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CONCURRENT PERFORMANCES: REINFORCEMENT BY DIFFERENT DOSES OF INTRAVENOUS COCAINE IN RHESUS MONKEYS[1]

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Different doses of intravenous cocaine reinforced the lever pressing of rhesus monkeys under two-lever concurrent or concurrent-chain schedules. Under the concurrent procedure, responding produced drug reinforcers arranged according to independent variable-interval 1-min schedules. Under the concurrent-chain procedure, responding in the variable-interval link led to one of two mutually exclusive, equal-valued, fixed-ratio links; completion of the ratio produced a drug reinforcer. Under both procedures, responding on one lever produced a constant dose of 0.05 or 0.1 mg/kg/injection, while on the other lever, dose was systematically varied within a range of 0.013 to 0.8 mg/kg/injection. Preference, indicated by relative response frequency on the variable-dose lever during the variable-interval link, was always for the larger of the doses. Relative response frequencies on the variable-dose lever roughly matched relative drug intake (mg/kg of drug obtained on variable lever divided by mg/kg of drug obtained on both levers). For many dose comparisons, responding occurred and reinforcers were obtained almost exclusively on the preferred lever. Overall variable-interval rates generally were lower than with other reinforcers, and these low rates, under the experimental conditions, may have occasioned the exclusive preferences.

That the intravenous injection of cocaine reinforces lever pressing in the rat, the rhesus monkey, and the squirrel monkey has been demonstrated in a number of studies (*e.g.*, Deneau, Yanagita, and Seevers, 1969; Goldberg, 1973; Goldberg, Hoffmeister, Schlichting, and Wuttke, 1971; Pickens and Thompson, 1968; Wilson, Hitomi, and Schuster, 1971). A finding common to many of these studies has been that over a range of cocaine doses, absolute rate of response is inversely related to reinforcer magnitude, *i.e.*, dose size in mg/kg/injection. Pickens and Thompson (1968), for example, demonstrated an inverse relationship between dose and response rate over a dose range of 0.25 to 3.0 mg/kg/injection in rats responding under continuous reinforcement (CRF) or fixed-ratio (FR) schedules. Similarly, response rates of rhesus monkeys under CRF schedules decreased as a function of dose between 0.05 and 1.2 mg/kg/injection (Wilson *et al.*, 1971; Woods and Schuster, 1968). Under FR 10, rhesus monkeys' rates were inversely related to dose as dose size increased from 0.05 to 0.2 mg/kg/injection (Goldberg *et al.*, 1971).

The observed inverse relationship between absolute response rate and cocaine dose size is provocative: it could reflect a decline in rein-

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forcer effectiveness with increased reinforcer magnitude. However, absolute rate of response under these single-schedule procedures may not be indicative of the reinforcing efficacy of different doses. Pickens and Thompson (1968) found that non-contingent intravenous injections of cocaine resulted in immediate cessation of fixed-ratio responding maintained by food reinforcement in the rat. The duration of the post-injection pause was directly related to dose size; when responding began again, it occurred at the usual, relatively constant rate. Similarly, using fixed-interval schedules of cocaine presentation in rats, Dougherty and Pickens (1973) demonstrated that an observed inverse relationship between dose and overall response rate was attributable to increases in the duration of the post-reinforcement pause with increasing dose; running rate (rate between the first response in the interval and the onset of drug injection) increased or remained unchanged. These findings strongly suggest that decreases in rate of drug-reinforced responding with increases in dose reflect a general, dose-related disruption of operant behavior occurring immediately after cocaine injection.

Additionally, in experiments employing single-schedule procedures and nutritive reinforcers—for which response-disrupting effects should be minimal—consistent magnitude-rate relationships have not been found. With increases in amount of reinforcer, absolute response rates have been found to increase (*e.g.*, Guttman, 1953; Stebbins, Mead, and Martin, 1959); to change only slightly, transiently, or unsystematically (Catania, 1963*a;* Jenkins and Clayton, 1949; Keesey and Kling, 1961); and to decrease (Goldberg, 1973; Pickens, Bloom, and Thompson, 1969). These single-schedule procedures thus appear to be of limited utility in investigating relationships between reinforcer efficacy and reinforcer magnitude.

Contrasting with results from single-schedule experiments are data obtained with concurrent scheduling procedures. Under these procedures, two equal-valued intermittent schedules, operating independently and concurrently, arrange the availability of different magnitudes, whose reinforcing efficacy is indexed by the preference demonstrated between them. Preference is defined as relative responding or relative time spent: responses emitted or time spent in one schedule condition divided by total responses emitted or time spent in both schedule conditions (Brownstein, 1971; Davis, Davison, and Webster, 1972; Neuringer, 1967; Pliskoff and Hawkins, 1967). A consistent finding has been that the value of the preference measure increases with increases in relative reinforcer magnitude: the reinforcer magnitude available under one schedule divided by the sum of the reinforcer magnitudes available under both schedules (Brownstein, 1971; Catania, 1963*a;* Neuringer, 1967; Walker and Hurwitz, 1971).

The demonstrated sensitivity of behavior under concurrent schedules to variations in reinforcer magnitude was an important consideration in the choice of tactics for the present experiment, which employed concurrent variable-interval scheduling procedures in evaluating the relative reinforcing efficacy of different doses of intravenously delivered cocaine in rhesus monkeys. The preference measure employed, relative response frequency, is obtainable without reference to absolute response rate. Additionally, then, these procedures appeared to offer a promising tool for minimizing the influence of rate-modifying effects of different doses of cocaine on the assessment of their reinforcing efficacy.

METHOD

Subjects

One female and three male rhesus monkeys (*Macaca mulatta*) weighing between 4 and 7 kg served in daily experimental sessions. One, Willis, which had had several months' experience in a preliminary dose-choice study with intravenous cocaine, died before the present study was completed. Another, Bernadette, previously had responded under fixed-ratio schedules with intravenous cocaine as the reinforcer. The other two, Boris and Rico, were experimentally naive. All were individually housed, had unlimited access to water, and twice daily were fed 15 Purina Monkey Chow biscuits, which had been treated by the manufacturer with 608.3 g/ton isoniazid for prevention of tuberculosis. This diet was supplemented with fresh fruit at least twice weekly.

Surgical Preparation

After at least two weeks of adaptation to the housing conditions and restraining apparatus

(described below), monkeys were anesthetized with sodium pentobarbital (30 mg/kg, intravenously delivered). A silicone rubber catheter (Rodhelm Reiss, Inc., Belle Mead, New Jersey) with an outer diameter of 0.24 cm and an inner diameter of 0.079 cm was secured in the internal jugular or the femoral vein, with the tip terminating at approximately the level of the right atrium. The distal end was passed subcutaneously to a midscapular point, where it exited through a stab wound. Further details of this catheterization procedure have been described elsewhere (Deneau *et al.*, 1969; Yanagita, Deneau, and Seevers, 1965).

Apparatus

General housing and restraint; infusion apparatus. Each monkey was housed in an enclosed wooden chamber 64 cm wide, 70 cm high, and 77 cm deep. An exhaust fan, mounted on the top, provided ventilation. A water bottle was located on one outside wall with a drinking tube projecting into the chamber; a food dish was located on the opposite inside wall. Two 6-W overhead white light bulbs provided general illumination. A wide-angled viewing lens mounted at the top of the chamber permitted observation of the monkey.

The restraining apparatus has been described in detail and diagrammed by Deneau *et al.* (1969). In brief, each monkey was restrained by a metal harness attached to a hollow, jointed, extension arm. The arm was fastened to the rear wall of the chamber so as to allow the monkey relatively free movement. The external end of the implanted catheter was attached to one end of a juncture located in the back of the harness; a second piece of identical catheter attached to the other end of the juncture passed through the restraining arm to the outside of the chamber. Here it was connected to the stem end of a Y-connector (Becton-Dickinson #3091), which, in turn, joined identical pieces of catheter leading from two syringe infusion pumps (Harvard #1100 or Sage #255-1).

