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Effect of Amphetamine on Behavior Maintained by Sucrose: Interaction of Reinforcement Schedule and Food Restriction

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SLAWECKI, C. J. AND H. H. SAMSON. *Effect of amphetamine on behavior maintained by sucrose: Interaction of reinforcement schedule and food restriction.* PHARMACOL BIOCHEM BEHAV **54**(3) 595-600, 1996. – A multiple schedule (Mult FR 10 VI 30″) was employed to examine the interaction of reinforcement schedule and food restriction on amphetamine's effects on lever pressing behavior. High response rates were observed in fixed ratio (FR) 10 components. Significantly lower response rates were observed under the variable interval (VI) 30″ schedule. In the nonrestricted feeding condition, significant decreases in high rate FR 10 responding occurred after administration of 1.0 mg/kg amphetamine while lower rates under the same schedule were increased by 0.30 and 1.0 mg/kg amphetamine. In contrast, VI 30″ responding was minimally effected at any amphetamine dose. Food restriction resulted in significant increases in responding in both schedule components. Under food restriction, significant decreases in responding were observed only in the FR 10 components at the highest amphetamine dose. The data indicate that amphetamine produced rate-convergent effects and the susceptibility of the animal to these effects was dependent on the schedule of reinforcement and food restriction.

Amphetamine Food restriction Multiple fixed ratio-variable interval schedule Rate dependency Rate constancy

THE EFFECTS of amphetamine on behavioral response rates have been linked to several variables. Factors that contribute to these effects are dose, rate of behavior prior to drug administration, and motivational states such as food restriction. The dose effects of amphetamine on a single behavior are generally biphasic. Relatively low doses (0.1–0.5 mg/kg) typically increase behavior (1,8,9,19,21,23,27) while high doses (>1.0 mg/kg) decrease behavior (8,9,21,25,33,34).

However, the differential effect of a given dose of amphetamine usually also depends upon the rate of the ongoing behavior, which has been termed rate dependency (6,15). This rate-dependent effect has been primarily studied using psychomotor stimulants but has been explored for benzodiazepines, barbiturates, and phenothiazine antipsychotics (15). For the psychomotor stimulants, the general finding is that for high rates of ongoing behavior, these drugs decrease response rate. For low rates of behavior, the same dose increases response rate. This effect has been explored using different schedules of reinforcement including fixed intervals (8,9), fixed ratios (25,29), random or variable interval (2,21,27), and multiple fixed ratio-fixed interval schedules (1,10,20,23).

The relationship of amphetamine's effects to ongoing behavior may also be modulated by other internal and external (environmental) stimuli. For example, food deprivation has been shown to modulate the effects of amphetamine. Samson (29) observed significant decreases in lever press behavior maintained by a 10% sucrose solution when a 0.5 mg/kg dose of amphetamine was administered to ad lib fed animals. After the introduction of food restriction (80% of ad lib weight) the same dose of amphetamine produced only a small, insignificant decrease in responding, indicating a shift in the dose effect curve to the right. Because dietary restriction has often been employed in most of the operant studies used to examine rate dependency, the interaction of this variable with various schedules may be important for a full characterization of a drug's effect.

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The present study was designed to examine the effects of amphetamine on sucrose-maintained lever pressing under both food-sated and restricted conditions using a different reinforcement schedule from those previously tested. A multiple schedule of reinforcement was used to established both high and low rates of behavior within the same operant session. The consequent alteration in response rate and pattern were then examined for a possible interaction between amphetamine's rate effects and feeding condition.

METHOD

Animals

Six 5-month-old male Wistar rats (Harlan-Sprague Dawley: Indianapolis, IN) were used in this study. The animals ranged in weight from 481 g to 562 g (mean = 522.3 g, SD = 27.1 g) at the start of the experiment. They were housed in standard hanging cages with ad lib access to food and water. Artificial lighting maintained a 12 L : 12 D (on from 0600 to 1800 h) with room temperature held at approximately 23°C.

Prior to this study, the animals had been used in an experiment related to alcohol self-administration. A sucrose-fading protocol (28) had been used for 3 months to induce ethanol self-administration. Each animal had been allowed to self-administer 10% EtOH (v/v) (between 8 to 14 30 min/session) before the start of the present study. During this time minimal ethanol exposure occurred.

