

*EFFECTS OF COCAINE ON FIXED-INTERVAL
RESPONDING REINFORCED BY
THE OPPORTUNITY TO RUN*

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Rate-dependent drug effects have been observed for operant responding maintained by food, water, heat, light onset, electrical brain stimulation, shock-stimulus termination, and shock presentation. The present study sought to determine if the effects of cocaine on lever pressing maintained by the opportunity to run could also be described as rate dependent. Seven male Wistar rats were trained to respond on levers for the opportunity to run in a wheel. The schedule of reinforcement was fixed-interval 60 s, and the reinforcing consequence was the opportunity to run for 60 s. On this schedule, overall rates of responding were low, usually below six presses per minute, and pauses frequently exceeded the 60-s interval. Despite these differences, an overall scalloped pattern of lever pressing was evident for each rat. Doses of 1, 2, 4, 8, and 16 mg/kg cocaine were administered 10 min prior to a session. Only at the 16 mg/kg dose did the responding of the majority of rats change in a manner suggestive of a rate-dependent drug effect. Specifically, lower response rates at the beginning of the intervals increased and higher rates at the end of the intervals decreased, as indicated by the fact that slopes from the regression of drug rates on control rates decreased. These data provide tentative support for the generalization of rate-dependent effects to operant responding maintained by wheel running. Differences in the baseline performance maintained by wheel running compared to those for food and water point to the need for further experimentation before this effect can be firmly established.

Key words: wheel-running reinforcement, fixed-interval schedule, rate dependency, cocaine, lever press, rats

Rate dependency refers to the observation that the effect of a drug on operant response rates depends on the control rate of responding. As Dews (1958) observed, on schedules of reinforcement that engender low control rates of responding, such as fixed-ratio (FR) 900 or fixed-interval (FI) 900-s schedules, low doses of methamphetamine increased responding. In contrast, on schedules of reinforcement that generate high rates of responding, such as an FR 50 or a variable-interval (VI) 60-s schedule, the same dose had little effect or decreased responding.

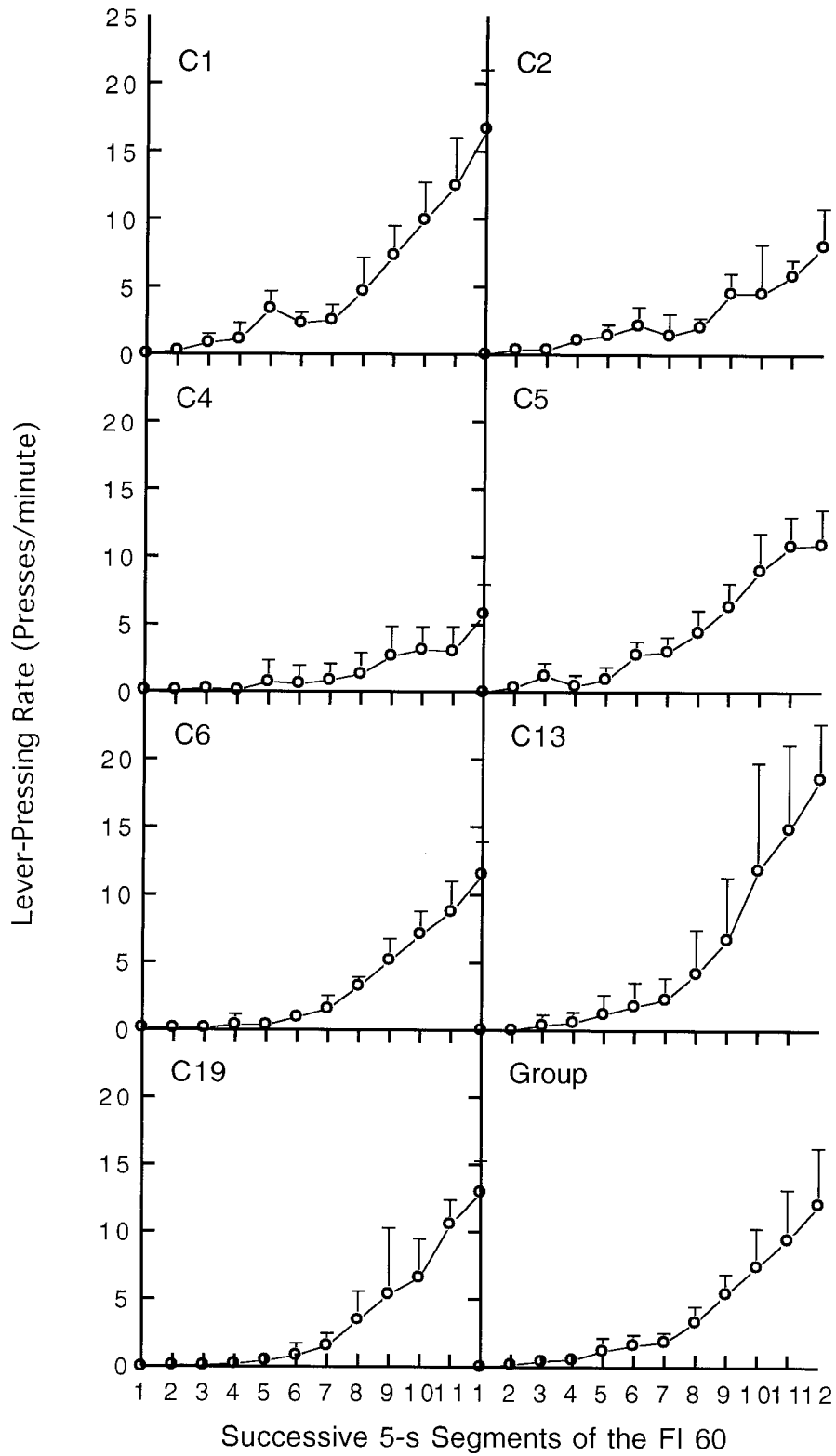
Since first observed by Dews (1958), rate-dependent drug effects have been demonstrated with a variety of maintaining events such as food (e.g., Barrett, Dworkin, & Zuc-

carelli, 1977; Gonzalez & Goldberg, 1977; Hearst, 1961; Heffner, Drawbaugh, & Zigmond, 1974; Logan, Carney, Holloway, & Seale, 1989), water (Hearst, 1961), heat (Weiss & Laties, 1963), light onset (Gomer & Jakubczak, 1974), shock presentation (Byrd, 1979; McKearney, 1973, 1974), shock-stimulus termination (Barrett et al., 1977; McKearney, 1980), and electrical brain stimulation (Carey & Goodall, 1973; Domino & Olds, 1972). Although originally assumed to be independent of the type of reinforcer maintaining operant responding, subsequent research suggested that "the type of event can be an important factor in determining the effects of certain drugs on behavior" (Barrett & Katz, 1981, p. 146). Consequently, Kida, Greenshaw, Sanger, and Blackman (1981) suggested that drug effects on operant responding need to be assessed over a variety of reinforcers.