Experimental apparatus. An aluminum chassis 30.5 cm wide, 20.5 cm high, and 7.5 cm deep was mounted on the inside of the front door of each living chamber at a height determined by the size of the monkey. On the front of the chassis were mounted three response levers (Lehigh Valley Electronics #1380) requiring a downward force of 0.49 N for operation. Two (side) levers were located 2 cm from the bottom of the panel with a distance of 16 cm between them. Centered 4.1 cm above each side lever was a circular aperture 2.9 cm in diameter covered by transluscent Plexiglas. A 6-W green Christmas-tree light mounted behind the Plexiglas could illuminate the left lever; a 6-W red Christmas-tree light, the right lever. The third (center) lever was mounted midway between the two side levers and 7 cm above them; it could be illuminated by a 6-W yellow pilot light 2.9 cm in diameter located 4.1 cm above it. Pairs of 6-W Christmas-tree lights—white, blue, red, and green—mounted overhead provided different houselight conditions. During experimental sessions, white masking noise was continuously present.

Standard electromechanical equipment automatically controlled experimental events. Digital counters and a six-channel event recorder (Ralph Gerbrands Company, #PC-2) recorded responses, reinforcements, and time intervals.

Drugs and Dosages

Cocaine hydrochloride was dissolved in 0.9% saline and diluted to the desired concentration; all doses are expressed as the salt. Drug dosage, for a given monkey, was manipulated by varying the volume of a constant-concentration solution injected over a constant time period. These variations were accomplished by the use of different pump motor speeds and/or different syringe sizes. The constant-concentration solution for each monkey resulted in delivery of a dose of either 0.05 or 0.1 mg/kg in a 0.375 ml injection.

PROCEDURES

Procedure A: Chain FR 1 Concurrent VI 1-min VI 1-min Timeout 5-min

Schedule specifications. The sequence of steps by which the terminal contingencies were attained varied among the monkeys, depending on experimental history. A schematic diagram of these terminal schedule conditions is shown in Figure 1. A cycle began with illumination of the yellow pilot light over the center lever and of the white houselight overhead (Condition 1, Figure 1). A single response on the center lever (FR 1): (1) darkened the yellow center-lever light; (2) illuminated the green

and red lights over the left and right side levers, respectively; and (3) initiated the concurrent variable-interval component (link) of the chain (Condition 2, Figure 1). During this component, two variable-interval tape timers, operating concurrently and independently for each side lever, arranged the availability of two drug doses. The average interreinforcement interval arranged for each variable-interval schedule was 1 min. When a reinforcement was scheduled for one lever, it remained available, while the variable-interval component was in effect, until collected. Thus, if both timers had scheduled a reinforcement at the time a reinforcement was obtained on one lever, the dose scheduled for the other lever was still available upon return to the variable-interval component. An individual tape timer was inactivated when it had arranged a reinforcement for a lever until after that reinforcement was collected, while the other timer continued to operate. Both timers were always inactivated from the onset of reinforcement on either lever until the variable-interval link was initiated in the following cycle.

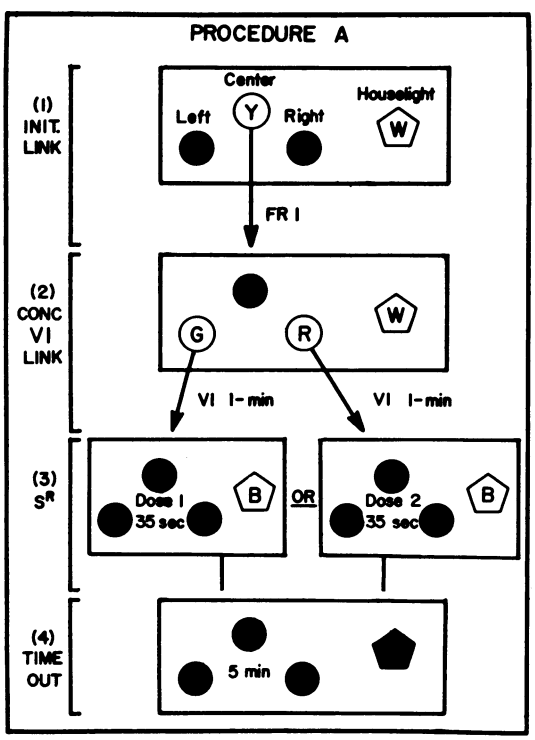

Fig. 1. Diagram of one cycle of Procedure A. Each box represents one possible state. Numbers on the left refer to successive experimental conditions. At the start of a cycle, the yellow center-lever light and white houselight are illuminated, and the side-lever lights are dark (Condition 1). A single center-lever response extinguishes the center-lever light and turns on the green and red side-lever lights (Condition 2). Responding on either side lever during the concurrent VI 1-min VI 1-min link leads to injection of one of two drug doses (Condition 3). During reinforcement, the houselight is blue and all lever lights are darkened. A 5-min timeout of total darkness follows reinforcement (Condition 4), after which the initial-link conditions are reinstated.

During the concurrent variable-interval component, a changeover delay (COD; Herrnstein, 1961) of 1.5 sec was employed. Responses occurring within 1.5 sec of a switch from one side lever to the other side lever were ineligible for reinforcement. The COD minimized the possibility that responding on one side lever would come under control of the injection dose scheduled for the other lever.

When a response was reinforced on one of the side levers, both side-lever lights were extinguished, the appropriate infusion pump was activated for 35 sec, and a blue houselight was illuminated for the duration of the injection (Condition 3, Figure 1). A 5-min timeout period of total darkness followed reinforcement (Condition 4, Figure 1). Responses occurring during reinforcement or timeout periods had no scheduled consequences. At the termination of the timeout, a new cycle began. Sessions ended after 30 reinforcements.

Dose variations. The behavior of two monkeys, Bernadette and Rico, was studied under this procedure. The order of dose comparisons and the number of consecutive sessions at each determination are shown for these animals in Columns 2, 3, and 5 of Table 1. Under the general strategy followed, equal doses of 0.1 mg/kg/injection initially were available on the two side levers. After behavior had stabilized under this condition (see below), one lever was selected as the constant-dose lever, on which the dose was kept at 0.1 mg/kg/injection, while a sequence of different comparison doses was presented on the other, variable-dose lever. After the sequence was completed, the equal-dose condition (0.1-0.1) was reinstated, the constant- and variable-dose levers were reversed, and a second sequence of comparisons was made. Minor deviations from this strategy occasionally occurred when fewer or more than two determinations were deemed appropriate for particular dose comparisons, but all determinations having the constant dose on the

same lever were considered as part of one sequence. The lever on which the constant dose was scheduled for each determination is indicated in Column 4 of Table 1.

Criteria for dose variation. Changes in the comparison dose were made when either of two kinds of behavioral criteria was satisfied. If responding and reinforcement continued to occur on both levers, a stability criterion was used. Behavior was considered stable when a minimum of 15 sessions had been conducted under a given dose comparison, when for five consecutive sessions the range of relative response frequencies on either lever in the concurrent variable-interval component did not exceed 0.10, and when there was no systematic trend in these relative frequencies.

If, on the other hand, after a monkey's initial exposure to any comparison, its relative frequency of responding in a session exceeded 0.99 on one lever, and/or it obtained all reinforcements on one lever (*i.e.,* received only one of the two doses), an "exclusive preference" was said to have occurred, and this occurrence also served as a criterion for changing the comparison dose in the next session.

Analysis of data. Data were summarized so as to represent the terminal performance of each animal at each determination. Accordingly, for determinations in which a stability criterion was attained, measures were individually calculated for each of the five terminal sessions and then averaged across these sessions. For determinations in which an exclusive preference developed, data were drawn only from the single terminal session that defined the preference as exclusive. Any further computations were made from data sets produced in this manner, with data points from each determination being equally weighted. Whether data points were drawn from one or five criterion sessions (*i.e.,* whether preference was exclusive) is indicated for each determination in Column 6 of Table 1.

