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CONTROL RATE OF RESPONSE OR REINFORCEMENT AND AMPHETAMINE'S EFFECT ON BEHAVIOR

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The roles of control response rate and reinforcement frequency in producing amphetamine's effect on operant behavior were evaluated independently in rats. Two multiple schedules were arranged in which one variable, either response rate or reinforcement frequency, was held constant and the other variable manipulated. A multiple differential-reinforcement-of-low-rate seven-second yoked variable-interval schedule was used to equate reinforcement frequencies at different control response rates between multiple-schedule components. Amphetamine increased responding under the differential-reinforcement-of-low-rate component but decreased responding under the variable-interval component. In contrast, amphetamine decreased responding equivalently between components of a multiple random-ratio schedule that produced similar control response rates at different reinforcement frequencies. The results provide experimental support to the rate-dependency principle that control rate of responding is an important determinant of amphetamine's effect on operant behavior.

Key words: rate-dependency principle, amphetamine, response rate, reinforcement rate, differential-reinforcement-of-low-rate schedule, variable-interval schedule, random-ratio schedule, lever press, rats

The rate-dependency principle originated from Dews' (1958) suggestion that control rates of operant responding could explain why amphetamine differentially alters behavior maintained by schedules of reinforcement. Specifically, amphetamine often increases rates of responding under schedules that usually produce low control response rates [differential-reinforcement-of-low-rate (DRL): Kelleher, Fry, Deegan, & Cook, 1961; Sidman, 1956; Zimmerman & Schuster, 1962; fixed-interval (FI): Clark & Steele, 1966; de Oliveira & Graeff, 1972]. In contrast, amphetamine usually decreases rates of responding under schedules that produce high control response rates [fixed-ratio (FR): Heffner, Drawbaugh, & Zigmond, 1974; Owen, 1960; variable-interval (VI): Bradshaw, Ruddle, & Szabadi, 1981; Lucki, 1983]. Behavioral effects of amphetamine that have been interpreted as response rate-dependent have subsequently been reported across a wide variety of species, using a number of reinforcement schedules, with several types of reinforcers, and for a range of responses with only a few exceptional circumstances (for reviews, see Dews & Wenger, 1977; Kelleher & Morse, 1968; Sanger & Blackman, 1976). Response rate-dependent behavioral effects have been reported with nearly every class of psychoactive drug and for so many behavioral situations that rate dependency is now considered one of the most important general principles of behavioral pharmacology (Dews, 1981).

The rate-dependency principle has remained most closely associated with amphetamine's behavioral effects because few other variables have been shown to modify its actions (Dews & Wenger, 1977). However, it is still important to systematically consider possible roles that other schedule variables may exert on amphetamine's behavioral effects. Reinforcement frequency could be a particularly critical variable of concern for the rate-dependency principle because it is highly correlated with response rate under ratio, interval, and response differentiation (DRL) schedules (Catania & Reynolds, 1968; Felton & Lyon, 1966; Staddon, 1965). As a consequence, reinforcement fre-

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quency is a schedule variable that could account for much of the evidence that currently supports the rate-dependency principle.

Previous studies have attempted to separate the interrelated effects of response rate and reinforcement frequency on amphetamine's behavioral actions. Three studies have attempted to vary response rate while maintaining reinforcer delivery rate constant by employing a tandem pacing requirement (DRL schedule) with an interval schedule. In two of the studies, low doses of amphetamine produced larger increases in responding and high doses produced smaller decreases in responding for the low-rate than for the high-rate schedules, results that are consistent with the rate-dependency principle (MacPhail & Gollub, 1975; Sanger & Blackman, 1975). However, Stitzer and McKearney (1977) employed a two-component multiple fixed-interval pacing schedule and found that pigeons failed to increase overall response rates to amphetamine in the low-rate component and, instead, increased overall response rates in the high-rate component. Stitzer and McKearney's results could suggest a possible limitation in generalizing drug effects obtained from tandem interval DRL schedules to the variety of simple reinforcement schedules that provide the bulk of the evidence supporting the rate-dependency principle.