Apparatus

Sessions were conducted in operant chambers housed in sound attenuated enclosures. The chambers have been described in detail previously (28). A single response lever was present on the front panel of the chamber. A 3-s delivery of 0.1 ml of 10% sucrose (w/v) was employed as the reinforcer (Gerbrands liquid dipper delivery system, model No. B-LH). For the entire study, data collection was accomplished by means of an IBM compatible PC using Med Associates (East Fairfield, VT) software.

Drugs

d-Amphetamine Sulfate was obtained from Sigma Chemicals (St. Louis, MO). All doses of *d*-amphetamine were dissolved in sterile physiological (0.9%) saline. Solutions were made each day prior to IP injections. Drug concentrations were prepared at 0.1, 0.3, or 1.0 mg/ml. All vehicle injections were with sterile saline.

Procedure

Over the first six sessions (one 30 min session/day; 5 days/week) the response schedule was increased from a fixed ratio 4 (FR 4) to an FR 10. Because the rats had previous experience in these chambers, no response shaping was required. When stable behavior was established on an FR 10, the animals were placed on a multiple schedule (Mult). In one component, an FR 10 was in effect and in the second component, reinforcement was presented on a variable interval 30-s schedule (VI 30″). VI intervals were assigned randomly by a subroutine based upon progression of means (7) within the Med Associates software. Each component of the Mult FR 10 VI 30″ was in effect for 5 min and components were signaled by the presence or absence of the houselight. Each component alternated throughout the 30-min session. Each session began with the houselight illuminated and the FR 10 schedule in effect. When responding had come under stimulus control, such that a high rate of lever press behavior was observed during the FR components and a lower rate observed in the VI components, a dose–effect curve for *d*-amphetamine was determined.

Animals were run daily (5 days/week) in the operant chamber, even on days in which no injections were given. Each session began at the same time each day (1400 h). Doses of 0.0, 0.1, 0.3, and 1.0 mg/kg (IP) amphetamine were tested twice, in an ascending order each time. No more than three injections were given per week, and there was always a minimum of 1 day between injections (i.e., maximum number of injections/week = 3 = injections on Monday, Wednesday, and Friday). On most weeks only two injections were administered. Injections were administered 20 min prior to each session.

After the initial determination of the amphetamine dose–effect curve, the animals were reduced over a 2-week period to 85% of their free-feeding body weights by limiting food availability. When this weight was reached, the animals were maintained by fixed daily food rations of 8–20 g. During the period in which weight reduction was occurring, daily operant sessions continued, but no injections were administered. Following stabilization of body weight, the amphetamine dose–effect curve was redetermined with a single evaluation at each dose in an ascending order. The rats were then provided with ad lib access to food, and the return to baseline responding was examined.

Data Analysis

Data consisted of total responses per session and responses during each component of the Multiple schedule. Each individual component of the Mult FR 10 VI 30″ schedule was analyzed independently to examine effects occurring within each component of the 30-min session. Additionally, comparisons were made between session components to assess overall effects of the variables being tested (i.e., feeding state, reinforcement schedule, and drug dose).

One-way repeated measures analysis of variance (ANOVA) was used to examine differences in total session responses, response rates between feeding conditions (ad lib vs. food restricted) for each of the multiple schedule components and between components (first FR vs. second FR vs. third FR) within the same feeding condition. When appropriate, multiple comparison procedures (Bonferroni *t*-tests) were then used to detect specific effects. Two-way repeated measures ANOVA were used to examine differences in amphetamine dose effects, schedule component effects, and the interaction between amphetamine dose and schedule component. Post hoc analyses for dose effect consisted of a one-way ANOVA with Bonferroni *t*-test multiple comparison against control. For analysis of drug effects, each amphetamine dose was compared against saline controls.

Statistical analyses were performed with a computerized statistical package (SigmaStat, Jandel Scientific). Cumulative records were visually inspected for changes in patterns of responding due to drug administration or food restriction. Med Associates Software SoftCr was used to examine the cumulative records.

RESULTS

At the end of the experiment, average weight had increased 106 ± 20 g (range: 570–651 g). During the portion of the ex-

periment that required food restriction, the weight of the animals was held at approximately 85% of free-feeding body weights determined from their ad lib weights prior to restriction (range: 538-631 g). Restricted body weights ranged from 447-532 g.