Procedure B: Chain FR 1 Concurrent (Chain VI 1-min FR x) (Chain VI 1-min FR x) Timeout 5-min

Schedule specifications. The terminal schedule conditions under this procedure are diagrammed in Figure 2. The schedule contingencies in the first two links (Conditions 1 and 2, Figure 2) were identical with those of Procedure A, with the exception of the duration of the COD in the concurrent variable-interval link, which was 0.5 sec. In this link, the VI 1-min schedules did not arrange the immediate availability of drug reinforcement, but rather the availability of access to the terminal-link conditions scheduled for each lever. When the terminal link was entered on a side lever (Condition 3, Figure 2), (1) the houselight color changed to match the color of

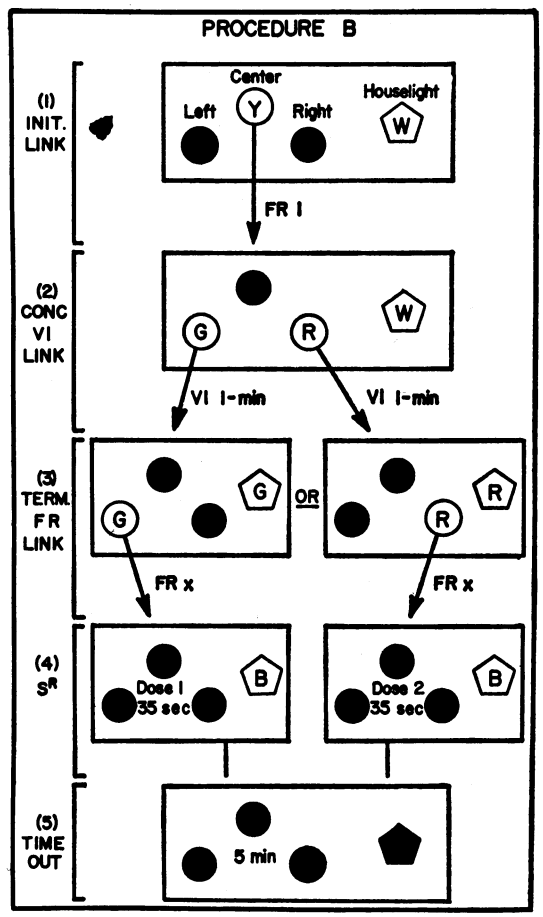

Fig. 2. Diagram of one cycle of Procedure B. Each box represents one possible state. Numbers on the left refer to successive experimental conditions. Initial-link and concurrent variable-interval link conditions (1 and 2) are the same as under Procedure A. Responding on either side lever during the concurrent variable-interval component leads, on a VI 1-min schedule, to one of two terminal-link states (Condition 3). During a terminal link on one side lever, the houselight color is changed to match that lever light, and the other side-lever light is darkened. The completion of a fixed-ratio requirement on the lighted side lever is then reinforced with one of two drug doses (Condition 4). Ratio values are the same on both levers, while drug doses usually differ. Stimulus conditions during reinforcement and timeout (Condition 5) are the same as those under Procedure A.

the light over that lever (*i.e.*, green if entry was into the left-lever terminal link, red if entry was into the right-lever terminal link); (2) the light over the other lever was extinguished; and (3) the variable-interval programmer for that lever was inactivated. In the presence of these terminal-link conditions, completion of an FR 5 (Boris) or an FR 15 (Willis) requirement on the lighted lever resulted in an injection of the dose available on that lever (Condition 4, Figure 2). Stimulus conditions during drug injection were identical to those in Procedure A.

The terminal-link fixed-ratio schedules for the two levers were mutually exclusive. Since retractable levers were not physically available to restrict terminal-link responding to the lighted lever, the following contingencies were imposed to prevent adventitious maintenance of responding on the other lever: (1) responses occurring on the unlighted side lever during the terminal link reset the ratio requirement to its initial value, if ratio responding had begun; (2) responses on the unlighted side lever during the terminal link resulted in a 15-sec blackout period, during which the houselight and lever lights were extinguished and the timer for the fixed-ratio period was stopped; (3) any further responses on any lever during a blackout period initiated a new 15-sec blackout. At the end of a blackout period during which no responses occurred, the appropriate terminal-link fixed-ratio conditions were reinstated.

As in Procedure A, a timeout of 5 min followed reinforcement (Condition 5, Figure 2), after which a new cycle began. Sessions again terminated after 30 reinforcements.

Dose variations. The behavior of two monkeys, Boris and Willis, was studied under this procedure. The order of dose comparisons and the number of consecutive sessions at each determination are shown for these monkeys in Columns 2, 3, and 5 of Table 1. For Boris, comparisons were made with constant doses of both 0.05 and 0.1 mg/kg/injection; again, for each constant dose, a sequence of determinations was defined as those comparisons for which the constant dose was on the same lever. For Willis, a single sequence of comparisons with a constant dose of 0.05 mg/kg/injection was completed before the monkey died. The constant-dose lever for each determination is indicated in Column 4 of Table 1.

Criteria for dose variation. Criteria for changes in comparison dose were the same as those under Procedure A.

Analysis of data. The method followed for summarizing results was also the same as that under Procedure A.

RESULTS

Concurrent Variable-Interval Performance

Since no systematic performance differences between Procedures A and B were observed, the data from the concurrent variable-interval links of both procedures are considered together. Relative response frequency on the variable-dose lever was calculated for each session by dividing the number of responses occurring on this lever by the total number of responses occurring on both levers. Criterion-session relative frequencies are presented for each determination in Column 9 of Table 1, and in Figure 3 are plotted for each monkey as a function of the dose available on the variable-dose lever. When the larger of the two doses was scheduled on the variable-dose lever, all monkeys consistently exhibited relative response frequencies of greater than 0.50 on this lever, whereas when the smaller of the two doses was scheduled on the variable-dose lever, all monkeys consistently exhibited relative response frequencies of less than 0.50 on this lever. With the same dose available on both levers, relative frequency of responding often deviated considerably from 0.50, especially for Willis and Rico; but within monkeys these deviations were never so extreme as those occurring when different doses were available on the two levers. These data point to the conclusion that the larger of the two doses presented for comparison was always the preferred.

To some extent, as the difference in size between the doses increased, the degree of preference demonstrated also increased. This relationship is particularly clearly illustrated in Figure 3 by Boris' data when 0.05 mg/kg/injection served as the constant dose, and by Bernadette's data as the comparison dose was increased from 0.025 or 0.05 mg/kg/injection to 0.2 mg/kg/injection. In these cases, relative response frequency on the variable-dose lever increased monotonically with the dose available on this lever.

However, in many cases the response proportions maintained by different doses on the same side of the constant dose cannot be

Table 1

Summary of dose-comparison data. Doses on the constant- and variable-dose levers are listed for each monkey in order of their presentation (Columns 2 and 3). The sequence to which a determination belongs is indicated in parentheses following the lever of the constant dose in Column 4. Column 6 indicates, for each determination, from how many criterion sessions the data values in Columns 1 to 10 and Column 12 were drawn: five when a stability criterion was attained; one when preference was exclusive. Column 13 gives the absolute values of the deviations of relative response frequency (Column 9) from relative intake (Column 12).