In the present study, the roles of control response rate and reinforcement frequency in determining amphetamine's effects on operant behavior were reexamined in two experiments. The experiments were complementary, in that multiple schedules held one variable, either response rate or reinforcement frequency, relatively constant while the other variable was allowed to fluctuate. The first experiment used a within-subject yoked-control procedure to examine amphetamine's actions on different rates of responding when the frequency of reinforcement was held relatively constant. The second experiment examined whether different reinforcement frequencies could exert an independent effect on amphetamine's behavioral actions when the baseline rates of responding were nearly equated. The results showed that amphetamine's effects varied according to the control response rate when equivalent reinforcement frequencies were maintained but that varying reinforcement frequencies failed to differentially alter amphetamine's actions when control response rates were held constant, in support of the rate-dependency principle.

EXPERIMENT 1

Method

Subjects

Five male hooded rats bred at the rat colony of the Department of Psychology at the University of Iowa were housed individually in a temperature-controlled (23 °C) colony maintained on a 12-hour light-dark cycle with lights on at 0800 hours. Starting from 110 days of age, each rat was maintained with free access to food at approximately 80% of its predicted body weight by restricting the amount of water given during a brief daily period 30 min after experimental sessions. Each rat's predicted body weight was readjusted upward 1 g per day until 150 days of age and was then held constant for the remainder of the experiment.

Apparatus

Five 30 by 23 by 24-cm operant conditioning chambers were used as described in detail previously by DeLong and Grisham (1980). Each chamber had two sidewalls and a hinged top made of clear Plexiglas and end panels made of aluminum attached to a grid floor. The chambers were individually enclosed within sound-attenuating chests, ventilated by an exhaust fan and provided 80-dB white masking noise from attached speakers during experimental sessions. A .6-cm diameter stainless steel lever projected 2.2 cm into the chamber, perpendicular to and at the midline of one of the end panels, 4.3 cm above the grid floor. The associated microswitch was activated by a .1-cm depression of the lever with a 6-g weight. Centered 6.2 cm above the lever was a 3.6-cm diameter aperture that provided access to a recessed water cup. The reinforcer was .1 ml of distilled water delivered to this cup by means of a constant pressure water system. Each chest could be illuminated by a 6-W 24-V dc houselight located behind the end panel on which the lever was mounted. Experimental control and data collection were provided from a separate room by a PDP 8/F computer (Digital Equipment Corp.) using the SKED software system (Snapper, Stephens, & Lee, 1974) to control a solid-state interface (Grisham & Frei, 1977).

Procedure

All rats had prior lever-pressing experience under a multiple DRL 15-sec yoked VI schedule for 60 sessions before being placed on a multiple DRL 7-sec yoked VI reinforcement schedule at 185 days of age. Sessions always began with presentation of the DRL schedule. Under the DRL schedule, signaled when the chambers were dark, a response was reinforced only when the time since the immediately previous nonreinforced response equaled or exceeded 7 sec (DRL 7-sec). Intervals between reinforcer deliveries during each DRL component were recorded and used to determine the number and temporal distribution of reinforcer availability during the next yoked VI component. Thus, during the yoked VI component, signaled by illumination of the chambers with the houselight, a reinforcer was presented immediately following the first response that occurred after the same temporal period that preceded the first reinforcer delivery in the prior DRL component. Subsequent periods of reinforcer availability in that component were determined similarly by the temporal distribution of reinforcer deliveries during the prior DRL component. Reinforcers made available during the VI component but not collected were lost. This occurred whenever a second reinforcer became available before the first had been delivered and whenever the yoked VI component ended before an available reinforcer was delivered. The DRL and VI schedule components were both 45 sec in length and were presented alternately 30 times each during the 45-min sessions. Experimental sessions were conducted 6 days per week between 1130 and 1230 hours. The rats were exposed to the multiple DRL 7-sec yoked VI schedule for 60 sessions before amphetamine's effect was examined.

Drugs

d-Amphetamine sulfate (Sigma Chemical Co.) was dissolved in sterile physiological saline just prior to use. Intraperitoneal injections of amphetamine or saline were administered 30 min prior to the start of experimental sessions in a volume of 1 ml/kg. Consecutive injections were spaced one week apart. Doses of amphetamine (expressed as the salt) were administered only once in the following sequence: 0 (saline), .25, .50, .1.0, 1.4, 2.8, 2.0, 4.0, and 5.7 mg/kg.

