Psychopharmacology (1985) 85: 154–161

Psychopharmacology

A parametric description of amphetamine's effect on response rate: changes in reinforcement efficacy and response topography

Gene M. Heyman[1] and Lewis S. Seiden[2]

[1] American Cyanamid Company, Medical Research Division of Lederle Laboratories, CNS Research, Pearl River, New York 10965, USA
[2] Department of Pharmacological and Physiological Sciences, University of Chicago, Chicago, IL 60637, USA

Abstract. A mathematical model was used to describe the effects of amphetamine on the rate of a reinforced response in the rat. The model provides measures of reinforcement efficacy and response topography for behavior maintained by variable-interval reinforcement schedules. In this study the measured behavior was a lever press, the reinforcer was water, and the variable-interval schedules provided five different rates of reinforcement, ranging from about 20 to 660/h. In each session the rats were exposed to each of the five schedules, and as reinforcement rate increased, the rate of lever pressing increased in a negatively accelerated manner that was closely approximated by the equation for a rectangular hyperbola. Amphetamine changed response rate and the parameters of the best-fitting hyperbolas. The 0.25–1.0-mg/kg doses increased response rate, and the parameter changes supported the interpretation that the increases were due primarily to an increase in reinforcement efficacy. The 2.0- and 3.0-mg/kg doses decreased response rates maintained by low reinforcement rates and increased response rates maintained by high reinforcement rates, and the parameter changes supported the interpretation that at higher doses amphetamine produced counteracting changes in reinforcement efficacy and response topography: reinforcement efficacy decreased, whereas response topography changed so as to increase response rates.

Key words: *d*-Amphetamine – Response rate – Reinforcement efficacy – Response topography – Matching law – Rate-dependency – Variable-interval schedule – Lever press – Rat

In experiments in which behavior is maintained by the presentation of a reinforcer, low and high doses of amphetamine typically have opposite effects on response rate. Low doses increase response rate, whereas high doses decrease rate (e.g., Carey and Goodall 1973; Dews 1958; Heffner et al. 1974; Wauquier and Niemegeers 1974). Two explanations of this effect have received most attention. One is in terms of reinforcement processes. For example, according to Berlyne et al. (1966) there is an optimum level of sensitivity to reinforcement, and low doses of amphetamine increase response rate because they bring the subject up to this optimum, whereas high doses decrease response rate because they push the subject past the optimum. The second account is in terms of the topography of the movements that comprise the reinforced response. For example, according to Lyon and Robbins (1975) low doses of amphetamine increase response rate by eliminating pauses (a topography change), while high doses decrease response rate by facilitating competing behaviors, such as rearing and excessive gnawing.

Although these two accounts have prompted much research (Lyon and Robbins 1975), it has not been possible to determine if they are correct, because of the problem of distinguishing between a motor effect and a reinforcement effect. For example, the evidence for Lyon and Robbins' motor hypothesis is compatible with the reinforcement hypothesis that low doses of amphetamine eliminate pauses because the reinforcer has become more efficacious. In order to resolve this methodological issue, we have adopted a method of analysis that provides logically independent measures of reinforcement efficacy and response topography. The method is based on a mathematical model of the relationship between response rate and reinforcement rate, referred to as the matching law (Herrnstein 1970).

One of the empirical results that led to the formulation of the matching law was that in experiments that used variable-interval reinforcement schedules, response rate was a simple, orderly function of reinforcement rate. Several mathematical descriptions were tested (e.g., de Villiers and Herrnstein 1976), and the equation for a rectangular hyperbola typically provided the most accurate description. The customary notation is:

$$B = \frac{kR}{R + R_e}, \quad (1)$$

where B stands for response rate, R stands for reinforcement rate, and k and R_e are parameters, whose values are obtained by fitting Eq. (1) to the rates of responding. These parameters can be differentially altered by either manipulating the response requirement, which affects k, or manipulating properties of the reinforcer, which affects R_e. In this study, amphetamine's effect on k and R_e are described.

The parameter k will be used to evaluate changes in response topography. Herrnstein (1970, 1974) suggested this definition on the basis of the formal relationship that k is equal to the estimated response rate asymptote. He pointed out that a brief response, such as a lever press, would have a relatively high asymptotic value, whereas a

Offprint requests to: G. M. Heyman

time consuming response, such as traversing a grid, would have a relatively low asymptotic value (assuming the same subject under the same reinforcement conditions). The evidence supports Herrnstein's predictions. Changes in the response requirement changed k while producing no systematic effects in R_e (Bradshaw et al. 1983; Hamilton and Stellar 1983; McSweeney 1978). For example, in an experiment with pigeons, McSweeney found that switching the response requirement from a key peck to a treadle kick produced a large decrease in k, but no associated changes in R_e, and in experiments with rats, Hamilton and Stellar (1983) and Bradshaw et al. (1983) found similar results by adding weights to the response lever.