Stable responding on the multiple schedule was established after 19 sessions. The average number of responses per session was 669 ± 33. During ad lib feeding conditions, the average rate of responding across FR 10 components was 30.9 ± 2.9 (SEM) responses/min, and in the VI components 8.4 ± 1.0 responses/min. The operant behavior was judged to be under stimulus control, as rapid decreases in response rate occurred at the transition from the FR 10 to VI 30″ component and rapid increases at the reverse schedule transition were noted in the cumulative records (Fig. 1a). Responding was greatest in the first 20 min of the session. Average response rates significantly decreased, $F(2, 40) = 5.416$, $p = 0.029$, across the three successive FR components (Fig. 2a, c, and e). Pair-wise comparisons revealed significant differences between the first and third FR components. Successive VI components (Fig. 2b, d, and f) under ad lib conditions also showed significant differences between the first and third VI components, $F(2, 40) = 5.294$, $p = 0.027$.

Response rates were more consistent under food restriction and typically lasted throughout the session (Fig. 1b). When compared to ad lib feeding, total session responses significantly increased to 1057 ± 59, $F(2, 142) = 53.0$, $p < 0.001$. Food restriction produced statistically significant increases in response rates in all FR, $F(5, 264) = 36.048$, $p < 0.001$, and VI, $F(5, 264) = 37.378$, $p < 0.001$, components of the multiple schedule when compared to the ad lib condition (Fig. 2a-f). The average response rate increased to 69.5 ± 4.5 responses/min during the FR components under food restriction and to 17.8 ± 2.7 responses/min during the VI components. Statistically significant increases in responding were observed in the first two FR components when compared to the third FR component, $F(2, 40) = 15.54$, $p < 0.001$. The first VI component response rate was significantly higher, $F(2, 40) = 12.72$, $p = 0.002$, than the second and third VI components.

Analysis of individual FR components within sessions during the ad lib condition revealed significant effects of amphetamine on responding. At the 1.0 mg/kg dose, significant decreases in response rates were observed in the first two (0-5 min and 10-15 min) FR components (Fig. 2a and c), $F(4, 44) = 16.086$, $p < 0.001$, and $F(4, 44) = 3.410$, $p = 0.016$, respectively. In the third (20-25 min) FR component (Fig. 2e), the 0.30 mg/kg dose significantly increased response rate, $F(4, 44) = 2.963$, $p = 0.030$. However, in the third component,