	Dose (mg/kg/inj)					Abs. Resp. Rates (resp/sec)		Relative with Respect to Var.- Dose Lever				Abs. Deviat. from Matching (|12-9|)
Monkey	Var.	Const.	Const.-Dose Lever	No. of Sess.	No. Crit. Sess.	Var.-Dose Lever	Const.-Dose Lever	Resp. Freq.	No. Rfts.	Dose	Intake	
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)
BERNADETTE	0.1	0.1	R (1)	51	5	0.65	0.80	0.45	0.47	0.50	0.47	0.02
	0.4	0.1	R (1)	21	1	0.45	0.04	0.92	1.00	0.80	1.00	0.08
	0.05	0.1	R (1)	27	5	0.48	0.97	0.33	0.44	0.33	0.28	0.05
	0.2	0.1	R (1)	24	5	1.82	0.30	0.86	0.85	0.67	0.92	0.06
	0.025	0.1	R (1)	17	1	0.02	1.81	0.01	0.10	0.20	0.03	0.02
	0.1	0.1	L (2)	26	5	0.88	0.67	0.57	0.49	0.50	0.49	0.08
	0.05	0.1	L (2)	32	5	0.59	0.92	0.39	0.48	0.33	0.31	0.08
	0.4	0.1	L (2)	9	1	0.29	0.02	0.93	1.00	0.80	1.00	0.07
	0.2	0.1	L (2)	20	1	0.78	0.00	1.00	1.00	0.67	1.00	0.00
RICO	0.1	0.1	R (1)	18	5	0.24	0.33	0.42	0.49	0.50	0.49	0.07
	0.2	0.1	R (1)	32	5	0.65	0.19	0.78	0.59	0.67	0.74	0.04
	0.05	0.1	R (1)	21	1	0.00	0.36	0.01	0.00	0.33	0.00	0.01
	0.4	0.1	R (1)	7	1	0.39	0.01	0.99	1.00	0.80	1.00	0.01
	0.1	0.1	L (2)	21	5	0.25	0.11	0.69	0.59	0.50	0.59	0.10
	0.05	0.1	L (2)	22	5	0.02	0.51	0.05	0.12	0.33	0.06	0.01
	0.2	0.1	L (2)	11	1	0.67	0.00	1.00	1.00	0.67	1.00	0.00
	0.067	0.1	L (2)	40	5	0.02	0.19	0.07	0.12	0.40	0.08	0.01
	0.2	0.1	L (2)	9	1	0.11	0.01	0.95	1.00	0.67	1.00	0.05
	0.025	0.1	L (2)	9	1	0.00	0.41	0.00	0.00	0.20	0.00	0.00
	0.4	0.1	L (2)	5	1	0.26	0.01	0.97	1.00	0.80	1.00	0.03

Table 1 *continued*

Monkey (*1*)	*Dose (mg/kg/inj)*		*Const.-Dose Lever* (*4*)	*No. of Sess.* (*5*)	*No. Crit. Sess.* (*6*)	*Abs. Resp. Rates (resp/sec)*		*Relative with Respect to Var.- Dose Lever*				*Abs. Deviat. from Matching (|12-9|)* (*13*)
	Var. (*2*)	*Const.* (*3*)				*Var.-Dose Lever* (*7*)	*Const.-Dose Lever* (*8*)	*Resp. Freq.* (*9*)	*No. Rfts.* (*10*)	*Dose* (*11*)	*Intake* (*12*)	
BORIS	0.05	0.05	R (1)	39	5	0.21	0.28	0.44	0.48	0.50	0.48	0.04
	0.2	0.05	R (1)	31	5	0.28	0.02	0.94	0.75	0.80	0.92	0.02
	0.1	0.05	R (1)	36	5	0.25	0.12	0.68	0.55	0.67	0.71	0.03
	0.05	0.05	R (1)	15	5	0.16	0.16	0.52	0.51	0.50	0.51	0.01
	0.025	0.05	R (1)	12	1	0.00	0.18	0.01	0.03	0.33	0.02	0.01
	0.1	0.1	R (1)	20	5	0.36	0.22	0.62	0.51	0.50	0.51	0.11
	0.4	0.1	R (1)	29	5	0.24	0.06	0.80	0.62	0.80	0.87	0.07
	0.05	0.1	R (1)	15	1	0.00	0.78	0.00	0.00	0.33	0.00	0.00
	0.8	0.1	R (1)	28	1	0.04	0.00	0.93	1.00	0.89	1.00	0.07
	0.2	0.1	L (2)	34	5	0.52	0.10	0.84	0.66	0.67	0.79	0.05
	0.025	0.1	L (2)	11	1	0.01	0.86	0.01	0.10	0.20	0.03	0.02
	0.4	0.1	L (2)	14	1	0.05	0.00	0.99	1.00	0.80	1.00	0.01
	0.2	0.1	L (2)	31	5	0.16	0.03	0.85	0.69	0.67	0.81	0.04
	0.1	0.1	L (2)	23	5	0.27	0.25	0.52	0.53	0.50	0.53	0.01
	0.05	0.05	L (2)	18	5	0.24	0.40	0.37	0.48	0.50	0.48	0.11
	0.2	0.05	L (2)	17	5	0.10	0.01	0.90	0.86	0.80	0.96	0.06
	0.025	0.05	L (2)	15	5	0.13	0.65	0.17	0.44	0.33	0.28	0.11
	0.1	0.05	L (2)	16	5	0.67	0.20	0.77	0.57	0.67	0.73	0.04
WILLIS	0.05	0.05	L (1)	55	5	0.25	0.10	0.71	0.63	0.50	0.63	0.08
	0.013	0.05	L (1)	8	1	0.00	0.54	0.00	0.07	0.21	0.02	0.02
	0.2	0.05	L (1)	27	1	0.11	0.00	0.33	0.47	0.50	0.47	0.14
	0.05	0.05	L (1)	44	5	0.22	0.44	0.99	1.00	0.80	1.00	0.01
	0.1	0.05	L (1)	8	1	0.20	0.00	1.00	1.00	0.67	1.00	0.00
	0.025	0.05	L (1)	11	1	0.00	0.57	0.01	0.03	0.33	0.02	0.01
	0.075	0.05	L (1)	22	1	0.38	0.00	0.99	0.90	0.60	0.93	0.06
	0.033	0.05	L (1)	15	1	0.01	0.77	0.01	0.13	0.40	0.09	0.08
	0.4	0.05	L (1)	20	1	0.01	0.00	1.00	1.00	0.89	1.00	0.00
	0.05	0.05	L (1)	20	5	0.21	0.70	0.23	0.47	0.50	0.47	0.24

