfield et al. (1992) study were 0.46 and 0.84 under the 8-s and 16-s delays, respectively. These proportions are considerably higher than the ones observed in the present study, which were 0.24 and 0.51 for the 8-s and 16-s delays, respectively. It is possible that this difference is due, in part, to the size of the chambers used in the Wilkenfield et al. study,

which were considerably smaller than those used in the present study. The probability of inoperative-lever responding should be inversely related to chamber size; as chamber size decreases the probability of inoperative-lever responding should increase. As the probability of inoperative-lever responding increases, the likelihood of such responding being adventitiously reinforced also increases. Thus, the higher proportions of inoperative-lever responding observed by Wilkenfield et al. (1992) as compared to the present findings may be due to an interaction of adventitiously reinforcement, the R > t contingency, and chamber size.

The present study extends the findings of prior studies by examining another index of learning, the development of stimulus control by the lever on which responses produced water. Although in the absence of drug substantial levels of operative-lever responding developed under all reinforcement procdedures within the first 100 min of the session, the development of stimulus control by the operative lever varied in speed and degree across procedures. Stimulus control developed rapidly when reinforcement was immediate. When reinforcement was delayed, stimulus control also developed under both 8-s nonresetting- and resetting-delay procedures, albeit less rapidly with the resetting delay. In contrast, despite substantial levels of operative-lever responding under the 16-s delay procedures, stimulus control did not develop at this delay under either nonresetting- or resetting-delay procedures. The present data suggest that response acquisition indexed as increases in operative-lever response rate may be less disrupted by

delayed reinforcement than response acquisition assessed in terms of the development of stimulus control by the operative lever. Grice (1948) previously reported that delaying reinforcement interfered with the development of stimulus control in rats performing a visual discrimination, which is consistent with the present findings. In contrast to these findings, however, he found substantial effects with delays as short as 2 s.

It is convenient to consider the two primary measures of response acquisition in the present study, overall level of operative-lever responding and level of operative-lever responding relative to inoperative-lever responding, as measures of reinforcement control and stimulus control, respectively, and we have made this distinction. Michael (1993), however, has pointed out that such contrasts are oversimplified because they "imply the absence of stimulus control when behavior change is accomplished by reinforcement" (p. 78). It is pehaps best to view the two idices of learning in the present study as representative of different forms of the function-altering effects of water deliveries. On the one hand, water deliveries establish an evocative relation between general features of the chamber and lever pressing in general; acquisition of this function is indexed by changes in rate of lever pressing. On the other hand, water deliveries establish an evocative relation between specific features of the operative lever and responses on it; acquisition of this function is indexed by changes in the proportion of inoperative responding. In light of the present findings, it appears that acquisition of the former relation is less disrupted by

delayed reinforcement than is acquisition of the latter relation.

Critchfield and Lattal (1993) were correct in asserting that recent findings of response acquisition with delayed reinforcement "prompt skepticism toward traditional assumptions . . . that substantial reinforcement delay prevents response acquisition (p.382)." Clearly, response acquisition can occur with delayed reinforcement. However, Schlinger and Blakely (1994) made the astute recommendation that what is needed is a thorough analysis of the variables that contribute to acquisition with delayed reinforcment. The present findings suggest that it will be important to discern the relative contribution of such variables to different aspects of acquisition.

The Present Findings in Relation to Prior Studies of Drug Effects on Learning

The major way in which the current study extends prior investigations of response acquisition with delayed reinforcement is by examining the effects of a drug, *d*-amphetamine, that is known to influence response acquisition under other free-operant assays. 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 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.

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

These findings are consistent with those of prior studies of the effects of *d*-amphetamine on repeated acquisition of behavioral chains. Generally, 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 increase within-session accuracy (learning) under repeated acquisition procedures, while moderate to high doses decrease within-session

accuracy, although acquisition still occurs (e.g., Evans & Wenger, 1992). While 5.6 and 10.0 mg/kg slowed response acquisition in the present study, these doses produced a general disruption of lever-pressing under all procedures by increasing stereotypies 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: "[T]here is no detrimental effect of these psychomotor stimulants on 'learning' until doses which produce a general behavioral disruption are achieved" (p. 636).

The present results are inconsistent with the effects of *d*-amphetamine on response acquisition under some other assays. For example, Robbins (1978) employed procedures (described above) similar to the ones used in the present study and found that response acquisition with conditioned reinforcement did not occur with any dose of *d*-amphetamine. One potential reason for the apparent difference in the effects of *d*-ampetamine reported by Robbins and those obtained in the present study is that different types of consequences (conditioned reinforcer versus unconditioned reinforcer) were arranged in the two studies. Because drug effects are known to be consequence-dependent under certain conditions of response maintenance (Barrett, 1981), drug effects on response acquisition also may be consequence-dependent.

An interesting finding of the present study was that the effects of *d*-amphetamine differed across delay value and delay type. Drug-

induced increases in overall rate of operative-lever responding were generally greater under the nonresetting-delay procedure than under the immediate-reinforcement and resetting-delay procedures. Moreover, such increases were greatest under the 16-s nonresetting delay. Increases in overall rates of responding are likely due to the drug's ability to increase locomotor activity (Seiden et al., 1993). Such activity might well lead to operation of the levers, and that the drug can increase lever pressing in the absence of any reinforcement contingencies is evident in Figure 7. For example, 1.0 mg/kg substantially increased rates of lever pressing under the no-water procedure relative to vehicle. Thus, any apparent enhancement of learning under the present procedures may be the result of generalized increases in locomotor activity. However, it is not clear why *d*-amphetamine increased overall response rates to a greater degree under the 16-s nonresetting-delay procedure than any other procedure.