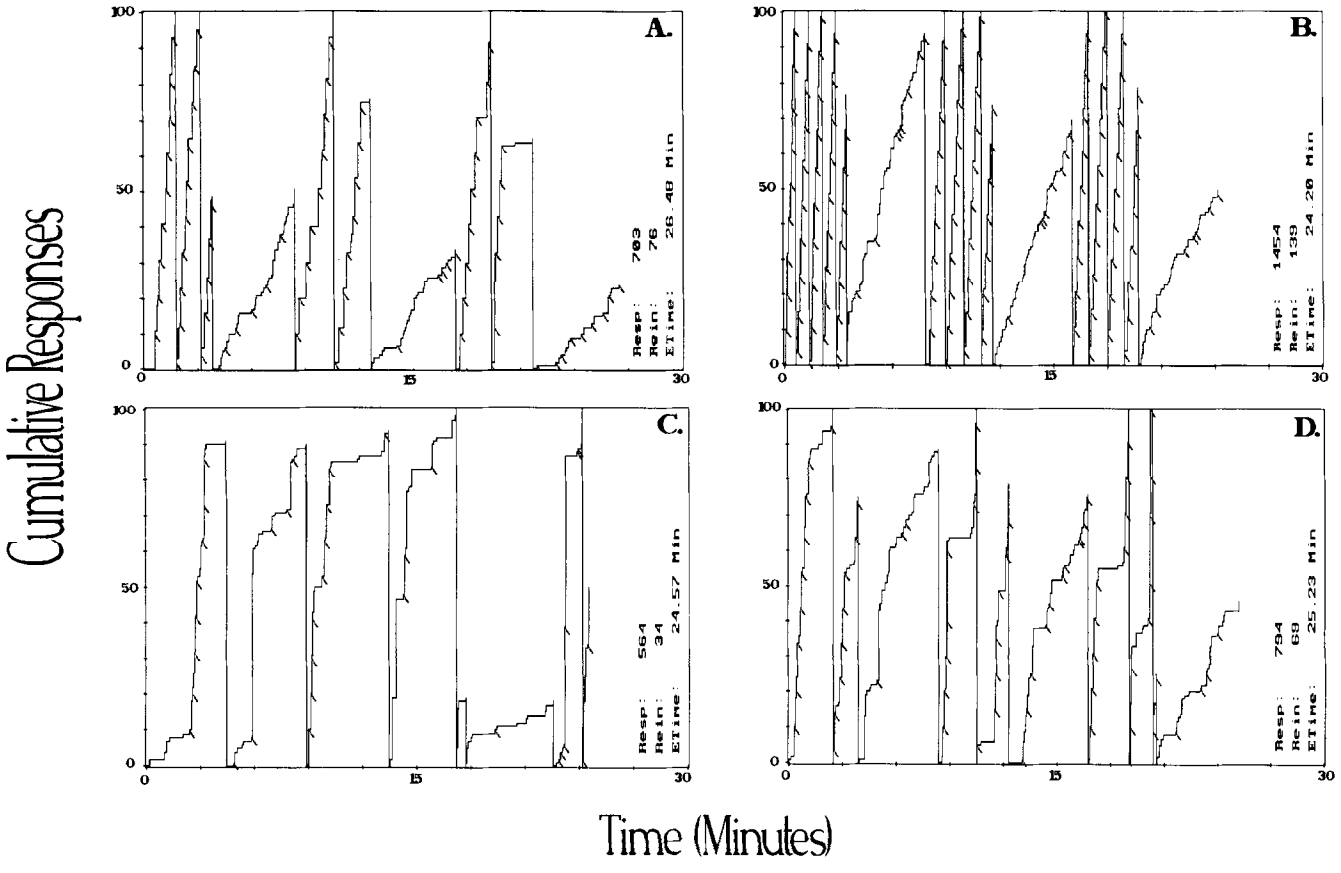

FIG. 1. Cumulative records depicting typical response patterns during the Mult FR 10 VI 30″ schedule. (A) Responding under ad lib feeding. (B) Responding under food restriction (85% free-feeding body weight). (C and D) Response patterns after 1.0 mg/kg amphetamine administered IP in two separate subjects in the ad lib (C) and the food restricted condition (D). Cumulative records were generated by Med-Associates SoftCR (East Fairfield, VT).

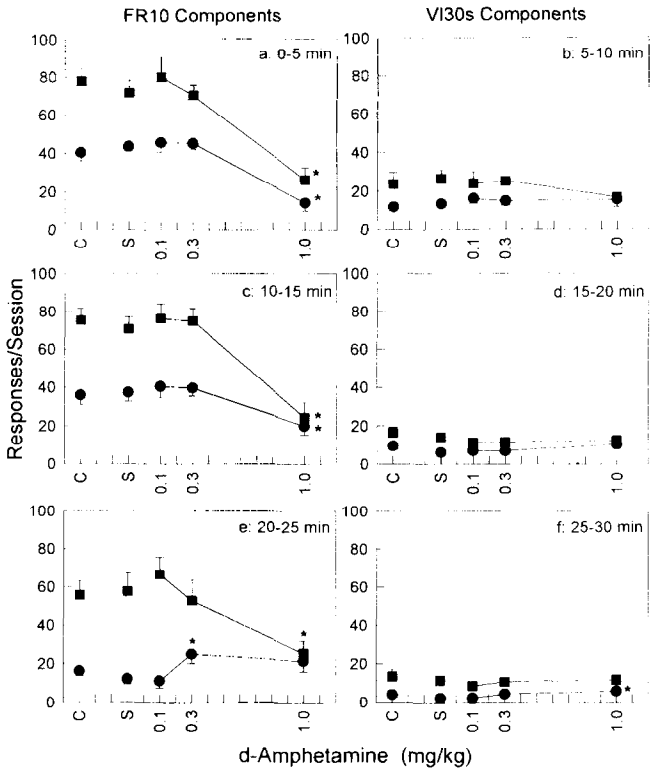

FIG. 2. Changes in response rates in individual schedule components as a function of increasing amphetamine dose. Filled squares depict responding under food restriction (n = 6); filled circles represent responding with ad lib feeding (n = 12). Error bars are the SEM. *Represents statistically significant difference from vehicle injection ($p < 0.05$). Total session length was 30 min. (a) Response rates in first FR component (0–5 min). (b) Response rates in first VI component (5–10 min). (c) Response rates in second FR component (10–15 min). (d) Response rates in second VI component (15–20 min). (e) Response rates in third FR component (20–25 min). (f) Response rates in third VI component (25–30 min).

the 1.0 mg/kg dose did not result in a significant difference from the saline control. The third VI component (25–30 min) at the 1.0 mg/kg dose (Fig. 2f) showed a significant increase in responding, $F(4, 44) = 2.830$, $p = 0.036$.

