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CONCURRENT PERFORMANCES:

REINFORCEMENT BY DIFFERENT DOSES OF INTRAVENOUS COCAINE

IN RHESUS MONKEYS

by

Carol Iglauer

A dissertation submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
(Psychology)
in The University of Michigan
1972

Doctoral Committee:

Assistant Professor James H. Woods, Chairman
Assistant Professor David B. Moody
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INTRODUCTION

That the intravenous infusion of cocaine reinforces lever pressing in the rat and the rhesus monkey has been demonstrated in a number of studies (Deneau, Yanagita, and Seevers, 1969; Goldberg, Hoffmeister, Schlichting, and Wuttke, 1971; Pickens and Thompson, 1968; Wilson, Hitomi, and Schuster, 1971). A finding common to these studies has been that over a wide 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 dose-rate relationship over a dose range of 0.25--3.0 mg/kg/injection in rats studied under continuous reinforcement (CRF) or fixed-ratio (FR) schedules. Similarly, response rates of rhesus monkeys 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, monkeys' response rates decreased as dose size increased from 0.05 to 0.2 mg/kg/injection (Goldberg et al., 1971).

Since absolute rate of response has frequently been considered to be a measure of reinforcer efficacy (e.g., Guttman, 1953, 1954; Hutt, 1954), the observed inverse relationship between absolute response rate and cocaine dose size is provocative: It could reflect a decline in reinforcer effectiveness with increased reinforcer magnitude. However, two kinds of considerations suggest that it is premature to interpret absolute rate of response under these single-schedule procedures as being indicative of the reinforcing efficacy of different doses. First, Pickens and Thompson (1968) have demonstrated that non-contingent

intravenous injections of cocaine result in an immediate and complete cessation of fixed-ratio responding maintained by food reinforcement in the rat. The duration of the post-injection pause is directly related to dose size; when responding begins again, it occurs at the usual, fairly constant rate, regardless of the dose injected. The net effect is that overall rate of food-reinforced responding is inversely related to infusion dose. These findings suggest that there is a general, dose-related disruption of operant behavior immediately following an infusion of cocaine, and that decreases in rate of drug-reinforced responding with increases in dose reflect this general disruption. Any changes in reinforcing efficacy, which might also occur with changes in dose and be reflected by changes in rate, would thus be obscured by these response-disrupting effects.

A second kind of consideration is raised by data from experiments employing single-schedule procedures and nutritive reinforcers, for which response-disrupting effects would be expected to be minimal. Although an increasing relationship between magnitude and absolute rate of responding has in some cases been demonstrated (e.g., Guttman, 1953; Stebbins, Mead, and Martin, 1959), frequently, weak effects, transient effects, or no effects of magnitude have been found with this measure (Catania, 1963a; Jenkins and Clayton, 1949; Keesey and Kling, 1961). Such results suggest that these procedures are, in general, of limited usefulness in the investigation of how reinforcer effectiveness varies with reinforcer magnitude.

Contrasting with these results from single-schedule experiments are data obtained with concurrent scheduling procedures. Under these procedures, two equal-valued intermittent schedules, operating independently

and concurrently, program the availability of different magnitudes, whose reinforcing efficacy is indexed in terms of the preference demonstrated between them. Frequently, the magnitudes have been scheduled on separate manipulanda, and preference has been defined as relative responding: the response output on a given manipulandum divided by the sum of the response outputs on both manipulanda (Neuringer, 1967; Pliskoff and Hawkins, 1967). Alternatively, only a single manipulandum has been available, and responses have served simply to change the schedule and stimulus conditions in effect, with the magnitudes available under the two schedules being intermittently presented on a response-independent basis. Preference is then defined as relative time spent in the presence of one of the stimulus conditions (Brownstein, 1971). In both cases the preference measure consistently has been found to increase 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, 1963a; Neuringer, 1967; Pliskoff and Hawkins, 1967; Walker and Hurwitz, 1971).

This demonstrated sensitivity of behavior to variations in reinforcer magnitude made under concurrent scheduling procedures was one important consideration in the choice of strategies for the present experiment, which used a preference measure in evaluating the relative reinforcing efficacy of different doses of intravenously delivered cocaine in rhesus monkeys. Two modifications of simple concurrent variable-interval (VI) schedules were employed; relative response frequency served as the measure of preference. Since this measure can be obtained without reference to absolute response rate when different magnitudes are concurrently available, the procedures appeared,

additionally, to offer a promising tool for minimizing the influence of response-disrupting effects of different doses of cocaine on the assessment of their reinforcing efficacy.

In many, but not all, concurrent-schedule studies in which reinforcer magnitude has been varied, the increasing relationship between relative reinforcement and relative responding or time spent has had the same mathematical form: Relative responding or time spent has equalled (matched) relative reinforcement magnitude (Brownstein, 1971; Catania, 1963a, Neuringer, 1967). The matching relationship has also been demonstrated, under equal concurrent schedules, with respect to relative immediacy of reinforcement (Chung and Herrnstein, 1967), under unequal concurrent variable-interval schedules with respect to relative rate of reinforcement (Baum and Rachlin, 1969; Catania, 1963b; Herrnstein, 1961), and under concurrent-chain schedules with respect to a number of different terminal-link parameters (e.g., Autor, 1960, 1969; Killeen, 1968; Schwartz, 1969; Ten Eyck, 1970). In most of these studies, nutritive reinforcers have been employed; and without exception, those studies in which matching to relative magnitude has been demonstrated in individual organisms have manipulated magnitude by varying duration of access to a nutritive reinforcer. A further question of interest, then, in the present experiment, was whether the matching relationship might be found when intravenously delivered cocaine served as the reinforcer, and magnitude was manipulated by varying dose size.

While in this study the relative response frequency measure received primary attention, absolute response rates were also examined. Concurrent-schedule experiments employing nutritive reinforcers have demonstrated that when magnitude or frequency of reinforcement under one schedule is held constant, absolute rate of response under this

schedule varies inversely with the magnitude or frequency of reinforcement available under the other schedule (Catania, 1963b; Rachlin and Baum, 1969; Walker, Schnelle, and Hurwitz, 1970). These data strongly suggest that changes in relative response frequencies maintained by one schedule with changes in the parameters of reinforcement available under this schedule reflect orderly variations in the absolute rates of response maintained by both schedules (Walker and Hurwitz, 1971). Cocaine dose was held constant on one lever in the present study; thus, another question of interest was how, as dose was varied on one lever, absolute rates on both levers would change. Additionally, since in single-schedule cocaine self-administration experiments decreases in response rate with increases in dose have been accompanied by some increase in average hourly drug intake (Goldberg et al., 1971; Wilson et al., 1971; Woods and Schuster, 1968), under the present procedures changes in intake as dose on one lever was increased and possible concomitant changes in overall rate were also examined.

METHOD

Subjects

One female and three male rhesus monkeys (Macaca mulatta) weighing between 4 and 7 kg served in daily experimental sessions. One, Willis, had had several months' experience in a preliminary dose-choice study with intravenous cocaine. Another, Bernadette, previously had been reinforced with different doses of cocaine under a fixed-ratio schedule. The other two, Boris and Rico, were experimentally naive. All were individually housed, had unlimited access to water, and were fed 15 Purina monkey chows twice daily. This diet was supplemented with fresh fruit at least twice weekly.

Surgical preparation

Briefly, 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 (Ronthor Reiss Corporation; outer diameter = 0.24 cm, inner diameter = 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, Yanagita, and Seevers, 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). Briefly, 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 16.2 cm between them. Centered 4.5 cm above each side lever was a circular aperture 3 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 3 cm in diameter located 4.5 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.

Drugs and dosages

Cocaine hydrochloride was diluted in 0.9% saline to the desired concentration; all concentrations were calculated on the basis of the salt. Drug dosage, for a given monkey, was manipulated by varying the volume of a constant-concentration solution infused 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 infusion.

Procedure

1. 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 previous experimental history. A schematic diagram of these terminal schedule conditions is shown for this procedure in Figure 1. A cycle

Figure 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 infusion 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.

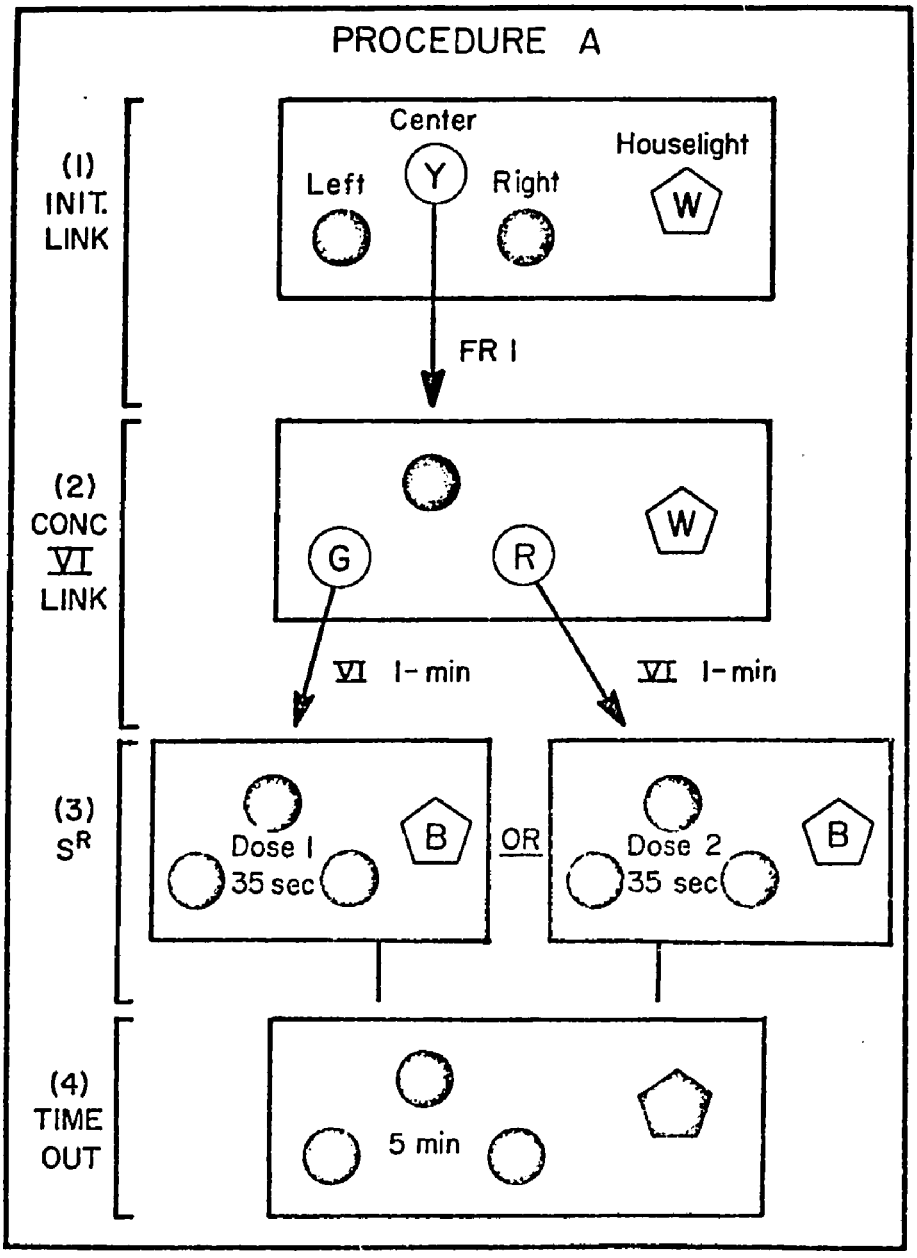

PROCEDURE A
(1) INIT. LINK
Center
Houselight
Left
Y
Right
W
FR 1
(2) CONC VI LINK
G
R
W
VI 1-min
VI 1-min
(3) S^R
Dose 1
35 sec
B
OR
Dose 2
35 sec
B
(4) TIME OUT
5 min