The faliure of *d*-amphetamine to increase operative-lever responding substantially under the resetting-delay procedure is likely due to the R > t contingency. Prior studies have shown that this contingency punishes established operants (Zeiler, 1971, 1976, 1979), and *d*-amphetamine characteristically does not increase behavior suppressed by punishment (Seiden et al., 1993). There is, however, evidence to suggest that amphetamines increase rates of operative-lever responding under resetting-delay procedures that arrange delays longer than those employed in the present study. For instance, Dews (1960) reported that methamphetamine increased rates of key pecking in

pigeons maintained under a 100-s resetting-delay procedure. Thus, the extent to which *d*-amphetamine enhances the acquisition of lever presssing under a resetting-delay procedure may depend on the length of the delay.

It is well documented that most drugs, including *d*-amphetamine, disrupt behavior to a greater extent when stimulus control is weak than when it is relatively strong (Picker & Negus, 1993; Poling, 1986; Thompson, 1978). In the present study, stimulus control as indexed by the proportion of overall inoperative-lever responding was weaker under the delayed-reinforcement procedures than under the immediate- reinforcement procedure. Thus, it is interesting that *d*-amphetamine did not disrupt acquisition to any greater degree under the delayed-reinforcement procedures than under the immediate-reinforcement procedure. No dose of the drug increased the mean overall proportion of inoperative-lever pressing (i.e., decreased stimulus control) to a greater extent under the delayed-reinforcement procedures than under the immediate reinforcment procedure. Moreover, although the development of stimulus control under the delayed-reinforcement procedures was slower, it was not disrupted by 1.0 mg/kg significantly more than under the immediate-reinforcement procedure. Thus, the relative degree to which stimulus control develops during conditioning does not appear to modulate the effects of *d*-amphetamine on response acquisition.

Procedural Issues

Even though procedures like those used in the present study appear to provide a tenable assay of drug effects on the acquisition of free-operant behavior, such procedures have two related limitations. First, because acquisition is studied during a single session in each subject, between-subjects experimental designs are necessitated. Behavior analysts have repeatedly emphasized that such designs are generally inferior to within-subject arrangements (e.g., Johnston & Pennypacker, 1993; Poling, Methot, & LeSage, 1995; Sidman, 1960), although such designs are necessary to address some experimental questions. Second, because between-subjects variability under such procedures is relatively large, greater numbers of subjects (as well as statistical data analysis) may be needed to reveal the effects of independent variables. Fortunately, the subjects in the present study were subsequently used in a semester-long undergraduate learning laboratory, which mimimized wastage of valuable animals.

Although between subjects variability under the present assay is somewhat problematic, prior studies have suggested that some of the uncontrolled variance in response acquisition may be accounted for statistically. For instance, Stolerman (1971a, b) found that measures of behavior during magazine training, such as latencies to procure the reinforcer, were significantly correlated with the subsequent rate of lever pressing during acqusition ($r = 0.70$, $p < .001$). It is possible, therefore, to account for a portion of the variability in response rates during acquisition by using measures of behavior during magazine

training as covariates, thus increasing the precision of detecting the effects of drugs and other variables on response acquisition.

The aforementioned limitations notwithstanding, there are some advantages to the present assay. It appears to be sensitive to and allows for rapid assessment of drug effects, even when those effects are irreversible. Moreover, it examines how drugs affect the provenance of operant responding, which few other assays do. The present data suggest that the assay may be useful to behavioral pharmacologists and toxicologists, but further research is necessary to determine its full potential. For instance, whether drugs from different classes (e.g., neuroleptics, anxiolytics) produce differential effects on response acquisition with delayed reinforcement will need to be determined.

Appendix A

IACUC Approval Form

WESTERN MICHIGAN UNIVERSITY
INVESTIGATOR IACUC CERTIFICATE

Title of Project: The effects of amphetamine on response acquisition with delayed reinforcement

The information included in this IACUC application is accurate to the best of my knowledge. All personnel listed recognize their responsibility in complying with university policies governing the care and use of animals.

I declare that all experiments involving live animals will be performed under my supervision or that of another qualified scientist. Technicians or students involved have been trained in proper procedures in animal handling, administration of anesthetics, analgesics, and euthanasia to be used in this project.

If this project is funded by an extramural source, I certify that this application accurately reflects all procedures involving laboratory animal subjects described in the proposal to the funding agency noted above.

Any proposed revisions to or variations from the animal care and use data will be promptly forwarded to the IACUC for approval.

_____ Disapproved ___✓___ Approved _____ Approved with the provisions listed below

Provisions or Explanations:

Leonard C. Green — IACUC Chairperson — 3-6-95 — Date

Acceptance of Provisions

Signature: Principal Investigator/Instructor — 3/12/95 — Date

IACUC Chairperson Final Approval — Date

Approved IACUC Number 95-02-01

Rev. 3/92

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