The purpose of the present study was to determine if rate-dependent drug effects occur for responding maintained by the opportunity to run. Wheel-running reinforcement differs from reinforcers previously assessed in a variety of ways. First, unlike shock presentation or shock-stimulus termination, wheel-

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running reinforcement does not involve exposure to aversive stimulation. Second, unlike food or water, but like heat, light onset, and, perhaps, electrical brain stimulation, running does not involve ingestion of a substance that meets a physiological need. Third, the duration of access to the reinforcer typically is much longer than for other types of reinforcement, and previous research has shown that the duration of the postreinforcement pause (PRP) varies directly with the duration of the reinforcement period (Belke, 1997; Belke & Dunbar, 1998).

Long PRPs have implications for the use of FI schedules. That is, depending on the relative durations of the interval requirement and the reinforcer duration, the percentage of PRPs in an experimental session that exceed the duration of the schedule interval may be higher than what is typical with other reinforcers (Belke & Dunbar, 1998). For example, long reinforcer durations, such as 60 s, may produce a distribution of PRPs in which most, if not all, of the pauses in a session are longer than the FI 15-s schedule under which the reinforcer is available. At the extreme, the interval schedule may come to be experienced as a continuous reinforcement schedule (FR 1) rather than an intermittent schedule, or as a schedule in which the periodicity of reinforcer availability is experienced to a lesser degree than is usual with food or water reinforcement.

Finally, unlike previously investigated reinforcers, wheel-running reinforcement offers the opportunity to investigate the effects of a drug on both operant and consequential behavior. For example, if the effect of a drug on operant behavior is interpreted in terms of an increase in the efficacy of a reinforcer, how does the consequential behavior change? Do changes in the consequential behavior support this interpretation? How is the rate of the consequential behavior related to the rate of the operant behavior?

In the present study, rather than assessing the effects of cocaine on operant and consequential behavior across different schedules of reinforcement, as Dews (1958) did, drug

Table 1

The dose order of cocaine injections for each rat. Each dose was administered by intraperitoneal injection three times before the next dose was studied.

Rat	Cocaine (mg/kg)				
	1	2	4	8	16
C1	1	2	3	4	5
C2	2	3	5	1	4
C4	3	4	5	2	1
C5	4	5	2	1	3
C6	5	3	1	2	4
C13	5	4	3	2	1
C19	4	3	2	1	5

effects were assessed on responding generated by an FI schedule. FI schedules generate patterns of responding that range from low rates in the period immediately following the termination of a reinforcer to high rates in the period immediately prior to the elapsing of the reinforcement interval. On these schedules, rate-dependent effects have been observed as an increase in the low rates near the beginning of the interval and a decrease in the high rates near the end of the interval (Dews & Wenger, 1977).