Calculation of Drug Effect

Control performance, expressed either as response rate or reinforcement frequency, was averaged over the three days prior to testing each dose of amphetamine. Drug effects were expressed as an output ratio calculated by dividing response rate at a particular dose of amphetamine by the control response rate, i.e., the mean response rate over the three days prior to administration of that drug dose. Drug effects were examined by analysis of variance.

Results

Control Performance

The multiple DRL 7-sec yoked VI schedule provided different control response rates under equivalent frequencies of reinforcement. Responding occurred 3.2 times more frequently during the VI component than during the DRL component of the multiple schedule, with mean lever press rates (± SEM) of 42.3 ± 9.2 and 13.2 ± 1.3 responses/min, respectively [$F(1, 4) = 158.6$, $p < .001$]. Although reinforcement frequencies were similar for both schedules, the number of reinforcers delivered under the DRL component (1.93 ± .12/min) was significantly greater than under the VI component [1.78 ± .12/min, $F(1, 4) = 20.5$, $p < .05$]. A small difference in reinforcement frequency was expected with this procedure and can be attributed to the consistent failure of the animals to collect an average of about 8% of the reinforcers that were available during the VI components of each session. The relatively small size of this difference and, importantly, that it was in the opposite direction of the response rate differences for both schedules suggest that this slight divergence in schedule reinforcement frequencies should not confound the examination of amphetamine's effect.

Reinforcement frequency significantly increased under both schedules over weeks of drug testing [$F(8, 32) = 3.82$, $p < .01$]. Mean VI response rates sharply increased during the second week, from 35 to 40 responses/min, and gradually continued to rise to a maximum of 44 responses/min over the remainder of the experiment. Mean DRL response rates did not vary significantly over the drug-testing period.

Effects of Amphetamine

Amphetamine's effects under both schedules are presented in Figure 1 as output ratios,

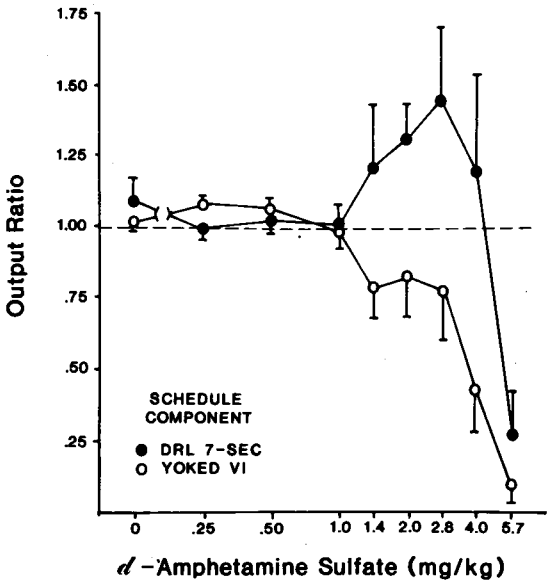

Fig. 1. Mean output ratios (± SEM) for each component of the multiple DRL 7-sec yoked VI schedule are shown as a function of the dose of amphetamine. Output ratio is defined as the response rate under amphetamine divided by the control response rate. The broken line when output ratio = 1.0 indicates where amphetamine produced no change in responding relative to control rates. Amphetamine differentially altered responding between the two schedule components (Schedule × Dose interaction, $p < .001$), according to analysis of variance.

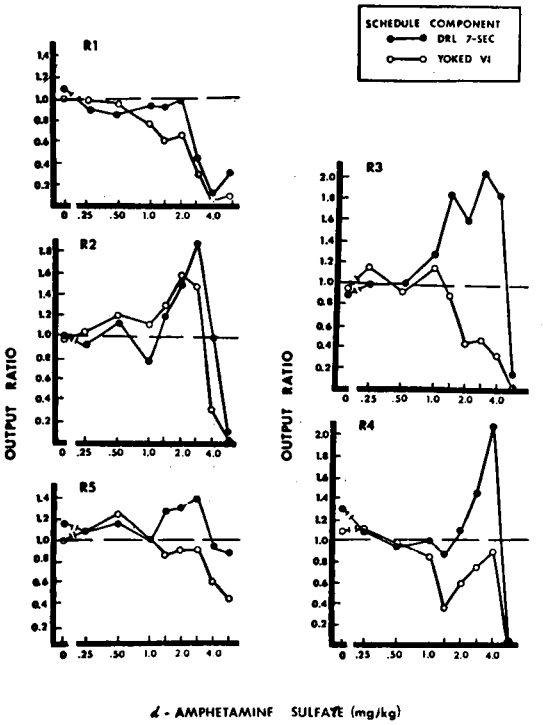

Fig. 2. Amphetamine's effect on responding under the multiple DRL 7-sec yoked VI schedule is shown for individual subjects. Individual control response rates (responses/min) for each subject averaged over the nine-week experiment were (DRL, VI): R1, 15.7, 32.7; R2, 12.5, 34.6; R3, 10.6, 70.2; R4, 16.9, 55.5; R5, 10.5, 18.3.

