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Effects of Cocaine in Pigeons Responding Under a Progressive-Ratio Schedule of Food Delivery

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JONES C. A., M. LESAGE, S. SUNDBY AND A. POLING. *Effects of cocaine in pigeons responding under a progressive-ratio schedule of food delivery.* PHARMACOL BIOCHEM BEHAV **50**(4) 527-531, 1995.—Although the progressive-ratio schedule has been used frequently to quantify the reinforcing effectiveness of self-administered drugs, it has seldom been used to examine the effects of drugs on food-maintained behavior and has never been used to evaluate the effects of cocaine on such behavior. In the present study, the effects of acute administrations of cocaine were evaluated in pigeons responding under a progressive-ratio 5 schedule of food delivery that continued for 1 h or until responding ceased for 5 consecutive min, whichever occurred first. The largest ratio completed each session (breaking point) was the primary dependent variable. In general, acute administrations of cocaine at 0.56 to 3.2 mg/kg increased breaking points, whereas doses above 5.6 mg/kg decreased breaking points. Although cocaine reduces food intake and subjective hunger for food, the present data indicate that the drug reduces the reinforcing effectiveness of food only at high doses.

Cocaine Progressive-ratio schedule Schedule-controlled behavior Pigeons

COCAINE reduces subjective desire for food in humans, and actual food intake in humans and nonhumans alike (1,3, 4,11,17,27). Given these effects, one might surmise that the drug would reduce food-maintained responding, regardless of the schedule under which behavior is maintained. But that is not the case. As with other drugs, the effects of cocaine on schedule-controlled responding are complex and are influenced by many variables, including dose, schedule type, rate of responding in the absence of drug, and the consequences of behavior (14,16). In general, cocaine appears to produce rate-dependent effects, increasing low-rate operants (e.g., those maintained under long fixed-interval schedules) at doses that decrease high-rate operants (e.g., those maintained under short fixed-ratio schedules) (10,12,14,25,26). These effects cannot be explained in terms of a motivational analysis alone.

To date, there are no published reports of the effects of cocaine on food-maintained responding under progressive-ratio (PR) schedules, which are often used to examine the relative reinforcing effectiveness of drugs and other stimuli [e.g., (2,5,6-8,10,18-20)]. The PR schedule increases the ratio requirement by a specified number of responses after each reinforcer until the subject fails to respond for a specified period, usually 5 to 15 min [e.g., (7,22,23)]. The subject's failure to respond ends the session and establishes the final completed ratio, called the breaking point, which is used as a measure of the efficacy of the reinforcer, or response strength (6). Thus, the primary index of the animal's behavior under the PR is not exclusively dependent on the response rate (10). This may be a useful feature in studying drugs that directly affect response rate, regardless of their possible motivational actions.

Researchers have used the PR schedule to study the relative reinforcing strength of a wide variety of drugs within the self-administration paradigm [e.g., (2,5,10,18-20)]. But the schedule has seldom been used to examine drug effects on food-maintained behavior. A noteworthy exception is a series of studies by Schulze and colleagues (21-24), who employed a complex multiple schedule to examine drug (THC, diazepam,

[1] The reported data were collected as part of a M. A. thesis submitted by C. A. Jones to Western Michigan University. Ms. Jones is currently at Oral Roberts University.

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d-amphetamine, and morphine) effects in rhesus monkeys. The same procedures were used in all of the studies. The PR schedule began with a value of either one or two lever presses, depending on the individual subject. After each food delivery, the response requirement was increased by the initial PR value. That is, if the initial requirement for food delivery was two lever presses, successive requirements were four lever presses, six lever presses, eight lever presses, and so on. The PR component was arranged within a multiple schedule that also involved 10-min components in which temporal response differentiation, delayed matching-to-sample, incremental repeated acquisition, and conditioned position responding were assessed. Although those procedures yielded a wide range of behavioral data in a brief (i.e., 50-min) session, it is questionable whether 10 min provides an adequate assessment of PR responding.