METHOD

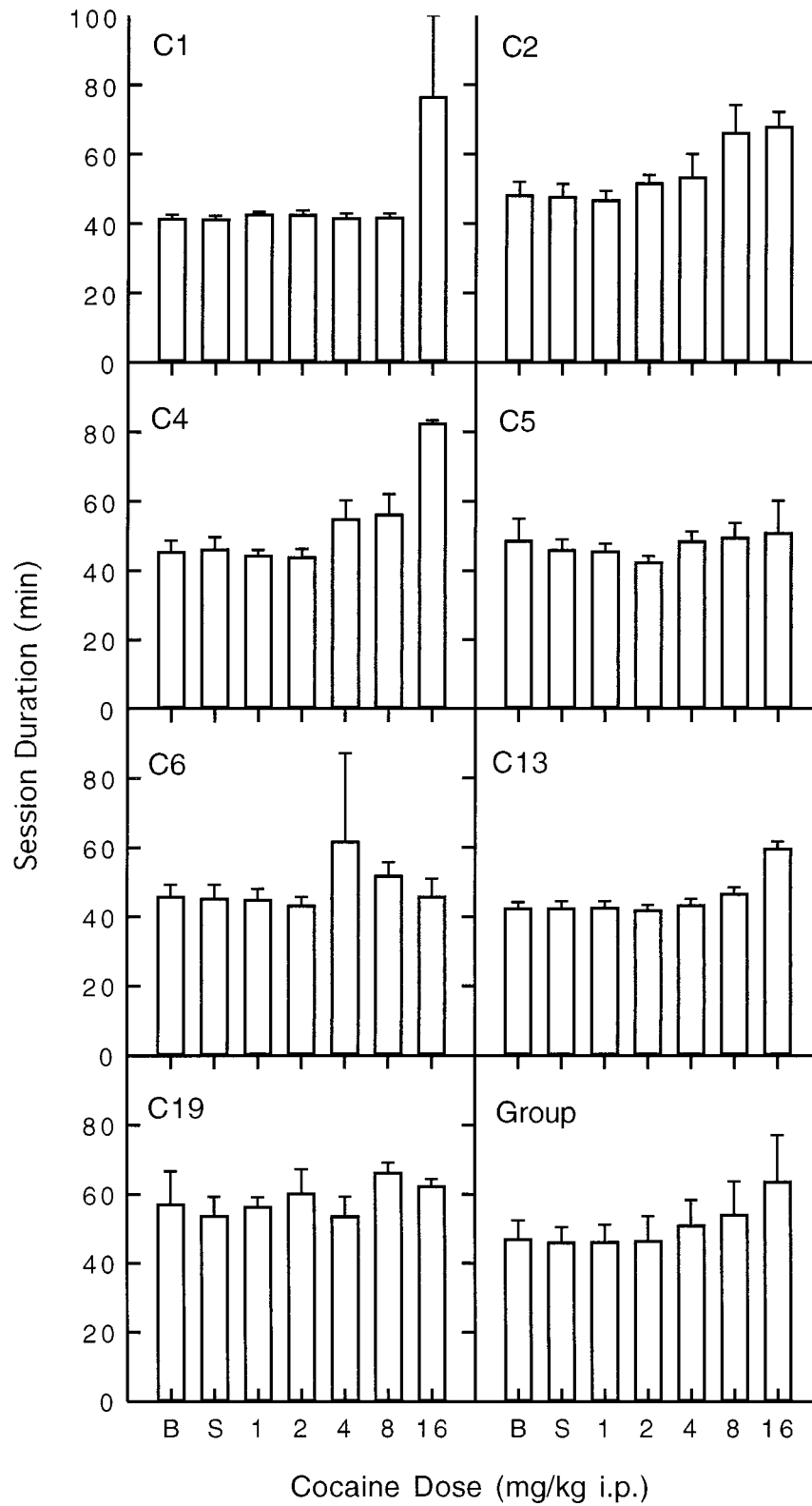
Subjects

Seven male Wistar rats obtained from Charles River Breeding Laboratories served as subjects. The animals were approximately 1 year old at the start of the experiment and had previously participated in a laboratory demonstration of operant conditioning. Following completion of the course, the 21 rats from the course were placed in running wheels for 30 min each day over a 10-day period. The number of wheel revolutions was recorded for each rat on each day. After 10 days, the rats used in the present study were selected based on their high rates of running.

When not in the experimental apparatus, rats were individually housed in standard polycarbonate cages (48 cm by 27 cm by 22 cm) in a colony room maintained at 20 °C with a 12:12 hr light/dark cycle (lights on at

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Fig. 1. Lever-pressing rates (presses per minute) across successive 5-s segments of the 60-s interval of the FI schedule averaged over five baseline sessions prior to the commencement of drug testing. Bars indicate 1 SD.



8:00 a.m.). Each subject was maintained at a target weight that was approximately 85% of a free-feeding body weight measured when its weight rose just above 400 g (i.e., adult weight). As a result, target weights varied around $340 \text{ g} \pm 10 \text{ g}$. Animals were maintained on food restriction because previous research in our laboratory showed that motivation to run varied inversely with body weight. Distilled water was freely available in the home cages.

Apparatus

Subjects were tested in activity wheels (three Wahmann and four Lafayette Instruments Model 86041A) without side cages. The diameters of the wheels were 35.5 cm. Each wheel was located in a soundproof shell equipped with a fan for ventilation and to mask extraneous noise. A retractable lever (Med Associates ENV-112) was mounted directly at the opening of each wheel. The lever extended 1.8 cm into the wheel through an opening (7 cm by 9 cm) in the center at the base of the wheel frame. A microswitch attached to the wheel frame recorded wheel revolutions. The force required to close the lever microswitches ranged between 18 and 27 g. Bulbs (24 V DC) mounted on the sides of the wheel frame served to illuminate the inside of the wheel. A solenoid-operated brake was attached to the base of each wheel. When the solenoid was operated, a rubber tip attached to a metal shaft contacted the outer rim of the wheel and stopped the wheel. Control of experimental events and recording of data were handled by IBM® personal computers interfaced to the wheels.

Procedure

Training the animals to press a lever for the opportunity to run began by shaping a lever press with sucrose reinforcement in standard operant conditioning chambers. Each lever press produced 0.1 ml of a 15% sucrose solution. When subjects reliably pressed the lever, the schedule of reinforcement was shifted

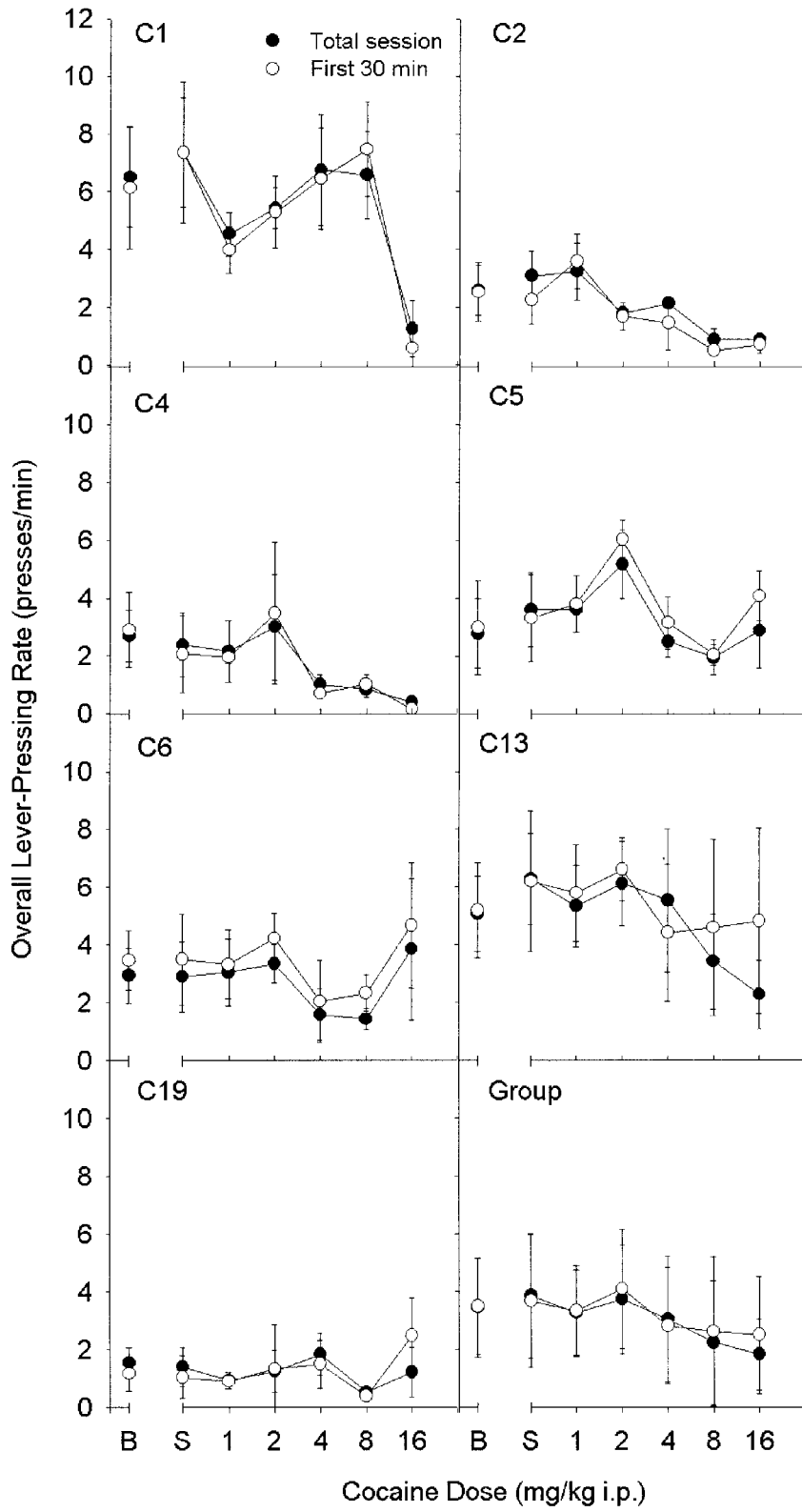
from an FR 1 schedule to a variable-ratio (VR) 3 schedule. This schedule remained in effect for approximately four sessions, with each session terminating when 50 sucrose reinforcers were obtained.