which express the drug effects in relation to the weekly control response rates. Amphetamine clearly produced different effects on responding under the two reinforcement schedules [Schedule × Dose interaction, $F(8, 32) = 5.64$, $p < .001$], altering responding under the two schedules in opposite directions between 1.4 and 4.0 mg/kg. Amphetamine increased responding under the DRL schedule up to a maximum at 2.8 mg/kg and eventually decreased responding at 5.7 mg/kg. In contrast, amphetamine decreased VI responding in a dose-related manner. Amphetamine, at doses of 2.0 mg/kg or higher, also significantly decreased to an equivalent extent the number of reinforcers earned under both reinforcement schedules [$F(8, 32) = 9.20$, $p < .001$].

The dose-effect curves for individual subjects are presented in Figure 2. R3, R4, and R5 showed increases in DRL responding at the same doses of amphetamine that decreased VI responding. R1 showed greater resistance to response suppression by amphetamine under the DRL than under the VI schedule. Amphetamine increased responding under both schedules in R2, but the greatest response increase was obtained under the DRL schedule and DRL responding was more resistant to suppression than VI responding.

Relative interresponse time (IRT) distributions are presented for the three animals that demonstrated the largest difference in amphetamine's effects between the DRL and VI schedules. Under the DRL 7-sec schedule (Figure 3, Control), the largest proportion of IRTs were of very short duration (1 to 2 sec) and a second group of IRTs were emitted of around 7-sec duration, which corresponded to the delay required between consecutive responses to obtain reinforcement. This bimodal IRT distribution was shown best by R3. The bimodal response pattern under DRL differed markedly from the IRT distribution obtained under the yoked VI schedule (Figure 4, Control), where nearly all responses occurred within 2 sec of the preceding response. Similar IRT distributions have previously been reported for DRL

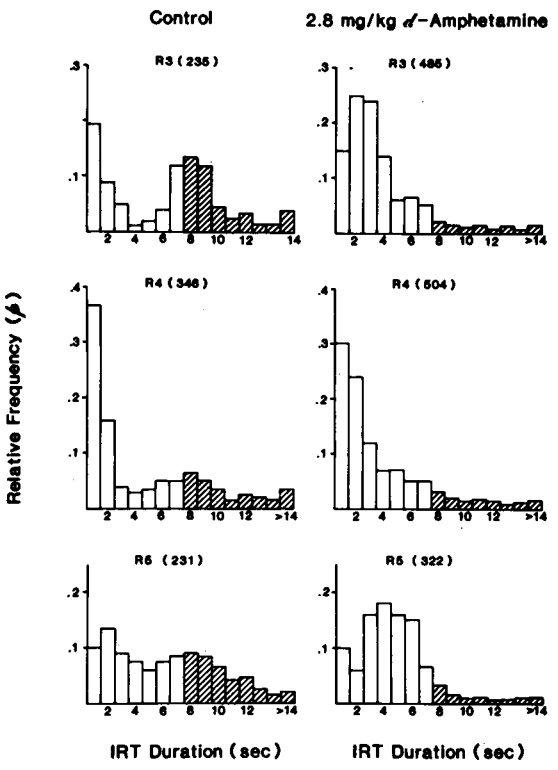

Fig. 3. Relative frequency distribution of interresponse times (IRTs) under the DRL 7-sec schedule is shown for three rats. The total number of IRTs emitted is shown in parenthesis next to the identification number of the animal studied. Diagonal-marked bars represent IRTs sufficiently long (> 7-sec) to produce reinforcement. IRT distributions shown on the left represent the control performance determined as the average from the three days preceding administration of 2.8 mg/kg *d*-amphetamine. IRT distributions shown on the right were collected in a single session 30 min following the injection of 2.8 mg/kg *d*-amphetamine.