The parameter R_e will be used to evaluate amphetamine's effect on reinforcement efficacy. It is measured in reinforcement rate units, e.g., pellets/h, and rearrangement of Eq. (1) shows that its magnitude is equal to the rate of reinforcement that maintains a one-half asymptotic response rate ($B = k/2$ when $R = R_e$). Consequently a change in R_e means that a given reinforcement rate supports more or less responding relative to the asymptotic rate. For example, an increase in R_e means that it takes more reinforcement to maintain a one-half asymptotic response rate. This formal definition suggests that R_e should change with changes in deprivation history or reinforcement conditions. Experiments support the inference. For example, an increase in hours of deprivation decreased R_e (Logan 1960; described in deVilliers and Herrnstein 1976); a decrease in amount of monetary reward increased R_e (Bradshaw et al. 1978), and, more generally, experiments in which just R_e changed were experiments in which either the reinforcer or deprivation conditions had been altered. (Note that the relationship between R_e and reinforcement efficacy is inverse: an increase in R_e is a decrease in efficacy.)

The concepts of reinforcement efficacy and response topography predate the field of psychopharmacology and have been adopted in order to help explain how drugs change behavior. In contrast, the rate-dependency principle arose as an empirical generalization within the field of psychopharmacology to summarize how drugs, especially amphetamine, change behavior (Dews 1958; Dews and Wenger 1977; Pickens 1977; Robbins 1981). According to the rate dependency-principle, amphetamine's effect on response rate depends on the subject's rate of responding in non-drug (baseline) conditions. Under certain conditions, this proposition yields predictions that are similar to those of Eq. (1) (Heyman 1983), but under other conditions the two approaches lead to different results. The areas of overlap and difference are outlined in the Discussion section of this report.

Materials and methods

Subjects. Eight male, albino Sprague Dawley rats (Holtzman Company, Madison, WI) served as subjects. The rats were approximately 4 months old at the start of the study. They were housed two to a cage in a colony room that was illuminated 16 h/day (lights on at 06:00 h). In the home cages there was free access to laboratory chow (Teklad Mouse and Rat Diet) and limited access to water: 25 ml/day plus the amount earned in experimental sessions.

Apparatus. The experiment was conducted in eight Gerbrands Model C operant conditioning chambers (23.0 × 21.5 × 19.0 cm). A lever was located on the front wall of each chamber, 3 cm from the right side and 3.8 cm from the grid floor (as measured from the lever top). To the left of the lever (6.5 cm) was a recessed opening that allowed the rat access to a 0.025-ml dipper of water. A downward force of more than 0.15 N operated the lever, and when the temporal component of the reinforcement contingency was fulfilled, a lever response raised the dipper into the recessed opening for 2.5 s. A Sonalert (dampened with resistors) and a light, located on the chamber back wall, signalled different phases of the experimental session. The chambers were connected to a PDP8/e computer, and a Super SKED Software System (Snapper et al. 1976) was used to control and record experimental events.

Procedure. Experimental sessions consisted of a series of five variable-interval (VI) reinforcement schedules (a five-component multiple schedule). Each schedule was available for 420 s and a 500-s time-out period separated consecutive schedules. The schedule order was random (without replacement) so that in each session the subject was exposed to five different reinforcement rates. The programmed rates were 24, 48, 120, 360, and 720/h, which corresponds to the series of schedules: VI 150 s, VI 75 s, VI 30 s, VI 10 s, and VI 5 s. The list of intervals for each schedule gave an approximately random temporal pattern of interreinforcement times (Fleshler and Hoffman 1962). During reinforcement, 2.5 s, and for the immediately following 1.5 s, the VI schedule timer did not operate and responses had no experimentally arranged consequences. The stimulus conditions were set by a houselight and Sonalert. The houselight was on when a reinforcement schedule was available and it was off during the time-out period. The rate of the Sonalert tone indicated which reinforcement schedule was available, with low rates signaling low reinforcement rates and high rates signaling high rates. The lowest signal rate was 7.5/min, the highest was 40/min, and the on time was 1 s.

In addition to the five VI schedules, each session began with a brief warm-up period. At the start of the session, the rat obtained six reinforcers according to the contingency that every fifth response or a 10-s interval without a response operated the dipper. The warm-up period was signalled by the houselight and was followed by a 120-s time-out period. During this time-out and the 500-s time-out periods between reinforcement schedules, the chamber light and Sonalert were off and responses had no experimentally arranged consequences, although they were recorded. The experiment was conducted five or six times a week at about the same time each day.

Drugs. Each rat received five different doses of *d*-amphetamine sulfate in the order: 0.50, 1.0, 0.25, 2.0, and 3.0 mg/kg. Each dose was administered on three occasions and eight saline (vehicle) injections were randomly interspersed between drug injections. The injection was delivered IP, 1 ml/kg, approximately 20 min before the start of the session. All injections occurred on Tuesdays and Fridays. The baseline condition was defined as a session of at least 2 days since the most recent drug injection. Each subject, then, was exposed to seven conditions: baseline (pre-drug and 18 inter-drug sessions), saline injections (eight sessions), and five doses of amphetamine (three sessions each dose).

