



# Quantitative analyses of methamphetamine's effects on self-control choices: implications for elucidating behavioral mechanisms of drug action

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## Abstract

The purpose of the present research was to utilize quantitative methods to identify behavioral mechanisms involved in the effects of stimulant drugs on choice in a self-control procedure. A logarithmic equation based upon a combination of the matching law and hyperbolic discounting was used to separate drug-induced changes in sensitivity to reinforcement delay from drug-induced changes in sensitivity to reinforcement amount. Pigeons responded under a concurrent-chains schedule. In the initial link, two keys were illuminated simultaneously and access to the terminal link was controlled by a single random-interval (RI) schedule; pecks on one or the other key lead to its terminal link with a 0.5 probability. In the terminal links, one alternative provided 1-s access to food (the smaller reinforcer) and the other alternative provided 4-s access to food (the larger reinforcer). The signaled delay to the smaller reinforcer always was 2 s, whereas the signaled delay to the larger reinforcer increased from 2 to 40 s within each session, across 10-min blocks. In general, intermediate doses of methamphetamine increased preference for the larger more delayed reinforcer. Quantitative analyses indicated that, in most cases, methamphetamine decreased sensitivity to reinforcement delay. In a few instances, concomitant decreases in sensitivity to reinforcement amount also occurred. These results suggest that a reduced sensitivity to reinforcement delay may be important behavioral mechanism of the effects of stimulants on self-control choices, and that this effect sometimes can be accompanied by a decreased sensitivity to reinforcement amount.

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## 1. Introduction

The discipline of behavioral pharmacology represents a fusion of behavior analysis and pharmacology (e.g., Blackman and Sanger, 1978; Branch, 1991; Pickens, 1977; Thompson and Schuster, 1968). A major contribution of behavioral pharmacology over the past 40 years has been to show repeatedly that environ-

mental contingencies controlling behavior can be powerful determinants of the behavioral effects of drugs (see Branch, 1991 for a review of some important examples). Such demonstrations suggest that an account of the behavioral actions of drugs cannot be confined to biochemical or pharmacological principles, but must include behavioral principles as well.

Some behavioral pharmacologists have suggested that the notion of *behavioral mechanisms* of drug action might provide a useful framework within which to conceptualize the role of environmental

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contingencies in modulating behavioral effects of drugs (Branch, 1984, 1991; Laties and Weiss, 1969; Thompson and Schuster, 1968; Thompson, 1984). Indeed, Branch (1991) stated that “the goal of behavioral pharmacology is to identify *behavioral mechanisms* of drug action” (p. 21). What is meant by “behavioral mechanism of drug action”?

Although several behavioral pharmacologists have written extensively about this notion, perhaps the most succinct characterization was offered by Thompson (1984):

By behavioral mechanism of drug action, we refer to a description of a drug’s effect on a given behavioral system expressed in terms of some more general set of principles regulating behavior. (p. 5)

Thompson went on to clarify the notion by saying that:

Specifying the behavioral mechanism(s) responsible for an observed effect involves (1) identifying the environmental variables which typically regulate the behavior in question, and (2) characterizing the manner in which those variables’ influence is altered by the drug. (p. 5)

According to this view, then, drugs can produce their behavioral effects by altering the way in which environmental variables control behavior. That is, drugs alter functional relations between environmental contingencies and behavior.

Despite the appeal of this notion, identifying behavioral mechanisms of drug action can be tricky. Among other things, the task is complicated by the fact that, even under highly controlled laboratory conditions, behavior is multiply determined. Thus, identifying which specific functional relation is altered by administration of a drug can be exceedingly difficult. For example, when administration of a given drug alters the rate of schedule-controlled operant behavior, it could do so by changing the organism’s capacity to execute the response, the effects of the establishing operation, the effects of the contingency between behavior and the consequent event, and/or the nature of the antecedent stimulus control, to name just a few of the possibilities (see Barrett, 1987; Witkin and Katz, 1991, for thoughtful discussions related to the difficulties in isolating behavioral mechanisms).

### 1.1. *Quantitative analyses and behavioral mechanisms of drug action*

In some cases, behavioral pharmacologists have found quantitative methods useful in elucidating behavioral mechanisms of drug action. This approach often involves characterizing drug-induced changes in one or more parameters of an equation or model that describes some relation between environmental contingencies and behavior. For example, Heyman and his colleagues (e.g., Heyman, 1983, 1992; Heyman and Monaghan, 1990) used Herrnstein’s (1970) hyperbolic equation relating absolute response rate to reinforcement rate in an attempt to isolate behavioral mechanisms associated with drug effects on schedule-controlled operant behavior.

Heyman found that certain drugs (e.g., amphetamine and methylphenidate) tended to change the value of parameter  $R_e$  (the reinforcement rate maintaining one half the asymptotic response rate) at doses that did not affect the parameter  $k$  (the asymptotic response rate). In contrast, at higher doses of these drugs, and at all doses of some other drugs (e.g., the neuroleptic pimoxide), concomitant decreases in  $k$  occurred. It was suggested that changes in  $R_e$  reflect drug-induced changes in reinforcement effectiveness, whereas changes in  $k$  reflect drug-induced changes in motor functioning. Egli et al. (1992) and Lancaster and Dallery (1999) also used this approach to investigate reinforcement mechanisms involved in effects of opiates.

Other investigators (e.g., Cohen, 1986; Egli et al., 1992) have attempted to characterize drug effects with the quantitative methods of behavioral momentum and resistance to change, with varying degrees of success. In this framework, drug administration is viewed as a behavioral disruptor, functionally similar to other disruptors such as extinction and supplemental presentation of the reinforcer (see Nevin, 1974, 1978; Nevin and Grace, 2000).

Because of the relatively precise specification of relations between environmental variables and their behavioral effects, quantitative methods seem particularly well suited to the challenging task of isolating behavioral mechanisms of drug action. In our opinion, however, the utility of this approach in behavioral pharmacology has yet to be fully exploited. Thus, the primary purpose of the present work was to intro-

duce and evaluate a quantitative approach to characterizing drug effects on choice in a self-control procedure. More specifically, we employed an analysis based upon a combination of the matching law and Mazur's (1987) hyperbolic discounting model in an attempt to isolate behavioral mechanisms associated with effects of the stimulant methamphetamine on choice in a self-control procedure.

### 1.2. Drugs and "self-control"

When an experimental subject is confronted with a choice between a smaller, more immediate reinforcer and a larger, more delayed reinforcer, the subject is said to behave "impulsively" when it chooses the former and show "self-control" when it chooses the latter (e.g., Ainslie, 1975; Logue, 1988; Rachlin, 1974). Recently, investigators have been interested in characterizing effects of drugs on choice under these conditions. Some of the data reported with psychomotor stimulants have been particularly interesting. Data from some of the initial studies indicated that drugs such as cocaine and *d*-amphetamine decrease the likelihood of choosing a larger, more delayed reinforcer (e.g., Charrier and Thiebot, 1996; Evenden and Ryan, 1996; Logue et al., 1992). Data from some more recent studies, however, suggest an opposite effect for this class of drugs. Using an adjusting-amount procedure, Richards and his colleagues (Richards et al., 1999; Wade et al., 2000) reported that amphetamines and other dopamine agonists actually increased the likelihood of choosing a larger, more delayed reinforcer. At this point, the reason(s) for these discrepancies is(are) not clear, although Richards et al. (1999) and Cardinal et al. (2000) have suggested some possibilities. Nevertheless, more work clearly is needed investigating effects of stimulants under self-control procedures. Thus, a second purpose of the present work was to provide additional data relevant to this issue.

### 1.3. Potential behavioral mechanisms involved in drug effects on self-control

Consider, for example, the case in which acute administration of moderate doses of methamphetamine increased the likelihood of selecting a larger, more delayed reinforcer (e.g., Richards et al., 1999). There are a number of potential behavioral mechanisms as-

sociated with this effect—at least two readily come to mind. For example, it is possible that methamphetamine increased the relative effectiveness of the larger food amount; that is, methamphetamine may have increased the sensitivity of the subjects' behavior to the difference in reinforcement amount. On the other hand, it also is possible that methamphetamine attenuated the discounting effects of reinforcement delay; that is, methamphetamine may have decreased the sensitivity of the subjects' behavior to the effects of delay. At this point, it is difficult to say which of these potential behavioral mechanisms may be relevant. Appropriate changes in either (or both) of these parameter(s) predict the obtained drug effect. In the present study, a quantitative approach was used to address the question: Are methamphetamine's effects on choice under a self-control procedure related to changes in the effects of reinforcement delay and/or reinforcement amount?

## 2. The present approach

Behavioral allocation in a two-choice self-control procedure can be described by the following version of the matching law:

$$\frac{R_L}{R_S} = \left( \frac{A_L/A_S}{D_L/D_S} \right) \quad (1)$$

where  $R_L/R_S$ ,  $A_L/A_S$ , and  $D_L/D_S$ , represent the ratios of responses, amounts, and delays, respectively, associated with the larger and smaller reinforcers. In this equation, increasing  $A_L/A_S$  has an increasing effect on  $R_L/R_S$ , whereas increasing  $D_L/D_S$  has a decreasing effect on  $R_L/R_S$ . In keeping with the frequent reports that delay discounting is best described by a hyperbolic function (e.g., Mazur, 1987; Richards et al., 1997) the term  $D_L/D_S$  was replaced with the term  $[1 + D_L]/[1 + D_S]$  in the present analysis. In addition, two free parameters were added, such that:

$$\frac{R_L}{R_S} = \left( \frac{(A_L/A_S)^{S_A}}{([1 + D_L]/[1 + D_S])^{S_D}} \right) \quad (2)$$

where  $S_A$  and  $S_D$  represent the sensitivities to effects of reinforcement amount and reinforcement delay, respectively (see Logue et al., 1984). Thus, according to this equation,  $R_L/R_S$  is an increasing power function of  $A_L/A_S$  and a decreasing power function of

$[1 + D_L]/[1 + D_S]$ . (For convenience, the free parameter  $k$  typically used in Mazur's, 1987 hyperbolic model was held constant at 1.0.)