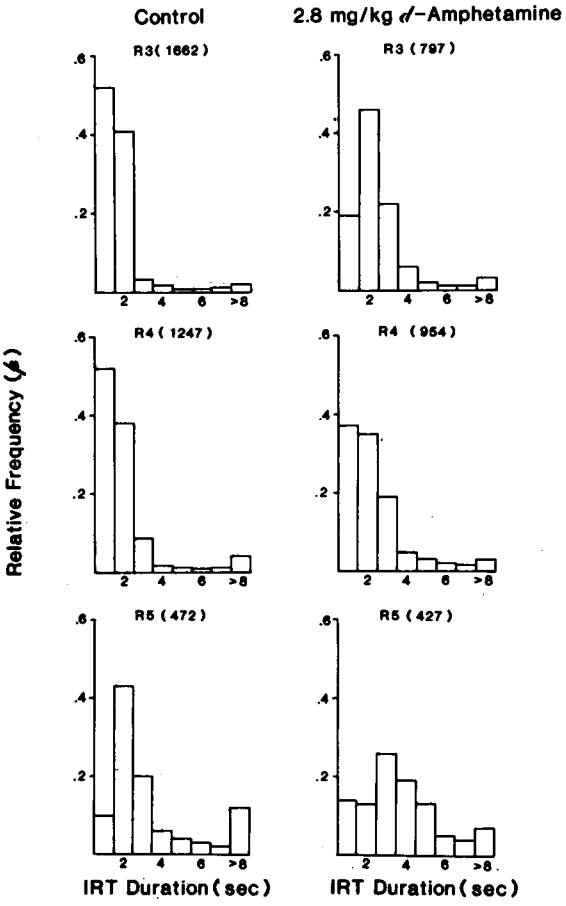

Fig. 4. Relative frequency distribution of interresponse times emitted during the yoked VI component of the multiple DRL 7-sec yoked VI schedule. Details of the figure are the same as for Figure 2.

and VI schedules studied individually (Anger, 1956; Malott & Cumming, 1964). The different IRT distributions for each schedule in the present study indicate strong control of responding by the two reinforcement schedules, especially since the frequency and density of reinforcement delivery between schedules was explicitly controlled.

Amphetamine affected the relative IRT distributions from the DRL and VI schedules differently. Under the DRL schedule (Figure 3), amphetamine changed the bimodal IRT distribution to a single, broad peak located midway between the two modes and reduced the proportion of both the shortest and longest duration IRTs. This was best seen with R3 and R5. Although amphetamine caused more responses to be emitted under the DRL schedule, fewer of the associated IRTs were of sufficient duration to produce reinforcement. In contrast, amphetamine decreased the number of responses emitted under the VI schedule (Figure 4). Under amphetamine, the preponderance of the VI IRTs were longer in duration than during control sessions. Interestingly, comparison of the IRT distributions for both schedules under amphetamine suggests that the two IRT distributions that had been different tended to resemble each other. Although the change produced by amphetamine in the number of IRTs for both schedules could be predicted by the rate-dependency principle, the IRT distributions indicate that differences in pattern of responding were reduced by amphetamine.

EXPERIMENT 2

METHOD

Subjects

Five male albino rats (Holtzman Co.) were 63 days of age upon arrival in the laboratory. From 73 days of age, each rat was maintained at approximately 80% of its predicted body weight by restricting the amount of water given during a brief daily period following within 30 min of experimental sessions. Each rat's predicted body weight was readjusted upward daily, with growth estimated from a second group of six rats that were allowed continued free access to food and water for the duration of the experiment.

Procedure

Following training to press the lever for immediate water delivery, the lever-press response was placed on a two-component multiple random-ratio (RR) reinforcement schedule. Random-ratio schedules assign every response a constant probability of reinforcement (p). The ratio requirement, determined by the value $1/p$, is the average number of responses expected to occur before a reinforcer is presented. A multiple RR 20 RR 50 schedule was used in which the probability of reinforcement following each response was .05 in the first component (RR 20) and .02 in the alternate component (RR 50). The stimulus signaling which reinforcement schedule was in effect was the houselight, which was randomly assigned to a particular schedule for each rat. Schedule components were 2 min in length and were presented alternately seven times each during daily 28-min sessions. The schedule that appeared first varied across experimental sessions, each occurring with an equal probability (.5).