Data analysis. For each subject in each condition, the average response and reinforcement rate for the five schedule components was determined. Equation 1 was then fitted to the response and reinforcement rates, so that each subject's performance could be summarized by a list of parameter values. Since Eq. (1) is nonlinear, the expression that minimizes the residuals is two nonlinear equations, each with two unknowns, k and R_e. The solutions were then obtained by the iterative method described by Wetherington and Lucas (1980). This technique gives the least-squares solution without the disadvantages that can occur with a reciprocal transformation of the response and reinforcement rates (see Wetherington and Lucas 1980). The significance level of changes in the values of k and R_e was determined by a paired t-test (Winer 1971). In addition group average response and reinforcement rates were calculated in order to provide an overall summary of the results.

Results

Response rates. Figure 1 and Table 1 show the average group response and reinforcement rates for each of the five schedule components in each condition. Table 2 lists the percentage changes in response rate. These were calculated by averaging the percentage changes for each of the eight rats. Doses of amphetamine between 0.25 and 1.0 mg/kg increased response rates, and the relative magnitude of the increases was inversely related to reinforcement rate. For example, in the lowest reinforcement rate component, VI 150 s (see Table 1), the 0.50-mg/kg dose increased response rate from 21.4 to 39.8/min, an 86% increment, whereas in the highest reinforcement rate component, VI 5 s, response rate increased from 101 to 116 responses/min, for a 15% increase. The 2.0-mg/kg dose produced a much different pattern of response rate changes. In each of the three lowest reinforcement rate components, response rate decreased, whereas in the highest reinforcement rate component, response rate increased. For example, in the VI 75-s schedule, second lowest reinforcement rate, response rate decreased from 33 to 26.1 responses/min, but in the VI 5-s schedule, response rate increased from 101 to 118.8 responses/minute. The 3.0-mg/kg dose had variable effects. Two subjects stopped lever pressing, two subjects pressed at lower rates in each schedule, and four pressed at lower rates in the four lowest reinforcement rate schedules but at baseline rates in the

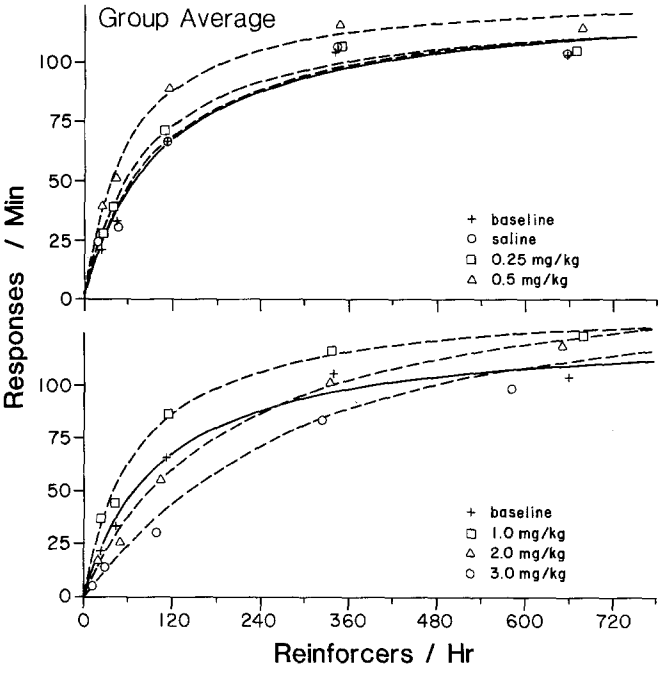

Fig. 1. Average response rate as a function of average reinforcement rate. Each data point is the average response rate for one of the five VI schedules. The *crosses* show baseline results, and the *open symbols* show saline and drug session results. For the baseline condition the averages were calculated from a sample of 18 sessions for each subject; for the saline condition, the sample was eight sessions for each subject; and for drug conditions, the sample was three sessions per subject. The *solid curves* correspond to the best fitting rectangular hyperbolas for the baseline condition, and the *broken curves* are the best fitting hyperbolas for saline and drug sessions. At the 3.0-mg/kg dose, the response rate is based on median rather than average values because of the large individual differences in responding at this dose

Table 1. Average response and reinforcement rates

Condition	VI 150 s		VI 75 s		VI 30 s		VI 10 s		VI 5 s	
	Reinf./h	Resp./min	Reinf./h	Resp./min	Reinf./h	Resp./min	Reinf./h	Resp./min	Reinf./h	Resp./min
Baseline	23.3	21.4 (3.3)[a]	43.5	33.0 (4.5)	113.0	66.3 (5.4)	338.9	104.3 (8.7)	657.6	101.0 (9.5)
Saline	22.9	25.8 (4.5)	46.6	32.4 (5.3)	113.8	71.0 (6.1)	336.5	107.4 (7.8)	666.0	103.0 (9.7)
0.25 mg/kg	25.9	27.6 (5.0)	44.1	39.4 (6.7)	109.6	70.6 (3.9)	348.8	106.9 (8.9)	670.4	105.0 (9.9)
0.50 mg/kg	25.3	39.8 (7.8)	44.8	51.9 (5.1)	114.9	89.3 (8.2)	345.5	117.3 (9.7)	677.5	116.0 (10.7)
1.0 mg/kg	22.6	37.3 (5.0)	42.5	43.9 (6.1)	115.6	86.0 (10.1)	337.0	115.9 (8.9)	680.1	123.4 (10.3)
2.0 mg/kg	20.8	17.9 (2.6)	50.8	26.1 (3.9)	106.0	56.4 (7.6)	333.6	102.9 (11.8)	649.8	118.8 (14.0)
3.0 mg/kg[b]	14.0	6.0 (0–33)	26.0	14.0 (5–35)	117.0	28.0 (6–94)	308.0	82.0 (0–134)	583.0	95.0 (27–207)