For the present analysis, Eq. (2) was transformed logarithmically:

$$\log\left(\frac{R_L}{R_S}\right) = S_A \log\left(\frac{A_L}{A_S}\right) - S_D \log\left(\frac{[1 + D_L]}{[1 + D_S]}\right) \quad (3)$$

In the study reported below,  $A_L/A_S$  was held constant at 4, while  $[1 + D_L]/[1 + D_S]$  was manipulated by changing  $D_L$ . Under these conditions, the model predicts that  $\log(R_L/R_S)$  is a decreasing linear function of  $\log([1 + D_L]/[1 + D_S])$ , with a slope  $S_D$  and  $y$ -intercept  $S_A \log(A_L/A_S)$ .

To illustrate how Eq. (3) was used to infer potential behavioral mechanisms associated with effects of methamphetamine on self-control, Fig. 1 presents two possible outcomes. In both panels of the figure, the solid line indicates the function relating  $\log(R_L/R_S)$  to  $\log([1 + D_L]/[1 + D_S])$  when both sensitivity parameters are 1.0. In the left panel, the dashed line illustrates an increase in the sensitivity to reinforcement amount ( $S_A$ ) to 2.0 while the sensitivity to delay ( $S_D$ ) remains at 1.0. This results in a parallel upward shift in the entire function; the  $y$ -intercept, but not the slope, is changed. Note that, with a constant

ratio of reinforcement amounts, this analysis assumes that *bias* (e.g., a position or color preference) remains constant. In the right panel, sensitivity to delay is decreased to 0.5, while sensitivity to amount remains at 1.0. This results in a change in the slope of the function, but not the  $y$ -intercept. Thus, in both of these examples, preference for a larger, more delayed reinforcer is increased. The effect, however, is manifested in different ways. That is, a drug-induced change in sensitivity to reinforcement amount occurs as a change in the  $y$ -intercept, whereas a drug-induced change in sensitivity to reinforcement delay occurs as a change in the slope. (Note: for clarity, an effect such as that presented in the right panel of Fig. 1, where the value becomes less negative, will be described as a *decrease* in the slope.)

### 3. Method

#### 3.1. Subjects

Four male White Carneau pigeons (*Columba livia*), designated 1809, 1863, 1845, and 1985, served as subjects. Each pigeon had previous experience, and had previously received drugs, under the procedures used

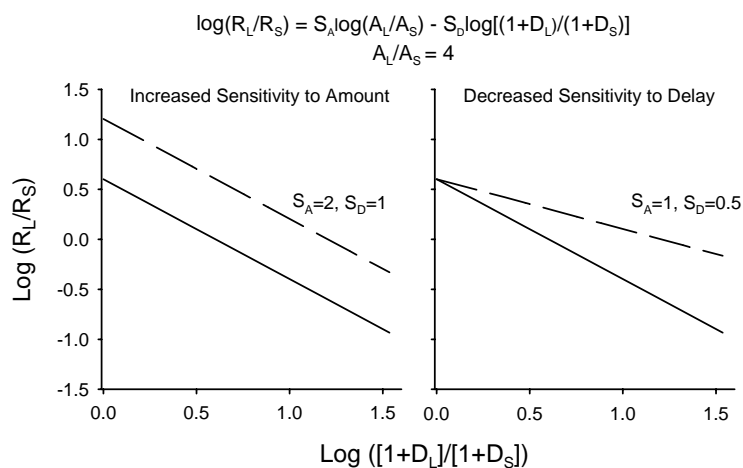


Fig. 1. Two hypothetical outcomes of a manipulation that increases choice of a larger, more delayed reinforcer. In these scenarios, the ratio of the large to small reinforcement amount ( $A_L/A_S$ ) is constant at 4, the delay to the smaller reinforcer is constant at 2 s, and the delay to the larger reinforcer ranges from 2 to 50 s. In these examples,  $\log(R_L/R_S)$  is plotted as a function of  $\log([1 + D_L]/[1 + D_S])$  and  $S_A$  and  $S_D$  represent the sensitivities to amount and delay, respectively. In both panels, the solid line shows the function when both  $S_A$  and  $S_D$  are 1.0. In the left panel, the dashed line shows the effect of increasing  $S_A$  to 2.0. In the right panel, the dashed line shows the effect of decreasing  $S_D$  to 0.5. See text for further discussion.

in the present study. Each pigeon was drug free for a minimum of 2 weeks prior to participating in the present study. All pigeons were housed individually in a colony room operating under a 12-h light:12-h dark cycle (lights on at 07:00 a.m.). The pigeons were maintained at 80% of their free-feeding weights by providing post-session access to mixed grain (Purina®) as needed. Continuous access to water and health grit was provided in the home cages.

### 3.2. Apparatus

Two identical operant-conditioning chambers were used (BRS/LVE, Inc. model SEC-002); each had an internal space measuring 35.0 cm deep by 30.5 cm wide by 36.0 cm high. One wall of each chamber was constructed of aluminum and contained three response keys arranged in a horizontal line, 26 cm from the floor and 8.5 cm apart (center to center). Each key was 2.5 cm in diameter and required approximately 0.25 N of force to activate its corresponding switch; only the two side keys were used in this study. Each side key was 9.0 cm from its adjacent wall and could be trans-illuminated red or green. A 5.0 cm × 6.0 cm aperture, through which mixed grain could be presented, was located 11.0 cm directly below the center key. When grain was presented, all key lights and houselights were off, and a white light illuminated the opening. A 1.2-W white houselight was located 6.5 cm directly above the center key. Green and red houselights were located 5 cm to the left and right of the white houselight, respectively. Each chamber was equipped with a ventilation fan, and white noise was present in the room to mask extraneous sounds. Experimental events were programmed and data were recorded from an adjoining room by an MS-DOS-controlled 80486 microcomputer using Med Associates® (Georgia, VT) software and interface equipment operating at 0.01-s resolution.

### 3.3. Behavioral procedure

Because of the pigeons' previous experience, no preliminary training was necessary. Experimental sessions consisted of exposure to a concurrent-chains procedure. During the initial link, the white houselight and the side keys were illuminated; one key was red and one was green. A single random-interval (RI)

1-min schedule governed access to the terminal links. The RI-schedule contingencies were programmed using a probability gate pulsed each second. A single RI schedule was used in the initial link to insure that both options were sampled. Once terminal-link access was set up by the RI schedule, another probability gate, set at 0.5, determined whether the red key or the green key was active. A peck on the active key turned off the white houselight and both side keys, illuminated the houselight that matched the color of the active key, and initiated the corresponding terminal link.

One terminal link (the smaller reinforcer) provided 1.5-s access to grain under a fixed-time (FT) 2-s schedule (i.e., this option provided access to the smaller reinforcer after a 2-s signaled delay). The other terminal link (the larger reinforcer) provided 4.5-s access to grain under an FT schedule. This option provided access to the larger reinforcer after a signaled delay that increased across blocks of the session (see below). For each reinforcement amount, the 0.5 s was included to allow the pigeon time to bring its head down to the food hopper (see Epstein, 1981). For the remainder of this paper, the values 1 and 4 s will be used to represent the smaller and larger reinforcement amounts, respectively.

A blackout followed each reinforcement delivery, after which the initial link was reinstated (with the red and green side keys and the white houselight illuminated). Post-reinforcement blackout time was adjusted to hold the duration from terminal-link entry to initial-link reinstatement at 60 s across the two choices (i.e., blackout = 60 s - [delay + amount]). A 5-s changeover delay (COD) was in effect during the initial link; a peck on a given key could not gain entry into a terminal link until 5 s had passed since a changeover to that key.

To obtain within-session delay functions, the delay to the larger reinforcer was increased across five blocks. Each block lasted 10 min, excluding time spent in the terminal links. The delay to the larger reinforcer was equal to that of the smaller reinforcer (2 s) during the first block and was 10, 20, 30, and 40 s during blocks 2–5, respectively. Blocks were separated by 75-s blackouts and sessions ended upon completion of the fifth block. If a block was scheduled to end while the food hopper was raised, the reinforcement cycle was allowed to finish before the block was terminated.

Key-color position and the keys corresponding to the larger and smaller reinforcers were counterbalanced across pigeons and held constant throughout the experiment. The conditions for each pigeons were as follows: 1809, left key: green/small, right key: red/large; 1863, left key: red/large, right key: green/small; 1845, left key: green/large, right key: red/small; 1985, left key: red/small, right key: green/large.

Sessions were conducted 5 days per week (Monday through Friday). Once stable performance was achieved under the concurrent-chains procedure described above, drug testing was initiated. Behavior was considered stable when the response rates on each key during the initial links of each block showed minimal variability and little trending over 10 consecutive sessions, as determined by visual inspection of daily plots.

### 3.4. Pharmacological procedure

Methamphetamine hydrochloride (Sigma®) was dissolved in saline (0.9% sodium chloride) and injected 15 min prior to selected sessions. Injections were given into the breast muscle (i.m.) using a solution volume of 1.0 ml/kg. Injections were administered on Tuesdays and Fridays, provided that the data from the session conducted the day before (the control session) were within the range of the previous 10 non-injection sessions; if this was not the case, the injection for that day was cancelled, but the session still was conducted. Injection sites alternated between the left and right breast muscle. The following doses of methamphetamine were tested (expressed in terms of the total salt): 0.3, 1.0, 1.7 and 3.0 mg/kg. Effects of each dose and the saline vehicle were determined at least twice; an additional determination of a dose was conducted if the data from the first two determinations were judged to be substantially different. Doses were administered in a mixed order, with the constraint that no dose was given a second time until all doses had been given once. Each determination of a dose-effect function was preceded by an assessment of the effects of saline (saline sessions).