Drugs

Injections of amphetamine or saline began after 65 sessions of training. Each dose was administered once in an ascending series and consecutive drug injections were separated by one week. Other procedures and the calculation of drug effects were the same as described for Experiment 1.

RESULTS

Control Performance

The mean control rates of responding and reinforcement under each component of the multiple random-ratio schedule provided the required baseline conditions for examining whether schedules with different baseline reinforcement frequencies might show different effects of amphetamine when control response rates are equated. Rats obtained 2.7 times as many reinforcers during the RR 20 schedule as during the RR 50 schedule, with mean reinforcement rates (± SEM) of 5.71 ± .23 and 2.13 ± .14 reinforcers/min, respectively [$F(1, 4) = 257.68$, $p < .001$]. Also, the mean rate of responding under the RR 20 schedule (112.8 ± 5.9 responses/min) was nearly identical to the RR 50 schedule [111.9 ± 8.5 responses/min; $F(1, 4) = 0.02$, $p > .05$].

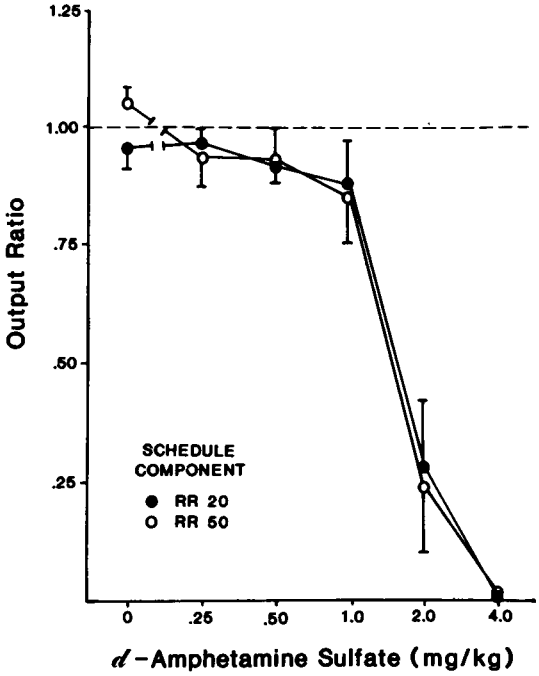

Fig. 5. The effect of amphetamine on responding under the multiple RR 20 RR 50 schedule, expressed as output ratios. Amphetamine altered responding under each component equivalently (Schedule × Dose interaction, $p > .05$), according to analysis of variance.

Effects of Amphetamine

Amphetamine's effect on responding is presented in Figure 5 as output ratios. Amphetamine produced a dose-dependent decrease in the output ratios of both random-ratio schedules [$F(5, 20) = 37.15$, $p < .001$]. More important, however, responding was altered equivalently by amphetamine under both random-ratio schedules, as indicated by the absence of a significant interaction between

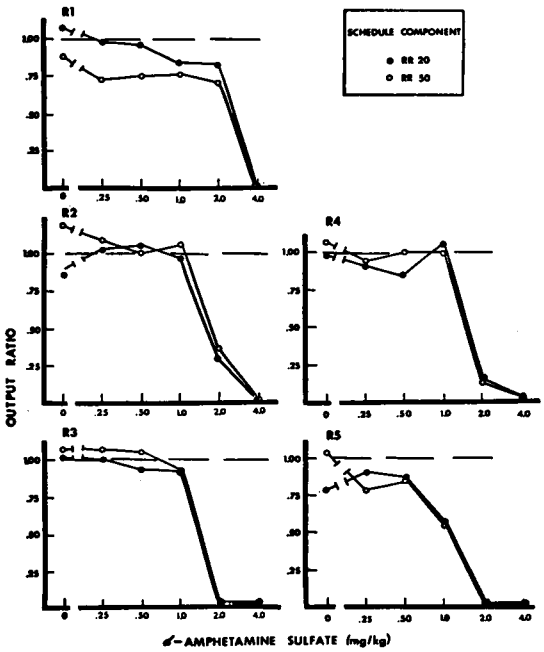

Fig. 6. Amphetamine's effect on responding under the multiple RR 20 RR 50 schedule is shown for each rat. Individual control response rates (responses/min) averaged over the six-week experiment were (RR 20, RR 50): RI, 99.9, 97.8; R2, 109.6, 97.4; R3, 104.2, 124.7; R4, 133.7, 139.2; R5, 116.5, 100.5.