After four sessions on the VR 3 schedule, sessions in the operant conditioning chamber were discontinued. At this point, the retractable lever in each wheel chamber was extended during the wheel-running sessions, and the opportunity to run for 60 s was made contingent upon a single lever press. When the reinforcement requirement was met, the lever retracted and the brake released, leaving the wheel free to turn for 60 s. Once 60 s had elapsed, the reinforcement period was terminated by the brake being applied and the lever extended. Each session consisted of 30 opportunities to run. The schedule of reinforcement was changed in the following sequence: FR 1, VR 3, VR 5, VR 9, and VR 15. Each schedule was in effect for four sessions before subjects advanced to the next schedule.

Following training on VR 15, the rats were placed on an FI 60-s schedule of reinforcement with a 60-s reinforcer duration. Each session consisted of 20 reinforcers. Over 100 days, the duration of the opportunity to run was varied as part of a different experiment (Belke, 2000). After this experimental manipulation was completed, the schedule was FI 60 s, with the opportunity to run for 60 s as the reinforcer, for 30 days prior to the commencement of drug testing. Subjects were then administered cocaine hydrochloride (dissolved in 0.9% saline) by intraperitoneal injection 10 min prior to a session at doses of 1, 2, 4, 8, and 16 mg/kg. The volume of the injection (in milliliters per kilogram) was based on the body weight of the animal from the previous day. Each dose was administered three times before proceeding to the next dose. Table 1 shows the dose order for each rat. Dose orders were selected at random from a list of dose orders for 5 animals. For the remaining 2 animals, ascending and de-

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Fig. 2. Mean effect of cocaine dose on session duration (minutes). Bars represent the standard deviation associated with each mean. Means for the baseline (B) and saline (S) conditions are based on the 15 sessions of each type that occurred over the entire series of drug administrations. Means for the drug doses are based on three administrations of each dose.



scending dose orders were assigned. Between drug administrations, a baseline session followed by a session preceded by a saline injection occurred. As a result, drug administration occurred once every 3 days.

Number of lever presses, time between the termination of a reinforcer and the first press (i.e., PRP), time between the first lever press following the termination of a reinforcer and the press that delivered the reinforcer (i.e., time spent lever pressing), and number of wheel revolutions were recorded for each reinforcer and cumulatively for the entire session. In addition, lever presses during each 5-s segment of the FI 60-s interval were cumulated over the entire session.

Throughout the experiment, animals were weighed and fed an amount of food sufficient to maintain their target body weights immediately following the session. Sessions were conducted 7 days per week.

Data Analysis

Responding on the FI schedule prior to and during the drug-administration phase was assessed using dependent variables derived from the previously described measures. Response rates in each 5-s FI segment were calculated as the total number of responses in the segment divided by 100 s (i.e., 5 s for each of 20 reinforcers) and multiplied by 60 to express the rate as presses per minute. Overall response rates, also expressed as presses per minute, were calculated in two ways. First, overall rates were calculated based on the total number of lever presses that occurred during a session divided by total time during which the schedule of reinforcement was in effect (i.e., session time minus time spent running). By this method, rates are calculated over a constant number of reinforcers. However, the time base over which rates are calculated can vary across animals, and this may influence the nature of the overall drug effect obtained across animals. To control for this, overall rates were also calculated based on a fixed time from the beginning of

the session (i.e., 30 min). That is, for those reinforcers that were completed within the first 30 min of the session, the total number of lever presses made while completing those reinforcers was divided by the time during which the schedule requirement was in effect. For rats that did not make their first response of the session until more than 30 min had elapsed, the rate was calculated as the single response that produced the first reinforcer divided by the latency to make that response.

A one-way repeated measures analysis of variance (ANOVA) was used to assess the effects of cocaine dose on operant responding. Comparisons between different dose levels were made using post hoc Dunnett *t* tests. The significance level for all tests was .05, as a two-tailed probability.