### 3.5. Data analysis

The following data were collected for each block: (a) overall response rate (per minute) on each key dur-

ing the initial link, and (b) the amount of time allocated to each option during the initial link. Time allocation to a given option was obtained by starting a timer upon the first peck to the corresponding key following either a peck to the other key or the start of the initial link and stopping the timer whenever the other key was pecked or when the terminal link was entered. Most of the data presented below were based upon data obtained from the last 5 min of each block, when performance presumably was most stable. For comparison, analyses from the first 5 min of each block also were conducted.

For each block (i.e., each delay value for the larger reinforcer), the ratio of the responses maintained by the larger reinforcer to the responses maintained by the smaller reinforcer ( $R_L/R_S$ ) was obtained. Average response ratios for control, saline, and each dose were plotted as a function of the term  $[1 + D_L]/[1 + D_S]$  and the resulting functions then were analyzed using Eq. (3). For each condition, sensitivity to reinforcement delay ( $S_D$ ) was obtained by taking the slope of the function, and sensitivity to amount ( $S_A$ ) was obtained by dividing the y-intercept by 0.6 (the logarithm of the amount ratio, which was 4). Functions for time allocation ( $T_L/T_S$ ) also were obtained.

Dose–response functions for methamphetamine on  $S_D$  and  $S_A$  also were obtained. For these analyses, log ratio functions were plotted for individual sessions and the corresponding slopes and y-intercepts were obtained. Mean  $S_D$  and  $S_A$  values were then plotted for control, saline, and each dose.

Stimulant drugs often produce “rate-dependent” effects on schedule-controlled operant behavior (see Dews and Wenger, 1977; Sanger and Blackman, 1976). That is, the observed drug effect can depend upon the rate of responding under baseline (non-drug) conditions. To assess the possibility of rate-dependent drug effects here, response rates from each block were subjected to the following analysis: At each drug dose, a percent-control value was obtained for each key in each block. Percent-control values were obtained by dividing the rate of responding on a given key in a given block after drug administration (“drug rate”) by the rate of responding obtained on that key in that block under control conditions (“control rate”) and multiplying the result by 100 ([drug rate/control rate]  $\times$  100). Thus, for each dose, a total of 10 percent-control values were obtained. These

values were then plotted against their corresponding control values on logarithmic coordinates. Any deviation in this function from a horizontal line indicates a rate-dependent effect (i.e., the dose affected some response rates differently than others).

#### 4. Results and discussion

##### 4.1. Control data

Fig. 2 shows initial-link response rates for each pigeon under control conditions. Rates maintained by the larger (filled symbols) and the smaller (unfilled symbols) reinforcers are plotted as a function of the delay to the larger reinforcer. For each pigeon, rates

maintained by the larger and smaller reinforcers decreased and increased, respectively, as a function of the delay to the larger reinforcer. Pigeons 1863, 1845, and 1985 responded more frequently on the key associated with the larger reinforcer at delays of 2 and 10 s, and responded more frequently on the key associated with the smaller reinforcer at delays of 20 s and longer (i.e., the functions crossed between 10 and 20 s). Pigeon 1809 showed a bias for the key associated with the smaller reinforcer; rates were higher on that key at all delay values.

Fig. 3 shows the response-ratio functions plotted according to Eq. (3);  $\log(R_L/R_S)$  is plotted as a function of  $\log([1 + D_L]/[1 + D_S])$ . Best-fit regression lines also are shown, along with the corresponding  $S_D$ ,  $S_A$ , and  $r^2$  values. The  $S_D$  values of these functions ranged

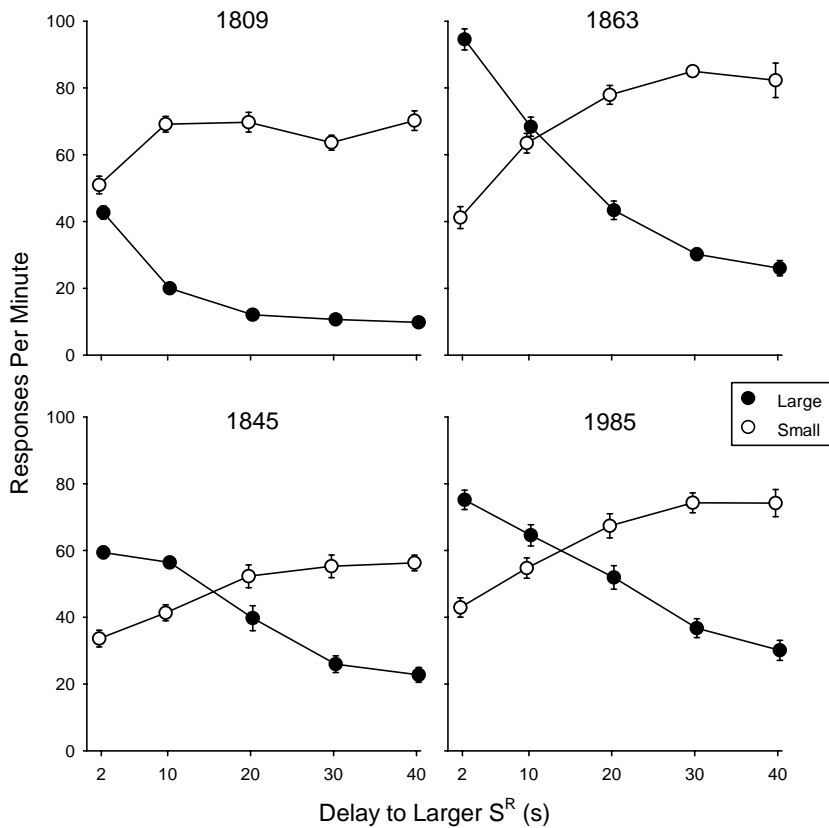


Fig. 2. Responses per minute on each key as a function of the delay associated with the larger reinforcer for each pigeon. The filled symbols show data for the key associated with the larger reinforcer and the unfilled symbols show data for the key associated with the smaller reinforcer. Values are means and vertical lines show S.E. The absence of an error bar indicates that it fell within the space covered by the data point. Values were obtained from between 11 and 15 observations.

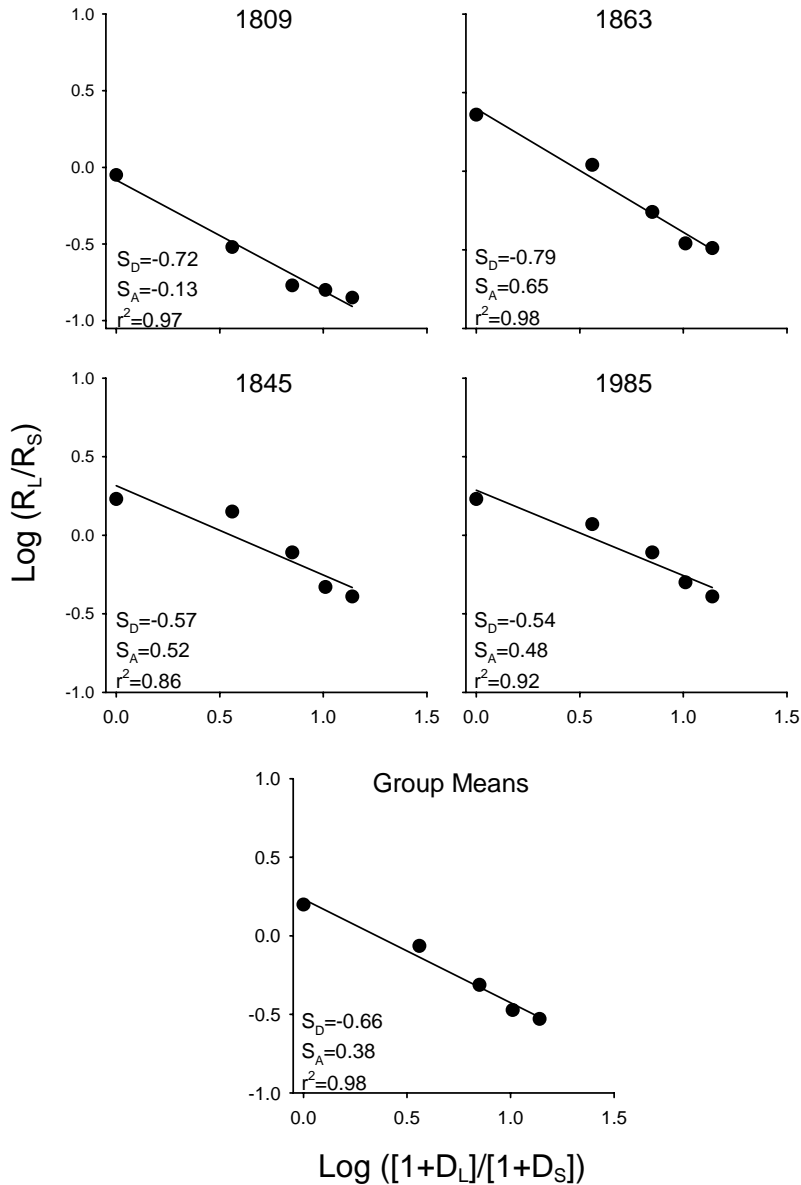


Fig. 3. Response-ratio/delay-ratio functions plotted according to Eq. (3) from control sessions for each pigeon, and for the group, along with their corresponding regression lines. In these graphs,  $\log(R_L/R_S)$  is plotted as a function of  $\log([1 + D_L]/[1 + D_S])$ . The  $S_D$  and  $S_A$  values obtained from Eq. (3) also are provided, along with  $r^2$  values.

from  $-0.79$  to  $-0.54$  and the  $S_A$  values ranged from  $-0.13$  to  $0.65$ . In each individual case, and with the group means, the linear regression line did a very good job of accounting for the data (individual  $r^2$  values ranged from  $0.86$  to  $0.98$ ).