Schedule and Dose of amphetamine [$F(5, 20) = 1.36$, $p > .05$]. The dose-effect curves for these schedules are nearly superimposable. Amphetamine also decreased average reinforcement frequency significantly under both schedules at doses greater than 1.0 mg/kg [$F(5, 20) = 17.92$, $p < .001$].

Dose-effect curves for individual rats are presented in Figure 6. All rats, except R1, demonstrated a similar decrease in output ratio under both random-ratio schedules as a function of dose of amphetamine. For RI, amphetamine produced slightly greater decreases in output ratio under the RR 20 schedule. However, since the rate of reinforcement under the RR 50 schedule was less than the RR 20 schedule, the results for R1 are not in the direction that would predict an inverse relationship between control reinforcement rate and amphetamine's effect.

DISCUSSION

Schedules of reinforcement were employed in this study to vary baseline rates of responding and reinforcement independently between components of multiple reinforcement schedules to examine the rate-dependency principle as an explanation for amphetamine's effects on schedule-controlled behavior. Two comparisons of amphetamine's effects were performed between schedule components: (1) response rate was varied but reinforcement frequency remained relatively constant (Experiment 1); and (2) response rate remained constant but reinforcement frequency was varied (Experiment 2).

The first comparison was performed using a procedure that yoked reinforcement availability under a VI schedule with the temporal pattern of reinforcement obtained by the same animal under a DRL schedule (multiple DRL 7-sec yoked VI), similar to Richardson (1973). Average rates of responding in the VI component were more than three-fold greater than the DRL rate, whereas reinforcement was at nearly equivalent rates and densities. Under these baseline conditions, amphetamine's effect was dependent not only on the dose but also on the reinforcement schedule. Amphetamine increased responding under the DRL schedule at the same doses that decreased responding under the VI schedule. This result with amphetamine is clearly consistent with expectations from the rate-dependency principle, because the DRL and VI schedules controlled different rates of responding.

The results of Experiment 1 are similar to those of other studies that have examined amphetamine's effect on pacing schedules that equate reinforcement frequencies at varying rates of responding. Two such studies have shown amphetamine's effect to vary as a function of the baseline response rate when reinforcement frequency was controlled (MacPhail & Gollub, 1975; Sanger & Blackman, 1975). However, a third study using pacing schedules (Stitzer & McKearney, 1977) did not show amphetamine's effect on overall response rate to vary in the manner predicted by the rate-dependency principle, and the effect on local response rates resembled local rates obtained from FI schedules where punishment contingencies were used to produce different response rates (McMillan, 1973). Procedures that suppress operant responding by punishment or other stimuli provide the few exceptional cases to the usual demonstrations of amphetamine's rate-dependent effects (Dews & Wenger, 1977).

In contrast to the studies using pacing schedules, the yoked-control procedure used in Experiment 1 employed schedules that have previously been used to support the rate-dependency principle. Amphetamine has been reported to increase the low response rates of DRL schedules and to decrease the higher response rates of VI schedules when these schedules are arranged individually (Bradshaw et al., 1981; Sidman, 1956; Zimmerman & Schuster, 1962), and these results have been used to support the rate-dependency principle. However, the possibility that amphetamine's effects were due more to different reinforcement frequencies was not considered. The present yoked-control procedure combined the DRL and VI schedules in a manner that explicitly controlled reinforcement frequency as a potentially confounding variable. The changes in DRL and VI responding observed in Experiment 1 are similar to amphetamine's effects when these schedules have been studied individually. In combination with the results from pacing schedules (MacPhail & Gollub, 1975; Sanger & Blackman, 1975), these results show that different reinforcement frequencies are not necessary to produce amphetamine's rate-dependent effects.

Although different amphetamine effects were obtained with the DRL and VI schedules of Experiment 1, the rate-dependency principle regards these changes as consistent with a single function relating amphetamine's effect to control rate of response (McKearney, 1981). Amphetamine's effect on behavior has been related systematically to the control rate of responding under a variety of schedules (Dews & Wenger, 1977; Kelleher & Morse, 1968; Sanger & Blackman, 1976), and the different amphetamine effects observed in Experiment 1 are consistent with these findings.