Figure 1

began with the 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, programmed the availability of two drug doses. The average interreinforcement interval programmed 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, and so might continue to be available during the variable-interval link of a number of cycles if responding were occurring primarily on the other lever. An individual tape timer was inactivated when it had scheduled a reinforcement for a lever until 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 initiation of the variable-interval link in the following cycle.

During the concurrent variable-interval component, a changeover delay (COD; Herrnstein, 1961) of 1.5 sec was employed. The first response on one side lever after a response on the other, and all subsequent responses within 1.5 sec, were ineligible for reinforcement. The COD minimized the possibility that responding on one side lever would come under the control of the dose scheduled for the other lever.

A reinforced response on one of the side levers extinguished both side-lever lights and turned on the appropriate infusion pump and a

blue houselight for a 35-sec period (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. (For Table 1, see p. 26.) 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. Upon completion of the sequence, 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. Within this broad strategy deviations were occasionally made 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 continued to occur and reinforcement continued to be obtained on both levers, a stability criterion was used. Behavior

was considered to be stable when a minimum of 15 sessions had been run under a given dose comparison, when for 5 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 initial exposure to any comparison, a monkey's relative frequency of responding in a session exceeded 0.99 on one lever, and/or he obtained all reinforcements on one lever (i.e., he 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 following session.

When such an exclusive preference developed for the constant-dose lever, its persistence frequently necessitated forcing an animal's exposure to the comparison dose on the variable lever after this dose had been changed. This was accomplished by preventing the variable-interval timer for the constant-dose lever from scheduling any reinforcers for a few cycles, so that in each of these cycles a monkey remained in the concurrent variable-interval link until he finally obtained the dose scheduled for the variable lever.

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, on the other hand, data were drawn only from the single terminal session which 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.

II. 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 variable-interval 1-min schedules did not program 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 the light over that lever (i.e., green if entry was to the left-lever terminal link, red if entry was to 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 a FR 5 (Boris) or a FR 15 (Willis) requirement on the lighted lever resulted in an infusion of the dose available on that lever (Condition 4, Figure 2). Stimulus conditions during infusion were identical with those in Procedure A.

The terminal-link fixed-ratio schedules for the two levers were mutually exclusive. Since retractable levers were not available to physically restrict terminal-link responding to the lighted lever,

Figure 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 variable-interval 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 in Procedure A.

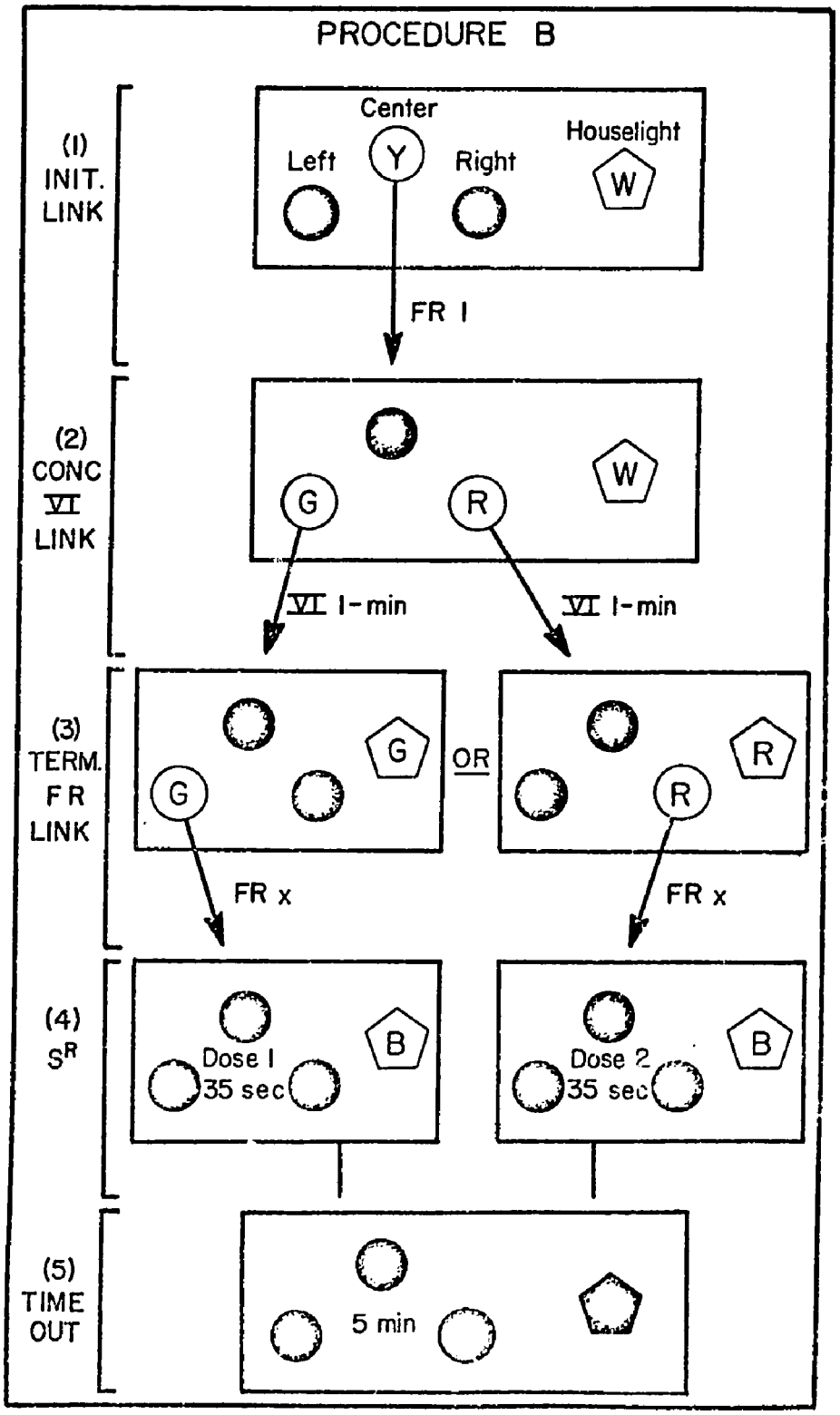

PROCEDURE B
(1) INIT. LINK
Center
Left
Y
Right
Houselight
W
FR 1
(2) CONC VI LINK
G
R
W
VI 1-min
VI 1-min
(3) TERM. FR LINK
G
G
OR
R
R
FR x
FR x
(4) S^R
Dose 1
35 sec
B
Dose 2
35 sec
B
(5) TIME OUT
5 min

Figure 2

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. Following initial training under these contingencies, during the terminal fixed-ratio links of most sessions both animals responded exclusively on the lighted lever.

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 made prior to his death. 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 used with Procedure A.

Analysis of data. The method followed for summarizing results was also the same as that used in 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, while 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

Figure 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. Closed circles: determinations in first sequence; open circles: determinations in second sequence. With repeated determinations in a sequence, only the first is joined to the line.