The data presented in Figs. 2 and 3 provide substantial evidence that performance of the individual pigeons was under good experimental control by the arranged contingencies. For all pigeons, preference for the larger reinforcer was a decreasing function of its

delay, an effect similar to that typically obtained in studies of delay discounting with both humans and non-humans (e.g., Madden et al., 1999; Mazur, 1987; Richards et al., 1997). Furthermore, the data in Fig. 3 indicate that Eq. (3) provided an excellent description of performance under the experimental conditions arranged here. Thus, the procedure used in this study appears to provide an effective method for assessing effects of reinforcement delay within sessions. Within-session methods such as the one used here may allow more efficient examination of variables affecting delay discounting than is possible with more commonly used methods (e.g., adjusting procedures). It should be noted, however, that the changing delay conditions within sessions may have recruited additional, unwanted, sources of control over choice. For example, the bias for the smaller reinforcer observed with 1809 may have resulted from the predictable escalation of the delay to the larger reinforcer across session blocks.

#### 4.2. Effects of methamphetamine

Fig. 4 shows effects of three doses of methamphetamine (1.0, 1.7, and 3.0 mg/kg) on the relation between  $\log([1 + D_L]/[1 + D_S])$  and  $\log(R_L/R_S)$  for each pigeon and for the group. The effects of the doses (unfilled symbols) are shown along with control data (filled symbols). In general, saline and 0.3 mg/kg had relatively little or no effect on responding and, thus, for clarity, these data are not presented in this figure. For three of the four pigeons (1809, 1863, and 1845) the major effect of methamphetamine was to elevate  $R_L/R_S$  at the higher  $[1 + D_L]/[1 + D_S]$  values (i.e., methamphetamine decreased the slope). It does not appear that the size of the effect depended upon the dose; comparable effects were obtained at all three doses. (Note, however, that the group-mean plot does appear to show a dose-dependent decrease in slope.) For 1809 and 1863, the change in the slope was accompanied by what appears to be a slight reduction in y-intercept at one (1809) or two (1863) doses. This resulted from a small reduction in preference for the larger reinforcer when the delays were equal. With 1985, methamphetamine tended to decrease preference for the larger reinforcer at the shorter delays. Thus, with this pigeon, there was a dose-dependent decrease in the y-intercept (also see Fig. 7). Only the highest dose (3.0 mg/kg)

increased preference for the larger reinforcer at the longer delays with this pigeon. This was accompanied by a substantial reduction in preference for the larger reinforcer during the first block. Thus, the slope of the log discount function for this pigeon was positive at 3.0 mg/kg. It should be noted that this dose produced relatively substantial decreases in overall levels of responding for 1985—average response rates for both keys were below 20 responses/min in all components and below 10 responses/min in most of the components for this pigeon.

Fig. 5 shows effects of only 1.7 mg/kg methamphetamine on the log response-ratio functions; corresponding regression lines also are included. For all four birds, this dose decreased the slope of the function. This was clearly the case with 1809, 1863, and 1845, and there was a hint of an effect with 1985. For two of the pigeons (1809 and 1845), this dose decreased the slope without substantially changing the y-intercept. For 1863, the change in slope was accompanied by a moderate decrease in the y-intercept; with this pigeon the function was nearly flat. For 1985, the major effect of this dose was to decrease the y-intercept. Recall that, for this bird, the function had a positive slope at 3.0 mg/kg, showing a change in both the y-intercept and the slope (see Fig. 4).

Fig. 6 shows effects of 1.0, 1.7, and 3.0 mg/kg methamphetamine on time allocation. In general, these functions resemble those for response allocation shown in Fig. 4. The most notable difference was the occasional increase in y-intercept (e.g., 1809 at 3.0 mg/kg and 1845 at 1.0 mg/kg) with time-allocation. Note also that the effects of methamphetamine on the slope for 1845 and y-intercept for 1985 appeared to be slightly greater for time allocation than for response allocation. Nevertheless, comparison of Figs. 4 and 6 indicates that, in general, the effects of methamphetamine were similar for both measures. For three of the birds, the most consistent effect of methamphetamine was a decrease in the slope of the function, whereas for the fourth bird, the most consistent effect was a change in the y-intercept.

Fig. 7 shows individual dose-effect functions for  $S_D$ , shown in the left panels, and  $S_A$ , shown in the right panels; these functions were derived from the response-allocation data; plots for group means also are shown. The values plotted for  $S_D$  are absolute values. (Note that the  $S_D$  for 1985 at 3.0 mg/kg actually

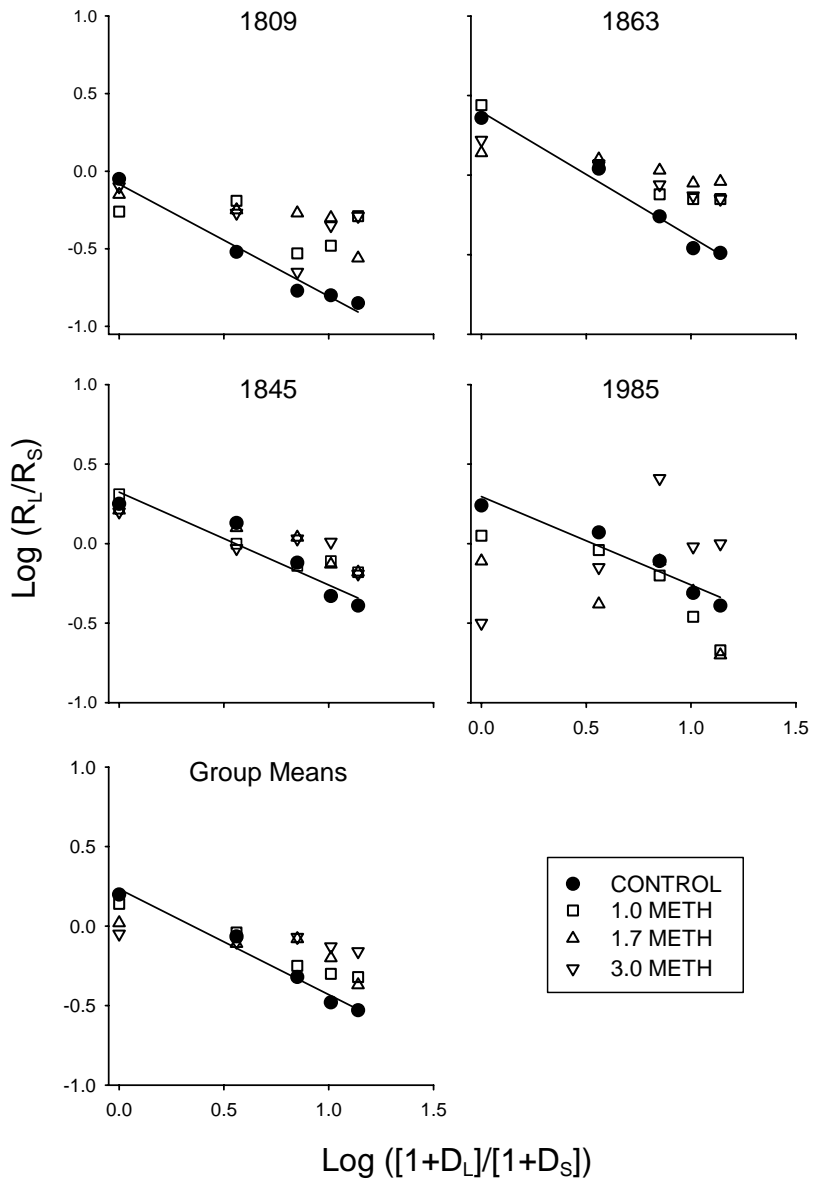


Fig. 4. Effects of three methamphetamine doses on the log-ratio function for each pigeon. Data from control sessions are shown with filled circles and effects of the methamphetamine doses are shown with open symbols. Squares show effects of 1.0 mg/kg, triangles show effects of 1.7 mg/kg, and inverted triangles show effects of 3.0 mg/kg. The regression lines were fitted to the data from control sessions. All other characteristics of this figure are as described for Fig. 3.

was positive—see Fig. 4. Because this effect represented a change in the slope that was in the same direction as the other data points, the slope at this dose for this bird was plotted at zero for convenience.) Fig. 7 shows that a primary effect of methamphetamine in all

birds was to flatten the log ratio functions. For 1809, 1863 and 1845, at least one dose reliably decreased  $S_D$  without reliably altering  $S_A$ . For all pigeons except 1809, at least one dose reliably decreased  $S_A$ . A one-way, repeated-measures ANOVA was conducted