However, the results obtained in Experiment 1 do not distinguish between several alterative accounts of rate dependency. First, the increase in low control rates and decrease in high control rates in Experiment 1 may indicate that amphetamine's effect on behavior is to produce a constant or stereotyped rate of responding (see Byrd, 1981; Ksir, 1981; Lyon & Robbins, 1975). Specifically, the increase produced by amphetamine in relative frequency of IRTs of 2 to 4 sec under both the DRL and VI schedules supports this view. Second, McKim (1981) has suggested that a loss of stimulus control may arise from nonspecific effects produced when a drug is injected, analogous to behavior changes that have been observed when an environmental stimulus is suddenly altered. This account must assume a major generalization decrement produced by amphetamine itself in the present Experiment 1, inasmuch as injections of saline had no comparable effect. Finally, because stimulus control is demonstrated by differential responding in the presence of different stimuli, the convergence of DRL and VI response rates under amphetamine in Experiment 1 could be described as a disruption of stimulus control (Laties, 1975; Thompson, 1978). It is most unlikely that amphetamine's alteration of the psychophysical difference between illumination conditions used as stimuli in Experiment 1 could account for its behavioral effects. Any explanation of the present results as disruption of stimulus control, then, must appeal to the stimulus effects of amphetamine itself that compete with previously established control of responding by illumination.

Experiment 2 examined the complementary question of whether reinforcement frequency exerts an independent effect on amphetamine's behavioral actions. A multiple random-ratio schedule was used to vary reinforcement frequencies between components by 2.7-fold, while control response rates were maintained at equivalent levels. This random-ratio behavior in rats agrees with previous reports of random-ratio effects in pigeons (Farmer & Schoenfeld, 1967; Sidley & Schoenfeld, 1964). The effect of amphetamine was to reduce responding under both random-ratio schedules.

The obtained decrease in responding under amphetamine was expected, given the high control response rates produced by the random-ratio schedules. However, the different reinforcement frequencies could have produced different effects on the descending limb of the dose-effect curves. In fact, the dose-effect curves for the two random-ratio schedules were nearly identical, and this was true for the individual subject dose-effect curves as well. In contrast, schedules controlling different response rates do show systematic variations on the descending limb of amphetamine's dose-effect curve, even though low doses of amphetamine never produce increased rates of responding (Heffner et al., 1974). The present failure to obtain differences in responding between ran-

dom-ratio schedules, however, was probably not caused by the inability of the animals to physically respond more rapidly, since chlordiazepoxide produces increases in responding under FR schedules in rats with even higher control response rates (Thomas, 1973; Wedeking, 1974).

There is virtually no information presently available on reinforcement frequency and drug effects, probably because it is so difficult to obtain behavior at equal response rates despite widely differing reinforcement frequencies, especially using the same subjects as in Experiment 2. Reinforcement frequency might determine amphetamine's effect at lower control response rates than those obtained in Experiment 2, or larger differences in reinforcement frequency might alter the effect of amphetamine. Random-ratio schedules have produced much larger differences in reinforcement frequency in pigeons (Farmer & Schoenfeld, 1967; Sidley & Schoenfeld, 1964), but the procedure involved successively retraining the pigeons at different ratio values and all response rates were uniformly high.

Of course, equivalent response rates at different frequencies of reinforcement provide no evidence of schedule control (i.e., that the schedule components differ for the subject). Nonetheless, amphetamine effects might have differed between schedule components of Experiment 2. Because this did not occur, a failure to reject the null hypothesis must be discussed. The significance of the present Experiment 2 rests on the strong similarity of dose-response functions obtained under the different reinforcement rates. Given so little variance in amphetamine's effect, despite large differences in reinforcement frequency, it is difficult to argue that reinforcement frequency alters amphetamine's behavioral effect.

In summary, the results of two complementary procedures were used to evaluate the roles of control rate of responding and reinforcement on amphetamine's behavioral actions. Amphetamine's effect was rate dependent when rates of reinforcement were controlled between schedules, but no alteration of amphetamine's effect was produced by variations in reinforcement frequency when control rates of responding were equivalent. Taken together, the present results support the view that an important factor determining the behavioral effect of amphetamine is the control rate of responding, regardless of the schedule used to obtain the response rates.

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