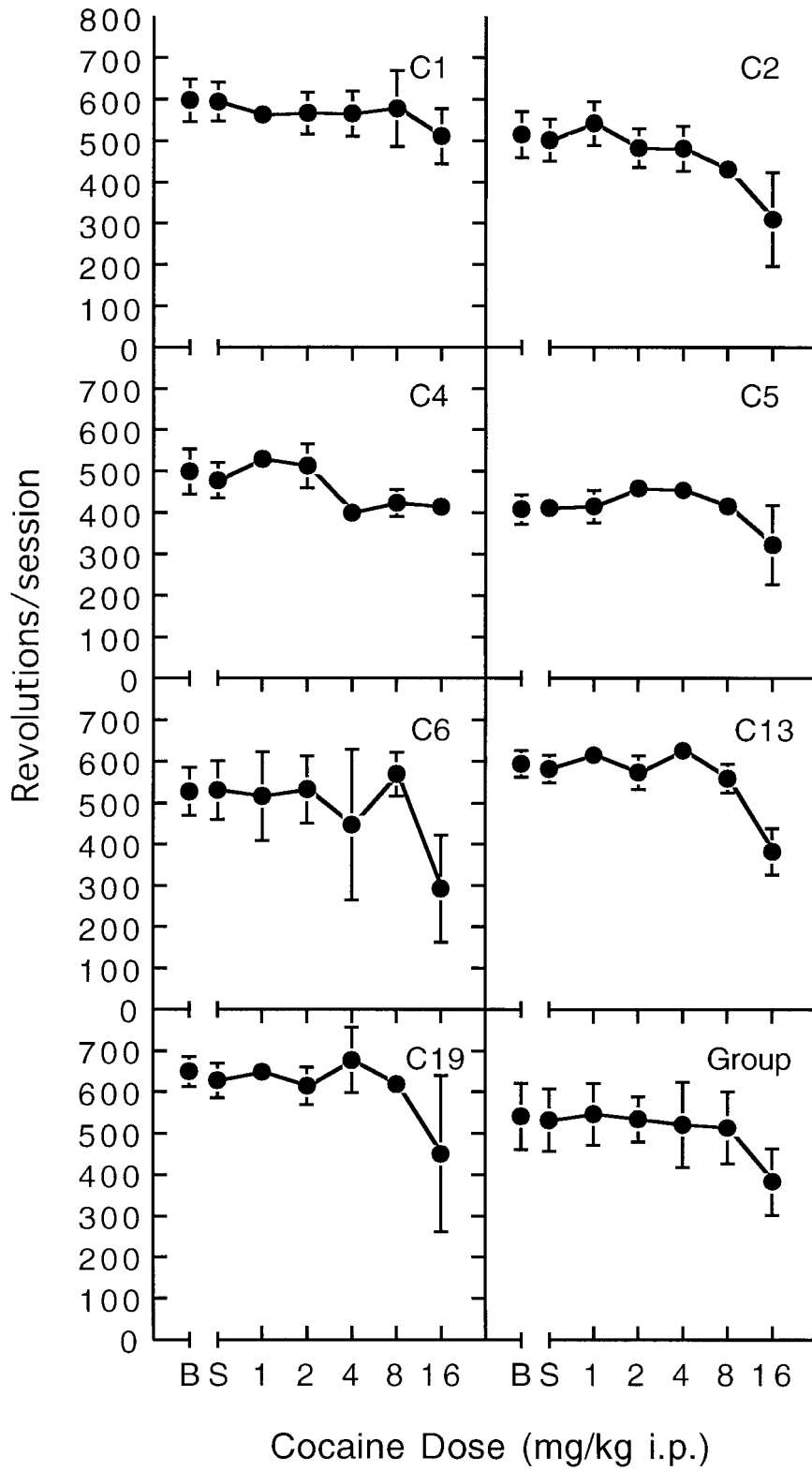
Finally, to determine if drug effects were rate dependent, the logs of drug rates during each 5-s segment were regressed on the logs of the control rates (i.e., saline). The slope of this regression was used to determine the extent to which the drug effects were consistent with the rate-dependency hypothesis. As responding within the fixed interval becomes more uniform over the duration of the interval due to an increase in low rates at the beginning of the interval and a decrease in higher rates the end of the interval, the slope of the regression line should approach zero.

RESULTS

Figure 1 shows baseline response-rate functions within the fixed interval for each animal and the group data averaged over the last five sessions prior to commencement of drug testing. The graphs show an increase in the likelihood of responding as the interval elapsed, but neither the rate of increase nor the highest rates achieved approximate those typical of food reinforcement. Response rates in the periods closest to reinforcement varied from 5.8 to 18.6 responses per minute. These relatively low response rates reflect a greater

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Fig. 3. Mean effect of cocaine dose on overall lever-pressing rates (presses per minute) on an FI 60-s schedule. Filled circles represent overall lever-pressing rates calculated based on the total session (i.e., the total time during which the schedule was in effect over all 20 reinforcers). Open circles represent overall response rates calculated for all reinforcers completed within the first 30 min of the session. Bars indicate ± 1 SD. Other details are as in Figure 2.



preponderance of PRPs longer than the schedule value. The mean percentage of total session reinforcers that were obtained with a single lever press following a variable period of time greater than 60 s across baseline sessions ranged from 9% to 66%, with a mean of 38.3%. Medians for the distributions of PRP values over the five predrug baseline sessions across animals varied from 31.3 to 68.1 s, with an average of 52.2 s.

Figure 2 shows the effect of cocaine on session duration. On average, session duration increased with dose, $F(5, 30) = 6.64, p < .01$; however, relative to saline only the 16 mg/kg dose significantly increased session duration, $td(30) = 4.66, p < .01$. Inspection of Figure 2 reveals that Rats C1 and C4 showed substantial increases in session duration at that dose. For these rats, the increases were largely a function of extended latencies to press the lever at the beginning of the session or long PRPs associated with the first few intervals of the session. For Rat C6, the increase at the 4 mg/kg dose was a function of a marked increase in total PRP duration associated with the third (4,027 s), but not the first (1,286 s) or second (1,310 s), administration of this dose. A marked decline in wheel revolutions also occurred for the third administration. The source of change in this animal's behavior is unknown.

Figure 3 shows the effects of cocaine dose on overall response rates. For rates calculated for the first 30 min of the session, mean overall lever-pressing rates for the 0, 1, 2, 4, 8, and 16 mg/kg doses were 3.7, 3.3, 4.1, 2.8, 2.6, and 2.5 presses per minute, respectively. No effect of dose, $F(5, 30) = 1.56, p > .10$, occurred for overall rates calculated in this way. For rates calculated on total session responding, mean overall rates for the equivalent doses were 3.9, 3.3, 3.7, 3.1, 2.2, and 1.8 presses per minute, respectively. For rates calculated in this way, there was a significant effect of dose, $F(5, 30) = 3.74, p < .05$. Dunnett *t*-test comparisons showed that relative to saline, the 8 and 16 mg/kg doses significantly decreased lever-pressing rates, $td(30) = 2.73, p < .05, td(30) = 3.42, p < .05$. Inspection of

Figure 3 shows considerable agreement between rates calculated by both methods for most doses. Notable exceptions are the higher overall rates based on the first 30 min for Rat C13 at the 8 and 16 mg/kg doses and Rats C5 and C19 at the 16 mg/kg dose. Also of note is that Rats C5, C6, and C19 all showed overall response rates for the first 30 min at the 16 mg/kg dose that were higher than the comparable values after saline injections.