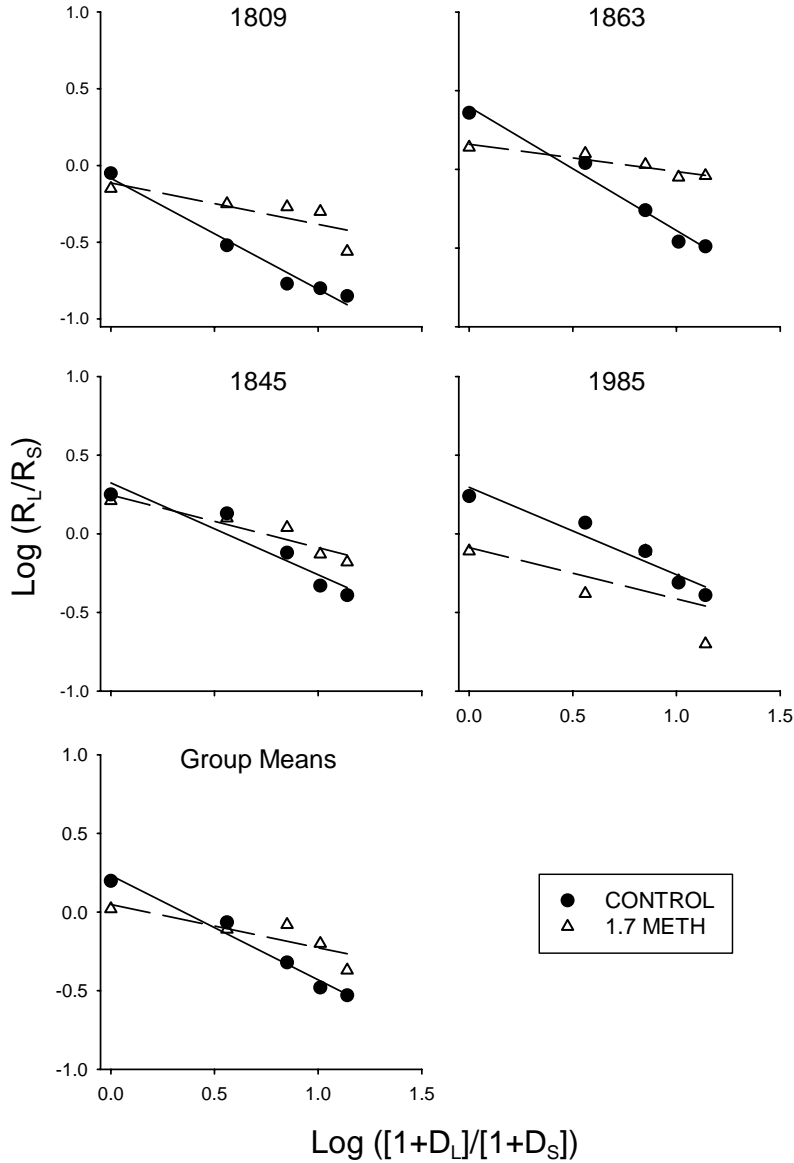


Fig. 5. Effects of 1.7 mg/kg methamphetamine on the log-ratio function for each pigeon. The solid regression line was fitted to the control data and the dashed regression line was fitted to the data for 1.7 mg/kg. All other characteristics of this figure are as described for Figs. 3 and 4. Note that for 1985 at the 20- and 30-s delays, the data points for 1.7 mg/kg are covered by the data points for control.

for the effects of methamphetamine on  $S_D$  and  $S_A$ , using the data for saline and each of the doses. Despite the small number of subjects, this analysis revealed a statistically significant effect of dose on  $S_D$  ( $F(4, 3) = 6.5, P = 0.005$ ); the data for  $S_A$  were not statistically significant ( $F(4, 3) = 1.64, P = 0.228$ ). Post hoc tests (Tukey's HSD) for  $S_D$  revealed significant differences

between the effects of saline and 1.7 mg/kg and the effects of saline and 3.0 mg/kg.

For comparison, data from the first 5 min of each component are shown for control and 1.7 mg/kg (triangles). In general, the effects of this dose on preference during the first and last 5 min of each component were similar, although for both  $S_D$  and

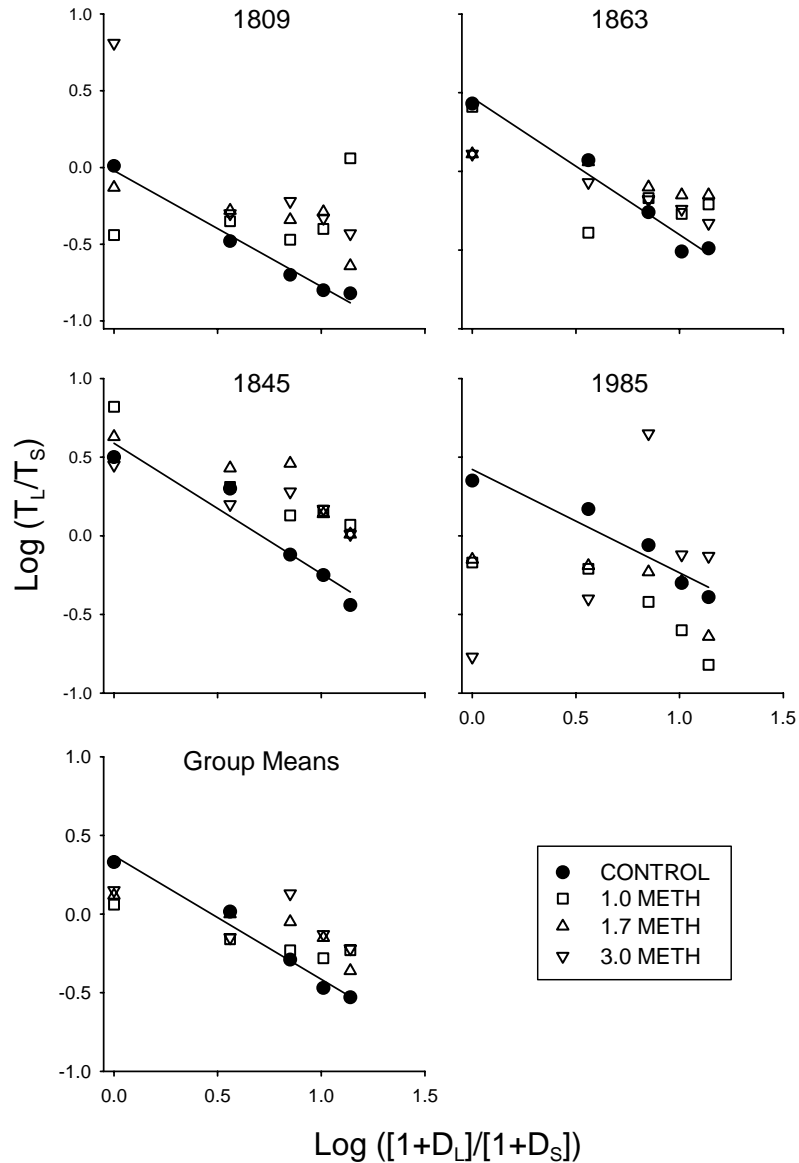


Fig. 6. Effects of three methamphetamine doses on the log discount functions for relative time-allocation ( $T_L/T_S$ ). All other characteristics of this figure are as described for Fig. 4.

$S_A$ , the effects were somewhat smaller during the first 5 min (except for 1845). Interestingly, for three of the pigeons (1809, 1863, and 1845),  $S_A$  values under control conditions were higher and the slopes of the functions were slightly steeper for the first 5 min than for the last 5 min; Thus, although preference appears to have been established relatively early

within each component, probably by virtue of the extensive history of exposure to a consistent escalation of delays to the larger reinforcer, there was some adjustment of preference within components. Furthermore, in most cases, behavior over the last 5 min of each component was more sensitive to the effects of methamphetamine.

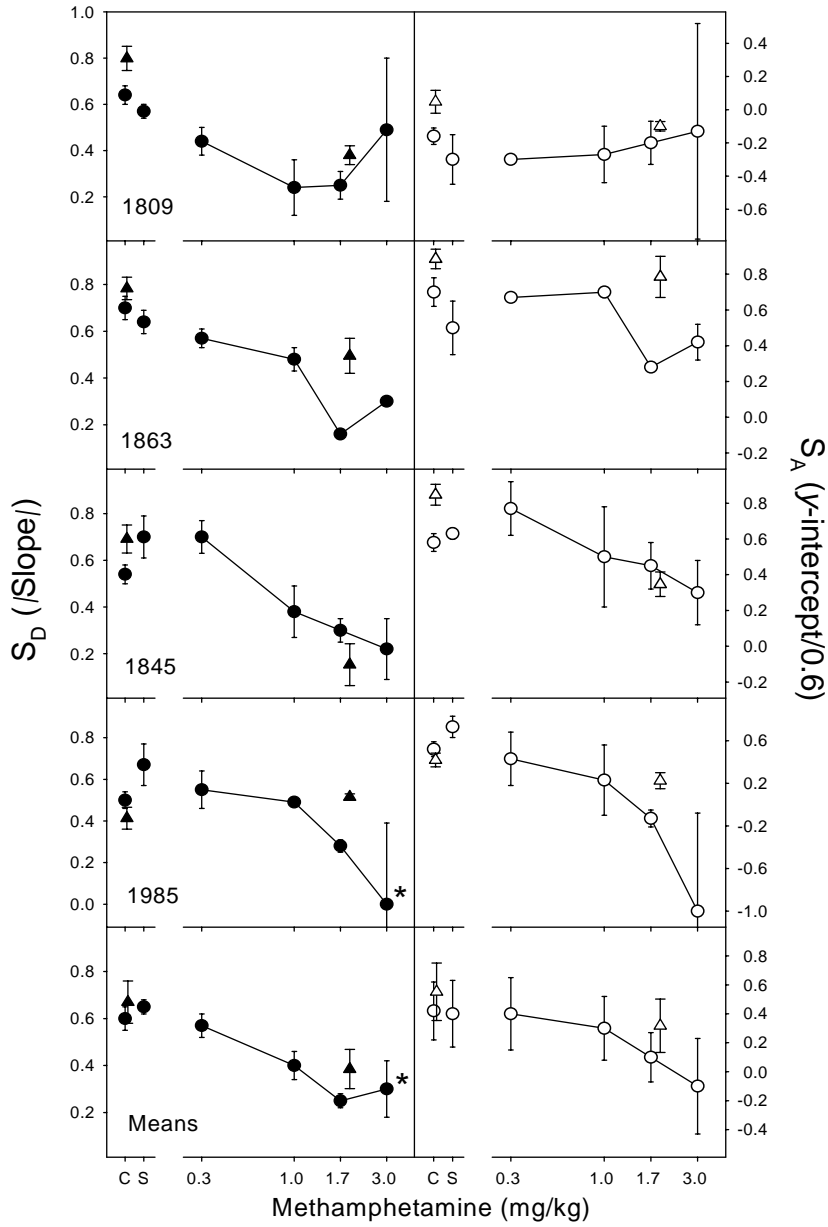


Fig. 7. Dose-effect functions for  $S_D$  (left panels) and  $S_A$  (right panels). Points above C show data from control sessions and points above S show effects of saline administration. Values are means from two to four determinations (saline and doses) and from 11 to 15 control sessions. Vertical lines show S.E. Data points for  $S_D$  are absolute values. Data points marked by an '\*' include a positive slope value (see text for details). Circles show data taken from the last 5 min of each component and triangles show data taken from the first 5 min of each component. Note that the y-axes for the  $S_A$  data are individualized.