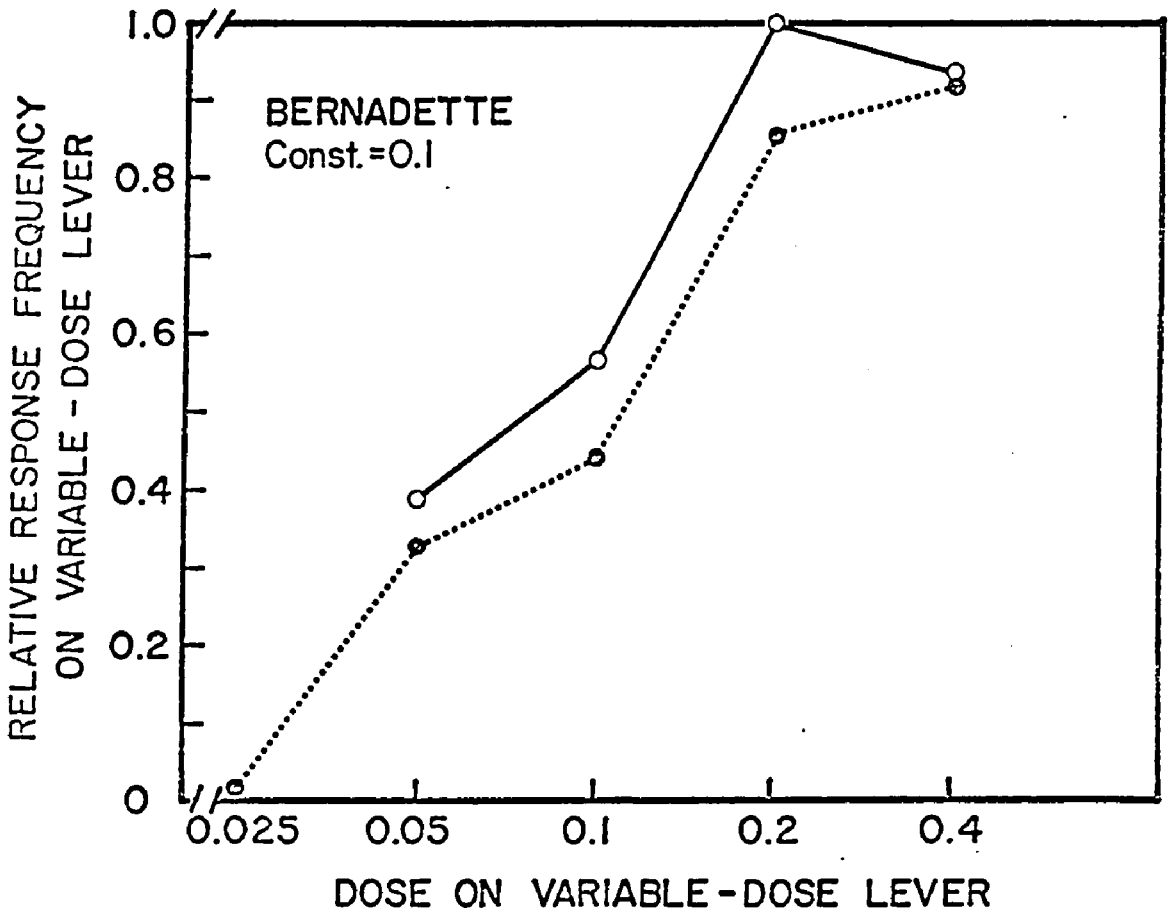

BERNADETTE
Const.=0.1
RELATIVE RESPONSE FREQUENCY ON VARIABLE-DOSE LEVER
1.0
0.8
0.6
0.4
0.2
0
0.025
0.05
0.1
0.2
0.4
DOSE ON VARIABLE-DOSE LEVER

Figure 3a

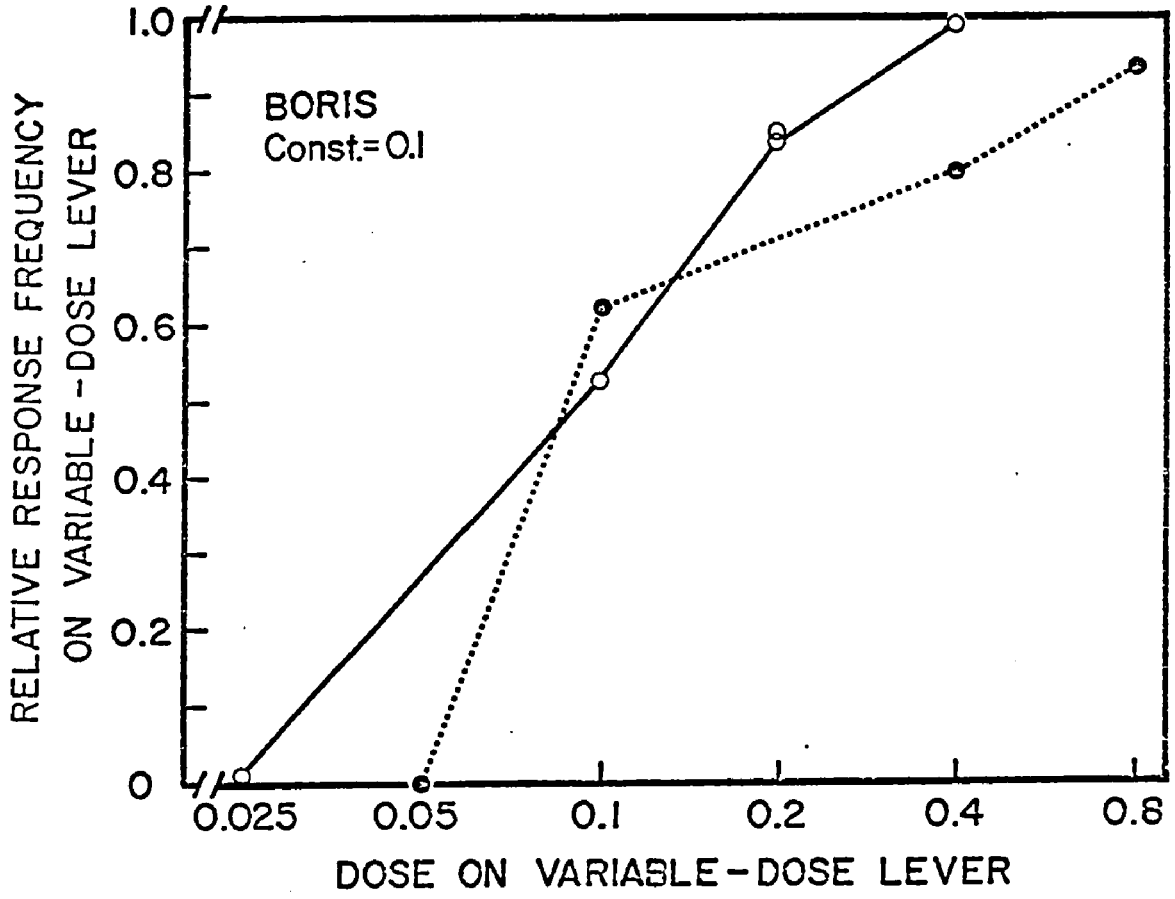

BORIS
Const.=0.1
RELATIVE RESPONSE FREQUENCY ON VARIABLE-DOSE LEVER
1.0
0.8
0.6
0.4
0.2
0
0.025
0.05
0.1
0.2
0.4
0.8
DOSE ON VARIABLE-DOSE LEVER

Figure 3b

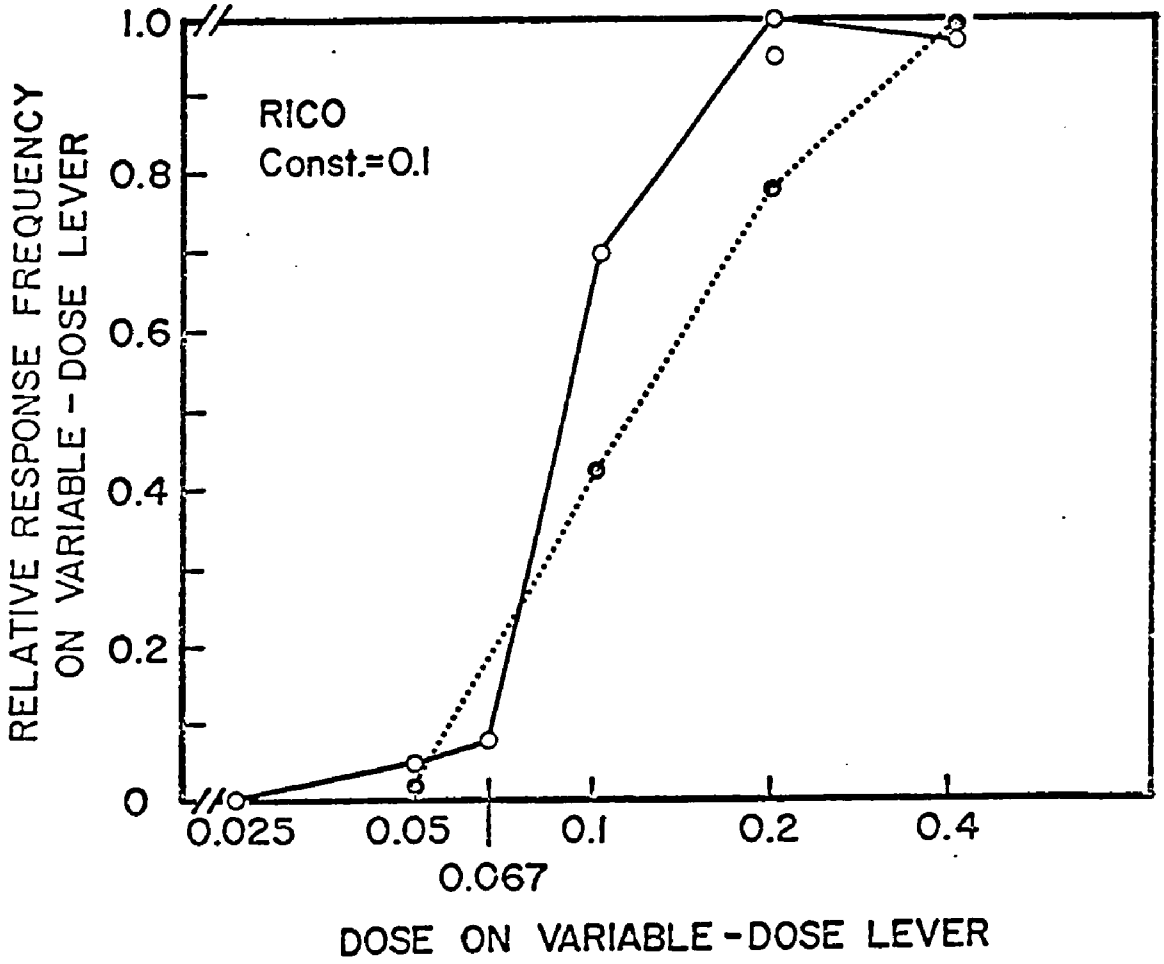

RICO
Const.=0.1
RELATIVE RESPONSE FREQUENCY ON VARIABLE - DOSE LEVER
1.0
0.8
0.6
0.4
0.2
0
0.025
0.05
0.067
0.1
0.2
0.4
DOSE ON VARIABLE - DOSE LEVER