[a] SE of the mean
[b] At 3.0 mg/kg the table lists median response and reinforcement rates and the parantheses enclose response rate range

highest reinforcement rate schedule. Since the between-subject variability was so large at 3.0 mg/kg, Table 1 lists the median rather than the average response and reinforcement rates at this dose.

Figure 2 shows response rates for a representative subject (Rat 1). Individual rats showed similar response rate changes. Lower doses tended to increase response rates associated with the lower reinforcement rate sched-

Table 2. Average percent change in response rate[a]

Condition	VI 150 s	VI 75 s	VI 30 s	VI 10 s	VI 5 s
Saline	+ 18	− 5	+ 7	+ 3	+ 3
	(11)[b]	(6)	(4)	(2)	(2)
0.25 mg/kg	+ 36	+ 20	+ 9	+ 2	+ 7
	(18)	(11)	(5)	(1)	(3)
0.50 mg/kg	+ 94	+ 87	+ 36	+ 13	+ 17
	(29)	(44)	(8)	(5)	(5)
1.0 mg/kg	+ 78	+ 43	+ 36	+ 12	+ 25
	(22)	(21)	(18)	(7)	(6)
2.0 mg/kg	− 9	− 39	− 14	− 2	+ 19
	(26)	(20)	(10)	(6)	(10)
3.0 mg/kg	− 78	− 70	− 59	− 14	+ 2
	(− 100, + 26)[c]	(− 81,+ 50)	(− 81,0)	(− 100, − 8)	(− 63, + 31)

[a] Entries were calculated from the individual subject results at each dose and each schedule
[b] Parentheses enclose the between subject standard error
[c] Entries at 3.0-mg/kg dose are medians and parantheses enclose the range