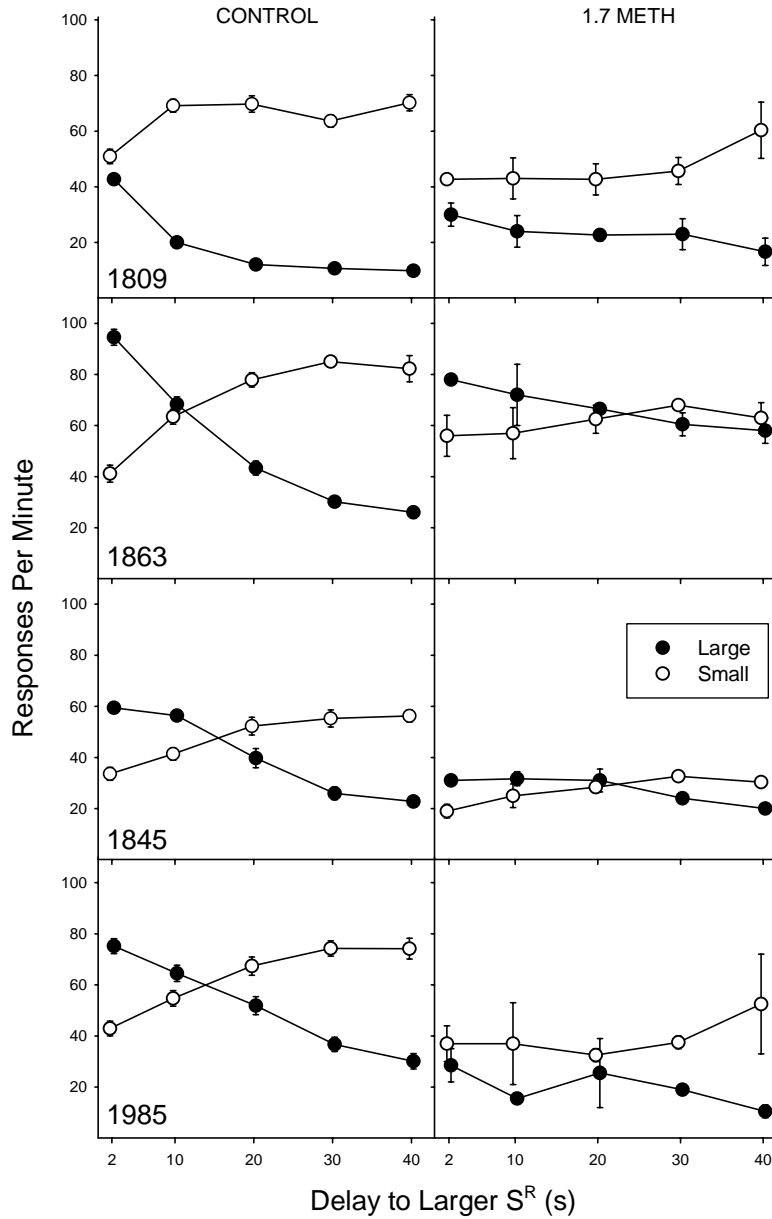


Fig. 8. Responses per minute for each pigeon as a function of the delay to the larger reinforcer for control sessions (left panels) and following administration of 1.7 mg/kg methamphetamine (right panels). All other characteristics of this figure are as described for Fig. 2.

To this point, methamphetamine's effects have been characterized entirely with relative measures. Fig. 8 shows the drug effects for absolute response rates on each key at each delay. The left panels show data from control sessions (these are the same functions

shown in Fig. 2) and the right panels show effects of 1.7 mg/kg. For all pigeons, a major effect of this dose was to flatten both functions and bring the rates on each key together. Interestingly, although the effects of this dose on the relative measures for 1809, 1863,

and 1845 were similar (see Fig. 5), they were achieved in slightly different ways. For 1809, the change in slope occurred as a result of slightly elevated rates on the “large key” and slightly lowered rates on the “small key” at delay values of 10 s and longer. A similar effect was obtained with 1863. In addition, for this pigeon, rates on the large key were lowered and rates on the small key were elevated in the first block (when the delays were equal); this resulted in the decrease in the *y*-intercept. On the other hand, for pigeon 1845, the change in slope appears to have occurred primarily as a result of lowered response rates on the small key at the longer delay values; response rates on the large key at the longer delays were relatively unaffected. Response rates on both keys were lowered during the first two blocks for this pigeon. For 1985, the change in the *y*-intercept occurred mainly as a result of substantially reduced rates on the large key during the first three blocks. Finally, it is worth pointing out here that, for 1863 and 1845, 1.7 mg/kg also changed the point at which the two functions crossed (what might be called the indifference point). For both of these pigeons, the crossover point was shifted to the right. That is, the delay value at which indifference occurred was increased.

#### 4.2.1. Rate-dependent analyses

As mentioned earlier, stimulants such as methamphetamine often produce rate-dependent effects. Under certain conditions, moderate doses of these drugs tend to affect different baseline response rates differentially. These doses often increase relatively low response rates (e.g., those occurring early during the interval under fixed-interval, or FI, schedules) and decrease relatively high response rates (e.g., those occurring late in the FI) (see Dews and Wenger, 1977; Sanger and Blackman, 1976).

Fig. 9 shows rate-dependency plots for the 1.7 mg/kg (left panels) and the 3.0 mg/kg (right panels) methamphetamine doses. In these graphs, percent control ( $[\text{drug rate}/\text{control rate}] \times 100$ ) is plotted as a function of the control rate on logarithmic coordinates; the dashed lines at 100 indicate an absence of a drug effect at all control rates. A regression line that is parallel to the no-effect line would indicate a drug effect that is a constant proportion of the control rate. In this figure, rate-dependent effects clearly occurred

with 1809, 1863, and 1845 at both doses, and with 1985 at 3.0 mg/kg. Pigeons 1809 (1.7 mg/kg) and 1863 (both doses) showed the classic rate-dependent pattern. In these cases, methamphetamine tended to increase lower rates (e.g., those maintained by the larger reinforcer during the later session blocks) and decrease higher rates (e.g., those maintained by the smaller reinforcer during the later session blocks). For 1809 at 3.0 mg/kg and for 1845 at both doses, the lowest control response rates were not affected and the higher control rates were decreased to a greater extent than were the intermediate control rates. With 1985, there were no rate-dependent effects at 1.7 mg/kg, but at 3.0 mg/kg, higher rates were decreased to a greater extent than were lower rates. It should be noted again, however, that responding on both keys for this pigeon in all blocks was substantially decreased throughout the session at this dose.

When examined in the context of the absolute response-rate data presented in Fig. 8, the rate-dependent effects shown in Fig. 9 might be described more effectively as rate-constant effects (see Gonzalez and Byrd, 1977; Ksir, 1981). That is, methamphetamine administration appears to have reduced the differences in the control response rates maintained under the different contingencies throughout the session; the different control rates tended to converge under the influence of the drug.

## 5. General discussion

In the present study, methamphetamine tended to increase choices of the larger reinforcer when it was delayed relative to the smaller reinforcer (i.e., in the later session blocks). For all pigeons, at least one methamphetamine dose decreased the slope of the delay function. For three pigeons, this effect occurred at several doses. For two of these pigeons, the slope decreases occurred without substantial changes in the *y*-intercept; for the third, the change in slope was typically accompanied by a modest decrease in the *y*-intercept. For the fourth pigeon, the primary effect of methamphetamine was a dose-related decrease in the *y*-intercept; the slope was changed substantially only at the highest dose. For all pigeons, doses that changed the slope also produced rate-dependent (or rate-constant) effects.

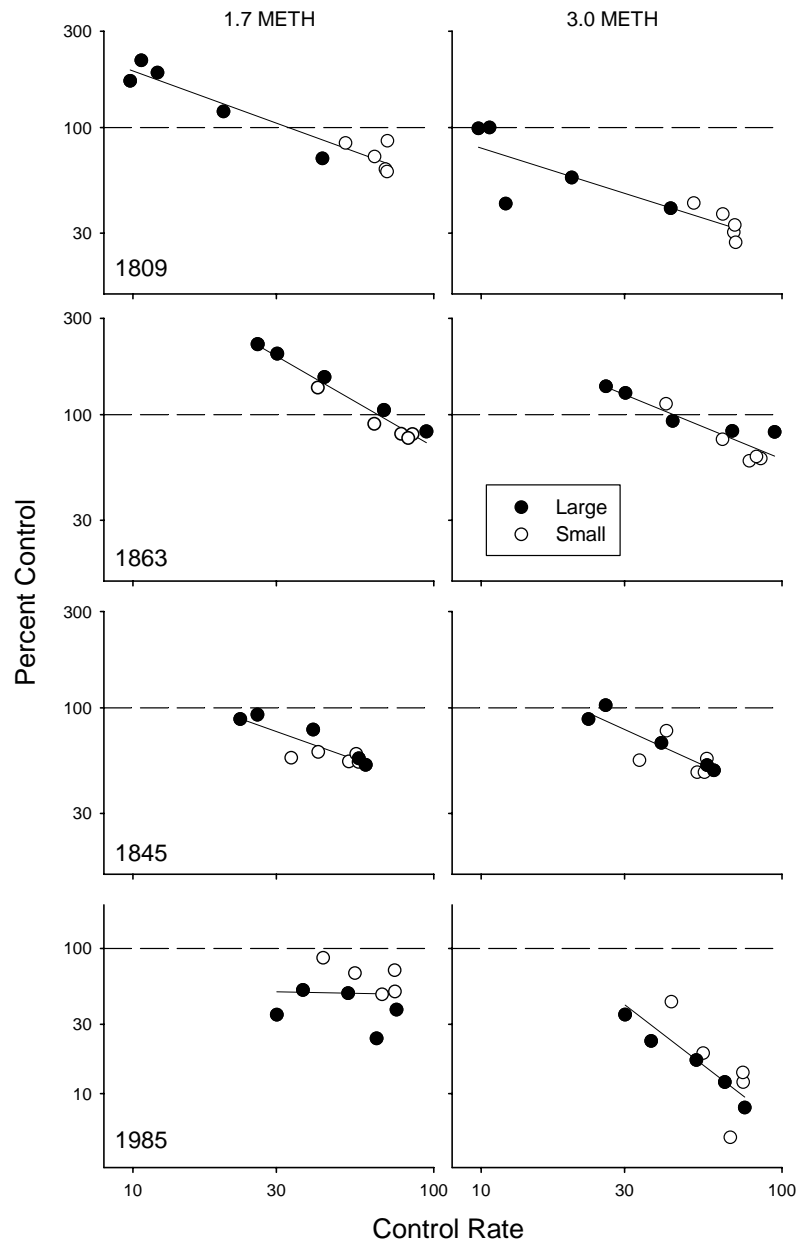


Fig. 9. Rate-dependency plots showing effects of 1.7 mg/kg (left panels) and 3.0 mg/kg (right panels) methamphetamine. In these graphs, percent control ( $[\text{drug rate}/\text{control rate}] \times 100$ ) is plotted as a function of the control rate. Filled symbols show data for behavior maintained by the larger reinforcer and unfilled symbols show data for behavior maintained by the smaller reinforcer. Horizontal lines show the absence of a drug effect. See text for additional details.