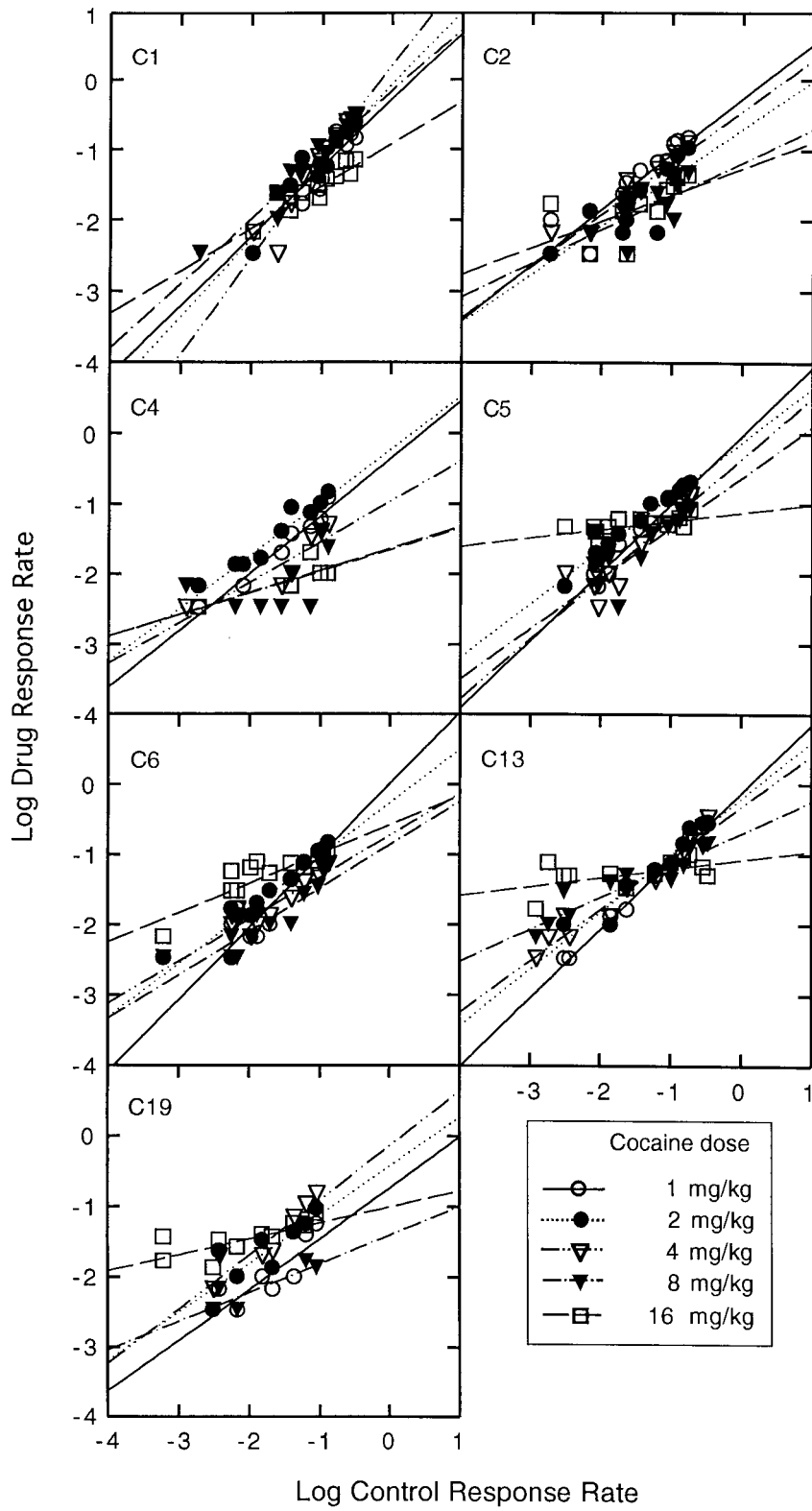
Cocaine also significantly affected running, $F(5, 30) = 13.89, p < .01$. Figure 4 shows, however, that total revolutions per session changed very little across doses between 1 and 8 mg/kg. The 16 mg/kg dose did decrease running relative to saline levels in all animals, $td(30) = 6.45, p < .01$.

Figure 5 depicts the regression of the logarithms of drug response rates on the logarithms of control rates from successive 5-s segments for each dose for each animal. Slopes from the regression analyses are presented in Table 2. In general, slopes declined as dose increased; however, a decline in slope, in and of itself, is not sufficient to conclude that there were rate-dependent effects. Specifically, the decline in slope must be due to an increase in responding early in the interval and a decline in responding later in the interval. A decline in slope can also occur due to suppression of responding that decreases responding throughout the interval. A statistical analysis of slope values will not differentiate between these two sources of change in slope values.

Inspection of Figure 5 suggests that at the 16 mg/kg dose, changes in the regression slopes for Rats C5, C6, C13, and C19 were consistent with rate-dependent effects. For these animals, the decline in slope was a function of an increase in response rates during the initial segments of the interval and a decline in later segments. That is, in Figure 5, data points for this dose in the left half of the graphs for these rats are elevated relative to the data points for other doses. The elevation of these data points reflects the increase in response rates early in the interval. Rat C2

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Fig. 4. Mean effect of cocaine dose on total session wheel revolutions for each rat and the group. Bars indicate ± 1 SD.



also showed some evidence of an increase in response rates earlier in the interval, although to a lesser degree than the aforementioned rats. Rat C1 showed the least effect of cocaine on response rates across the entire dose series, and the decline in the slope at the 16 mg/kg dose was largely due to suppression of responding. That is, response rates at this dose generally decreased across the entire range of control values. This reflects a decrease in responding throughout the interval, but particularly in the later segments. Similarly, the decline in slope evident at the 8 and 16 mg/kg doses for Rat C4 was due to a suppression of responding.

Figure 6 shows mean PRPs across reinforcers for saline and the 16 mg/kg dose of cocaine. Inspection of this figure suggests two different patterns. Rats that showed evidence of rate-dependent effects of cocaine (i.e., Rats C5, C6, C13, and C19) had PRPs shorter than values after saline for reinforcers early in the session. Shorter PRPs would be consistent with the assertion that responding increased earlier in the interval. Interestingly, shorter PRPs early in the session gave way to PRPs equivalent to and then longer than those in the saline condition for reinforcers later in a session. The point at which this change occurred differed across animals. For Rat C13, only the initial latency to lever press and PRPs for the next five reinforcers were shorter than those for saline. For Rat C5, PRPs for the 2nd through the 12th reinforcers were shorter than those for the saline condition.

