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FIXED-INTERVAL RESPONDING UNDER SECOND-ORDER SCHEDULES OF FOOD PRESENTATION OR COCAINE INJECTION[1]

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Squirrel monkeys operated a key under second-order schedules in which every tenth completion of a 5-minute fixed interval resulted in either presentation of food or intravenous injection of cocaine. When a 2-second light was presented at the completion of the component fixed-interval schedules, positively accelerated responding developed and was maintained in each component. Over a tenfold range of doses of cocaine (30 to 300 μg/kg/injection) and amounts of food (0.75 to 7.5 g/presentation), the second-order schedule of cocaine injection maintained higher average rates of responding than the second-order schedule of food presentation. Substituting saline for cocaine or eliminating food presentations decreased average rates of responding. When no stimulus change occurred at the completion of the first nine component fixed-interval schedules, but the 2-second light and food presentation or cocaine injection still occurred after the tenth component, only low and relatively constant rates of responding were maintained in each component. Patterns of responding characteristic of 5-minute fixed-interval schedules were maintained by the 2-second light paired with either cocaine injection or food presentation, though the maximum frequency of cocaine injection or food presentation was less than once per 50 minutes.

Key words: cocaine, self-administration, second-order schedules, fixed interval schedules, key pressing, squirrel monkey

The control of behavior by environmental stimuli that are intermittently associated with drug injections can be studied systematically with second-order schedules of drug injections. This type of higher-order schedule treats a pattern of behavior controlled by a schedule (the first-order or component schedule) as a response that can itself be controlled by a schedule (the second-order schedule). When a brief visual stimulus is presented at the completion of each component schedule, second-order schedules of drug injection can maintain orderly sequences of responding even when injections occur infrequently.

Fixed-interval schedules of fixed-ratio components have been frequently used as second-order schedules of drug injection (Goldberg, 1975; Kelleher, 1975). In one series of experiments with squirrel monkeys, for example, a brief visual stimulus was presented whenever the monkey completed a 30-response fixed-ratio schedule; the first fixed-ratio component completed after a 5-min fixed-interval elapsed produced both the brief visual stimulus and an intravenous injection of 100 μg/kg of cocaine (Goldberg, 1973*b*). The monkeys characteristically paused briefly at the beginning of each fixed-ratio component and then responded rapidly until the brief stimulus was presented, and average rates of responding exceeded one per second.

In squirrel monkeys and rhesus monkeys, similar performances have been maintained under 10- or 30-response fixed-ratio components of a 60-min fixed-interval schedule of injection of cocaine or morphine (Goldberg, 1975, 1976; Goldberg, Morse, and Goldberg, 1976; Goldberg and Tang, 1976; Kelleher, 1975). When the brief stimuli were not presented, fixed-ratio patterns of responding were disrupted and rates of responding decreased.

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Because the brief stimuli controlled rates and patterns of responding characteristic of fixed-ratio schedules, high average rates of responding were maintained under the second-order schedule.

Fixed-ratio schedules of fixed-interval components have been frequently used in studies of second-order schedules of food presentation (Byrd and Marr, 1969; de Lorge, 1964, 1967; Kelleher, 1966*a, b;* Marr, 1969, 1970; Stubbs, 1971) but not in systematic studies of second-order schedules of drug injection. Fixed-interval performance is generally characterized by an initial period of no responding followed by acceleration of responding to a rate that is sustained until the end of the interval. Performances under fixed-interval schedules are of interest because patterns of responding characteristic of such schedules have been maintained under various conditions by diverse events, including presentations of brief stimuli associated with occasional presentation of food or electric shock (Byrd, 1972; Byrd and Marr, 1969; Kelleher, 1966*a, b;* Kelleher and Morse, 1968). Preliminary results indicate that patterns of responding characteristic of fixed-interval schedules can be maintained in the squirrel monkey by the presentation of a brief visual stimulus under a second-order schedule of cocaine injection (Goldberg, Kelleher, and Morse, 1975).

The present study concerns performances of squirrel monkeys under schedules of brief presentation of a visual stimulus in fixed-interval components of a second-order fixed-ratio schedule of food presentation or cocaine injection. The effects of varying the amount of food and the dose of cocaine and of omitting the brief visual stimuli were studied systematically. Sequences of responding characteristic of fixed-interval schedules were maintained by presentations of the brief visual stimulus which was intermittently paired with either food presentation or cocaine injection though the maximum frequency of food presentation or cocaine injections was less than once per 50 min.