## 5.1. Behavioral mechanisms?

### 5.1.1. Sensitivity to effects of reinforcement delay and/or amount

The changes in slope obtained in the present study are consistent with the interpretation that methamphetamine administration attenuated the discounting effects of reinforcement delay. That is, this finding suggests that methamphetamine altered the function relating delay to reinforcement effectiveness such that the sensitivity of the organism's behavior to changes in delay was reduced. This interpretation of methamphetamine's effects contains both characteristics involved in specifying behavioral mechanisms of drug action that were outlined by Thompson (1984): (1) important environmental variables typically regulating the behavior in question were identified (e.g., reinforcement amount and delay), and (2) the manner in which the variables' influence is altered by the drug was characterized (change in sensitivity to delay).

The occasional decreases in  $y$ -intercept obtained with some of the pigeons suggest another potential behavioral mechanism involved in stimulant effects on self-control choices, a drug-induced decrease in the sensitivity to reinforcement amount. The occasions in which choice of the larger reinforcer was decreased during the first block of the session, when the delays for the larger and smaller reinforcer were equal, indicate that reinforcement amount played a smaller role under the influence of the drug than under control conditions. It must be noted that, because only a single amount ratio was used, it is not possible to untangle drug-induced changes in sensitivity to amount from drug-induced changes in bias (e.g., for a particular side key or color). A more definitive assessment of the effects of methamphetamine on sensitivity to reinforcement amount requires drug administration at several amount ratios.

Interestingly, these two potential behavioral mechanisms, attenuation of the effects of reinforcement delay and reinforcement amount, represent opposing influences on self-control choice. A reduction in the sensitivity to effects of reinforcement amount would be expected to shift preference toward the smaller, more immediate reinforcer, whereas a reduction in the sensitivity to effects of reinforcement delay would be ex-

pected to shift preference toward the larger, more delayed reinforcer. Thus, in those instances in which the  $y$ -intercept was decreased, the drug-induced increases in preference for the larger reinforcer when it was delayed (during the later blocks within the session) may have been less than would otherwise have been the case.

It is possible that these two opposing behavioral mechanisms also may have played important roles in some of the discrepancies in the literature on effects of stimulants on self-control. Recall that, in some studies, these drugs tended to decrease choices of a larger, more delayed reinforcer (Charrier and Thiebot, 1996; Evenden and Ryan, 1996; Logue et al., 1992), whereas in other studies, the opposite effect was found (Richards et al., 1999; Wade et al., 2000). In general, the data in the present study were consistent with the latter studies. It is possible, however, that the particular effect obtained depends upon which of these two mechanisms is most readily expressed within the procedure used. Interestingly, in those studies in which stimulant administration "increased self-control," explicit stimuli were correlated with the delay. On the other hand, in those studies in which stimulants "decreased self-control," the stimuli present during the delay were not unique (i.e., they also were present during the intertrial intervals). Furthermore, Cardinal et al. (2000) found that effects of *d*-amphetamine on choice with delayed reinforcement depended upon whether the delay was signaled or not. Thus, it may be that with explicitly signaled delays, the most likely outcome of stimulant administration is a reduction in the sensitivity to delay. In contrast, when the delays are not explicitly signaled, a reduction in the sensitivity to amount may be a more likely outcome. At any rate, more work clearly is needed to identify the exact conditions under which stimulant administration will increase or decrease the likelihood of choosing a larger, more delayed reinforcer.

Of course, it is quite possible that behavioral mechanisms other than changes in sensitivities to effects of reinforcement delay and amount may have been involved in the effects of methamphetamine in the present study. It has been shown repeatedly that stimulant drugs produce: (a) rate-dependent/rate-constant effects, (b) effects on conditioned reinforcement, and (c) effects on timing.

### 5.1.2. Rate-dependency/rate-constancy

Rate-dependency actually does not qualify as a behavioral mechanism in the sense discussed by Thompson (1984). Indeed, as Branch (1984) points out, rate-dependent analyses do not specify behavioral processes altered by drug administration, rather, they simply identify a drug effect on a dependent variable in relation to characteristics of that same dependent variable under non-drug conditions. Nevertheless, rate-dependent (or rate-constant) effects did occur in the present study. In fact, whenever a change in the slope occurred, rate-dependent effects were observed. The question therefore arises: Were the effects obtained in the present study “purely” rate-dependent and, thus, unrelated to alterations in sensitivity to delay and amount? This question is difficult to answer conclusively, but some features of the data weaken such an interpretation. First, the data for time-allocation generally were similar to those for response allocation. Although “time-dependent” drug effects also may have occurred, the time-allocation data suggest that the changes in slope obtained with response allocation were not simply a result of changes in local rates of responding on each key. Second, for 1863 and 1845, the drug-induced changes in slope were accompanied by changes in the crossover point of the absolute-rate functions for the larger and smaller reinforcers (see Fig. 8). That is, methamphetamine appeared to increase the delay value at which indifference occurred. Theoretically, the rates of responding on each key at the crossover point were equal and, thus, should not have changed differentially if the effects were purely rate-dependent.

Rather than producing the drug effects on preference, perhaps the rate-dependent effects observed in the present study actually occurred as a result of drug-induced alterations in the behavioral processes controlling choice. For example, any manipulation that decreases sensitivity to reinforcement delay will increase relatively low rates maintained by a larger, more delayed reinforcer and decrease relatively high rates maintained by a smaller, more immediate reinforcer. To some degree then, rate-dependent effects are an inevitable outcome of this behavioral mechanism.

An interpretation of the present data in terms of behavioral mechanisms, with rate-dependency as an artifact, is consistent with previous research on effects of stimulants on responding maintained under

single VI schedules with varying reinforcement rates. Rate-dependent effects for stimulants have been reported for single VI schedules (e.g., Bradshaw et al., 1981; Lucki, 1983), in which drug administration produces differential effects on the different response rates maintained by different reinforcement rates. Interestingly, however, Heyman and Monaghan (1990) point out that, in single VI schedules with different reinforcement rates, manipulations that decrease the parameter  $R_e$  in Herrnstein's single-alternative matching equation will result in typical rate-dependent effects. Furthermore, they found that the matching equation provided a better account of amphetamine's effects under single VI schedules than did a two-parameter rate-dependency equation described by Dews and Wenger (1977). Therefore, baseline reinforcement rate (an independent variable) appears to provide a better account of amphetamine's effects under VI schedules than does baseline response rates (a dependent variable). Similarly, Lancaster and Dallery (1999) found that the matching equation performed just as well as rate-dependency in describing effects of opiates under single VI schedules. Thus, although rate-dependency may be an important empirical generalization regarding effects of drugs on operant behavior, its utility as a general theoretical account of drug action is questionable (see Branch, 1984; Odum et al., 2002 for excellent discussions of the theoretical utility of rate-dependency).

### 5.1.3. Stimulants and conditioned reinforcement

Stimulants have been shown to elevate rates of responding maintained by conditioned reinforcement (e.g., Files et al., 1989; Hill, 1970; Robbins, 1978). As a result, some investigators have suggested that stimulants may increase choices of a larger, more delayed reinforcer by enhancing the effectiveness of the conditioned reinforcers present during the delay (e.g., Cardinal et al., 2000; Richards et al., 1999). In most procedures used to study drug effects on self-control, the smaller reinforcer is presented immediately (with no delay). In these arrangements, only choices of the larger reinforcer produce an explicit conditioned reinforcer. Thus, a drug-induced increase in self-control is consistent with an interpretation involving enhanced conditioned reinforcement. In the present study, however, both the larger and smaller reinforcers were presented following a completely sig-

naled delay. Thus, each choice involved presentation of a conditioned reinforcer. Therefore, an interpretation of the present results in terms of a drug-induced enhancement of the effectiveness of conditioned reinforcement would seem to require additional processes (e.g., a change in sensitivity to the duration of the delay).

#### 5.1.4. Stimulants and “timing”

To the extent that choice in the present study was under discriminative control of the relative delay durations experienced within each block, it is worth considering the potential contribution of drug-induced changes in “timing.” Following administration of certain doses of stimulants, subjects often respond earlier than usual under procedures typically used to assess temporal discrimination (e.g., Eckerman et al., 1987; Maricq et al., 1981; Meck, 1983). That is, under temporal-discrimination procedures, stimulants appear to produce an overestimation of the passage of time; subjects respond as if more time has elapsed than is actually the case. Furthermore, Maricq et al. (1981) found that methamphetamine produced a constant proportional change in “time perception” across all tested durations. Thus, the effects of methamphetamine in the present study are not easily interpreted as resulting from an overestimation of delay duration. Recall that both the larger and smaller reinforcers were delayed in the present study. If methamphetamine increased the effects of the delays to both reinforcers by a constant proportion, the slopes of the log discount functions should not have changed. At this point, then, the relevance of timing to drug-effects under self-control procedures is unclear.