The second pattern consisted of latencies and PRPs longer than those in the saline condition. Rats C1 and C4 had long latencies to lever press for the first reinforcer compared to the saline condition. In contrast, Rat C2 did not show a long initial latency to lever press at the beginning of a session, but showed PRPs longer than the saline condition for most of the first 10 reinforcers. PRPs longer than the schedule value (i.e., greater than 60 s) lead reinforcers to be acquired with a single lever press, and the responses producing these reinforcers would not have contributed to the cumulative response func-

Table 2

Slopes from the regression of log drug rates on log control rates from successive 5-s segments of the 60-s fixed interval as a function of dose for each rat (see Figure 5).

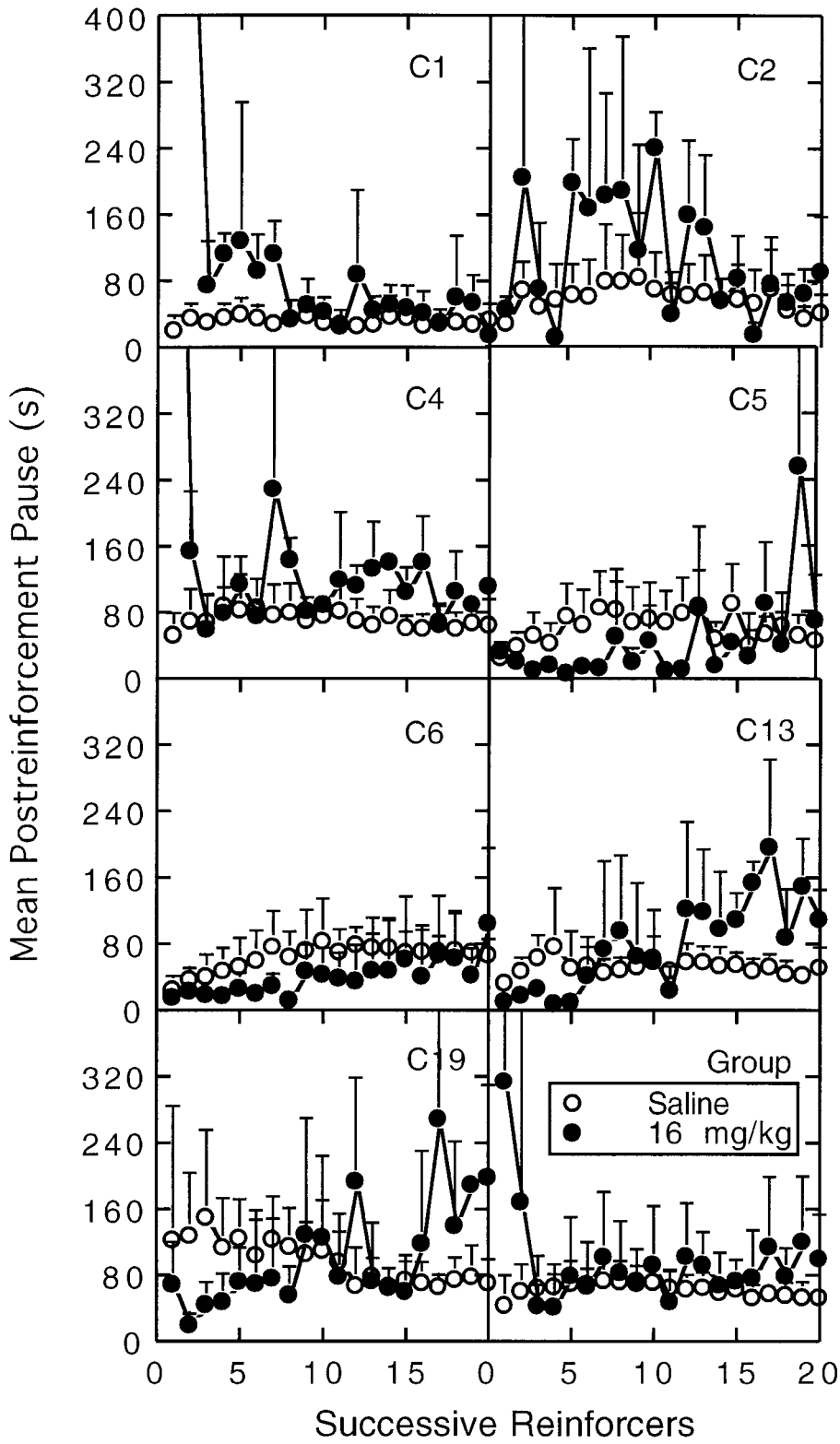
Rat	Cocaine (mg/kg)				
	1	2	4	8	16
C1	0.97	1.10	1.37	0.91	0.60
C2	0.79	0.68	0.73	0.47	0.37
C4	0.82	0.75	0.58	0.31	0.31
C5	0.97	0.77	0.85	0.72	0.12
C6	1.03	0.76	0.60	0.62	0.42
C13	0.97	0.81	0.73	0.46	0.13
C19	0.72	0.69	0.78	0.41	0.23
<i>M</i>	0.90	0.79	0.80	0.56	0.31

tions. Therefore, a drug effect that increased PRP durations would decrease the number of reinforcers that contributed responding to the cumulative response function and thereby decrease the cumulative response function.

In contrast, a rate-dependent effect that increased responding earlier in the interval across several reinforcers would increase the number of reinforcers that contribute to the cumulative response function. Such a result is shown in Table 3. This table shows the mean number of reinforcers per session (of a total of 20 reinforcers) for which the reinforcer was obtained with a single lever press for the predrug, baseline, saline (0), 1, 2, 4, 8, and 16 mg/kg conditions. Rats C1, C2, and C4, which failed to show effects on response rates consistent with rate dependency, showed an increase in reinforcers obtained with a single lever press in the 16 mg/kg condition relative to the saline condition. Rats C5, C6, and C19, which showed rate-dependent drug effects, showed a reduction in the number of reinforcers obtained with a single lever press in the 16 mg/kg condition. However, Rat C13, which showed changes in local response rates within the fixed interval consistent with rate dependency, showed an increase in reinforcers obtained with a single press in the 16 mg/kg condition.

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Fig. 5. Regression of log drug rates on log control (i.e., saline) rates from successive 5-s segments of the 60-s FI cumulated over the entire session for each dose for each rat. See Table 2 for slopes.