METHOD

Subjects

Five male squirrel monkeys (*Saimiri sciurea*), weighing 600 to 900 g, were handled according to procedures described by Kelleher, Gill, Riddle, and Cook (1963). Two of these monkeys (S-467 and S-474) had been used in previous studies of cocaine self-administration (Goldberg and Kelleher, 1976). In the three monkeys used in the cocaine experiments (S-59, S-467, and S-474), polyvinyl chloride catheters (inside diameter, 0.38 mm; outside diameter, 0.76 mm) had been inserted by way of the left or right external jugular vein into the superior *vena cava* at the level of the right atrium. The distal end of the catheter was passed through the skin in the middle of the monkey's back and was protected by a leather jacket that the monkey wore at all times. Each day, the catheters were flushed with saline (0.9% NaCl) and sealed with stainless-steel obturators. The surgical procedures and catheterization techniques have been described by Herd, Morse, Kelleher, and Jones (1969). The two monkeys (S-538 and S-542) used in the food experiments were maintained at about 80% of their free-feeding body weights. Between experimental sessions, the monkeys lived in individual cages.

Apparatus

During experimental sessions, the monkeys sat in a Lucite restraining chair (Herd *et al.*, 1969) within a sound-attenuating isolation chamber (Model AC-3, Industrial Acoustics Company, Bronx, N.Y.). Continuous white noise in the chamber further masked extraneous sounds. In the first set of experiments with food presentation, a larger isolation chamber (Model AC-2) was used. A response key (Lehigh Valley Electronics rat lever, #1352) was mounted on a transparent Lucite wall in front of the monkey. When the monkey pressed the key with a force of 0.28 N or more, there was an audible relay click and a response was recorded. Pairs of 6-W bulbs mounted at eye level behind the Lucite wall could illuminate the experimental chamber with green or amber light.

For studies of responding maintained by injections of cocaine, the distal end of the implanted catheter was connected by polyethylene tubing to a syringe located outside the chamber. The syringe was driven by a 110-V ac motor that could be energized by automatic programming equipment; a small dc voltage braked the motor between injections. Each injection delivered 0.18 ml in about 200 msec. For studies of responding

maintained by food presentation, a food-pellet dispenser (Model D-1, Ralph Gerbrands Company, Arlington, Mass.) was mounted behind the transparent Lucite wall. When an electrical pulse of about 150 msec energized the dispenser, it delivered a 0.25-g SKF food pellet (Riddle, Rednick, Catania, and Tucker, 1966) to a tray, which the monkey could reach through a rectangular opening in the center of the Lucite wall.

Procedure

Experimental sessions were conducted daily, Monday through Friday. Except as noted, each session ended after the third cocaine injection or food presentation.

The basic second-order schedule was a fixed ratio (FR) of fixed-interval (FI) components (Kelleher, 1966*a*, *b*). During preliminary training, the first response occurring after 5 min in the presence of a green light turned off the green light and simultaneously turned on an amber light; the amber light was presented for 2 sec before, and remained on during food presentation or cocaine injection. Then, all lights were turned off for a timeout period during which responses had no scheduled consequences. Within 20 experimental sessions, the number of these FI components required for cocaine injection or food presentation was increased from one to 10. This schedule is designated FR 10 (FI 5:S).

Two sets of experiments were conducted to determine the effects of: (1) varying the amount of food or dose of cocaine at each presentation and (2) eliminating the brief-stimulus change at the completion of each FI 5-min component except the last one.

(1) The amount of food presented at the completion of each 10-component sequence was varied by delivering different numbers of 0.25-g food pellets in succession (about 150 msec between pellet deliveries). The duration of the timeout period was 100 sec. Responding was maintained initially by 0.75 g per presentation (three pellets) of food. The amount was subsequently varied over a range of zero (no food pellets) to 7.5 g per presentation (30 pellets). The order of conditions was 0.75, 2.5, 0, and 7.5 g per presentation. The performance of each monkey (S-538 and S-542) was studied for six to nine sessions under each condition.

The dose of cocaine injected at the completion of each 10-component sequence was varied by changing the concentration of the cocaine solution delivered in a single injection. Responding was maintained initially by 100 μg/kg/injection of cocaine. All lights were turned off for a 100-sec timeout period after each injection. The dose was subsequently varied over a range of zero (saline solution) to 600 μg/kg/injection. The order of conditions was 100, 30, 10, 0, 300, 100, and 600 μg/kg/injection. The performance of each monkey (S-467 and S-474) was studied for five to 17 sessions under each condition. During the last seven of the 13 sessions with saline, the 2-sec stimulus change was eliminated.

To diminish the possibility of direct effects of cocaine on subsequent responding, two procedural modifications were studied in some experiments: (a) the 100-sec timeout period was extended by 60 min, *i.e.*, each timeout lasted 61 min and 40 sec, and the session ended after the second injection cycle (Monkeys S-59 and S-474); (b) each session ended after the first timeout period (Monkey S-474). In these experiments, each dose of 300 or 600 μg/kg comprised 10 successive injections of 30 or 60 μg/kg each (about 150 msec between injections).