## 6. Concluding remarks

Despite the difficulties in specifying behavioral mechanisms of drug action unequivocally, we agree with Branch (1984, 1991) that this represents an important goal of behavioral pharmacology. Along with substantial empirical and theoretical implications, identifying fundamental behavioral processes that are altered by drugs has significant therapeutic implications. Although quantitative methods have been used by behavioral pharmacologists to make inferences

about behavioral mechanisms, we believe that the utility of this approach has yet to be fully appreciated. Clearly, data from a single experiment cannot provide sufficient evidence of a specific behavioral mechanism. Nevertheless, we hope that the work presented here provides sufficient evidence of the value of the approach, and that it will inspire further efforts to elucidate behavioral mechanisms of drug action.

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## References

- Ainslie, G., 1975. Specious reward: a behavioral theory of impulsiveness and impulse control. *Psychol. Bull.* 82, 463–496.
- Barrett, J.E., 1987. Non-pharmacological factors determining the behavioral effects of drugs. In: Meltzer, H.Y. (Ed.), *Psychopharmacology: The Third Generation of Progress*. Raven Press, New York, pp. 1493–1501.
- Blackman, D.E., Sanger, D.J. (Eds.), 1978. *Contemporary Research in Behavioral Pharmacology*. Plenum Press, New York.
- Bradshaw, C.M., Ruddle, H.V., Szabadi, E., 1981. Relationship between response rate and reinforcement frequency in variable-interval schedules. III. The effects of D-amphetamine. *J. Exp. Anal. Behav.* 36, 29–40.
- Branch, M.N., 1984. Rate dependency, behavioral mechanisms and behavioral pharmacology. *J. Exp. Anal. Behav.* 42, 511–522.
- Branch, M.N., 1991. Behavioral pharmacology. In: Iversen, I.H., Lattal, K.A. (Eds.), *Experimental Analysis of Behavior, Part 2*. Elsevier, Amsterdam, pp. 21–77.
- Cardinal, R.N., Robbins, T.W., Everitt, B.J., 2000. The effects of *d*-amphetamine, chlordiazepoxide,  $\alpha$ -flupenthixol, and behavioural manipulations on choice of signalled and

- unsignalled delayed reinforcement in rats. *Psychopharmacology* 152, 362–375.
- Charrier, D., Thiebot, M.H., 1996. Effects of psychotropic drugs on rats responding in an operant paradigm involving choice between delayed reinforcers. *Pharmacol. Biochem. Behav.* 54, 149–157.
- Cohen, S.L., 1986. A pharmacological examination of the resistance-to-change hypothesis of response strength. *J. Exp. Anal. Behav.* 46, 363–379.
- Dews, P.B., Wenger, G.R., 1977. Rate-dependency of the behavioral effects of amphetamine. In: Thompson, T., Dews, P.B. (Eds.), *Advances in Behavioral Pharmacology*, vol. 1. Academic Press, New York, pp. 167–227.
- Eckerman, D.A., Segbefia, D., Manning, S., Breese, G.S., 1987. Effects of methylphenidate and *d*-amphetamine on timing in the rat. *Pharmacol. Biochem. Behav.* 27, 513–515.
- Egli, M., Schaal, D.W., Thompson, T., Cleary, J., 1992. Opioid-induced response-rate decrements in pigeons responding under variable-interval schedules: reinforcement mechanisms. *Behav. Pharmacol.* 3, 581–591.
- Epstein, R., 1981. Amount consumed as a function of magazine-cycle duration. *Behav. Anal. Lett.* 1, 63–66.
- Evenden, J.L., Ryan, C.N., 1996. The pharmacology of impulsive behavior in rats: the effects of drugs on response choice with varying delays of reinforcement. *Psychopharmacology* 128, 161–170.
- Files, F.J., Branch, M.N., Clody, D., 1989. Effects of methylphenidate on responding under extinction in the presence and absence of conditioned reinforcement. *Behav. Pharmacol.* 1, 113–121.
- Gonzalez, F.A., Byrd, L.D., 1977. Mathematics underlying the rate-dependency hypothesis. *Science* 195, 546–550.
- Herrnstein, R.J., 1970. On the law of effect. *J. Exp. Anal. Behav.* 13, 243–266.
- Heyman, G.M., 1983. A parametric examination of the hedonic and motoric effects of drugs: pimoizide and amphetamine. *J. Exp. Anal. Behav.* 40, 113–122.
- Heyman, G.M., 1992. Effects of methylphenidate on response rate and measures of motor performance and reinforcement efficacy. *Psychopharmacology* 109, 145–152.
- Heyman, G.M., Monaghan, M.M., 1990. Contributions of the matching law to the analysis of the behavioral effects of drugs. In: Barrett, J.E., Thompson, T., Dews, P.B. (Eds.), *Advances in Behavioral Pharmacology*, vol. 7. Erlbaum, Hillsdale, NJ, pp. 39–77.
- Hill, R.T., 1970. Facilitation of conditioned reinforcement as a mechanism of psychomotor stimulation. In: Costa, E., Garattini, S. (Eds.), *International Symposium on Amphetamines and Related Compounds*. Raven Press, New York, pp. 781–795.
- Ksir, C., 1981. Rate-convergent effects of drugs. In: Thompson, T., Dews, P.B., McKim, W.A. (Eds.), *Advances in Behavioral Pharmacology*, vol. 3. Academic Press, New York, pp. 39–59.
- Lancaster, J.S., Dallery, J., 1999. The effects of morphine on responding under variable-interval schedules: rate-related effects. *Behav. Pharm.* 10, 337–347.
- Laties, V., Weiss, B., 1969. Behavioral mechanisms of drug action. In: Black, P. (Ed.), *Drugs and the Brain*. The Johns Hopkins Press, Baltimore, pp. 115–133.
- Logue, A.W., 1988. Research on self-control: an integrating framework. *Behav. Brain Sci.* 11, 665–679.
- Logue, A.W., Rodriguez, M.L., Pena-Correal, T.E., Mauro, B.C., 1984. Choice in a self-control paradigm: quantification of experienced-based differences. *J. Exp. Anal. Behav.* 41, 53–67.
- Logue, A.W., Tobin, H., Chelonis, J.J., Wang, R.Y., Geary, N., Schachter, S., 1992. Cocaine decreases self-control in rats: a preliminary report. *Psychopharmacology* 109, 245–247.
- Lucki, I., 1983. Rate-dependent effects of amphetamine on responding under random-interval schedules of reinforcement in the rat. *Pharmacol. Biochem. Behav.* 18, 195–201.
- Madden, G.J., Bickel, W.K., Jacobs, E.A., 1999. Discounting of delayed rewards in opioid-dependent outpatients: exponential or hyperbolic discounting functions? *Exp. Clin. Psychopharmacol.* 7, 284–293.
- Maricq, A.V., Roberts, S., Church, R.M., 1981. Methamphetamine and time estimation. *J. Exp. Psychol. Anim. Behav. Process.* 7, 18–30.
- Mazur, J.E., 1987. An adjusting procedure for studying delayed reinforcement. In: Commons, M.L., Mazur, J.E., Nevin, J.A., Rachlin, H. (Eds.), *Quantitative Analysis of Behavior*, vol. 5. The Effect of Delay and of Intervening Events on Reinforcement Value. Erlbaum, Hillsdale, NJ, pp. 55–73.
- Meck, W.H., 1983. Selective adjustment of the speed of internal clock and memory processes. *J. Exp. Psychol. Anim. Behav. Process.* 9, 171–201.
- Nevin, J.A., 1974. Response strength in multiple schedules. *J. Exp. Anal. Behav.* 21, 389–408.
- Nevin, J.A., 1978. Reinforcement schedules and response strength. In: Zeiler, M.D., Harzem, P. (Eds.), *Advances in the Analysis of Behaviour*, vol. 1. Reinforcement and the Organization of Behaviour. Wiley, Chichester, England, UK, pp. 117–158.
- Nevin, J.A., Grace, R.C., 2000. Behavioral momentum and the law of effect. *Behav. Brain Sci.* 23, 73–130.
- Odom, A.L., Lieving, L.M., Schaal, D.W., 2002. Effects of *D*-amphetamine in a temporal discrimination procedure: selective changes in timing or rate dependency? *J. Exp. Anal. Behav.* 78, 195–214.
- Pickens, R., 1977. Behavioral pharmacology: a brief history. In: Thompson, T., Dews, P.B. (Eds.), *Advances in Behavioral Pharmacology*, vol. 1. Academic Press, New York, pp. 229–257.
- Rachlin, H., 1974. Self-control. *Behaviorism* 2, 94–107.
- Richards, J.B., Mitchell, S.H., de Wit, H., Seiden, L.S., 1997. Determination of discount functions in rats with an adjusting-amount procedure. *J. Exp. Anal. Behav.* 67, 353–366.
- Richards, J.B., Sabol, K.E., de Wit, H., 1999. Effects of methamphetamine on the adjusting amount procedure, a model of impulsive behavior. *Psychopharmacology* 146, 432–439.
- Robbins, T.W., 1978. The acquisition of responding with conditioned reinforcement: effects of pipradrol, methylphenidate, *d*-amphetamine, and nomifensine. *Psychopharmacology* 58, 79–87.
- Sanger, D.J., Blackman, D.E., 1976. Rate-dependent effects of drugs: review of the literature. *Pharmacol. Biochem. Behav.* 4, 73–83.

- Thompson, T., 1984. Behavioral mechanisms of drug dependence. In: Thompson, T., Dews, P.B., Barrett, J.E. (Eds.), *Advances in Behavioral Pharmacology*, vol. 4. Academic Press, New York, pp. 1–45.
- Thompson, T., Schuster, C.R., 1968. *Behavioral Pharmacology*. Prentice-Hall, Englewood Cliffs, NJ.
- Wade, T.R., de Wit, H., Richards, J.B., 2000. Effects of dopaminergic drugs on delayed reward as a measure of impulsive behavior in rats. *Psychopharmacology* 150, 90–101.
- Witkin, J., Katz, J., 1991. Analysis of the behavioral effects of drugs. *Drug Dev. Res.* 20, 389–409.