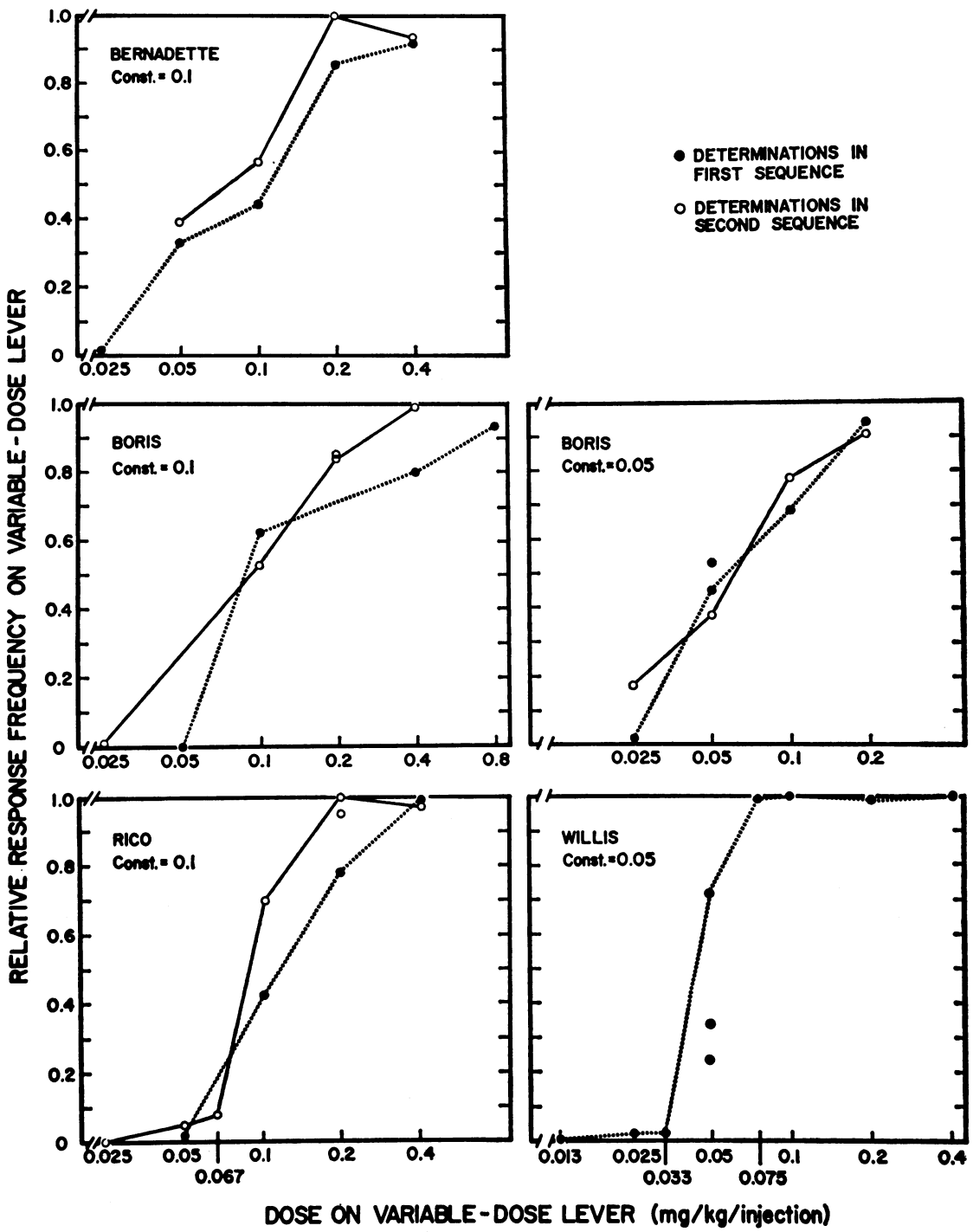

Fig. 3. Relative response frequency on the variable-dose lever as a function of dose on this lever. Doses are logarithmically spaced. The constant dose is indicated on each graph under the monkey's name. Data are from the criterion sessions (five or one) at each determination. With repeated determinations in a sequence, only the first is joined to the line.

clearly ordered. Willis' data provide an example of one source of ambiguity: Willis exclusively preferred 0.05 mg/kg/injection to all lower doses and exclusively preferred all higher doses to 0.05, so that the relative response frequency *versus* dose function is essentially flat between all doses on the same side of 0.05. No other monkey consistently exhibited this pattern of extreme preferences. But the tendency of all monkeys to prefer exclusively the higher of two doses, regardless of the difference in dose size, is evident in the asymptotic portions of the individual functions, where relative response frequencies approach or equal either 0.00 or 1.00. Furthermore, between two sequences of determinations the relative response frequency *versus* dose functions for each animal often differ considerably: functions sometimes increase monotonically within a sequence, but show inversions or are flat across sequences. These between-sequence differences cannot be accounted for by any consistent lever biases. Thus, the objective of ordering the reinforcing efficacy of a number of different doses without presenting them for direct comparison, by ordering the relative response frequencies that they maintained when compared to the same constant dose, generally was not attained.

Relative drug intake on the variable-dose lever was employed in the present study as the measure of relative reinforcement magnitude. Drug intake obtained on each lever over an experimental session is calculated by multiplying the number of reinforcements received on a lever by the dose available on it. Relative drug intake on the variable-dose lever is then calculated by dividing the intake obtained on this lever by the total intake obtained on both levers. This statistic, like Neuringer's (1967) "relative total access to reinforcement" (the proportion of reinforcer time under one schedule, when magnitude is varied by varying duration of reinforcer presentation), takes into account the effect of responding on the distribution of reinforcements between the schedules. The influence of monkeys' preferences on the distribution of reinforcements is indicated by Column 10 of Table 1, which shows that the relative number of reinforcers obtained on the variable-dose lever usually rose sharply above 0.50 with comparison doses larger than the constant dose, and fell sharply below 0.50 with comparison doses smaller than the constant dose. Relative intake thus usually did not approximate closely the scheduled relative magnitude of reinforcement, relative dose (dose available on the variable-dose lever divided by the sum of the doses available on both levers; Column 11, Table 1), except under equal-dose conditions.

Figure 4 plots each monkey's relative response frequencies on the variable-dose lever against that monkey's corresponding relative drug intakes. The diagonal line represents the locus of perfect matching, where equality exists between the measures. Most points on the individual graphs quite closely approximate this matching line. Willis exhibited unaccountably strong lever preferences under equal-dose conditions; as a result, these data show the widest absolute deviations of relative response frequency from relative intake, 0.24 and 0.14 (Column 13, Table 1). Still, across all determinations, Willis' average absolute deviation from matching was only 0.06. Absolute deviations from matching, averaged across determinations, were for the other monkeys slightly smaller: 0.03 for Rico, and 0.05 for Bernadette and Boris (deviations under both constant-dose conditions considered together). The most extreme absolute deviation from matching for these three monkeys was 0.11.

Absolute response rates on the two levers are presented in Columns 7 and 8 of Table 1, and in Figure 5 are plotted for each monkey as a function of dose on the variable lever. Response rate on the variable-dose lever first increased with the dose available on this lever, and then declined at the highest dose(s). Rate on the constant-dose lever, after sometimes increasing and sometimes decreasing as the dose on the variable lever was increased to 0.05 mg/kg/injection, then decreased monotonically with further increases in the comparison dose. Thus, dose changes on the variable lever clearly affected response rates on both the variable- and constant-dose levers, so that changes in relative response frequencies on the variable lever reflected absolute rate changes occurring on both levers.

The upper portions of the graphs in Figure 5 present overall response rates in the concurrent variable-interval link, averaged for each monkey across determinations (when more than one determination was made), and show how both these rates and average hourly drug intake changed with the dose available on