(2) During sessions in which the 2-sec stimulus change was eliminated, the green light remained on continuously until 10 consecutive FI 5-min components had been completed. At the completion of the tenth component, the amber light was presented and remained on during food presentation or cocaine injection. Thus, performances under FR 10 (FI 5) were compared with performances under FR 10 (FI 5:S).

Under the schedule of food presentation, the effects of eliminating the brief stimulus for six (S-538) or seven (S-542) sessions were studied while performance was maintained by 2.5 g per presentation (S-538) or 2.5 and 7.5 g per presentation (S-542). Otherwise, the procedures were as described previously.

Under the schedule of cocaine injection, the effects of eliminating the brief stimulus for seven (S-59) or 16 (S-474) sessions were studied while performance was maintained by doses of 300 μg/kg (S-59) or 600 μg/kg (S-474). In these experiments, each dose comprised 10 successive injections of 30 or 60 μg/kg each, and the timeout period lasted for 61 min and

40 sec. Sessions ended after the second injection cycle. In one experiment, performances under FR 10 (FI 5) and FR 10 (FI 5:S) were compared in Monkey S-59 during 30 sessions in which saline was injected at the end of each sequence.

Analysis of results. Average response rate under the second-order schedule was computed for each session by dividing total responses in the presence of the green light by total time during the green light. Responses in the presence of the amber light were excluded from the computations. The number of responses in each tenth of the fixed-interval components was recorded over the entire session. These data were used to compute quarter-life values. The quarter life, calculated by linear interpolation, is the time taken to complete the first quarter of the responses in the fixed interval. This estimated quarter-life value provides an indication of the temporal patterning of responding, which is relatively independent of rate of responding (Gollub, 1964; Herrnstein and Morse, 1957). Responding in each session was recorded on cumulative-response recorders.

Drugs. Cocaine hydrochloride was dissolved in saline (0.9% NaCl). All doses are expressed as the salt.

RESULTS

Cocaine injections and food presentations maintained qualitatively similar performances at appropriate parameter values (Figures 1 and 2). Responding seldom occurred during 2-sec presentations of the amber light or during 100-sec timeout periods. Within each fixed-interval component, an initial brief period of no responding was followed by increasing responding until a response produced the 2-sec amber light and ended the component. The numbers of responses in consecutive fixed-interval components varied markedly throughout each 10-component sequence under FR 10 (FI 5:S), although responding was usually lowest in the first component. Both the patterns of responding within components and the variations in numbers of responses among components are characteristic of performances under fixed-interval schedules.

As the dose of cocaine per injection was increased under FR 10 (FI 5:S), average rates of responding generally increased up to 100 or 300 μg/kg/injection and then decreased at 600

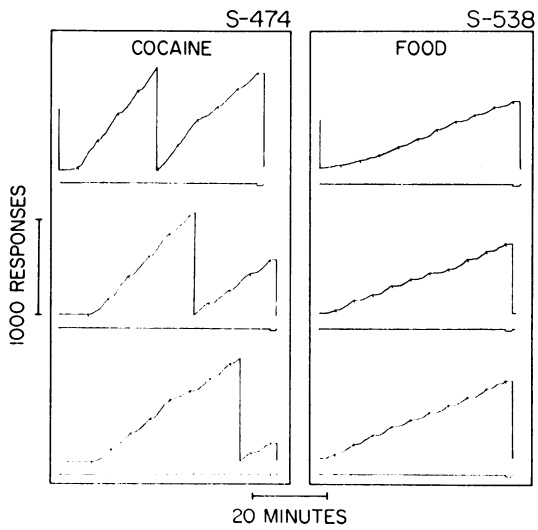

Fig. 1. Positively accelerated responding within 5-min fixed-interval components of the second-order schedule of intravenous cocaine injection (300 μg/kg/injection; left panel) or food presentation (2.5 g/presentation; right panel). Ordinate: cumulative responses; abscissa: time. Each panel shows a complete experimental session composed of three successive completions of the second-order schedules (from top to bottom). The recording pen reset whenever 1100 responses had cumulated and at the end of the time-out period. The motor of the recorder stopped but responses still cumulated during 2-sec presentations of the amber light, indicated by short diagonal strokes on the cumulative record, and during cocaine injections or food presentations, indicated by the downstroke of the event pen. The event pen remained down until the end of the 100-sec timeout period. Records shown are from the sixth session at 2.5 g/presentation of food (S-538) and from the seventh session at 300 μg/kg/injection of cocaine (S-474).