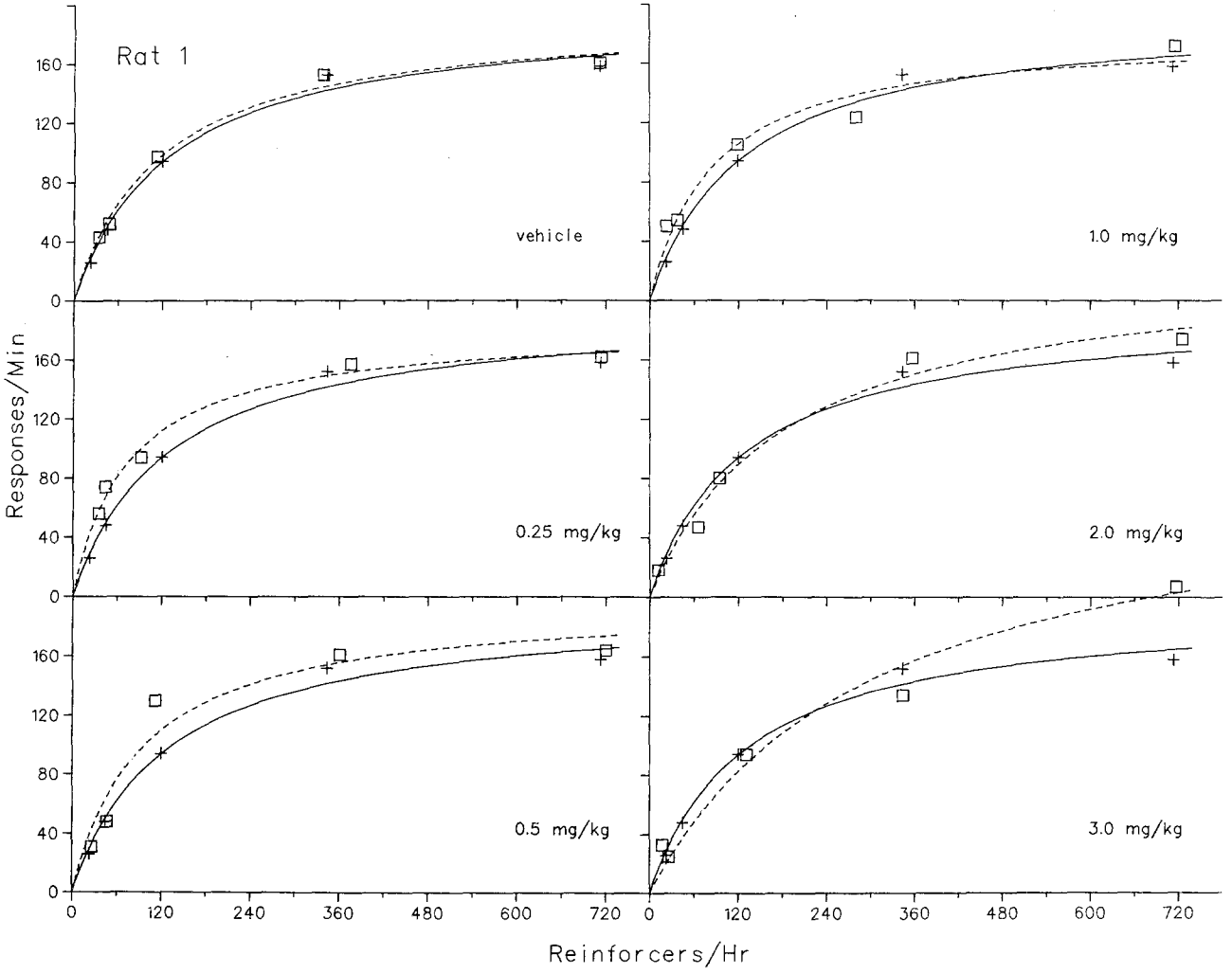

Fig. 2. Response rate as a function of reinforcement rate for Rat 1. Each data point is the average response rate for one of the five VI schedules. The *crosses* show the baseline condition results; the *open squares* show results for the condition indicated by the panel. The *solid curve* is the best fitting rectangular hyperbola for baseline, and the *broken curve* is the hyperbola for the experimental conditions

ules and higher doses tended to increase response rates associated with the higher reinforcement rate schedules. However, there were individual differences in sensitivity to amphetamine. At the lowest dose, three subjects showed little or no change in response rates, and at the highest dose, two pressed at lower rates in each of the five reinforcement schedules, and two stopped lever pressing altogether, suggesting that all of the rats would have stopped at doses above 3.0 mg/kg. Thus, individual rats were similar in terms of the pattern of response rate changes, but were different in terms of the magnitudes of the changes.

Amphetamines effect on k and R_e. Figure 3 shows changes in k and R_e. For each subject at each dose, Eq. (1) was fitted to the response rate results. The criterion for goodness of fit was the complement of the ratio of the squared residuals,

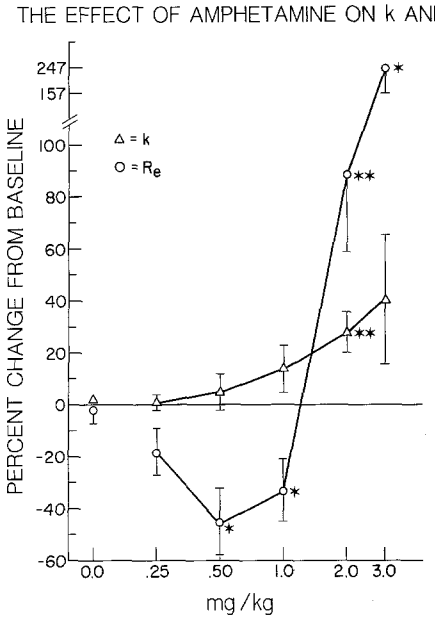

Fig. 3. The percentage change from baseline in k and R_e as a function of drug dose. Each data point represents the group average parameter value, expressed as a percentage difference from the baseline values. The x-axis scale is logarithmic. The *error bars* represent the standard error of the differences between baseline and treatment condition, expressed as a percentage of the baseline value. * $P < 0.05$; ** $P < 0.01$, according to a paired t-test

error, to the variance in response rates, r^2. In baseline sessions, the subject that provided the median fit yielded an r^2 of 0.97, and the range was 0.78 to 0.99. This means that the difference between the predicted and obtained response rates was typically about 3% as large as the largest possible difference. In drug sessions the fit was about the same. The median r^2 was 0.96 and the range was 0.77–0.99.

Changes in R_e were a nonmonotonic function of dose. At 0.25 to 1.0 mg/kg, amphetamine decreased R_e, whereas at 2.0 and 3.0 mg/kg amphetamine increased R_e. The 0.5-mg/kg dose produced the largest decrease, 45% ($P < 0.05$) and the 0.25- and 1.0-mg/kg doses produced decreases of 18% and 33% ($P < 0.05$), respectively. The decreases in R_e shown in Fig. 3 correspond to the increases in response rate at the lower reinforcement rates shown in Figs. 1 and 2. In contrast, the 2.0-mg/kg dose increased R_e by 89% ($P < 0.01$), and the 3.0-mg/kg dosed increased this parameter by 247% ($P < 0.05$). This increase in R_e corresponds to the decreases in response rate at the lower reinforcement rates shown in Figs. 1 and 2. The changes in R_e mean that depending on dose amphetamine had opposing effects on the proportion of asymptotic responding maintained by a given rate of reinforcement. Low doses increased the proportion of responding; high doses decreased the proportion of responding.