Figure 3c

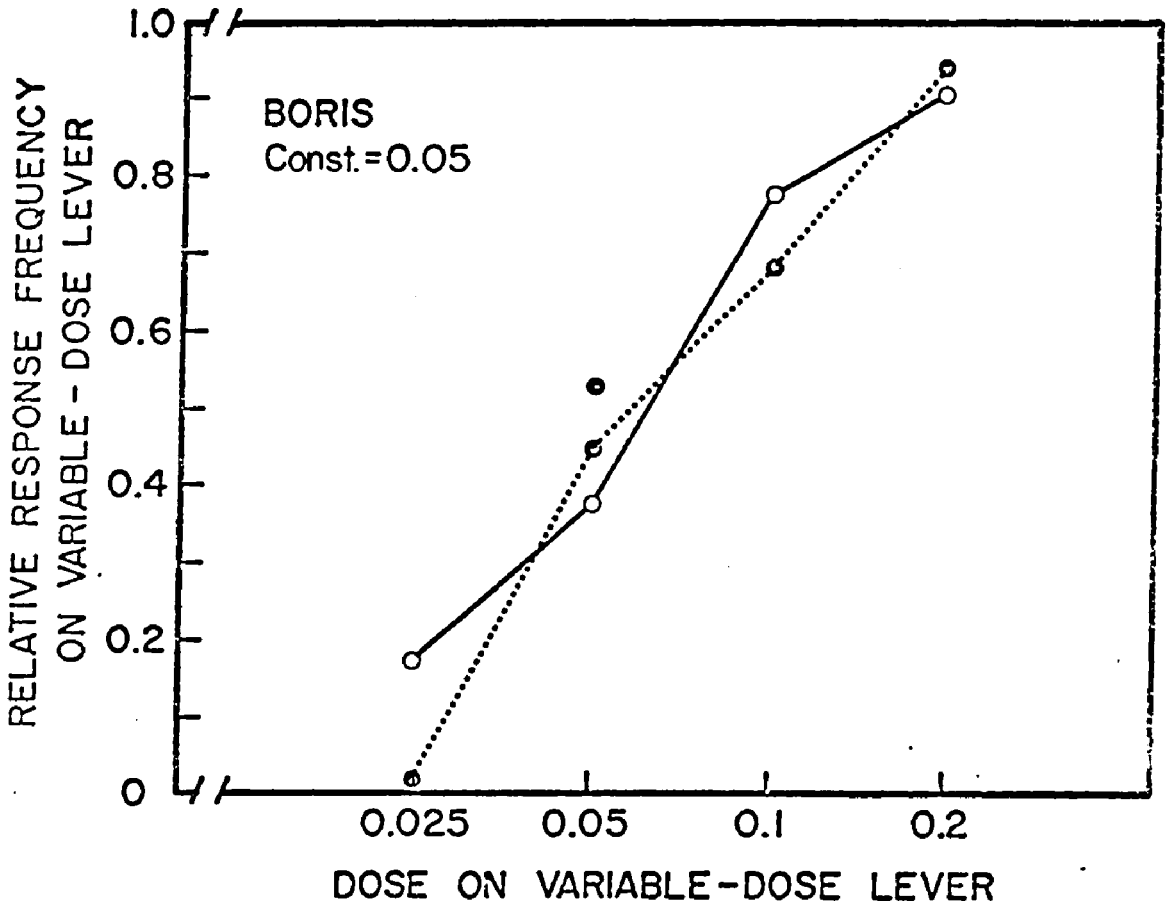

BORIS
Const.=0.05
RELATIVE RESPONSE FREQUENCY ON VARIABLE-DOSE LEVER
1.0
0.8
0.6
0.4
0.2
0
0.025
0.05
0.1
0.2
DOSE ON VARIABLE-DOSE LEVER

Figure 3d

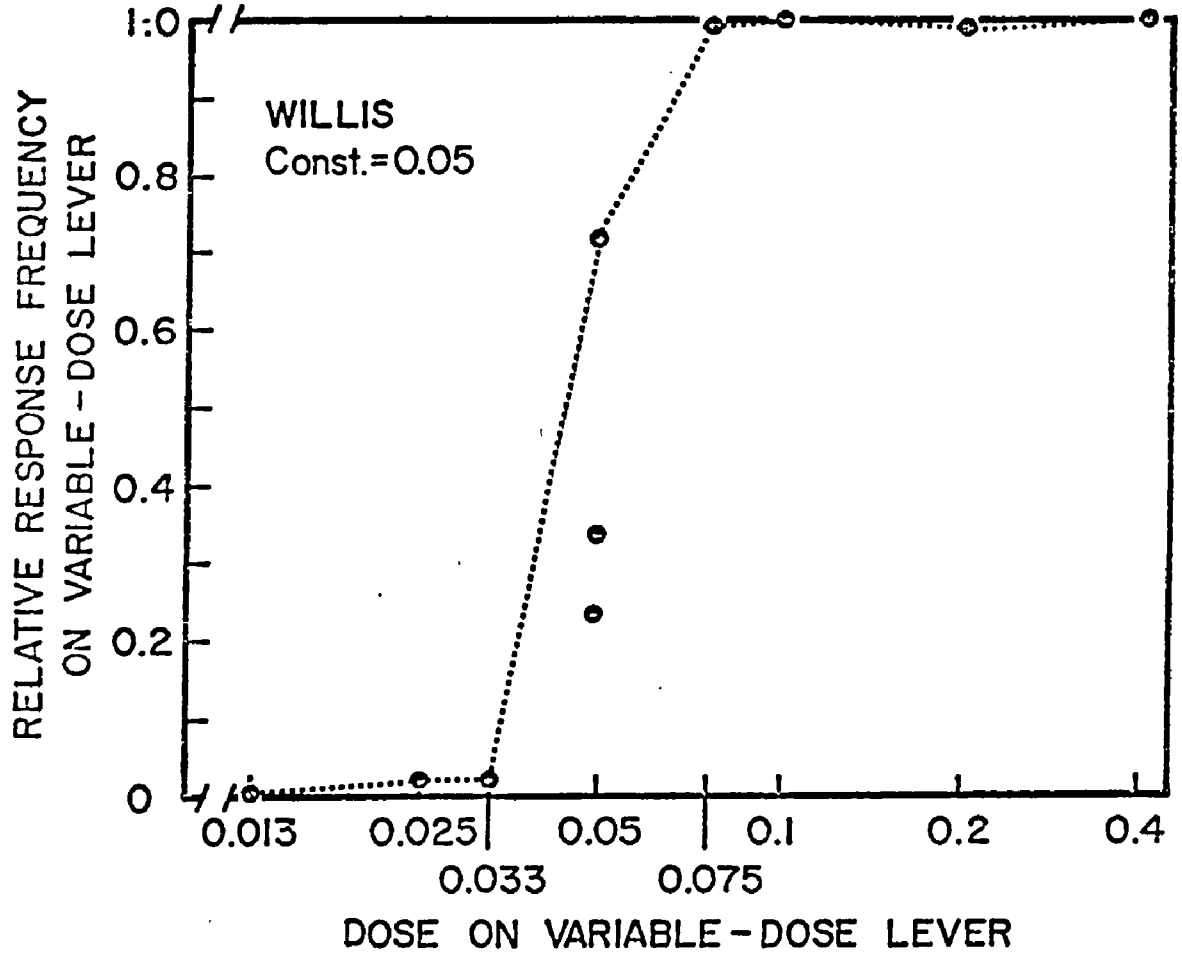

1:0
0.8
0.6
0.4
0.2
0
WILLIS
Const.=0.05
RELATIVE RESPONSE FREQUENCY
ON VARIABLE-DOSE LEVER
0.013
0.025
0.033
0.05
0.075
0.1
0.2
0.4
DOSE ON VARIABLE-DOSE LEVER

Figure 3e

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--10 and Column 12 were drawn: 5 when a stability criterion was attained; 1 when preference was exclusive. Column 13 gives the absolute values of the deviations of relative response frequency (Column 9) from relative intake (Column 12).

TABLE 1

Monkey (1)	Dose (mg/kg/inj) Var. (2)	Dose (mg/kg/inj) Const. (3)	Const.-Dose Lever (4)	No. of Sess. (5)	No. Crit. Sess. (6)
BERNADETTE	0.1	0.1	R (1)	51	5
	0.4	0.1	R (1)	21	1
	0.05	0.1	R (1)	27	5
	0.2	0.1	R (1)	24	5
	0.025	0.1	R (1)	17	1
	0.1	0.1	L (2)	26	5
	0.05	0.1	L (2)	32	5
	0.4	0.1	L (2)	9	1
	0.2	0.1	L (2)	20	1
RICO	0.1	0.1	R (1)	18	5
	0.2	0.1	R (1)	32	5
	0.05	0.1	R (1)	21	1
	0.4	0.1	R (1)	7	1
	0.1	0.1	L (2)	21	5
	0.05	0.1	L (2)	22	5
	0.2	0.1	L (2)	11	1
	0.067	0.1	L (2)	40	5
	0.2	0.1	L (2)	9	1
	0.025	0.1	L (2)	9	1
	0.4	0.1	L (2)	5	1

TABLE 1--Continued

Abs. Resp. Rates (resp/sec)		Relative with Respect to Var.-Dose Lever				Abs. Deviat. from Matching (|12-9|) (13)
Var.-Dose Lever (7)	Const.-Dose Lever (8)	Resp. Freq. (9)	No. Rfts. (10)	Dose (11)	Intake (12)	
0.65	0.80	0.45	0.47	0.50	0.47	0.02
0.45	0.04	0.92	1.00	0.80	1.00	0.08
0.48	0.97	0.33	0.44	0.33	0.28	0.05
1.82	0.30	0.86	0.85	0.67	0.92	0.06
0.02	1.81	0.01	0.10	0.20	0.03	0.02
0.88	0.67	0.57	0.49	0.50	0.49	0.08
0.59	0.92	0.39	0.48	0.33	0.31	0.08
0.29	0.02	0.93	1.00	0.80	1.00	0.07
0.78	0.00	1.00	1.00	0.67	1.00	0.00
0.24	0.33	0.42	0.49	0.50	0.49	0.07
0.65	0.19	0.78	0.59	0.67	0.74	0.04
0.00	0.36	0.01	0.00	0.33	0.00	0.01
0.39	0.01	0.99	1.00	0.80	1.00	0.01
0.25	0.11	0.69	0.59	0.50	0.59	0.10
0.02	0.51	0.05	0.12	0.33	0.06	0.01
0.67	0.00	1.00	1.00	0.67	1.00	0.00
0.02	0.19	0.07	0.12	0.40	0.08	0.01
0.11	0.01	0.95	1.00	0.67	1.00	0.05
0.00	0.41	0.00	0.00	0.20	0.00	0.00
0.26	0.01	0.97	1.00	0.80	1.00	0.03