μg/kg/injection (Figures 3 and 4). Rates of responding maintained by 10 μg/kg/injection were similar to those maintained by saline injections. At 600 μg/kg/injection of cocaine, each injection was followed by low rates of responding (Figure 4, S-467) or long periods of pausing (Figure 4, S-474), resulting in relatively low-average rates of responding. Average quarter-life values ranged from 39 to 43% in Monkey S-467 and from 33 to 39% in Monkey S-474 and were not systematically related to dose per injection. Varying the amount of food per presentation under the FR 10 (FI 5:S) schedule had different effects in the two monkeys studied (Figure 5). The highest rates of responding were maintained by 7.5 g per presentation in Monkey S-538 and by 0.75 g per presentation in Monkey S-542. Average quar-

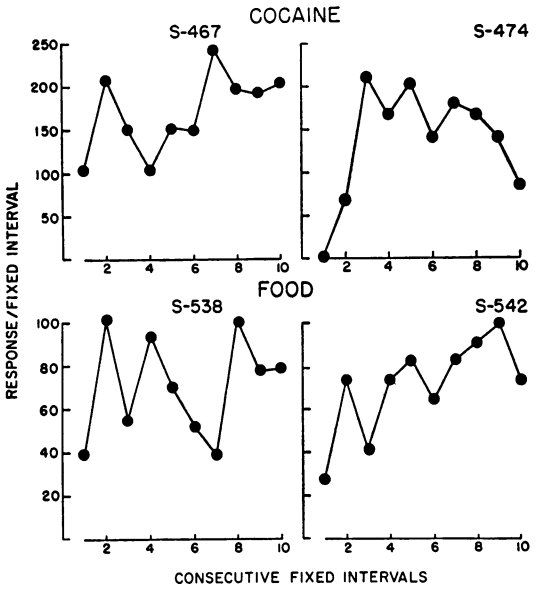

Fig. 2. Variability in the number of responses per fixed-interval component. Each frame presents data from the second sequence of 10 consecutive fixed-interval components from one selected session. Each sequence terminated with the injection of 100 μg/kg of cocaine (upper graphs) or presentation of 2.5 g of food (lower graphs). Note the difference in scales of the ordinates in the upper and lower graphs. The schedule parameter values were the same as in Figure 1.

ter-life values ranged from 33 to 46% in Monkey S-538 and from 32 to 36% in Monkey S-542 and were not systematically related to the amount of food presented. The average rates of responding maintained at 30 to 300 μg/kg/injection of cocaine were higher than those maintained at any amount of food per presentation that was studied.

Table 1

Average rates of responding and average quarter-life values for Monkey S-474 as a function of cocaine dose (μg/kg) under the second-order FR 10 (FI 5:S) schedule of intravenous cocaine injection.[a]

Cocaine Dose	*Response/Sec*[b]	*Quarter Life*[b]
0	0.10 ± 0.02	43.0 ± 0.6
100	0.34 ± 0.05	38.0 ± 0.6
300	0.33 ± 0.03	39.8 ± 0.6
300[c]	0.36 ± 0.03	37.8 ± 0.5
600	0.36 ± 0.01	40.8 ± 2.3

[a]A 61-min and 40-sec timeout period followed the injection of cocaine and the session ended after the second timeout period.

[b]The mean and standard error for the last four sessions at each condition are shown.

[c]The session ended after the first timeout period.

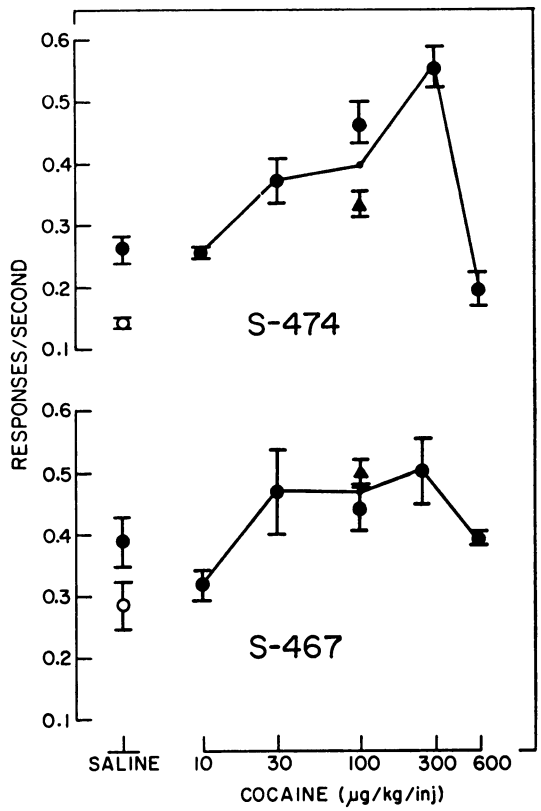

Fig. 3. Effects of dose of cocaine per injection on mean rates of responding under the second-order schedule. Filled points: FR 10 (FI 5:S); unfilled points: FR 10 (FI 5). Each point is the mean of the last four sessions under each condition; bracketed vertical lines indicate ± one standard error of the mean. At 100 μg/kg, the lines were drawn through the means of the first (triangles) and second (circles) determinations.