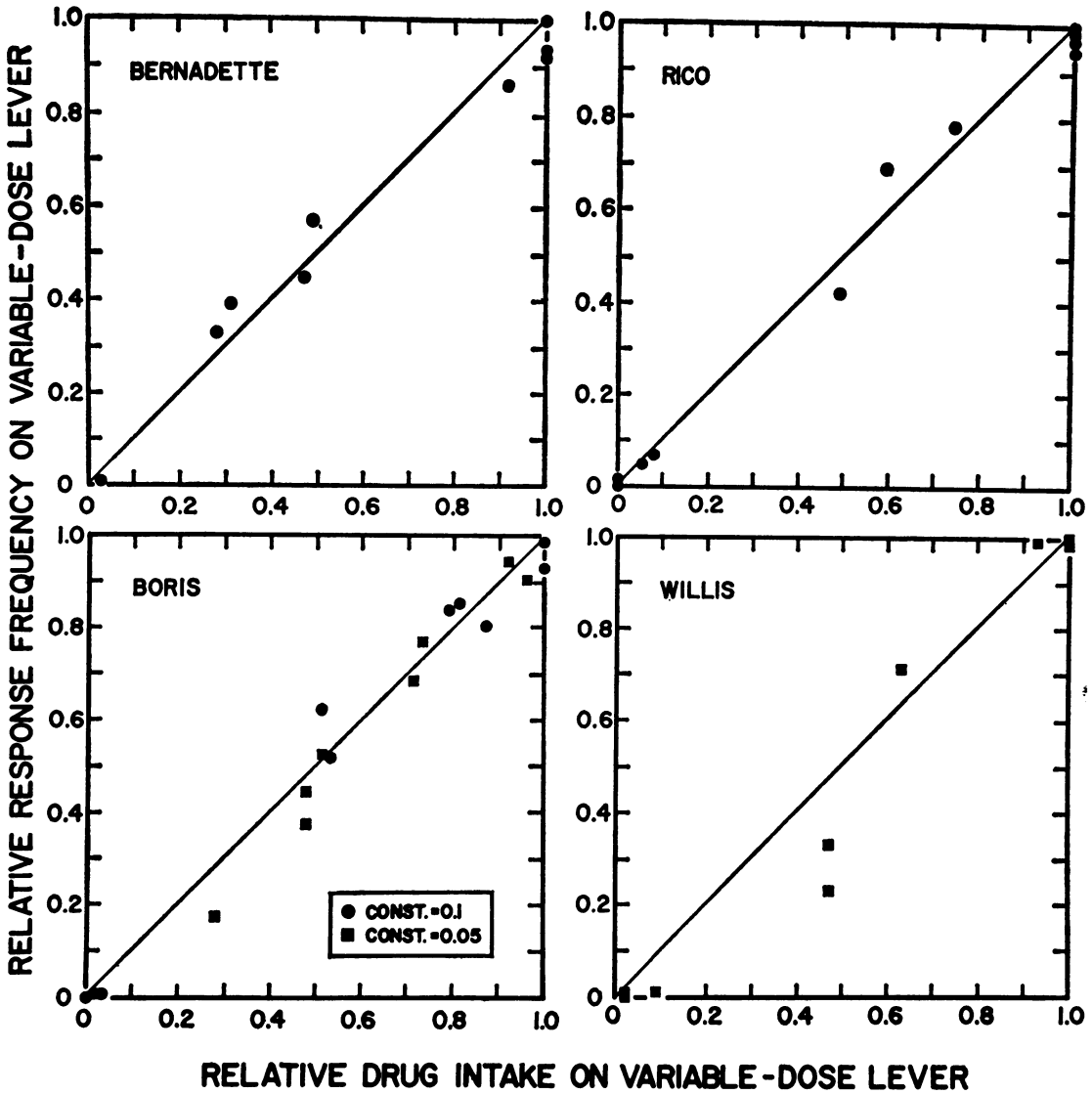

Fig. 4. Relative response frequencies on the variable-dose lever plotted against relative drug intake on the variable-dose lever. Drug intake on a lever is the number of reinforcements obtained on that lever multiplied by the dose available on it. Relative drug intake on the variable-dose lever is the drug intake on this lever divided by the sum of the intakes on both levers. The diagonal line represents the locus of perfect matching. Data are drawn from the criterion sessions (five or one) at each determination.

the variable lever. For any dose comparison, the range of overall rates that a monkey exhibited across sequences of determinations may be obtained from the lower portion of its graph, since the overall rate for any determination is the sum of the rates on the two levers. Between-sequence variability in drug intake was negligible.

While considerable between-sequence variability in response rates is evident, responding appeared to follow one of two patterns as dose on the variable-dose lever was increased. For Willis, and for Boris when 0.1 mg/kg/injection served as the constant dose, average overall response rates generally decreased with increases in the dose available on the variable lever. For Bernadette and Rico, and for Boris when 0.05 mg/kg/injection served as the constant dose, overall rates appeared unrelated to dose on the variable lever over most of the comparison-dose continuum, and then declined at the highest comparison-dose value.

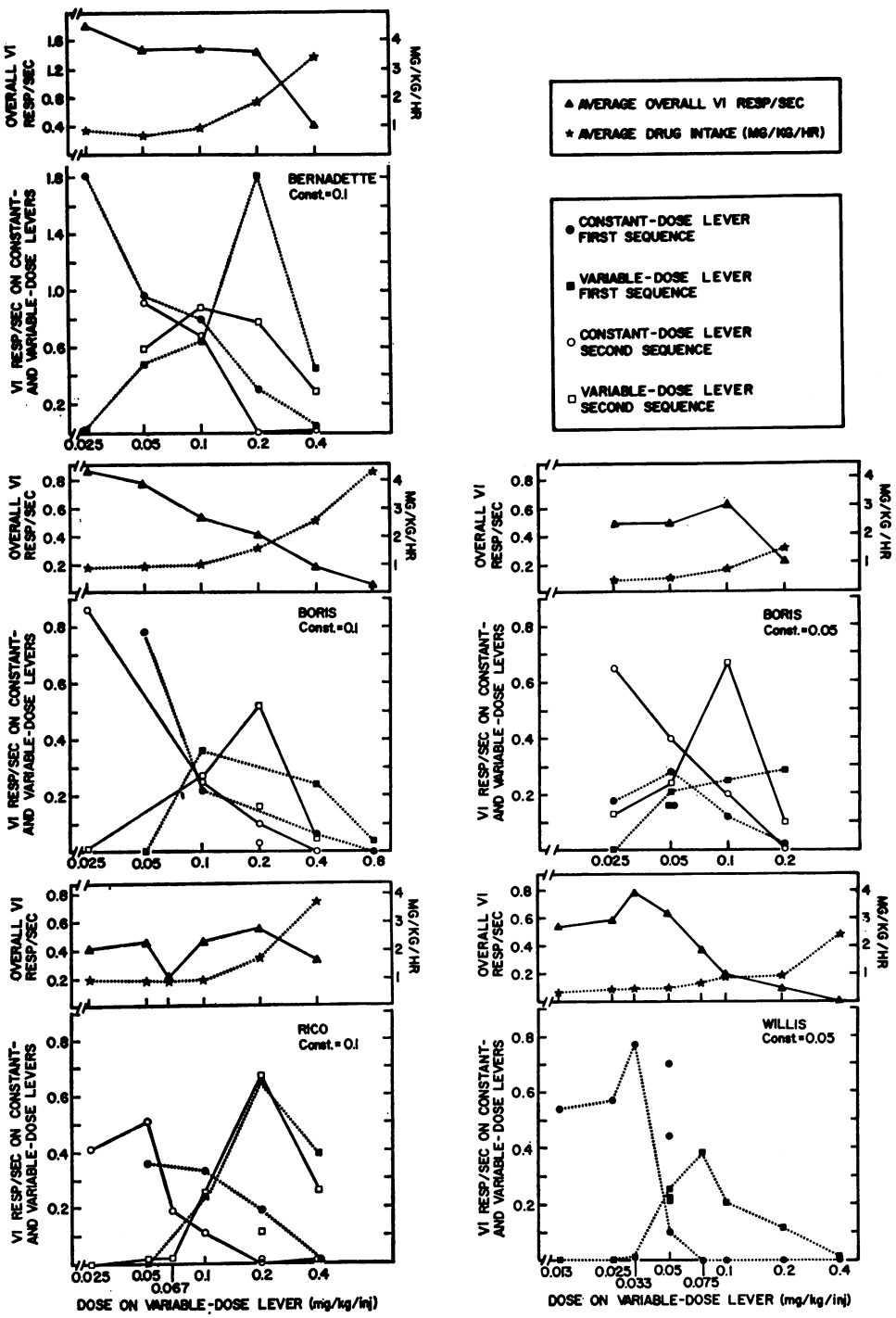

Fig. 5. Absolute variable-interval response rates (responses per second) and hourly drug intake (mg/kg/hour) plotted against dose on the variable-dose lever. Doses are logarithmically spaced. The constant dose is indicated on each graph under the monkey's name. The bottom portion of each graph shows absolute variable-interval rates on the constant- and variable-dose levers; data are from the criterion sessions (five or one) at each determination. With repeated determinations in a sequence, only the first is joined to the line. The top portion of each graph shows overall absolute variable-interval response rates and hourly drug intake for each dose comparison; data for each animal are averaged across determinations.

Hourly drug intake was determined primarily by the temporal parameters of the procedures, which limited the number of possible reinforcements to fewer than 10 per hour, and by the doses that were available. The preferences of the animals, by influencing the relative number of reinforcements obtained on each lever, also influenced hourly intake, but to a lesser extent because of the low hourly rate of reinforcement and the actual dose values compared. With comparison doses below or equal to the constant dose, these combined influences resulted in an essentially constant intake of approximately 0.9 to 1.0 mg/kg/hour (constant dose = 0.1 mg/kg/injection) or 0.4 to 0.5 mg/kg/hour (constant dose = 0.05 mg/kg/injection). As the comparison dose was increased over the constant dose, hourly drug intake increased, a finding that would be expected unless the animals had obtained reinforcements at a rate much less rapid than possible. That the animals' strong preferences resulted in the majority of reinforcements being obtained on the higher-dose lever meant that intake rose somewhat more sharply than if the number of reinforcers obtained on the two levers had been equal.

When rate and intake are considered together, Figure 5 indicates that each animal's highest drug intake under a given constant-dose condition was correlated with a low average overall rate of response. For all monkeys but Rico, this was the lowest average overall response rate that occurred. Since changes in hourly drug intake with changes in the dose available on the variable lever followed a uniform pattern, while changes in overall response rate did not, other consistent intake-rate relationships are not apparent in the data.