The purpose of the present study was to examine the effects of acute administrations of cocaine in pigeons responding under a PR 5 schedule of food delivery that continued for 1 h or until responding ceased for 5 consecutive min, whichever occurred first. Despite the fact that the PR schedule may be well suited for quantifying motivational effects of cocaine, and such effects have been suggested outside the behavioral pharmacology literature, there are no published reports of the effects of cocaine under PR schedules.

METHOD

Subjects

Six White Carneau pigeons, maintained at 80% of their free-feeding weights, served as subjects. Three birds were experimentally naive; three had histories of acute exposure to hallucinogenic drugs under repeated acquisition procedures. The nonnaive pigeons were drug free for at least 6 months prior to the start of the present study. Each bird was individually housed with unlimited access to grit and to water in a colony area with controlled lighting (16 h light, 8 h dark each day), temperature (22–24°C), and humidity (60–70%). The research project was approved by the Institutional Animal Care and Use Committee of Western Michigan University before implementation.

Apparatus

Subjects were tested in four operant conditioning chambers (Lehigh Valley Electronics, BRS/LVE, Lehigh Valley, PA), measuring 32 cm long, 36 cm high, and 35 cm wide. In each chamber, three response keys 2.5 cm in diameter were located 23 cm from the bottom of the front wall, approximately 5.5 cm apart. Only the center key, illuminated in white, was operative in the present study. The key was operated by a minimum of 0.2 N of pressure. An aperture horizontally centered