When the timeout period was lengthened or sessions ended after one injection cycle, responding was well maintained in Monkey S-474 at doses of cocaine ranging from 100 to 600 μg/kg (Table 1). At 300 μg/kg of cocaine, performances with the longer timeout period (61 min and 40 sec) were similar to those obtained with one injection cycle per session. Again, quarter-life values were not systematically related to dose of cocaine.

Eliminating the 2-sec presentations of the amber light at the completion of fixed-interval components consistently decreased rates of responding maintained by either cocaine injection or food presentation (Figure 6). Steady low rates of responding in most fixed-interval components (Figure 7) resulted in quarter-life values approaching 25%. When the 2-sec amber light was presented again, rates of re-

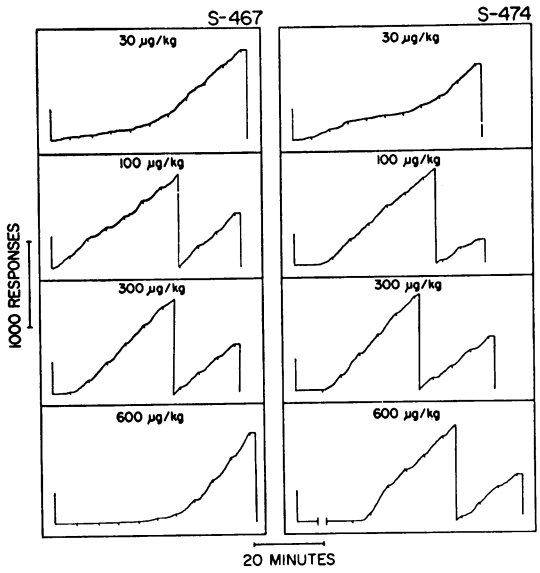

Fig. 4. Effects of dose of cocaine per injection on patterns of responding under the second-order FR 10 (FI 5:S) schedule. Ordinate: cumulative responses; abscissa: time. Each panel shows a representative sequence of 10 consecutive fixed-interval components followed by a 100-sec timeout period after the injection. Each record is from the second of the three sequences of that experimental session. The recording pen reset whenever 1100 responses had cumulated and at the end of the timeout period. The motor of the recorder stopped but responses still cumulated during 2-sec presentations of the amber light, indicated by short diagonal strokes on the record, and during the injection of cocaine at the completion of the tenth fixed interval. The bracketed space in the record in the lower-right panel indicates the omission of 15 min in which no responding occurred.

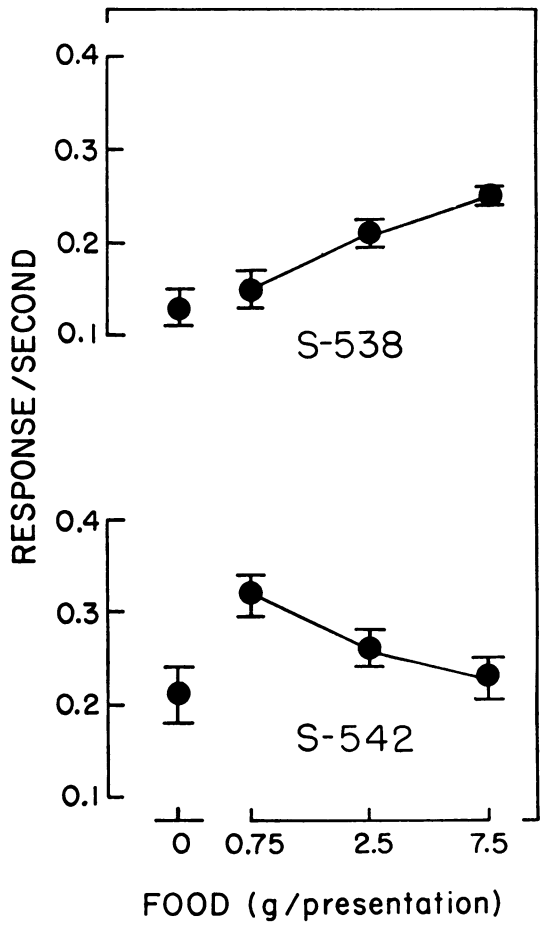

Fig. 5. Effects of amount of food per presentation on mean rates of responding under the second-order FR 10 (FI 5:S) schedule. Each point is the mean of the last four sessions under each condition; bracketed vertical lines indicate ± one standard error of the mean.

sponding and quarter-life values increased and the original patterns of responding were recovered (Figures 6 and 7).