In the food restricted condition, amphetamine produced statistically significant decreases in response rates in all three FR components (Fig. 2a, c, and e) at the dose of 1.0 mg/kg [first FR: $F(4, 20) = 11.597$, $p < 0.001$, second FR: $F(4, 20) = 15.306$, $p < 0.001$, and third FR: $F(4, 20) = 3.638$, $p = 0.022$]. No statistically significant effect of amphetamine at any dose was observed in VI components (Fig. 2b, d, and f).

When ad lib feeding was reinstated, a statistically significant decrease in total session responding was observed in comparison to responding during the food restricted condition, $F(2, 142) = 53.0$, $p < 0.001$. Total session responses decreased to 721.5 ± 20. Total session responding during the final ad lib condition was not different from responding during the first ad lib feeding condition.

Visual examination of cumulative records after administration of 1.0 mg/kg amphetamine indicated four major response patterns: 1) delayed onset of responding, 2) early termination of responding, 3) increased duration and frequency of pausing, 4) and a constant rate of responding. These characteristics were often found in combination. Delayed onset of responding was characterized by either highly decreased or termination of responding within the first 15 min of the session. Early termination was characterized by cessation of responding or low rate sporadic responding. When prolonged pauses were not present, the response rate was relatively constant throughout several components of the session (Fig. 1c-d). These effects were observed across both feeding conditions.

DISCUSSION

In animals maintained with ad lib food, administration of a 1.0 mg/kg dose of amphetamine resulted in significant decreases in lever press behavior in the first two FR components of the multiple schedule while 0.30 mg/kg amphetamine produced significant increases in the third FR component. The 1.0 mg/kg amphetamine dose also produced a significant increase in lever pressing only in the third VI component. Food restriction resulting in an 85% reduction of free-feeding body weight produced significant increases in responding across all components of the multiple schedule. In the food-restricted condition, significant decreases in responding were observed in all FR components at the 1.0 mg/kg dose. No effect of amphetamine was observed in the VI components under food restricted conditions.

Dose-response curves for amphetamine on FR responding in both feeding conditions were in good agreement with previous reports for high amphetamine doses, for instance, 1.0 mg/kg amphetamine produced decreases in responding in most of the FR components (8,26,33). The FR component in which a significant increase in responding was observed, the third FR component in the ad lib feeding condition, differed from the other FR components by its low response rate, 15–20 responses/min. Other studies have also reported increases or no change in FR responding under multiple schedules at this amphetamine dose when similar low response rates occurred (23,34). In addition, increases or no change in lever press behavior under different reinforcement schedules have been reported in rats at doses of amphetamine greater than 1.0 mg/kg when similar low rates were generated (1,21). The most consistent decreases in FR responding over a wide range of amphetamine doses have been reported when response rates are greater than 100 responses/min (8,25,26). The present finding of decreases in response rates between 40 to 80 responses/min suggests intermediate rates of FR responding under a multiple schedule of reinforcement are similarly susceptible to the rate decreasing effects of high dose amphetamine as are high rates generated under a simple FR schedule.

Only in the third VI component under ad lib feeding when responding was lowest (<10 responses/min) did the 1.0 mg/kg dose of amphetamine produce a small but statistically significant increase in response rates. The lack of effect during the VI components contrasts with much of the literature (2,20,26). However, this study is not the only one that reports a lack of effect of amphetamine on VI schedule responding (21,22,30). Using a 20% sucrose reinforcer, Shah (30) observed small decreases in responding during a VI 80 s when doses of amphetamine as low as 0.2 mg/kg were administered and control rates of responding were approximately 25/min. Using a random interval schedule Lucki (22) observed that at response rates similar to those generated in this experiment,

administration of 0.25 and 1.0 mg/kg amphetamine did not significantly alter response rate, while 0.5 mg/kg of amphetamine did increase response rates. It is possible that alterations in response rate would have occurred had an intermediate dose between 0.3 and 1.0 mg/kg been administered. In addition, it has been reported by Lucki and De Long (22) that amphetamine doses as high as 1.0 mg/kg have no effect on response rates similar to those generated in this study during a multiple DRL yoked-VI schedule. These data taken together suggest that a lack of susceptibility to amphetamine's rate changing effects is uncommon but not irreconcilable with the literature.