TABLE 1--Continued

Monkey (1)	Dose (mg/kg/inj) Var. (2)	Dose (mg/kg/inj) Const. (3)	Const.-Dose Lever (4)	No. of Sess. (5)	No. Crit. Sess. (6)
BORIS	0.05	0.05	R (1)	39	5
	0.2	0.05	R (1)	31	5
	0.1	0.05	R (1)	36	5
	0.05	0.05	R (1)	15	5
	0.025	0.05	R (1)	12	1
	0.1	0.1	R (1)	20	5
	0.4	0.1	R (1)	29	5
	0.05	0.1	R (1)	15	1
	0.8	0.1	R (1)	28	1
	0.2	0.1	L (2)	34	5
	0.025	0.1	L (2)	11	1
	0.4	0.1	L (2)	14	1
	0.2	0.1	L (2)	31	5
	0.1	0.1	L (2)	23	5
	0.05	0.05	L (2)	18	5
	0.2	0.05	L (2)	17	5
	0.025	0.05	L (2)	15	5
	0.1	0.05	L (2)	16	5
WILLIS	0.05	0.05	L (1)	55	5
	0.013	0.05	L (1)	8	1
	0.2	0.05	L (1)	27	1
	0.05	0.05	L (1)	44	5
	0.1	0.05	L (1)	8	1
	0.025	0.05	L (1)	11	1
	0.075	0.05	L (1)	22	1
	0.033	0.05	L (1)	15	1
	0.4	0.05	L (1)	20	1
	0.05	0.05	L (1)	20	5

TABLE 1--Continued

Abs. Resp. Rates (resp/sec)		Relative with Respect to Var.-Dose Lever				Abs. Deviat. from Matching (|12-9|) (13)
Var.-Dose Lever (7)	Const.-Dose Lever (8)	Resp. Freq. (9)	No. Rfts. (10)	Dose (11)	Intake (12)	
0.21	0.28	0.44	0.48	0.50	0.48	0.04
0.28	0.02	0.94	0.75	0.80	0.92	0.02
0.25	0.12	0.68	0.55	0.67	0.71	0.03
0.16	0.16	0.52	0.51	0.50	0.51	0.01
0.00	0.18	0.01	0.03	0.33	0.02	0.01
0.36	0.22	0.62	0.51	0.50	0.51	0.11
0.24	0.06	0.80	0.62	0.80	0.87	0.07
0.00	0.78	0.00	0.00	0.33	0.00	0.00
0.04	0.00	0.93	1.00	0.89	1.00	0.07
0.52	0.10	0.84	0.66	0.67	0.79	0.05
0.01	0.86	0.01	0.10	0.20	0.03	0.02
0.05	0.00	0.99	1.00	0.80	1.00	0.01
0.16	0.03	0.85	0.69	0.67	0.81	0.04
0.27	0.25	0.52	0.53	0.50	0.53	0.01
0.24	0.40	0.37	0.48	0.50	0.48	0.11
0.10	0.01	0.90	0.86	0.80	0.96	0.06
0.13	0.65	0.17	0.44	0.33	0.28	0.11
0.67	0.20	0.77	0.57	0.67	0.73	0.04
0.25	0.10	0.71	0.63	0.50	0.63	0.08
0.00	0.54	0.00	0.07	0.21	0.02	0.02
0.11	0.00	0.99	1.00	0.80	1.00	0.01
0.22	0.44	0.33	0.47	0.50	0.47	0.14
0.20	0.00	1.00	1.00	0.67	1.00	0.00
0.00	0.57	0.01	0.03	0.33	0.02	0.01
0.38	0.00	0.99	0.90	0.60	0.93	0.06
0.01	0.77	0.01	0.13	0.40	0.09	0.08
0.01	0.00	1.00	1.00	0.89	1.00	0.00
0.21	0.70	0.23	0.47	0.50	0.47	0.24

relationship is particularly clearly illustrated in Figure 3d by Boris's data when 0.05 mg/kg/injection served as the constant dose, and by Bernadette's data (Figure 3a) 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 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 his relative response frequency versus dose function is essentially flat between all doses on the same side of 0.05 (Figure 3e). 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 determination, 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. This between-sequence variability contributes to the difficulty in ordering the doses in terms of the relative response frequencies which they maintained.

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 this lever by the dose (mg/kg/injection) 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 9 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), except under equal-dose conditions.

Figure 4 plots relative response frequency on the variable-dose lever against relative drug intake obtained on this lever, for each monkey. Most points on the individual graphs quite closely approximate the diagonal line, which represents the locus of perfect matching. Willis, as a result of his unaccountably strong lever preferences under equal-dose conditions, was the monkey for whom absolute deviations of relative response frequency from relative intake were widest, at 0.24 and 0.14 (Column 13, Table 1). Still, across all determinations, he showed an average absolute deviation from matching of only 0.06.

Figure 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. Closed circles: determinations at a constant dose of 0.1 mg/kg/injection. Closed squares: determinations at a constant dose of 0.05 mg/kg/injection.

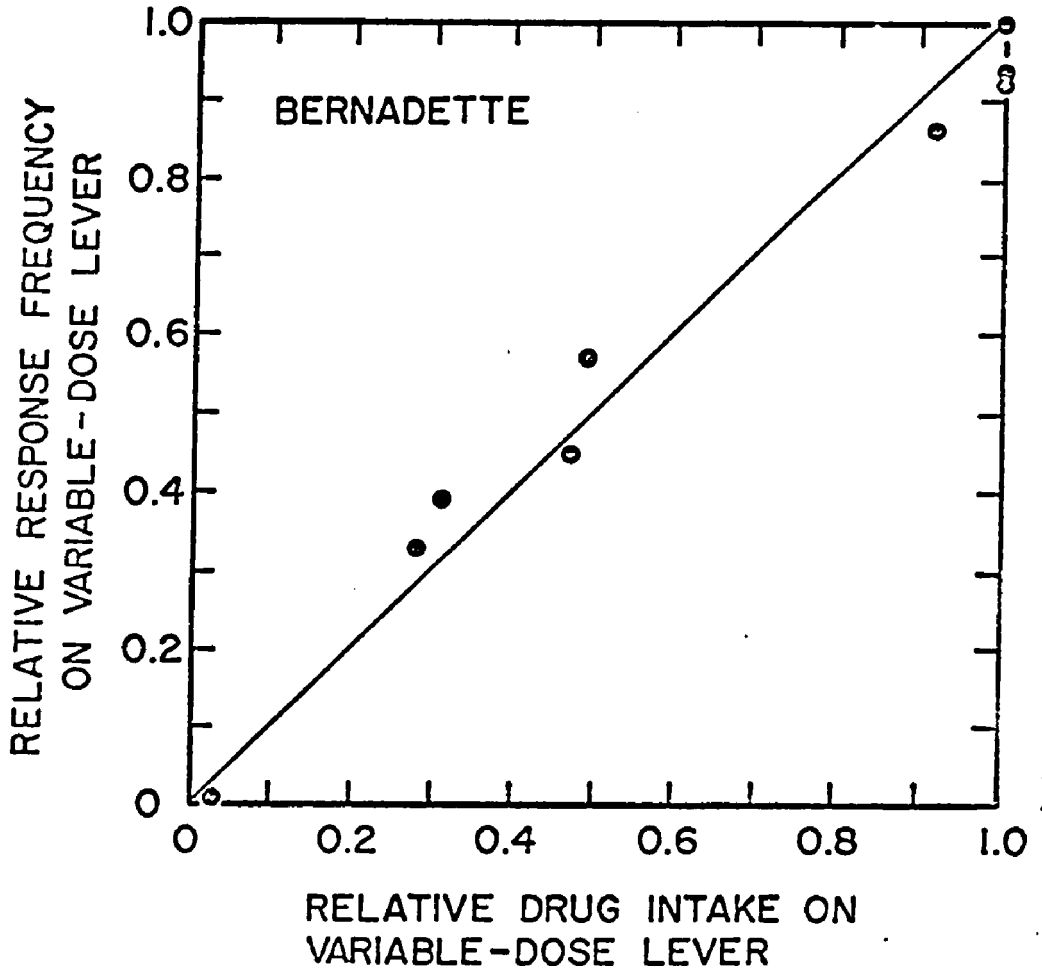

BERNADETTE
RELATIVE RESPONSE FREQUENCY ON VARIABLE-DOSE LEVER
RELATIVE DRUG INTAKE ON VARIABLE-DOSE LEVER
0
0.2
0.4
0.6
0.8
1.0

Figure 4a

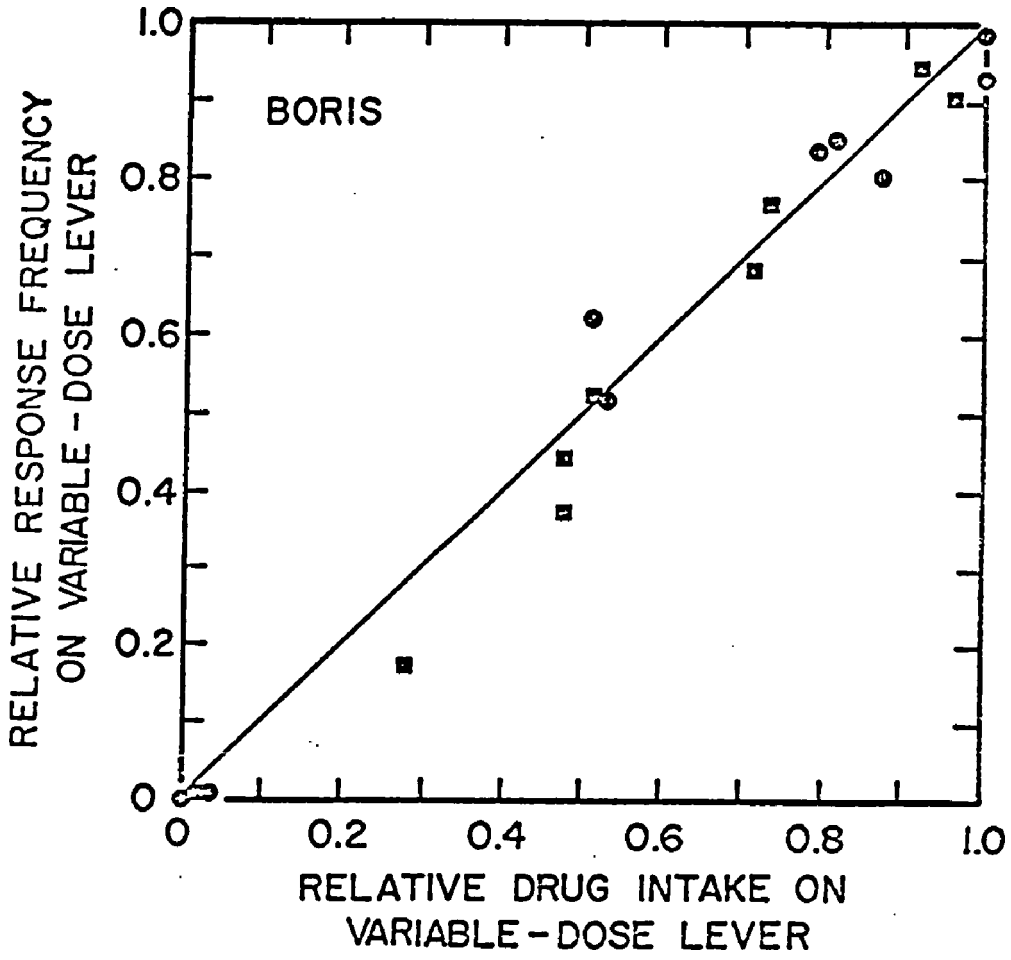

BORIS
RELATIVE RESPONSE FREQUENCY ON VARIABLE-DOSE LEVER
RELATIVE DRUG INTAKE ON VARIABLE-DOSE LEVER
0
0.2
0.4
0.6
0.8
1.0