The 2-sec presentations of the amber light controlled rates and patterns of responding in Monkey S-59 over many sessions after saline injections were substituted for cocaine injections (Figure 8). During saline sessions in which the brief stimulus was omitted, rates of responding declined and quarter-life values were low. When the brief stimulus was presented again, rates of responding increased and patterns of responding characteristic of fixed-interval schedules were recovered, despite the continued absence of cocaine injections.

DISCUSSION

The present results indicate that a brief stimulus intermittently associated with intravenous injections of cocaine in the squirrel monkey can maintain characteristic patterns of positively accelerated responding in the fixed-interval components of a second-order schedule. A useful perspective on the characteristics of performances under schedules of drug injection can be gained by directly comparing such performances with those maintained under similar schedules by other consequent events, such as food presentations. In a previous study of squirrel monkeys under second-order schedules with fixed-ratio components, repeated sequences of rapid responding characteristic of fixed-ratio schedules were maintained by stimuli associated with either cocaine injections or food presentations (Goldberg, 1973*a*). Similarly, in the present study,

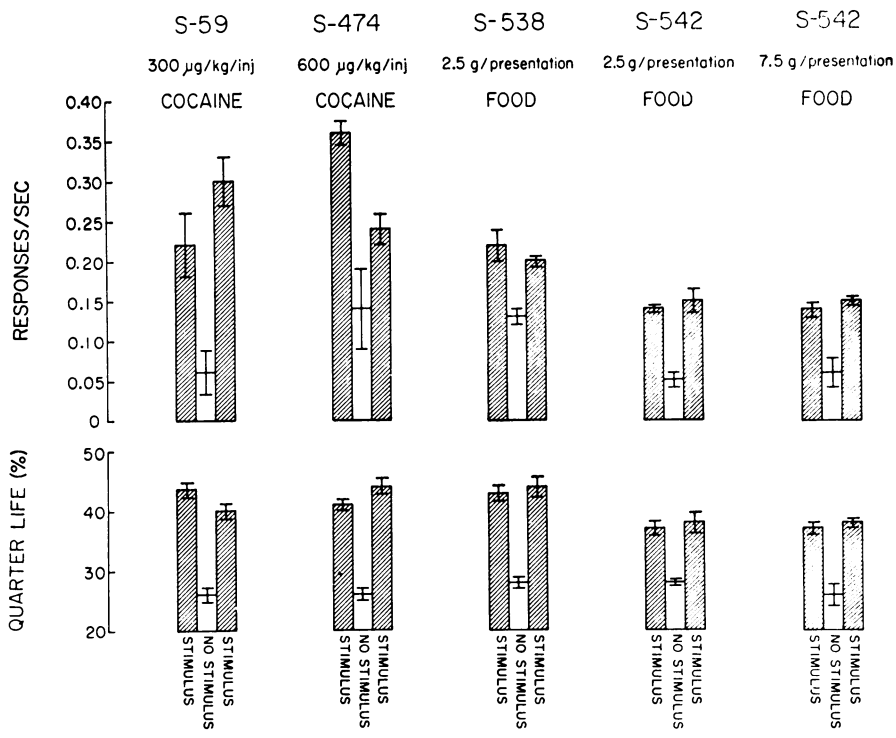

Fig. 6. Decreases in mean rates of responding and quarter-life values when the brief stimulus was omitted under the second-order schedule of cocaine injection or food presentation. Each bar is the mean of the last four sessions under each condition; bracketed vertical lines indicate ± one standard error of the mean.

patterns of responding in the fixed-interval components of a second-order schedule of food presentation were similar to those maintained under the second-order schedule of cocaine injection. The present results are also consistent with those of previous studies in which appropriate responding was maintained in fixed-interval components of second-order schedules of food presentation in the rat (de Lorge, 1964) and the pigeon (Kelleher, 1966*a*, *b*) and of electric-shock delivery in the squirrel monkey (Byrd, 1972).