Changes in k, the asymptotic response rate, were a monotonic function of dose. At the 0.25-mg/kg dose there was no apparent change in k, four subjects showing small increases and four subjects showing small decreases. At doses above 0.25 mg/kg, subjects typically showed an increase in k. The percentage increments were 6%, 17%, 27% ($P < 0.01$), and 29% (the probability of this value was not less than 0.05, because of between subject variability and the reduced sample size at the 3.0-mg/kg dose). The increments in k, shown in Fig. 3, correspond to the increases in response rate at the highest reinforcement rates shown in Figs. 1 and 2. For doses up to 1.0 mg/kg, then, the parameter changes were cooperative in the sense that each was associated with response rate increases. At the 2.0- and 3.0-mg/kg doses, however, the parameter changes were antagonistic in the sense that the change in R_e reflected response rate decreases (at the lower reinforcement rates) and the change in k reflected response rate increases (at the higher reinforcement rates).

Rate dependency. According to Dews and Wenger (1977) a straight line with a negative slope should describe the

Table 3. Average parameter values

Condition	k (responses/min)	SE[a]	R_e (reinforcers/h)	SE	r^{2c}
Baseline	126	12	112	21	0.97
Saline	129	11	110	20	0.94
0.25 mg/kg	127	12	92	17	0.97
0.50 mg/kg	132	13	62	11	0.96
1.0 mg/kg	144	11	75	27	0.96
2.0 mg/kg	161	19	212	28	0.98
3.0 mg/kg[b]	177	45	389	150	0.90

[a] Between subject standard error
[b] Parameter estimates at 3.0-mg/kg dose were based on median response rates for each subject, see text
[c] Median r^2 values for the eight subjects

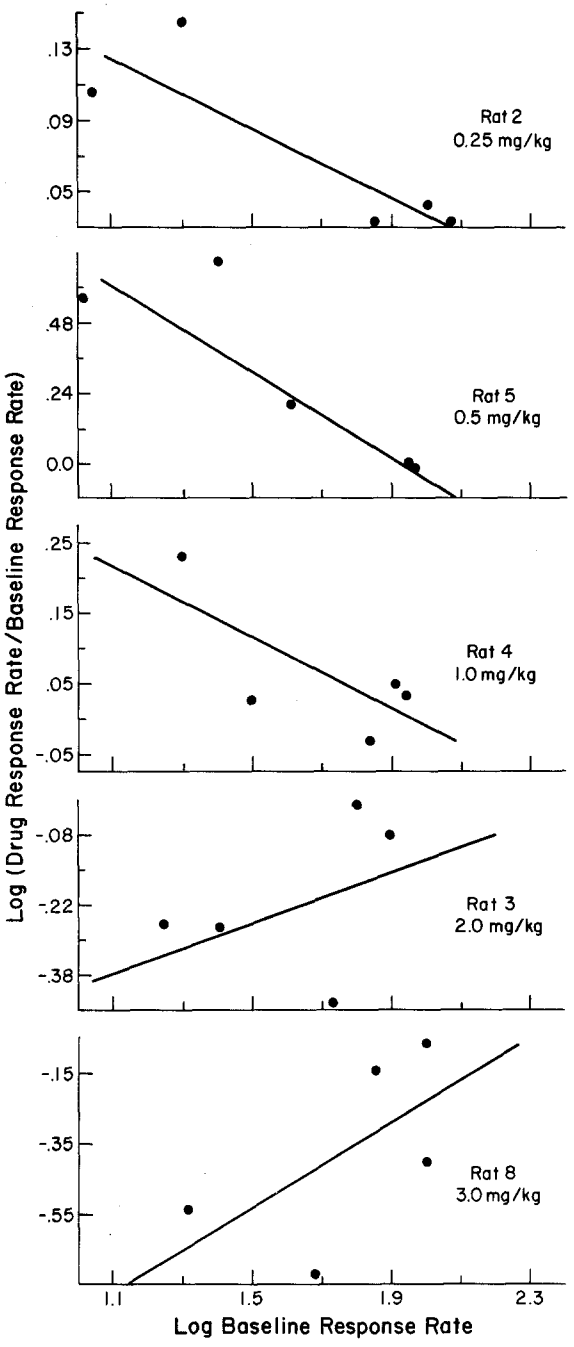

Fig. 4. The logarithm of the ratio of drug to baseline response rate as a function of the logarithm of the baseline response rate. The *straight lines* were fitted by the method of least-squares, and each panel shows the results for the subject that provided the median fit, (the fourth or third largest r^2 value). The median r^2 for all rats at all dose levels was 0.58

relationship between baseline response rate and the ratio of drug to baseline response rates (drug effect) when these measures are plotted in logarithmic coordinates. Figure 4 tests this proposition: each panel shows the correlation between baseline response rate and drug effect at each dose level for the subject that provided the median linear fit. In other words, this figure parallels Table 3 which lists the median fit for individual subjects according to Eq. (1). For doses between 0.25 and 1.0 mg/kg there was a negative correlation between baseline response rate and drug effect, as predicted. However, for the 2.0- and 3.0-mg/kg doses, the correlation was typically positive. The change in slope occurred because amphetamine either decreased low response rates more than high response rates or increased high rates more than low ones at the 2.0- and 3.0-mg/kg doses. Independently of slope, the median fit for the predicted linear relation was an r^2 value of 0.58. This means that the predicted linear relation between baseline response rate and drug effect resulted in discrepancies that were about 42% as large as the maximum possible discrepancy.