DISCUSSION

This study was an attempt to extend the study of the effects of pharmacological agents, such as cocaine, to operant responding maintained by an unconventional reinforcer: the opportunity to run. The results provide tentative support for the generalization of the rate-dependent effect of psychomotor stimulants. Of the rats tested, a majority showed changes in overall response rates, PRPs, and cumulative response-rate functions at the high dose (16 mg/kg) of cocaine that appear to be consistent with rate-dependent effects. That is, an increase in low response rates early in the interval and a decrease in higher rates later in the interval occurred, as reflected in a reduction in regression slopes toward zero and a decrease in PRPs within the session. Of the rats that did not show an effect, 2 paused for long periods of time at the beginning of the session. The durations of the pauses were almost as long as the 25-min half life for cocaine (Ma, Falk, & Lau, 1999). Casual observation of the rats during these pauses suggested that the animals were engaging in stereotypic behavior.

Although some rats showed changes consistent with rate dependency, the fact that this effect occurred predominantly at the highest dose suggests that a conclusion that rate-dependent effect of cocaine occurs for operant lever pressing maintained by wheel running should be regarded as tentative. This is because the baseline performance on the FI schedule differed markedly from that typically observed for more conventional reinforcers such as food or water (Lowe & Harzem, 1977; Lowe, Harzem, & Spencer, 1979). With conventional reinforcers, responding within each interval increases as the interval elapses and, cumulatively over all the intervals within a session, this produces the scalloped pattern of responding typical of FI schedules. With wheel-running reinforcement, the cumulative pattern suggestive of scalloping occurs; how-

ever, the frequency of intervals with no responding due to long PRPs is much higher than with conventional reinforcers. This appears to be a critical difference between FI performances maintained by wheel running and these more conventional reinforcers.

Consistent with this, overall response rates were lower than those typically obtained under an equivalent FI schedule with other reinforcers. Overall response rates averaged between three and four lever presses per minute. This raises the possibility that control rates of responding were less susceptible to enhancement by cocaine (Dews & Wenger, 1977). Verhave (1958, as reported in Dews & Wenger, 1977) found that operant level lever-pressing rates of approximately one press per hour were not increased by methamphetamine. In the present study, lever-pressing rates may have fallen within a range below which cocaine would show rate-enhancing effects.

Further experimentation is required to understand the differences in operant responding maintained by wheel running and by more conventional reinforcers. Understanding these differences may be important for interpreting the effects of cocaine on operant responding in the context of a reinforcer that generates long PRPs. For example, if the longer PRP is due to momentary fatigue after wheel running, then the effects of cocaine on fatigue may be important for understanding its effects on responding maintained by wheel-running reinforcement. Previous research with dextroamphetamine shows that low doses increase the endurance of rats to run on treadmills (Gerald, 1978). However, a similar study using cocaine suggested that intraperitoneal injections of 12.5 and 20 mg/kg doses reduced running endurance on treadmills due to rapid muscle glycogen depletion and early fatigue (Bracken, Bracken, Winder, & Conlee, 1989). To the extent that this result can be generalized to the current

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Fig. 6. Effect of the 16 mg/kg dose of cocaine on mean PRP per reinforcer across successive reinforcers within a session for each rat and the group. Bars indicate 1 *SD*. Open circles represent the mean PRPs per reinforcer in the saline condition. Filled circles represent the mean PRPs across administrations of the 16 mg/kg dose. Not depicted are the PRPs for the first two reinforcers for Rat C1 and the first reinforcer for Rat C4. Mean latencies to lever press from the beginning of the session for Rats C1 and C4 were 955 s (*SD* = 1,536.3) and 1,066 s (*SD* = 889.8), respectively. The mean PRP for the second reinforcer for Rat C1 was 737.6 s (*SD* = 1,042.6).

Table 3

Mean number of reinforcers out of 20 total session reinforcers in which the reinforcer was obtained with a single lever press for predrug, baseline (B), saline (0), and 1, 2, 4, 8, and 16 mg/kg cocaine sessions.

Rat	Predrug	B	Cocaine (mg/kg)					
			0	1	2	4	8	16
C1	1.8	1.6	1.3	3.0	1.7	1.3	0.7	7.7
C2	7.8	8.6	7.1	8.0	9.3	8.7	14.7	12.0
C4	13.2	10.8	11.4	13.0	11.3	16.3	15.0	17.3
C5	7.2	8.3	7.6	8.3	5.7	8.3	10.0	3.7
C6	8.2	8.7	9.4	6.3	9.0	11.7	13.3	4.7
C13	5.2	6.2	4.6	6.0	3.7	4.3	12.7	9.7
C19	10.2	14.3	14.2	15.0	16.3	13.3	18.0	10.7

findings, it suggests that high doses of cocaine do not delay or diminish fatigue, but rather hasten it. With respect to fatigue as the basis of the long PRPs, however, Belke (2000) recently showed that correlations between revolutions run and the duration of the immediately following PRP for rats responding on FI schedules for the opportunity to run were modest and accounted for less than 10% of the variance in PRP duration. Thus, fatigue appears to contribute to pause duration, but not as much as might be expected.

Cocaine also had little effect on running, as measured by total session revolutions, except for suppression at the highest dose. This result is inconsistent with Tainter's (1943) finding that cocaine at doses of 7.5, 15, and 30 mg/kg increased running in female rats over a 7-hr period. The lack of an increase in running in the present study may be a function of the manner in which the opportunity to run was arranged. Rather than continuous access over an extended period, the present study constrained running to brief periods. One consequence of this constraint is that animals run at higher rates per unit time of opportunity to run than they do under continuous-access conditions. As a result of these higher rates of running, it may be less likely that psychomotor stimulants increase running under these constrained conditions. Consistent with this interpretation, Belke and Neubauer (1997) did not observe increases in contingent running in a similar paradigm at doses of amphetamine that had been reported to increase running under continuous-access conditions (Glavin, Pare, Vincent, & Tsuda, 1981; Jakubczak & Gomer, 1973;

Tainter, 1943). As was the case for operant responding, however, the lack of an effect on running at the session level may obscure effects that may be occurring either within the session across reinforcers or, perhaps, even within the reinforcement duration itself. Future research should investigate these possibilities.

The results of the present study suggest that the study of pharmacological effects of drugs on operant behavior can be extended to responding maintained by the opportunity to run. In this study, some, but not all, rats showed changes in operant responding on FI schedules of wheel-running reinforcement under the influence of cocaine that suggest a rate-dependent drug effect. Further experimentation is needed to clarify this effect, particularly in light of differences in operant responding that occur when the opportunity to run for a brief period of time serves as the reinforcing consequence rather than the opportunity to consume a small amount of food.

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