Because of this finding, it would appear that response rate is not the single determinant of amphetamine effects. The multiple schedule in the present study generated similar rates of responding during different components. For example, the rates of responding in all VI components and the third FR component under ad lib feeding were comparable (15–25 responses/min), but the FR component was more susceptible to alteration by amphetamine at 0.30 mg/kg. McMillan also (23) observed differences in the rate effects of 0.3 mg/kg amphetamine on FI 5 min limited hold (LH) 160 s and FR 250 (LH 720 s) schedules that generated similar rates of behavior. In addition, it was reported that the length of a limited hold (20 or 160 s) differentially affected rate in an FI 5 min schedule. In combination with the present study, these data suggest that ongoing rate of behavior is not the single determinant of the rate altering effects of amphetamine. The nature of the schedule maintaining the behavior appears to play a key role in the rate altering effects of amphetamine.

The failure of amphetamine to increase low response rates in the VI components when comparable to low-rate FR responding suggests that a rate-dependent hypothesis alone cannot explain the results of this study. Rate convergence may provide an explanation for the data. Examination of the dose–response curves reveal that response rates may be converging in the FR components. The convergence point for the FR components approximates the average rate in the VI components (20 responses/min). Additionally, increases in VI responding were observed when responding was lowest. Ksir (15) has noted that several studies that report rate-dependent phenomena can also be interpreted as rate convergence when their dose–effect curves are examined. Similar convergence of high and low rates in a multiple schedule were observed by McMillan (23) in a Mult FR 250 FI 60 LH 720. In this study, FI response rates decreased significantly with increasing amphetamine doses while FR rates slightly decreased to result in approximately equal final response rates. If the rate convergence theory is true, the lack of alteration of VI response rate could be attributed to the fact that the VI rate was being maintained at the convergence rate in this experimental paradigm.

The increase in total session responding during food restriction was a result of both an increased rate of responding within each component and longer duration of responding during the session (Fig. 2a–f). Increased intake of the sucrose reinforcer would be expected in food-restricted animals due to its caloric content. Although experience may account for the slight increase in total session responding upon return to ad lib feeding conditions, the large increases and decreases in responding following the start and end of food restriction suggests that the most parsimonious explanation would be an increased need for calories. However, several authors have shown food restriction can increase intake of noncaloric reinforcers in operant paradigms, for instance, food deprivation can alter the self-administration patterns of many reinforcers including alcohol, cocaine, amphetamine, phencyclidine, and heroin, resulting in increased drug self-administration regardless of caloric content (4,16). Increases in operant responding maintained by both caloric and noncaloric reinforcers induced by food restriction suggests that complex motivational alterations, in addition to caloric need, may be operating to increase behavior. Evidence for changes in motivational processes has been reported by Harrington (11). Using a conditioned place-aversion paradigm, a dose of 0.8 mg/kg alphaflupenthixol given over 8 days produced conditioned place aversion in food-sated rats; however, the same dose resulted in a conditioned place preference in food-restricted rats. This suggests that motivational changes induced by drugs, along with rate effects, are dependent on the context in which the drug is administered.

A possible explanation for the anomalous effect of amphetamine on behavioral rate may be attributed to stimulus control. Stimulus control of behavior appeared to become more robust with the introduction of food restriction in the present study. Examination of cumulative records revealed rapid changes in response rate in concert with changes in the houselight stimulus associated with the reinforcement schedule in effect (Fig. 1b). However, the apparent alteration in stimulus control by food restriction may only be a function of increased responding, and not due to changes in the cues salience. That is, the changes in response rate with stimulus change may only appear to be more distinct due to the decreases in local pausing throughout the session. More direct measures of stimulus control distinct from response rate measures must be employed to further address this issue.