Figure 4b

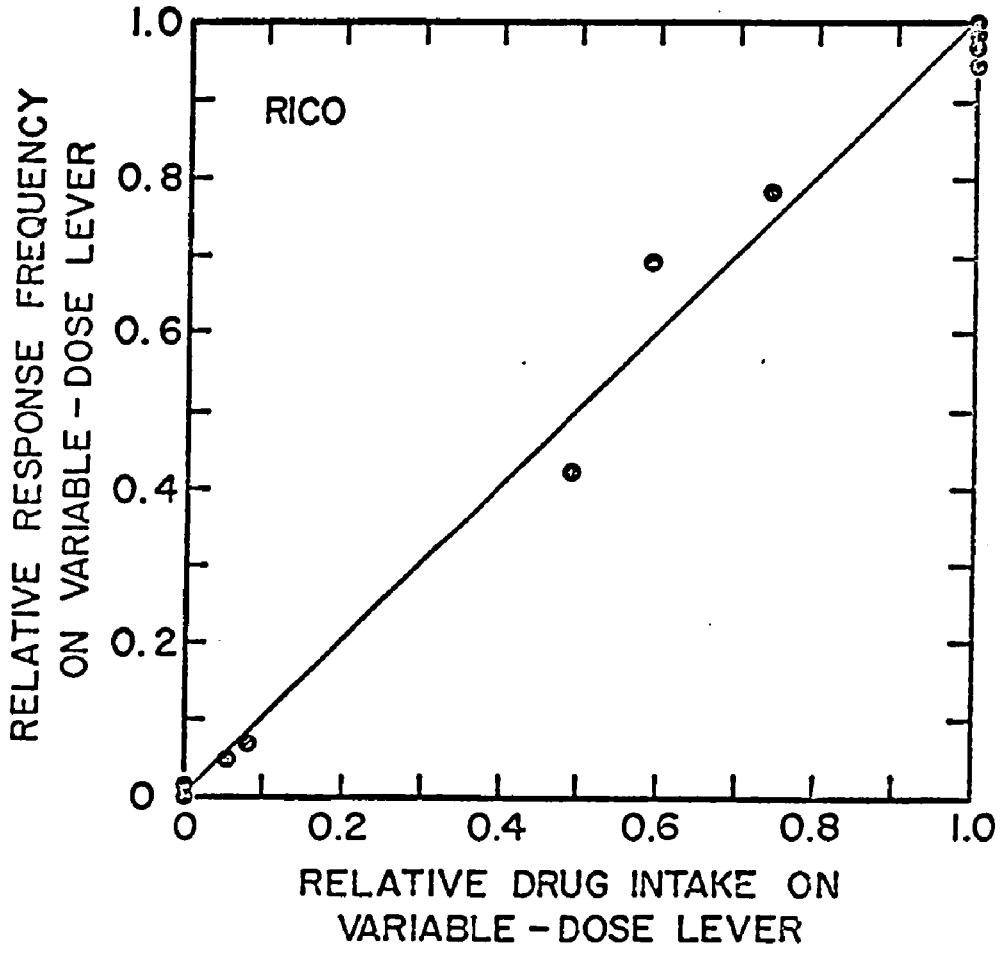

RICO
RELATIVE RESPONSE FREQUENCY ON VARIABLE-DOSE LEVER
RELATIVE DRUG INTAKE ON VARIABLE-DOSE LEVER
0
0.2
0.4
0.6
0.8
1.0

Figure 4c

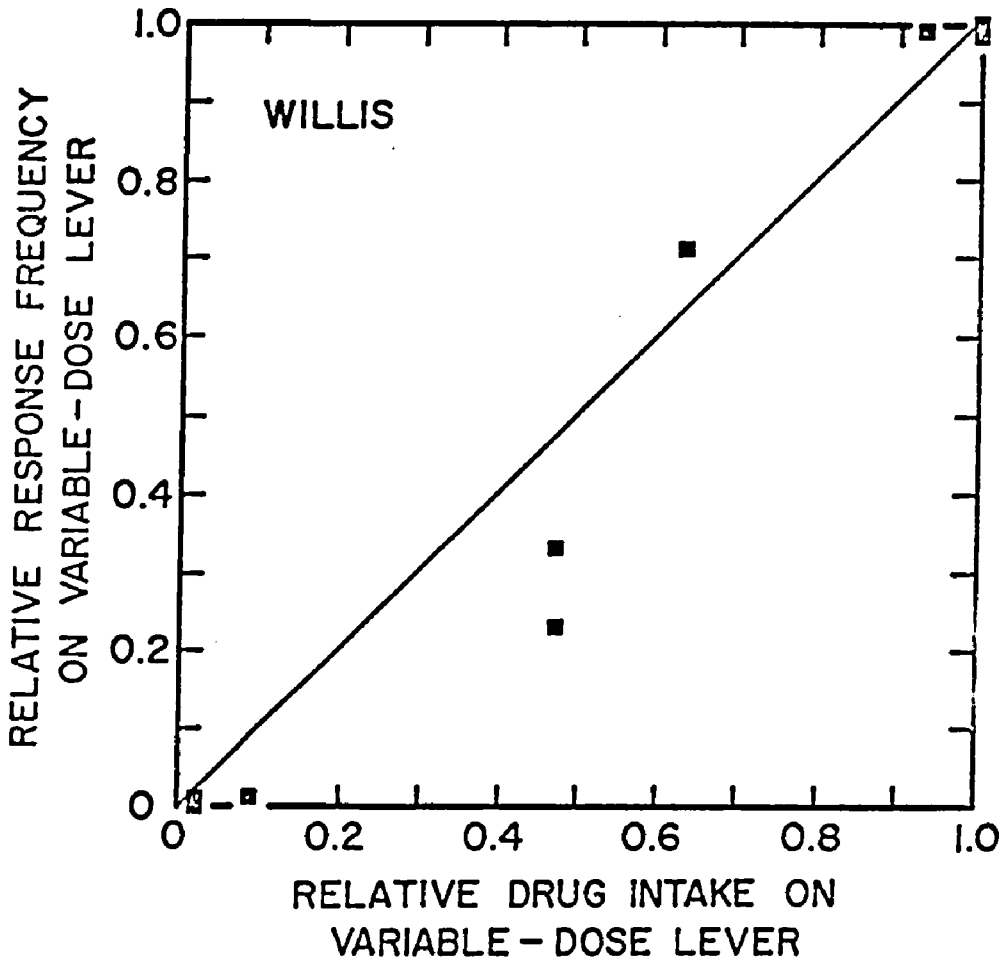

WILLIS
RELATIVE RESPONSE FREQUENCY ON VARIABLE-DOSE LEVER
RELATIVE DRUG INTAKE ON VARIABLE-DOSE LEVER
0
0.2
0.4
0.6
0.8
1.0

Figure 4d

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, which the relative response frequencies reflect, are presented in Columns 7 and 8 of Table 1, and in the lower portions of the graphs in Figure 5 are plotted for each monkey as a function of dose on the variable lever. Rate changes for all monkeys followed the same rough pattern under both constant-dose conditions. Response rate on the constant-dose lever, after sometimes increasing and sometimes decreasing as the dose available on the variable lever was increased to 0.05 mg/kg/injection, then decreased monotonically with further increases in the comparison dose beyond 0.05. Absolute rate on the variable-dose lever first increased with the dose available on this lever, and then declined at the highest dose(s). These data clearly indicate that changes in relative response frequency on one lever as dose was varied on this lever reflected changes in the absolute rates of responding on both levers.

The upper portions of the graphs in Figure 5 present overall response rates in the concurrent variable-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 the variable lever. For any dose comparison the range of overall rates which a monkey exhibited may be obtained from the lower portion of his graph, since the overall rate

Figure 5. Absolute variable-interval response rates (responses/sec) 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 response rates on the constant- and variable-dose levers; data are from the criterion sessions (five or one) at each determination. Closed circles: responses/sec on constant-dose lever, first sequence of determinations. Closed squares: responses/sec on variable-dose lever, first sequence of determinations. Open circles: responses/sec on constant-dose lever, second sequence of determinations. Open squares: responses/sec on variable-dose lever, second sequence of determinations. 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. Triangles: overall responses/sec; stars: hourly drug intake. Bernadette's rate scales in both portions of her graph differ from those of the other monkeys, while her intake scale is the same.