Discussion

According to the definitions that k measures response topography and R_e measures reinforcement efficacy, the results can be summarized as follows. At the 0.25- and 0.50-mg/kg doses, amphetamine increased reinforcement efficacy, but had little effect on response topography. At the 1.0-mg/kg dose, amphetamine continued to increase reinforcement efficacy, and it also produced sizeable, rate increasing changes in response topography. At the 2.0- and 3.0-mg/kg doses, amphetamine produced counteracting changes in the two factors: reinforcement efficacy decreased below baseline levels, but response topography showed even larger rate enhancing effects.

Amphetamine's effect on response rate varied as a function of reinforcement rate. For example, at the two lowest doses, changes in response rate became relatively smaller as reinforcement rate increased. This pattern can be explained in terms of how changes in the factors measured by R_e interact with reinforcement rate, and, more generally, inspection of Eq. (1) reveals two possible patterns of response rate change for behavior maintained by variable-interval schedules of reinforcement.

According to Eq. (1) the ratio of drug to baseline response rates is

$$\frac{B'}{B} = \frac{k'R}{R + R_e'} \Big/ \frac{kR}{R + R_e} = \frac{k'(R + R_e)}{k(R + R_e')}, \qquad (2)$$

where the prime marks indicate drug treatment. If a drug changes response rates so that k but not R_e changes then Eq. (2) reduces to a constant, k'/k. This means that the response rates in drug sessions were proportional to the response rates in baseline sessions. In contrast if a drug changes response rates so that R_e but not k changes, then the ratio of drug to baseline response rates is$(R + R_e)/(R + R_e')$. This quotient will vary from approximately R_e/R_e' to 1/1 as reinforcement rate increases. Consequently, if R_e (but not k) changes, it is necessarily the case that the drug effect is inversely related to reinforcement rate. At the 0.25- and 0.50-mg/kg doses, amphetamine produced this inverse pattern of response rate changes, whereas in studies in which the response requirement was changed (e.g., Bradshaw et al. 1983; Hamilton and Stellar 1983; McSweeney 1978), the treatment produced the proportional pattern of changes in response rate. Put somewhat differently, a change in reinforcement efficacy is synonymous with reinforcement dependent changes in the ratio of drug to baseline response rates, whereas a change in response topography is synonymous with reinforcement independent changes in the ratio of drug to baseline response rates.

Since response rate is a function of reinforcement rate, a second implication of a change in reinforcement efficacy is that there will be a negative correlation between baseline response rate and the magnitude of the change in response rate. This implication is similar to the predictions of the rate-dependency principle, but with the qualification that the correlation between baseline response rate and drug effect is secondary to reinforcement rate. Three findings support the primacy of reinforcement rate in variable-interval schedules.

First, Eq. (1) which includes the influence of reinforcement rate, provided a more accurate description of amphetamine's effect on response rates. This was determined by fitting Eq. (1) and the linear rate dependency model to the response rates for each subject at each dose. Both models have two parameters, and the ratio of the squared residuals to the variance has been the customary criterion for evaluating the precision of each approach. In 36 of 38 tests, (two subjects did not respond at the 3.0-mg/kg dose), Eq. (1) provided the more accurate fit, and for this sample of 38 data sets, the matching law approach produced a median r^2 of 0.96 and the rate dependency approach produced a median r^2 of 0.58. Fitting the two models to the group average response rates, listed in Table 1, improved the accuracy of the rate dependency model to a median r^2 of 0.84, however, it is possible that averaging produced artifactual response rate patterns.

Second, the slope of the rate dependency switched from negative to positive at the 2.0- and 3.0-mg/kg doses. This reversal is compatible with a reversal in reinforcement efficacy, but is not compatible with Dews and Wenger's (1977) statement of rate-dependency for amphetamine.

Third, in instances in which the predictions based on Eq. (1) and rate-dependency qualitatively differed, the Eq. (1) predictions approximated the results. For example, for a number of subjects the two highest reinforcement rates maintained nearly equivalent response rates, because responding had approached the estimated asymptotic rate. In this situation, rate dependency predicts that the two response rates should change by about the same amount and in the same direction. In contrast, according to Eq. (1) it is possible for response rates to differentially change if the pattern of change produces an increase in R_e. For example, the 3.0-mg/kg dose produced a 229% increase in R_e and response rate at the VI 10-s schedule decreased from 152 to 134 responses/min, whereas response rate at the VI 5-s schedule increased from 158 to 207/min (there was a simultaneous increase in k). In other words, nearly equal baseline response rates either decreased or increased as a function of reinforcement rate (Table 1 shows similar results for the group data).