In order for drug injections to maintain characteristic schedule performances, the reinforcing effects of the drug injection relative to its other pharmacological effects on behavior have to be controlled. For example, pretreatment with cocaine enhances and then, at higher doses, suppresses responding independently of the type of event maintaining the behavior (Barrett, 1976; Gonzalez and Goldberg, 1977; Smith, 1965). Under conditions in which responding results in frequent injections of a drug, the rate of responding may be limited by these other effects of the drug on responding. This may, to some extent, account for the frequent finding that over a range of doses, rate of responding is inversely related to dose under simple fixed-ratio shedules of drug injection (*e.g.*, Hoffmeister and Goldberg, 1973; Pickens and Thompson, 1968; Wilson, Hitomi, and Schuster, 1971; Woods and Schuster, 1968). The number and frequency of drug injections can be controlled by limiting the number of injections in each session and by imposing timeout periods between successive schedule components. Balster and Schuster (1973), for example, studied rhesus monkeys responding under a 9-min fixed-interval schedule of intravenous cocaine injection, with 15-min timeout periods separating successive interval components. They found that response rate was directly related to dose over a range from 25 µg/kg/injection to 400 or 800 µg/kg/injection. In contrast, response rate of rhesus monkeys is inversely related to dose when studied over this range under simple fixed-ratio schedules (Goldberg, Hoffmeister, Schlichting, and Wuttke, 1971; Wilson *et al.*, 1971). Goldberg (1973*a*, *b*) studied squirrel monkeys respond-

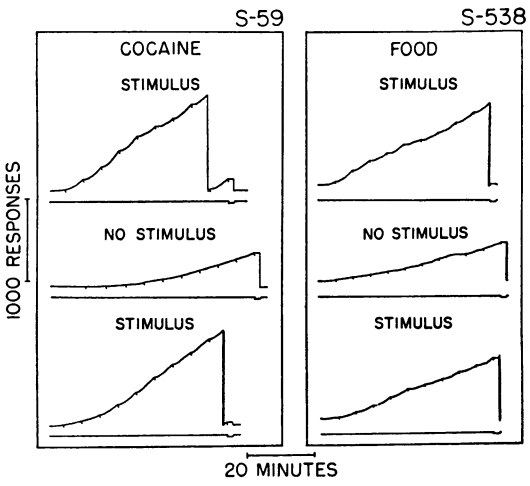

Fig. 7. Influence of the brief stimulus on patterns of responding under second-order schedules of cocaine injection (300 μg/kg/injection; left panels) or food presentation (2.5 g/presentation; right panels). Ordinate: cumulative responses; abscissa: time. The recording pen reset whenever 1100 responses had cumulated and at the end of the timeout period. Upper and lower panels: the motor of the recorder stopped but responses still cumulated during 2-sec presentations of the amber light, indicated by short diagonal strokes on the cumulative record, and during cocaine injections or food presentations, indicated by the downstroke of the event pen. The event pen remained down until the end of the 100-sec timeout period. Middle panels: recording was the same as in the upper and lower panels, but no stimulus change occurred until completion of the tenth interval and short diagonal strokes on the cumulative record indicate only the completion of each fixed-interval component. Each record is from the second sequence of fixed intervals in that session. Positively accelerated responding within fixed-interval components was lost and overall rates of responding decreased when the brief stimulus was omitted, but characteristic performances recovered when the brief stimulus was presented again.

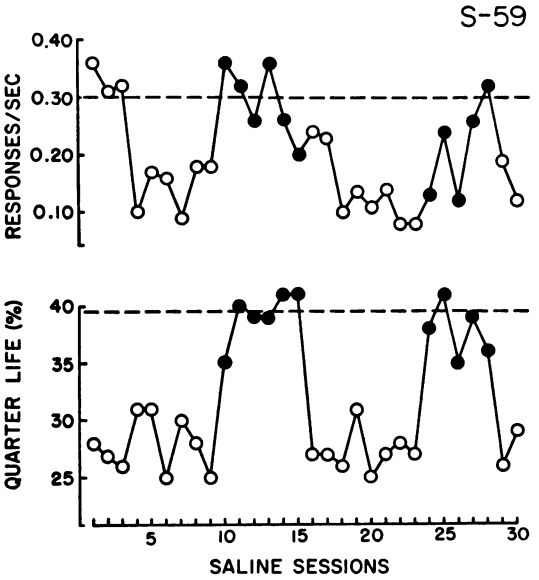

Fig. 8. Effects of the brief visual stimulus on mean rates of responding (upper graph) and quarter-life values (lower graph) in successive daily sessions after saline was substituted for cocaine (Monkey S-59). Unfilled points: no stimulus; filled points: stimulus. Mean response-rate and quarter-life values (± one standard error of the mean) from the last four sessions under the second-order schedule of cocaine injection (300 μg/kg/injection) were 0.30 ± 0.03 responses per second and 39.5 ± 1.3 per cent; these mean values are indicated by dashed lines in the upper and lower graphs. Note the relatively high rates of responding and high quarter-life values when the brief stimulus was presented at the completion of each fixed-interval component.

ing under a second-order schedule in which completion of each fixed ratio produced a brief light and the first fixed ratio completed after a 5-min interval produced both the light and an intravenous injection of cocaine. Each injection was followed by a 1-min timeout period and each session ended after 15 injections. Under this second-order schedule, mean response rates increased slightly as the dose of cocaine was varied from 25 to 200 μg/kg/injection and the optimal doses for maintaining high response rates were 100 to 200 μg/kg/injection. In contrast, under simple fixed-ratio schedules, response rate of squirrel monkeys first increased and then decreased as dose of cocaine was increased from 12 to 200 μg/kg/injection and optimal doses for maintaining high response rates were 12 to 25 μg/kg/injection (Goldberg, 1973*a*; Goldberg and Kelleher, 1976).