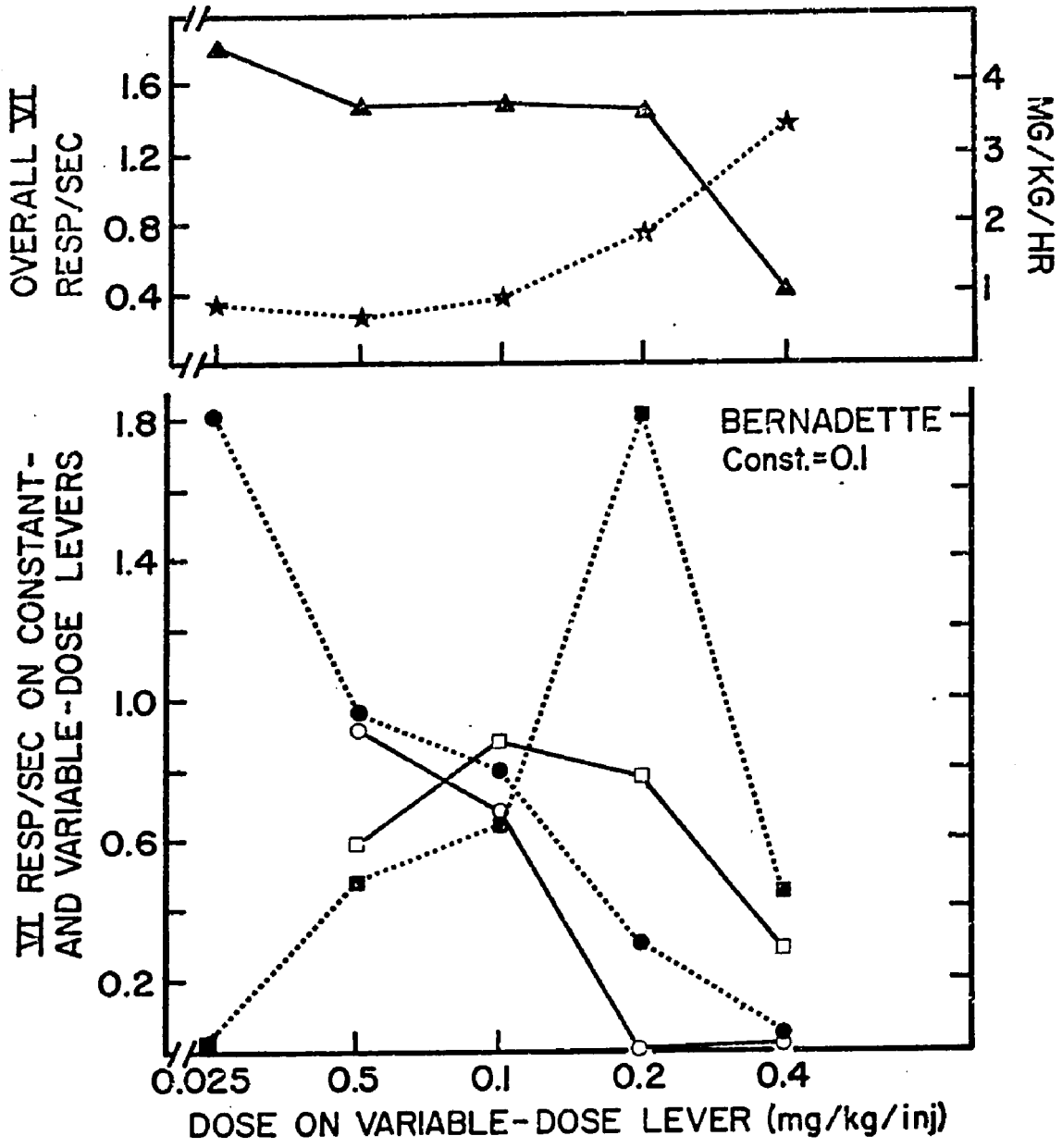

OVERALL VI RESP/SEC
1.6
1.2
0.8
0.4
4
3
2
1
MG/KG/HR
VI RESP/SEC ON CONSTANT- AND VARIABLE-DOSE LEVERS
1.8
1.4
1.0
0.6
0.2
BERNADETTE
Const.=0.1
0.025
0.5
0.1
0.2
0.4
DOSE ON VARIABLE-DOSE LEVER (mg/kg/inj)

Figure 5a

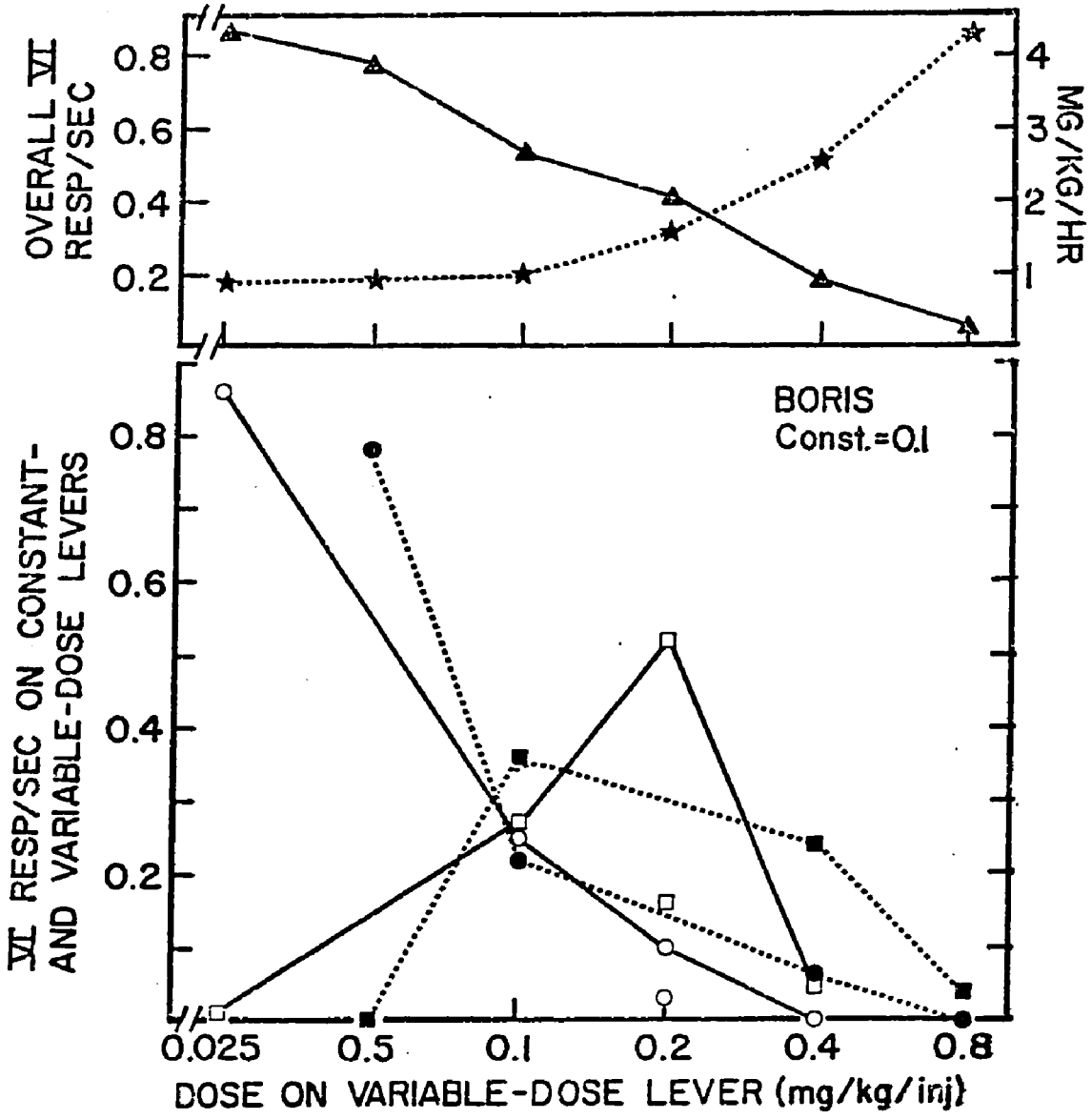

OVERALL VI RESP/SEC
0.8
0.6
0.4
0.2
4
3
2
1
MG/KG/HR
BORIS
Const.=0.1
VI RESP/SEC ON CONSTANT- AND VARIABLE-DOSE LEVERS
0.8
0.6
0.4
0.2
0.025
0.5
0.1
0.2
0.4
0.8
DOSE ON VARIABLE-DOSE LEVER (mg/kg/inj)

Figure 5b

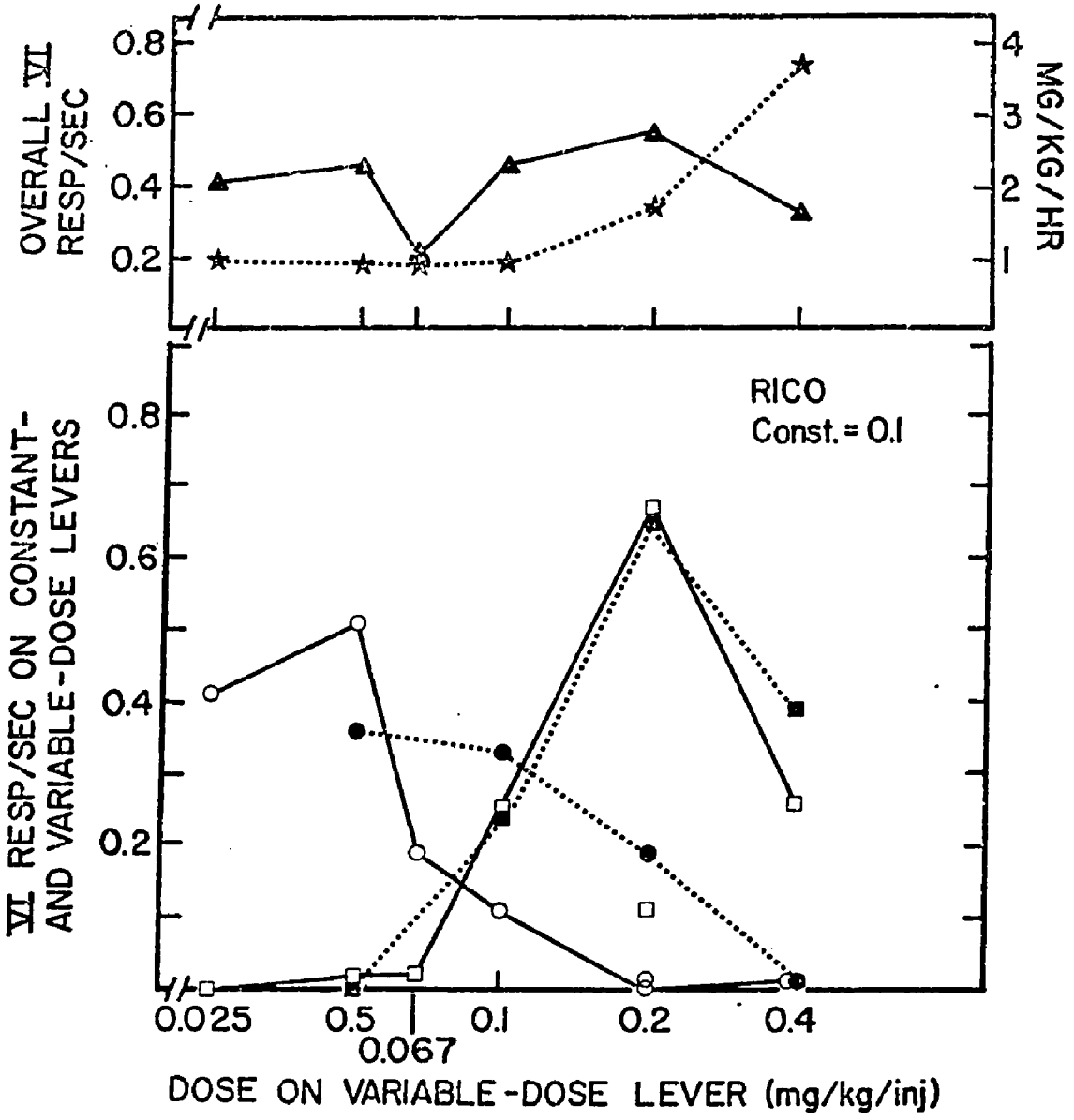

OVERALL VI RESP/SEC
MG/KG/HR
RICO
Const. = 0.1
VI RESP/SEC ON CONSTANT- AND VARIABLE-DOSE LEVERS
0.025
0.5
0.067
0.1
0.2
0.4
DOSE ON VARIABLE-DOSE LEVER (mg/kg/inj)