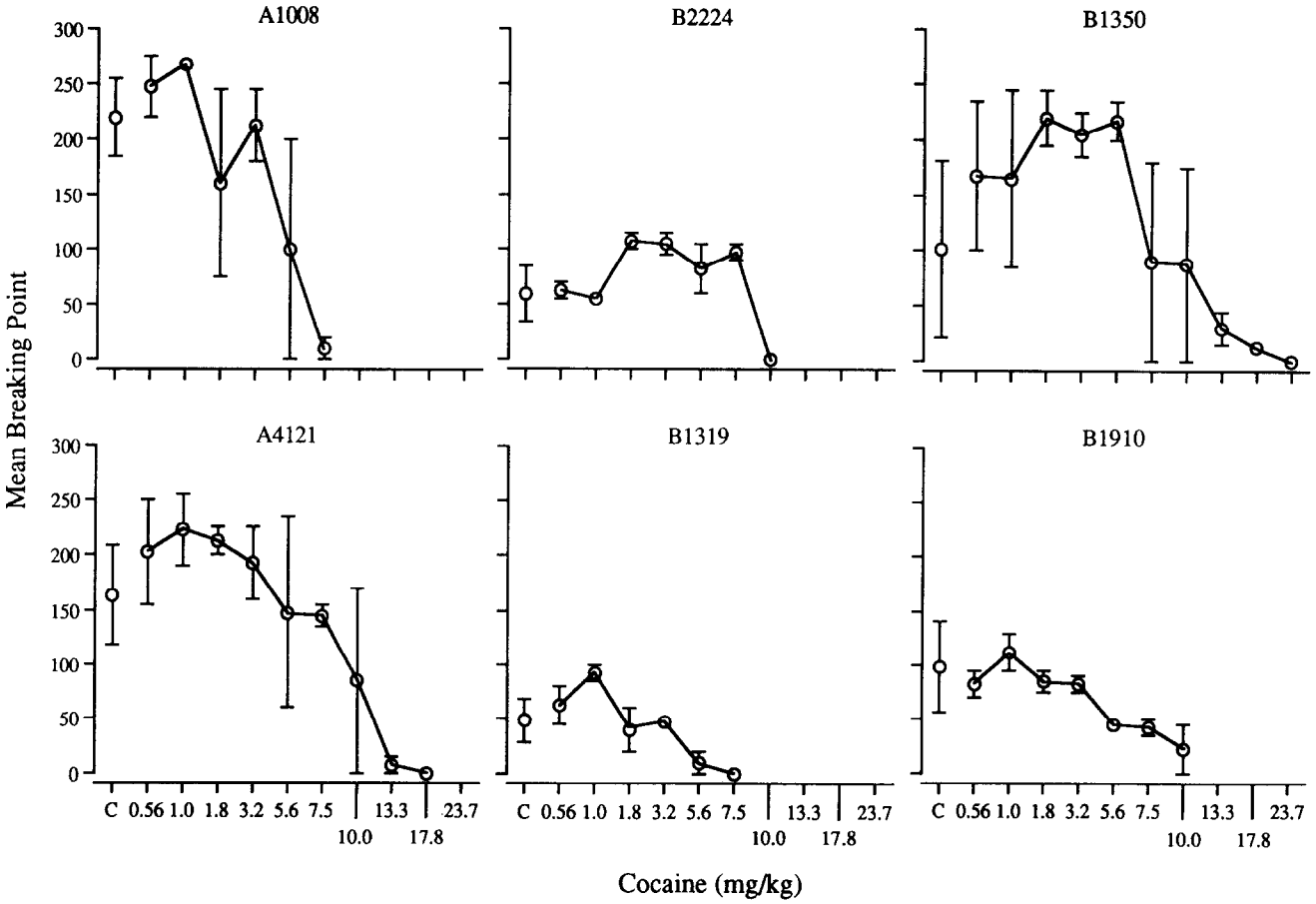

FIG. 1. Mean breaking points (with ranges) for individual pigeons exposed to a PR 5 schedule under all experimental conditions. Control (C) data represent performance in all sessions immediately prior to drug injections. Drug data for each dose represent two administrations.