Using conditional probability measurements, Katz (13,14) has reported that changes in response rate due to amphetamine administration, traditionally attributed to decreases in stimulus control, are not due to alterations in stimulus control regardless of its strength. It is possible that the drastic changes in response patterns after high dose amphetamine could be due to motoric problems such as stereotypy; however, no gross motoric problems were observed during the course of the session. In addition, similar doses of amphetamine have been shown to have a more pronounced effect on reinforcing factors than motoric factors. In an investigation of the matching law, Heyman (12) found that over a wide does range, parameters associated with motoric variables were less systematically altered than were those relating the to reinforcing efficacy. Thus, motoric problems are not thought to be the primary reason for decreases in response rates in this paradigm.

If stimulus control was affected, an increase in the salience of the sucrose reinforcer under the food restricted condition might be expected to decrease the ability of amphetamine to reduce response rates. In support of this hypothesis, Samson (29) reported a shift to the right in the dose–response curve for amphetamine in rats when food restriction was imposed. In the present study, the dose–effect curve did not shift to the right. The 0.3 and 1.0 mg/kg doses of amphetamine in the final FR component actually resulted in a shift to the left in the dose–effect curve, the opposite result from that found by Samson (29). In the first two FR components the decreases in responding were greater in magnitude than the decreases seen in the ad lib condition. The reason for this difference could be a result of schedule, stimulus cues available, or the extent of behavioral control present in a given situation.

This study examined the interaction of food restriction, schedule control, and dose of amphetamine on lever-press re-

sponse rate using a Mult FR 10 VI 30″ schedule. The data indicated that food restriction increased response rate and possibly stimulus control across both portions of the multiple schedule. Although increases in low-rate behavior and decreases in high-rate behavior were observed, the lack of effect of amphetamine in components with similar response rates suggests the rate dependency hypothesis does not best describe the data. Examination of dose-effect curves for amphetamine and cumulative records suggest that a rate-convergent effect may have resulted from amphetamine administration.