Psychopharmacological research based on the matching law equation (Herrnstein 1970) shows that low doses of amphetamine increased the reinforcing efficacy of food (Bradshaw et al. 1981; Heyman 1983), whereas low doses of pimozide decreased the reinforcing efficacy of both food (Heyman 1983; Heyman and Coons 1981) and brain stimulation (Hamilton and Stellar 1983). The present study used water as the reinforcer and used a wider range of doses than did previous experiments based on Eq. (1). The results corroborated and extended the earlier studies. At doses similar to those used in the previous experiments, reinforcement efficacy was increased. At higher doses, however, effects not seen in the previous studies appeared. The parameter measuring response topography was significantly altered and reinforcement efficacy was decreased. The present experiment also used a wider range of reinforcement rates than did previous studies. This made it possible to compare Eq. (1) and the rate-dependency principle over a wide range of baseline response rates. The analyses showed that rate-dependent effects in variable-interval reinforcement schedules could be explained in terms of changes in reinforcement efficacy.

Acknowledgements. We thank H. deWit, M. Fischman, C. Johanson, and W. Woolverton for their thoughtful and constructive comments and thanks to B. X. Knight and C. Nardella for their technical assistance. This work was supported by U.S. Public Health Service Grant MH-11191-18; GMH supported by USPHS MH-14274, Training Grant; L.S.S. recipient of Research Scientist Award MH-10562.

References

Berlyne DE, Koenig JDV, Hirota T (1966) Novelty, arousal and reinforcement of diversive exploration in the rat. J Comp Physiol Psychol 87: 222–226

Bradshaw CM, Ruddle HV, Szabadi E (1981) Relationship between response rate and reinforcement frequency in variable-interval schedules: III. the effect of *d*-amphetamine. J Exp Anal Behav 36: 29–39

Bradshaw CM, Szabadi E, Bevan P (1978) Effect of variable-interval punishment on the behavior of humans in variable-interval schedule of monetary reinforcement. J Exp Anal Behav 29: 161–166

Bradshaw CM, Szabadi E, Ruddle HV (1983) Herrnstein's equation: effect of response force requirement on performance in variable-interval schedules. Behav Anal Lett 3: 93–100

Carey RJ, Goodall EB (1973) A comparison of the effects of amphetamine on fixed interval performance maintained by electrical stimulation of the brain versus food reinforcement. J Pharmacol Biochem Behav 1: 237–239

deVilliers PA, Herrnstein RJ (1976) Toward a law of response strength. Psychol Bull 83: 1131–1153

Dews PB (1958) Studies on behavior IV. Stimulant actions of methamphetamine. J Pharmacol Exp Ther 122: 137–147

Dews PB, Wenger GR (1977) Rate-dependency of the behavioral effects of amphetamine. In: Thompson T, Dews PB (eds) Advances in behavioral pharmacology, Vol. I. Academic Press, New York, pp 167–227

Fleshler M, Hoffman HS (1962) A progression for generating variable-interval schedules. J Exp Anal Behav 5: 529–530

Hamilton AL, Stellar JR (1983) A simple method for distinguishing factors which affect reward from those affecting motor performance in responding for electrical stimulation of the brain. Abstract: Eastern Psychological Association Meetings, Philadelphia, PA

Heffner TG, Drawbaugh RB, Zigmond MJ (1974) Amphetamine and operant behavior in rats: Relationship between drug effect and control response rate. J Comp Physiol Psychol 86: 1031–1043

Herrnstein RJ (1970) On the law of effect. J Exp Anal Behav 13: 243–266

Herrnstein RJ (1974) Formal properties of the matching law. J Exp Anal Behav 21: 159–164

Heyman GM, Coons W (1981) The effects of pimozide on reinforced responding. Abstract: Eastern Psychological Association Meeting, New York

Heyman GM (1983) A parametric evaluation of the hedonic and motoric effects of drugs: pimozide and amphetamine. J Exp Anal Behav 40: 113–122

Logan FA (1960) Incentive. Yale University Press, New Haven

Lyon M, Robbins TW (1975) The action of central nervous system drugs: A general theory concerning amphetamine effects. In: Essman W, Valzelli L (eds) Current developments in psychopharmacology, Spectrum, New York, pp 81–163

McSweeney FK (1978) Prediction of concurrent keypeck and treadle-press responding from simple schedule performance. Anim Learn Behav 6: 444–450

Pickens R (1977) Behavioral pharmacology: a brief history. In: Thompson T, Dews PB (eds). Advances in behavioral pharmacology, Vol. I. Academic Press, New York, pp 229–257

Robbins TW (1981) Behavioral determinants of drug action: rate dependency revisited. In: Cooper SJ (ed) Theory in psychopharmacology, Vol. I. Academic Press, London, pp 1–63

Snapper AG, Stephens KR, Cobez RI, Van Haaren F (1976) The SKED Manual 2: OS/8 and Time Share SKED. Kalamazoo, MI, The SKED Users Group

Wauquier A, Niemegeers CJE (1974) Intracranial self-stimulation as a function of various stimulus parameters. Psychopharmacologia 34: 265–274

Wetherington CL, Lucas TR (1980) A note on fitting Herrnstein's equation. J Exp Anal Behav 34: 199–206

Winer BJ (1971) Statistical principles in experimental design. McGraw Hill, New York

Received October 4, 1983; Final version September 20, 1984