Terminal-Link Fixed-Ratio Performance

Table 2 presents terminal-link fixed-ratio rates (responses per second) on each lever for the two animals, Boris and Willis, whose behavior was studied under Procedure B. Relative fixed-ratio rate on the variable-dose lever was calculated, when possible, for the criterion session(s) of a comparison: fixed-ratio rate on the variable-dose lever divided by the sum of the fixed-ratio rates on both levers. For six of 28 determinations, an exclusive preference developed in which there were no entries into one terminal link in the final session (all reinforcements were obtained on one lever), so that a meaningful relative rate could not be computed.

Table 2

Response rates (responses per second) on each lever during the terminal fixed-ratio link for monkeys whose behavior was studied under Procedure B. Data from the criterion sessions (five or one) at each determination are ordered by the dose available on the variable lever; the sequence (first or second) to which each determination belongs is indicated in parentheses following the constant dose. Where a dash (—) occurs, during the criterion session of the determination the monkey did not enter into the terminal link on the lever so indicated, obtaining all reinforcements on the other lever.

Dose (mg/kg/inj)		*FR Rate (resp/sec)*	
Var.	*Const.*	*Var.-Dose Lever*	*Const.-Dose Lever*
BORIS (FR 5)			
0.025	0.1 (2)	1.0	1.6
0.05	0.1 (1)	—	2.9
0.1	0.1 (1)	2.0	2.9
0.1	0.1 (2)	1.5	1.2
0.2	0.1 (2)	2.5	1.4
0.2	0.1 (2)	1.6	1.0
0.4	0.1 (1)	2.1	1.7
0.4	0.1 (2)	1.4	—
0.8	0.1 (1)	0.2	—
0.025	0.05(1)	1.8	2.5
0.025	0.05(2)	1.0	1.4
0.05	0.05(1)	0.4	0.7
0.05	0.05(1)	0.5	1.8
0.05	0.05(2)	1.1	0.8
0.1	0.05(1)	0.6	1.4
0.1	0.05(2)	1.4	1.0
0.2	0.05(1)	0.6	1.5
0.2	0.05(2)	0.9	0.4
WILLIS (FR 15)			
0.013	0.05(1)	1.0	0.8
0.025	0.05(1)	1.5	1.6
0.033	0.05(1)	1.0	2.6
0.05	0.05(1)	0.5	0.6
0.05	0.05(1)	1.3	1.1
0.05	0.05(1)	1.8	2.0
0.075	0.05(1)	1.9	0.2
0.1	0.05(1)	0.6	—
0.2	0.05(1)	0.3	—
0.4	0.05(1)	0.2	—

Figure 6, which plots relative fixed-ratio rates against relative variable-interval response frequencies from the same criterion session(s), shows the extent to which relative responding under the mutually exclusive fixed-ratio schedules was influenced by dose manipulations, as compared to relative responding under the concurrently available variable-interval schedules. Had there been an equal effect on responding in both links, points would have fallen along

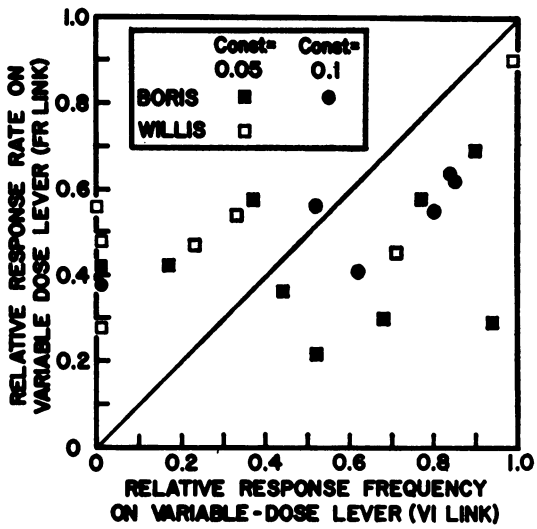

Fig. 6. Relative response rates on the variable-dose lever during the terminal fixed-ratio link plotted against relative response frequencies on this lever during the concurrent variable-interval link. Relative response rate was calculated by dividing the terminal-link fixed-ratio rate on the variable-dose lever by the sum of the fixed-ratio rates on both levers. Relative frequency of responding was calculated by dividing the number of responses on the variable-dose lever during the concurrent variable-interval link by the total number of responses on both levers during this link. Data points are from the criterion sessions (five or one) at each of 22 determinations. For six additional determinations, entry occurred exclusively into one terminal link, so that a meaningful relative rate could not be calculated. If responding in both links had been equally influenced by dose manipulations, points would have fallen along the diagonal line.

the diagonal line. Since most points lie between 0.3 and 0.7 on the ordinate, any effect of magnitude variation on fixed-ratio responding is clearly weaker than its effect on concurrent variable-interval responding. That dose manipulations may have exerted a minor influence on terminal-link fixed-ratio responding is suggested by the finding that a majority of points below 0.5 on the abscissa also lie below 0.5 on the ordinate, while a majority of points above 0.5 on the abscissa lie above 0.5 on the ordinate. Relative fixed-ratio rate, therefore, tended to be somewhat higher on the lever maintaining the higher variable-interval relative response frequency.

Latencies

Average latencies to respond on the lighted center lever at the termination of the timeout period were computed separately for center-lever responses after each of the two doses. For Rico, latencies were unrelated to preceding dose, ranging from 3 to 15 sec. For the other three monkeys, effects of preceding dose were not apparent for doses below 0.4 mg/kg/injection (Boris and Bernadette) or 0.2 mg/kg/injection (Willis); following doses lower than these, average center-lever latencies ranged from 1 to 25 sec. Following the higher doses, average latencies were occasionally longer, *e.g.*, 145 sec after 0.8 mg/kg/injection (Boris); 72 sec after 0.4 mg/kg/injection (Bernadette, one determination); 52 sec after 0.2 mg/kg/injection (Willis).

DISCUSSION

All monkeys in the present experiment consistently preferred the larger of two cocaine doses presented for comparison. Similarly, when different amounts of nutritive reinforcer, as well as different intensities or durations of electrical brain stimulation, have been compared under concurrent scheduling procedures, clear preferences for the larger magnitude have occurred (Brownstein, 1971; Davis *et al.*, 1972; Neuringer, 1967; Walker, Schnelle, and Hurwitz, 1970). All monkeys in the present experiment demonstrated quite close matching between relative response frequency (the measure of preference) and relative drug intake (the measure of relative obtained reinforcement). Similarly, in many concurrent-schedule studies in which different magnitudes of nutritive reinforcer have been compared, matching has occurred (Brownstein, 1971; Catania, 1963*a*; Neuringer, 1967); more generally, for nutritive reinforcers the matching relationship has been found to hold with respect to a number of different parameters of reinforcement evaluated under a variety of concurrent scheduling procedures (*e.g.*, Autor, 1960, 1969; Baum and Rachlin, 1969; Catania, 1963*b*; Chung and Herrnstein, 1967; Herrnstein, 1961; Schwartz, 1969; Ten Eyck, 1970).

In the present experiment, when dose was changed on one lever, all monkeys' changes in preference reflected changes in their absolute response rates on both levers, with rate on the constant lever varying inversely with dose on the variable lever over most of the dose range. Similarly, in concurrent-schedule experiments employing other reinforcers, when magnitude

or frequency of reinforcement has been held constant under one schedule, absolute response rate under this schedule usually has varied inversely with magnitude or frequency of reinforcement available under the other schedule (Catania, 1963*b*; Rachlin and Baum, 1969; Walker *et al.*, 1970); and preference changes have reflected changes in response rates under both schedules when these rates both have been free to vary (Catania, 1963*b*; Pliskoff and Hawkins, 1967; Walker and Hurwitz, 1971). The present data, then, extend the generality of relationships previously found with other, non-drug reinforcers to include intravenously delivered cocaine as the reinforcer.