As the dose of cocaine per injection was increased in the present study, rates of responding increased, reaching a maximum at a dose of 300 μg/kg, and then decreased at a dose of 600 μg/kg. In a previous study of performance under a 5-min fixed-interval schedule of cocaine injection, the functional relations between rate of responding and dose per injection were similar, but rate of responding decreased at 100 μg/kg/injection (Goldberg and Kelleher, 1976). In the present study, responding was well maintained under FR 10 (FI 5:S) by 600 μg/kg when a timeout period of slightly more than 60 min followed the injection cycle. When the time between an injection and the next period of measured responding is about

23 hr, responding can be well maintained by doses of cocaine as high as 1.5 mg/kg (Goldberg, 1976; Goldberg and Kelleher, 1977). The time between an injection of cocaine and the beginning of the next period in which responding is measured is a primary determinant of how much the dose of cocaine can be increased before responding decreases.

Varying the amount of food per presentation associated with the brief stimulus under the second-order schedule of fixed-interval components had less consistent effects on performance than varying the amount of cocaine. As the amount of food per presentation was increased, rates of responding increased for one monkey but decreased for the other monkey. In a previous study of the performance of pigeons under a second-order schedule with fixed-interval components, decreasing the duration of food presentation from 30 sec to 3 sec decreased the rate of responding in one bird, but had no effect on performances of the other two birds (Kelleher, 1966*a*). In a study of squirrel monkeys under second-order schedules with fixed-ratio components, the effects of varying the dose of cocaine per injection were similar to the effects of varying the amount of food per presentation (Goldberg, 1973). The maintenance of qualitatively similar performances under second-order schedules of food presentation and cocaine injection at certain parameter values in the present study seems more remarkable than the differences in the effects of varying the amount of food and dose of cocaine. With such quantitative variations, the possibility of varied effects is increased because there are so many ways in which food presentation and cocaine injection differ. As just one example, the dose of cocaine injected and its rate of injection are controlled by the experimenter, whereas the amount of food ingested and its rate of ingestion are controlled by the monkey.

Performance under the second-order schedules in the present study was jointly controlled by the brief stimulus and by the presentation of food or injection of cocaine. Omission of the brief stimulus at completion of the first nine component fixed-interval schedules immediately decreased average rates of responding and eliminated the recurring patterns of positively accelerated responding (quarter-life values decreased to between 25 and 30%). In previous studies of similar second-order schedules, omission of the brief stimulus had the same effect on patterns of responding in fixed-interval components; however, average rates of responding were not consistently affected (Kelleher, 1966*a;* Byrd, 1972). Some experiments with second-order schedules of the type used in this study indicate that the brief stimulus controls patterns of responding characteristic of fixed-interval schedules only when it is occasionally paired with another consequent event that can function as a reinforcer (Byrd and Marr, 1969; de Lorge, 1969; Kelleher, 1966*a;* Marr, 1969), whereas other experiments indicate that such pairing is unnecessary (Stubbs, 1971). In the present study, no experiments were conducted to determine whether pairings between the brief stimulus and the presentation of food or the injection of cocaine were essential to the behavioral control exerted by the brief stimulus.

Omission of food presentations or substitution of saline for cocaine decreased average rates of responding while having little effect on quarter-life values of component fixed-interval schedules. Although the development and maintenance of behavior under the second-order schedules used in the present study ultimately depended on the presentation of food or the injection of cocaine, the maintained behavior could be as rapidly modified by omitting the brief stimulus as by omitting food or cocaine.

In addition to functioning as a reinforcer, cocaine can have other direct effects upon behavior. Second-order schedules should be particularly useful for analyzing behavior maintained by injections of cocaine or other drugs because brief stimuli that have been paired with injections can provide schedule control over responding at times when the direct effects of the drug are minimal or absent. The control of rates and patterns of responding by the brief stimulus in the present study was apparent when the brief stimulus was omitted and then presented again during successive sessions in which saline was substituted for cocaine. Even when rates of responding had decreased to low levels and quarter-life values were near 25% during sessions in which neither the brief stimulus nor cocaine was presented, rates and patterns of responding returned to near control levels when the brief stimulus was presented again. These results, as well as those obtained with long

timeout periods, indicate that control of performance by scheduled presentations of the brief stimulus previously associated with injections of cocaine was not dependent on the presence of psychomotor stimulant effects of cocaine.

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