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REFERENCES

1. Allen, R. A.; MacPhail, R. C. Effects of triadimefon on a multiple schedule of fixed-interval performance: Comparison with methylphenidate, *d*-amphetamine and chlorpromazine. Pharmacol. Biochem. Behav. 40:775–780; 1990.
2. Bradshaw, C. M.; Ruddle, H. V.; Szabadi, E. Relationship between response rate and reinforcement frequency in variable-interval schedules: III. The effects of *d*-amphetamine. J. Exp. Anal. Behav. 36:29–39; 1981.
3. Brown, R. M.; Seiden, L. S. Inter-response time changes as a function of water deprivation and amphetamine. J. Pharmacol. Exp. Ther. 193(2):701–712; 1973.
4. Carroll, M. E.; Meisch, R. A. Determinants of increased drug self-administration due to food deprivation. Psychopharmacology (Berlin) 74:197–200; 1981.
5. Dews, P. B. Studies on behavior. II. The effects of pentobarbital, methamphetamine, and scopolamine on performances in pigeons involving discriminations. J. Pharmacol. Exp. Ther. 115:380–389; 1955.
6. Dews, P. B. Interactions of behavioral effects of drugs. Ann. NY Acad. Sci. 281:50–63; 1976.
7. Fleshler, M.; Hoffmanm, H. A progression for generating variable interval schedules. J. Exp. Anal. Behav. 5:529–530; 1962.
8. Glick, S. D.; Jerussi, T. P. Spatial and paw preferences in rats: Their relationship to rate-dependent effects of amphetamine. J. Pharmacol. Exp. Ther. 188(3):714–725; 1974.
9. Goudie, A. J. Comparative effects of cathinone and amphetamine on fixed-interval operant responding: A rate-dependency analysis. Pharmacol. Biochem. Behav. 23:355–365; 1985.
10. Graeff, F. G. Effect of cyproheptadine and combinations of cyproheptadine and amphetamine on intermittently reinforced lever-pressing in rats. Psychopharmacology (Berlin) 50:65–71; 1976.
11. Harrington, F.; van der Kooy, D. Deprivation state determines the motivational effects of neuroleptics in rats. Psychobiology 20(4):294–299; 1992.
12. Heyman, G. M. A parametric analysis of the hedonic and motoric effects of drugs: Pimozide and amphetamine. J. Exp. Anal. Behav. 40(2):113–122; 1983.
13. Katz, J. L. Effects of drugs on stimulus control of behavior. I. Independent assessment of effects on response rates and stimulus control. J. Pharmacol. Exp. Ther. 223(3):617–623; 1982.
14. Katz, J. L. Effects of drugs on stimulus control of behavior. II. Degree of stimulus control as a determinant of effect. J. Pharmacol. Exp. Ther. 226(3):756–763; 1983.
15. Ksir, C. Rate-convergent effects of drugs. In: Thompson, T. T.; Dews, P. B.; McKim, W. A., eds. Advances in behavioral pharmacology. Vol. 3. New York: Academic Press Inc.; 1981:39–57.
16. La Garza, R.; Johanson, C. E. The effects of food deprivation on the self-administration of psychoactive drugs. Drug Alcohol Depend. 19:17–27; 1987.
17. Laties, V. G.; Weiss, B. Influence of drugs on behavior controlled by internal and external stimuli. J. Pharmacol. Exp. Ther. 152(3): 388–396; 1966.
18. Laties, V. G. The modification of drug effects on behavior by external discriminative stimuli. J. Pharmacol. Exp. Ther. 183(1): 1–13; 1972.
19. Laties, V. G.; Wood, R.; Rees, D. C. Stimulus control and the effects of *d*-amphetamine in the rat. Psychopharmacology (Berlin) 75:277–282; 1981.
20. Leander, J. D.; McMillan, D. E. Rate-dependent effects of drugs. I. Comparisons of *d*-amphetamine, pentobarbital and chlorpromazine on multiple and mixed schedules. J. Pharmacol. Exp. Ther. 188(3):276–739; 1974.
21. Lucki, I. Rate-dependent effects of amphetamine on responding under random-interval schedules of reinforcement in the rat. Pharmacol. Biochem. Behav. 18:195–201; 1983.
22. Lucki, I.; DeLong, R. E. Control rate of reinforcement and amphetamine's effect on behavior. J. Exp. Anal. Behav. 40(2):123–132; 1983.
23. McMillan, D. E. Effects of *d*-amphetamine on performance under several parameters of multiple fixed-ratio, fixed interval schedules. J. Pharmacol. Exp. Ther. 167:26–33; 1969.
24. Nielsen, E. B.; Appel, J. B. The effects of drugs on the acquisition of stimulus control in a conditioned suppression procedure. Psychopharmacology (Berlin) 85:80–86; 1985.
25. Owen, J. E. The influence of *dl*-, *d*-, *l*-amphetamine, and *d*-methamphetamine on a fixed-ratio schedule. J. Exp. Anal. Behav. 3:293–310; 1960.
26. Peterson, D. W.; Sparber, S. B. Increased fixed ratio performance and differential *d*- and *l*-amphetamine action following norepinephrine depletion by intraventricular 6-hydroxydopamine J. Pharmacol. Exp. Ther. 191(3):349–357; 1974.
27. Phillips, G.; Willner, P.; Sampson, D.; Nunn, J.; Muscat, R. Time-, schedule-, and reinforcer-dependent effects of pimozide and amphetamine. Psychopharmacology (Berlin) 104(1):125–131; 1991.
28. Samson, H. H. Initiation of ethanol reinforcement using a sucrose-substitution procedure in food- and water-sated rats. Alcohol. Clin. Exp. Res. 10(4):436–442; 1986.
29. Samson, H. H. Effect of amphetamine on sucrose-reinforced lever pressing: Interaction with food deprivation. Drug Alcohol Depend. 17:323–330; 1986.
30. Schaal, D. W.; Branch, M. N. Changes due to food deprivation in the effects of cocaine on the responding of pigeons. Behav. Pharmacol. 3:5–9; 1992.
31. Shah, K.; Bradshaw, C. M.; Szabadi, E. Interaction between antidepressants and *d*-amphetamine on variable-interval performance. Psychopharmacology (Berlin) 100:548–554; 1990.
32. Sparber, S. B.; Tilson, H. A. Environmental influences upon drug-induced suppression of operant behavior. J. Pharmacol. Exp. Ther. 179(1):1–9; 1971.
33. Tilson, H. A.; Sparber, S. B. The effects of *d*- and *l*-amphetamine on fixed interval and fixed ratio behavior in tolerant and nontolerant rats. J. Pharmacol. Exp. Ther. 187(2):372–379; 1973.
34. Wagner, G. C.; Jarvis, M. F. Evaluation of the pharmacological similarities between phenylpropanolamine and amphetamine: Effects on schedule-controlled behavior. Synapse 6:101–105; 1990.