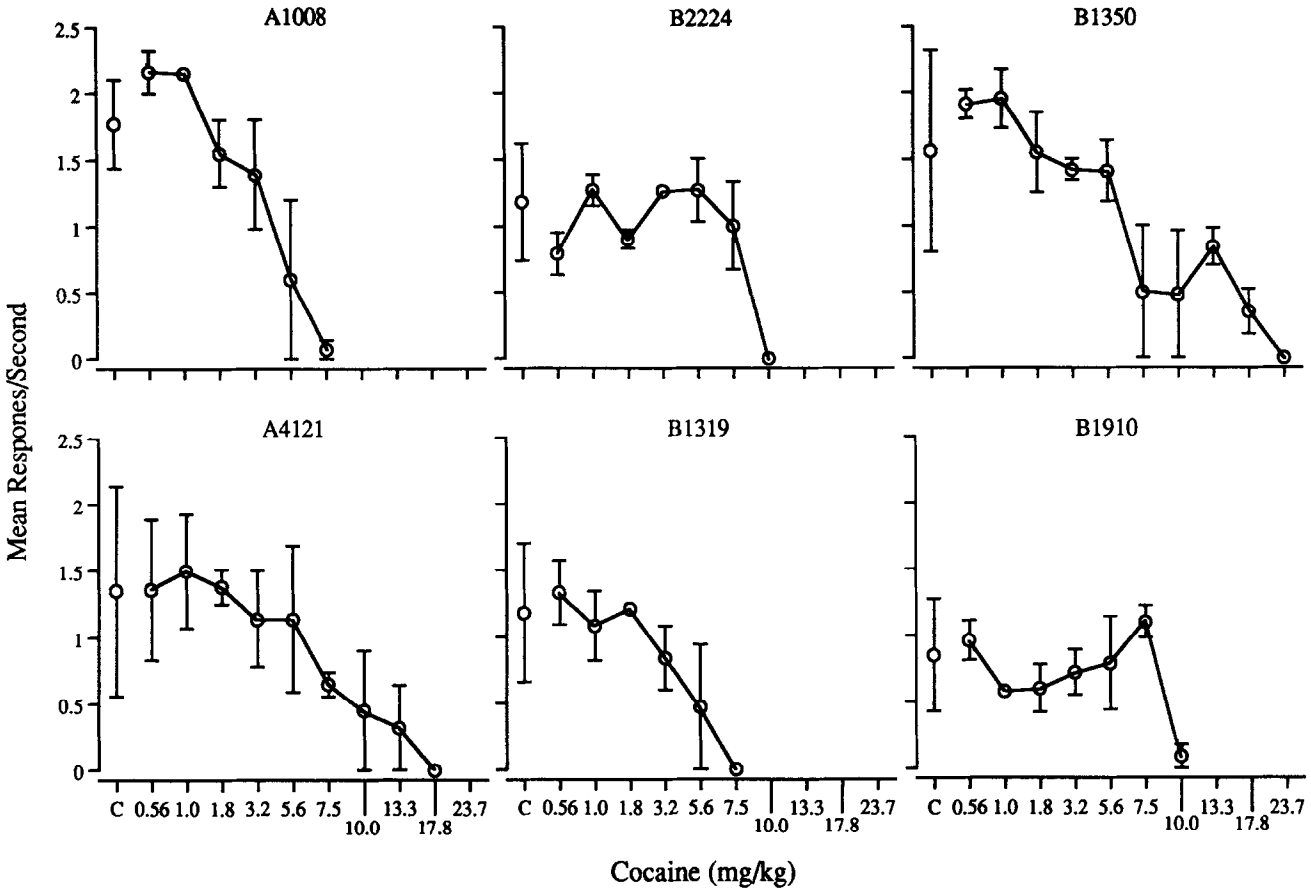

FIG. 2. Mean response rates (with ranges) for individual pigeons exposed to a PR 5 schedule under all experimental conditions. Control (C) data represent performance in all sessions immediately prior to drug injections. Drug data for each dose represent two administrations.

in the front wall 7.5 cm above the floor allowed access to a grain feeder. When raised, the feeder was illuminated by a 7 W bulb and was filled with Purina Pigeon Grain (Ralston-Purina, St. Louis, MO). A 7 W white bulb (houselight) centrally located 30 cm above the chamber floor on the front wall provided ambient illumination. An exhaust fan mounted on the back wall of the chamber supplied continuous masking noise and ventilation. Additional masking noise was provided by a white noise generator through a speaker mounted on the lower right corner of the intelligence panel. An ALR Flyer 32DT microcomputer with MED-PC software (Med Associates, East Fairfield, VT) was used for controlling experimental events and recording data.

Procedure

After preliminary keypeck training, each bird was exposed to fixed-ratio (FR) schedules that were gradually increased to FR 50. Once keypecking was reliable under the FR 50 schedule, a PR 5 schedule of food delivery was implemented for each pigeon. The PR schedule began with a ratio value of 5 at the beginning of each session and was increased by an additional value of 5 each time the subject earned a reinforcer. Thus, the requirement for food delivery across the course of each session was 5, 10, 15, 20, 25. . . . Completion of each ratio requirement was followed by 3-s access to grain. The white center key and the chamber light remained on throughout the session. The session continued for 1 h or until the bird ceased to respond for 5 consecutive min, whichever occurred first, at which time the session ended and key light and chamber light were turned off. The breaking point was defined as the value of the final ratio completed during each session and was recorded. Sessions were conducted 7 days per week, at about the same time each day.

After data for breaking points were stable (i.e., showed no visible trend across 10 consecutive sessions), drug evaluation began. On average, responding stabilized after 70 sessions of exposure to the PR 5; the range across subjects was 61 to 86 sessions. Prior to drug injections, each pigeon was injected intramuscularly with a vehicle of isotonic saline for 2 days consecutively to desensitize the subject to injection. Each subject was then returned to baseline for 4 days, after which the dose–response determination began. During this determination, each bird was exposed to two ascending series of acute cocaine administrations. Cocaine hydrochloride (Sigma Chemical Co., St. Louis, MO) was dissolved in isotonic saline solution prepared at an injection volume of 1 ml/kg. Injections were made into the pectoral muscle 5 min prior to selected sessions. To minimize bruising, the injections were alternated between left and right pectoral muscles.