An outstanding feature of behavior under both procedures was the predominance of exclusive preferences. Of 36 determinations involving unequal doses, 22 resulted in exclusive preferences: either the proportion of responding on one lever was greater than 0.99, the proportion of reinforcements obtained on one lever was 1.00, or both. By contrast, exclusive preferences have not occurred in most other concurrent-schedule studies of variations in reinforcer magnitude, nor have they usually occurred in concurrent-chain studies in which terminal-link reinforcement parameters have been varied. The difference in findings between the present study and these others may relate to the differing extent to which response rates and schedule parameters have promoted an effect of preference on obtained reinforcement.

In other concurrent and concurrent-chain experiments, overall variable-interval rates typically have been relatively high, variable-interval values relatively long, or both. Pliskoff and Hawkins (1967), for example, employing a concurrent-chain procedure, reported rats' overall rates under initial-link concurrent VI 1-min VI 1-min schedules to be between 1 and 2.5 responses per second. Catania (1963*a*) found pigeons' overall rates under concurrent VI 2-min VI 2-min to average about 1.3 responses per second. In such studies, the relative number of reinforcers obtained under each schedule usually has been observed to be close to 0.50.

By comparison, in the present experiment overall rates of all monkeys (except Bernadette) were usually below 0.8 responses per second, often falling much lower. The likelihood that the distribution of responses between the two levers would affect the distribution of reinforcers was increased by these low rates: when responding on the non-preferred manipulandum occurs infrequently with respect to time, reinforcers scheduled for this manipulandum may not be collected for a number of cycles, instead of being collected as soon as they become available. Additionally, the likelihood that preference would influence the distribution of reinforcers was increased by the 1-min average interreinforcement interval scheduled for each lever: at a given response rate, the shorter the average interreinforcement interval, the more probable it becomes that reinforcers scheduled for the preferred manipulandum will be obtained soon after they become available, while reinforcers scheduled for the non-preferred manipulandum will be held across variable-interval periods. Conditions in the present experiment thus favored the monkeys' obtaining unequal numbers of reinforcers on the two levers.

It is reasonable to assume, as Killeen (1972) argued, that once responding has influenced the relative reinforcement obtained, it is this obtained reinforcement, rather than that which was scheduled, that influences subsequent behavior. Preference for the manipulandum on which the larger magnitude is available should then increase. If the relative number of reinforcements obtained on this manipulandum is thereby still further increased, then preference for this manipulandum should once again increase, and so on. Most or all responding and reinforcement might, therefore, eventually occur on one manipulandum, as happened in the present experiment.

Data lending indirect support to these lines of argument have been reported by Fantino, Squires, Delbrück, and Peterson (1972) and Davis, Davison, and Webster (1972). In the Fantino *et al.* experiment, pigeons' responding under equal concurrent variable-interval schedules was reinforced with either 1.5 sec or 6 sec of access to grain (scheduled relative magnitude of reinforcement = 0.80). Schedule values were varied among 600 sec, 60 sec, and 10 sec, all with a COD of 1.5 sec. Under concurrent VI 10-sec VI 10-sec only, preferences for the 6-sec key were close to exclusive by the criteria of the present experiment: relative response frequencies on this key averaged 0.93, and the relative number of reinforcers obtained averaged 0.87.

Conditions created by the concurrent VI 10-sec VI 10-sec schedules employed by Fantino *et al.* may be compared to those engendered by low response rates in the present experiment. Under very small variable-interval values, even at moderately high absolute response rates, relatively infrequent responding on one key will result in that key's reinforcements being held through a number of variable-interval periods. A lowering in the relative number of reinforcers obtained on that key to below 0.50 will result. Additionally, the COD (1.5 sec) employed by these experimenters may have promoted an effect of preference on obtained reinforcement: when the COD is relatively long in comparison to the variable-interval value, the influence of the distribution of responses on the distribution of reinforcers will be more pronounced (Shull and Pliskoff, 1967). Exclusive or near-exclusive preferences thus might have been expected to develop in the Fantino *et al.* experiment.

In the Davis *et al.* study (1972), pigeons' preferences for different intensities or durations of electrical brain stimulation were assessed under concurrent VI 30-sec VI 30-sec schedules. The authors reported that low overall response rates were typical (exact values could not be computed from the data presented). Again, these low rates, coupled with the relatively small variable-interval values employed, should be expected to favor the occurrence of exclusive preferences; at the more extreme magnitude differences, most pigeons did, indeed, show close-to-exclusive responding on the higher-intensity or longer-duration key. Additionally, it appears from the data reported that at these extreme magnitude differences, most or all reinforcers were obtained on the higher-magnitude key. The same circular processes, then, may partially account for the development of exclusive and near-exclusive preferences in this study, the Fantino *et al.* study, and the present one.

In Figure 4, data points from exclusive and near-exclusive preferences are clustered in the lower left-hand and upper right-hand corners of the matching functions. Although at these points relative intake deviates widely from relative dose (relative scheduled reinforcement; compare Columns 11 and 12, Table 1), the data are consistent with the usual matching formulation, which evaluates matching with respect to obtained, rather than scheduled, reinforcement (Herrnstein, 1970; Killeen, 1972; Rachlin, 1971). As Herrnstein (1970) pointed out, however, the matching function has greatest empirical content when the number of responses far exceeds the number of reinforcers, that is, when reinforcement strongly affects responding while responding has little effect on reinforcement. In the present experiment, with exclusive preferences for the highest doses, response-to-reinforcer ratios sometimes fell as low as 3 or 4 to 1, and extreme response distributions generally had a significant influence on relative reinforcement obtained. Thus, the finding of approximate equality between relative response frequencies and relative intake is often somewhat vacuous, and the replication of the matching relationship seen in these data should not be over-emphasized.

Data from other cocaine experiments suggest that most disruption of operant responding occurs immediately after intravenous cocaine injection (Dougherty and Pickens, 1973; Pickens and Thompson, 1968). In the present study, two delays between drug injection and the variable-interval period were imposed: the 5-min timeout, and the latency to respond on the lighted center lever after the timeout. To the extent that these techniques succeeded in averting rate-modifying drug effects on variable-interval responding, the timeout apparently played the stronger role. Among animals, overall rates bore no consistent relationship to dose on the variable-dose lever or to intake, except at the higher doses, while center-lever latencies were also unrelated to the preceding dose except at the higher dose values. Latencies after the higher doses were sometimes longer than after lower doses; nevertheless, overall rates were depressed in sessions in which these doses were evaluated, as maximum hourly intake for each animal was attained. These findings, together with the finding that variable-interval rates usually were considerably lower than in comparable concurrent-schedule studies employing other reinforcers, suggest that the two post-reinforcement delays never entirely prevented response-disrupting drug influences from decreasing overall variable-interval rates. Other observations (Balster and Schuster, 1973) suggest that longer timeouts and/or longer interreinforcement intervals might have had the desired effect. With 15-min timeouts following reinforcement, rhesus monkeys'

response rates under a fixed-interval 9-min limited-hold 3-min schedule of intravenous cocaine presentation were directly related to injection dose over a dose range of 0.0 to 0.4 or 0.8 mg/kg/injection. Therefore, under the schedule parameters selected, the influence of response-disrupting drug effects on rate of drug-reinforced responding was apparently significantly minimized.

In the present study, the degree of preference demonstrated for the larger dose appeared, on inspection, unrelated to hourly drug intake or to overall absolute response rate. Thus, the data might be interpreted as indicating that the relative response frequency measure was not significantly influenced by drug effects that apparently decreased overall responding. However, since there are strong indications that the unusually low response rates observed, coupled with the variable-interval values employed, played a role in the development of exclusive preferences, the eventual effects of the dose manipulations on preference do, in fact, seem partially dependent on the absolute response rates the doses maintained. The present concurrent scheduling procedures cannot, therefore, be said to provide a measure of the reinforcing efficacy of different doses that is clearly impervious to their rate-decreasing effects. That such schedule-dependent and/or rate-dependent modulations of preference development are not unique to cocaine as a reinforcer, but rather, must also be considered when other, non-drug reinforcers are evaluated under concurrent scheduling procedures is evident from the data of Fantino *et al.* (1972) and Davis *et al.* (1972).

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