The drug regimen began with 0.56 mg/kg of cocaine, and doses were increased progressively for each bird until the rate of responding was suppressed to below 10% of the control (no drug) level. Dosage increases were in quarter-log units to 5.6

mg/kg (i.e., 0.56, 1, 1.8, 3.2, and 5.6 mg/kg, expressed as the salt), and in eighth-log units above 5.6 mg/kg (i.e., 7.5, 10, 13.3, 17.8, and 23.7 mg/kg). For each pigeon, doses were given according to a BBBBCD design, where B represents baseline sessions (no injection), C vehicle control sessions (saline injections), and D drug sessions (cocaine injection).

RESULTS

For four birds, sessions almost always ended because responding ceased for 5 consecutive min, not because the 1 h session limit expired. The other birds (A1008, A4121) characteristically responded for the maximum time during control sessions and in sessions in which cocaine doses below 5.6 were administered. When a bird responded throughout a 1-h session, the largest completed ratio in that session was considered as the breaking point. Figure 1 shows the average breaking points and ranges for individual subjects during drug and vehicle control conditions. Relative to vehicle control levels, four of the six subjects had increased breaking points (no overlap in ranges compared to conrol levels) at one or more low doses of cocaine (0.56 to 3.2 mg/kg) and decreased breaking points at high doses. The other two birds (A4121, B1910) exhibited increased average breaking points relative to control values at certain doses; however, the ranges of control and drug data overlapped.

The average overall rate of responding (total responses/total session time) for individual pigeons under all experimental conditions are presented in Fig. 2. In four of six subjects, response rates decreased in generally dose-dependent fashion. In the other two birds (B2224 and B1910), relatively high doses decreased responding substantially but, at lower doses, responding did not decline as an orderly function of increased dosage.

DISCUSSION

In all birds, certain doses below 5.6 mg/kg increased average breaking points relative to control values, whereas higher doses decreased them. If breaking points under the PR schedule are assumed to provide an index of the reinforcing effectiveness of the scheduled event (i.e., food delivery), as many authors claim them to be (6–8), the present data suggest that cocaine generally increased the reinforcing effectiveness of food at low doses, and decreased it a higher doses. Moreover, previous PR data suggest that *d*-amphetamine at doses from 0.3 and 1.0 mg/kg also increased the reinforcing effectiveness of food (22). Such conclusions are inconsistent with the general perception that stimulants decrease, not increase, the reinforcing effectiveness of food (1,3,4,11,17,27). Drugs may influence schedule-controlled responding through many behavioral mechanisms (14,16), and it should not be automatically assumed that drug-induced changes in PR breaking points provide an uncontaminated index of the relative effectiveness of the scheduled reinforcer. This caution may be important in studies designed to evaluate how one drug influences the reinforcing effectiveness of a second compound.

Although the PR schedule has not been used to examine the effects of cocaine on food-maintained behaviors, the FR schedule has been employed for this purpose. For example, Hoffman, Branch, and Sizemore (9) investigated the acute effects of cocaine in pigeons responding under FR schedules of food delivery. They used a three-component multiple schedule comprising an FR 5, FR 25, and FR 125. Acute administrations of cocaine (1 to 10 mg/kg) produced dose-dependent rate reductions under each of the FR components. Similar results have been reported in other studies that employed FR schedules (12,14,25).

It is not clear why cocaine at low doses decreased response rates under FR schedules in prior investigations, but increased breaking points under the PR schedule in the present study. Like other stimulants, cocaine has rate-dependent effects. Low doses generally decrease high-rate operants and increase low-rate operants, whereas high doses reduce all operant behavior (13,15,26). Although overall rates under the PR schedule were relatively high, and were not increased by cocaine administration, it is possible that rates toward the end of the session (when ratios were high) were relatively low; hence, increased by the drug. Data relevant to this possibility were not collected in the present study, but merit attention in future investigations.

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