Figure 5c

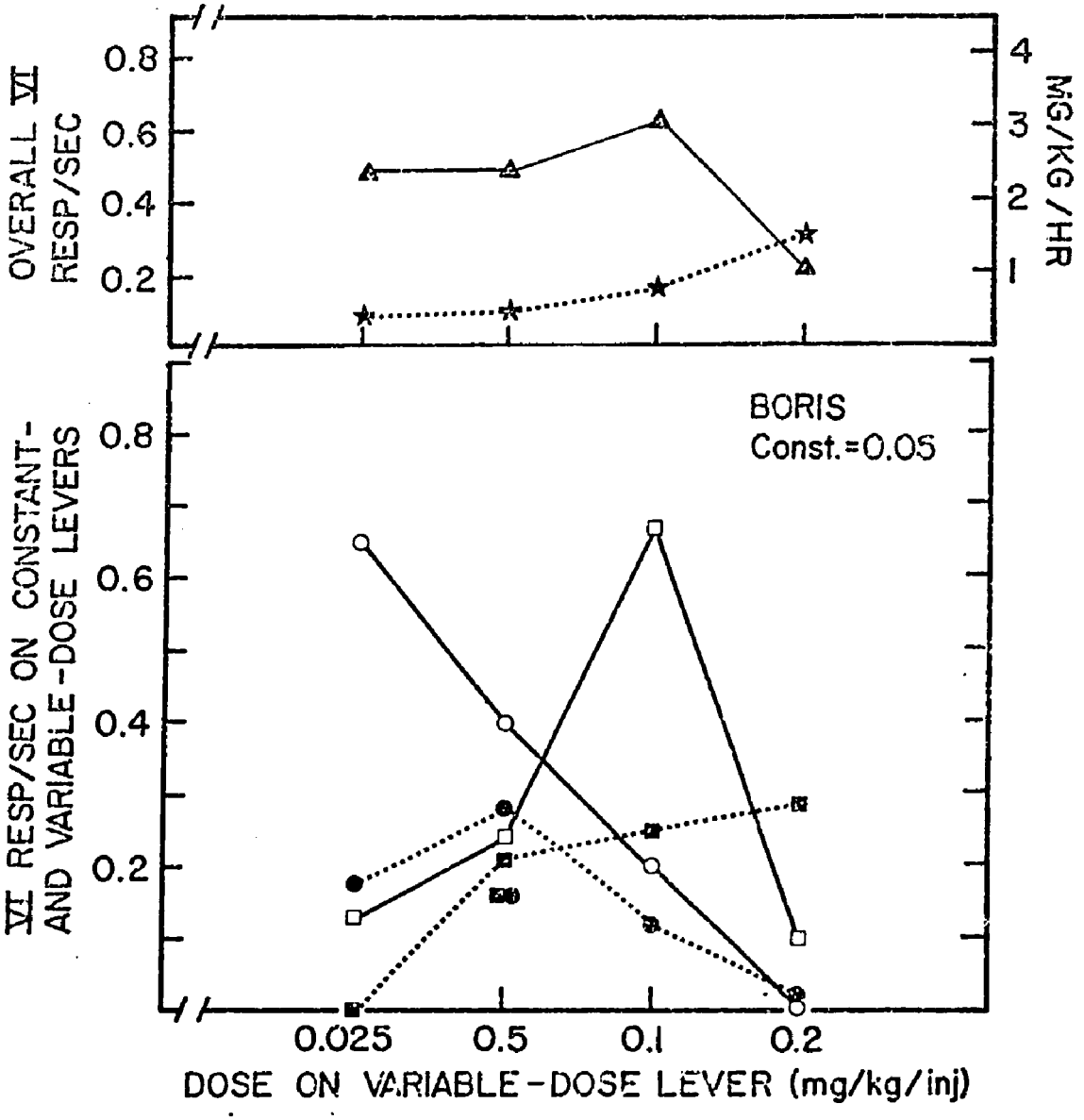

OVERALL VI RESP/SEC
0.8
0.6
0.4
0.2
4
3
2
1
MG/KG/HR
VI RESP/SEC ON CONSTANT- AND VARIABLE-DOSE LEVERS
BORIS
Const.=0.05
0.025
0.5
0.1
0.2
DOSE ON VARIABLE-DOSE LEVER (mg/kg/inj)

Figure 5d

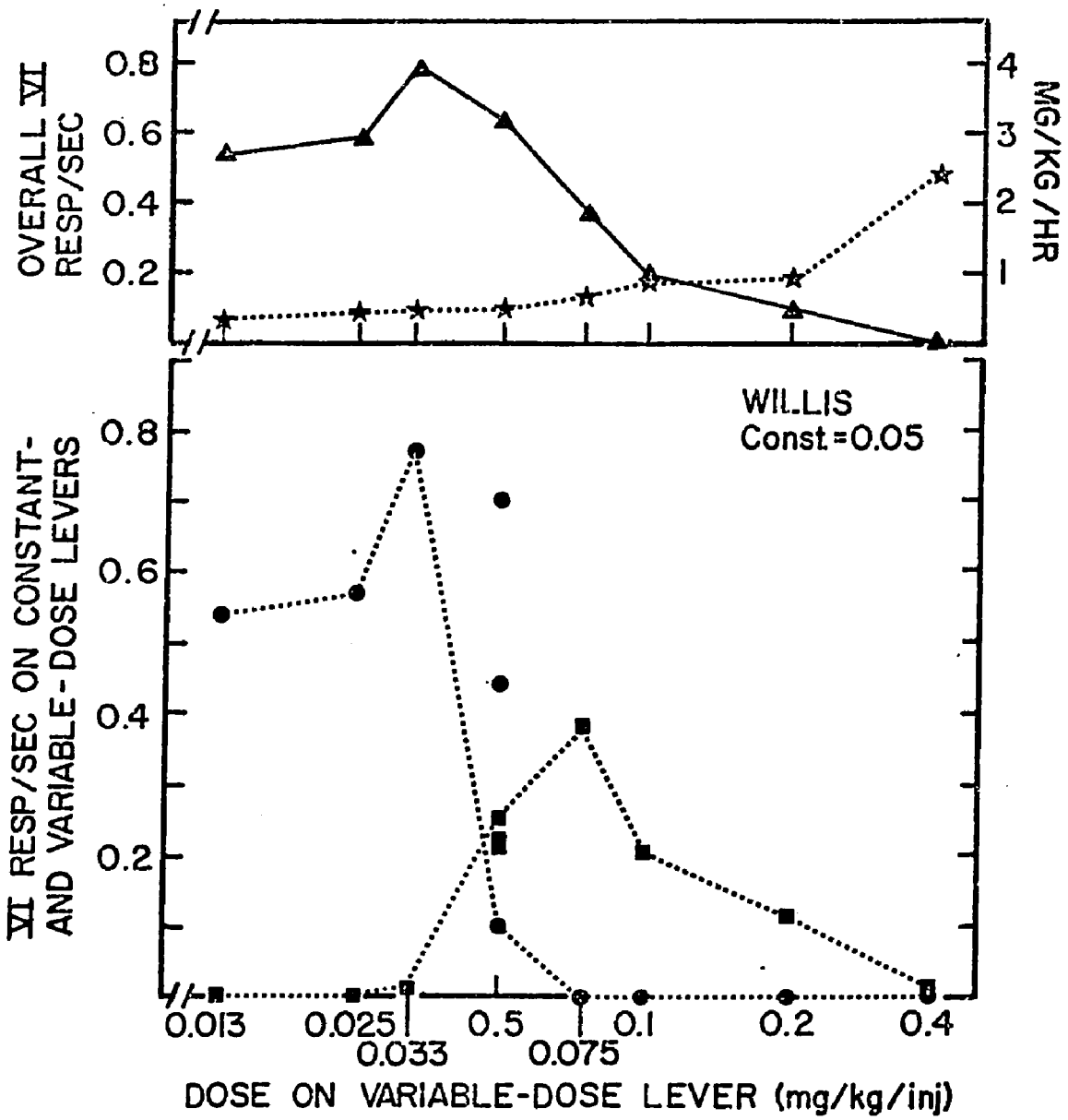

OVERALL VI RESP/SEC
0.8
0.6
0.4
0.2
4
3
2
1
MG/KG/HR
WILLIS
Const=0.05
VI RESP/SEC ON CONSTANT- AND VARIABLE-DOSE LEVERS
0.8
0.6
0.4
0.2
0.013
0.025
0.033
0.5
0.075
0.1
0.2
0.4
DOSE ON VARIABLE-DOSE LEVER (mg/kg/inj)

Figure 5e

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, as dose on the variable-dose lever was increased, responding appeared to follow one of two patterns. For Willis, and for Boris when 0.1 mg/kg/injection served as the constant dose, average overall response rates 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 were unrelated to dose on the variable lever over most of the comparison-dose continuum, and then declined at the highest comparison-dose value.

Hourly drug intake was determined primarily by the temporal parameters of the procedures, which limited the number of possible reinforcements to fewer than ten per hour, and by the doses which 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--1.0 mg/kg/hour (constant dose = 0.1 mg/kg/injection) or 0.4--0.5 mg/kg/hour (constant dose = 0.05 mg/kg/injection). As the comparison dose was increased over the constant dose, hourly drug increased, a finding which 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 which 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/sec) 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 6 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.

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

Table 2. Response rates (responses/sec) on each lever during the terminal fixed-ratio link for monkeys 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.

TABLE 2

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. 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 6 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.

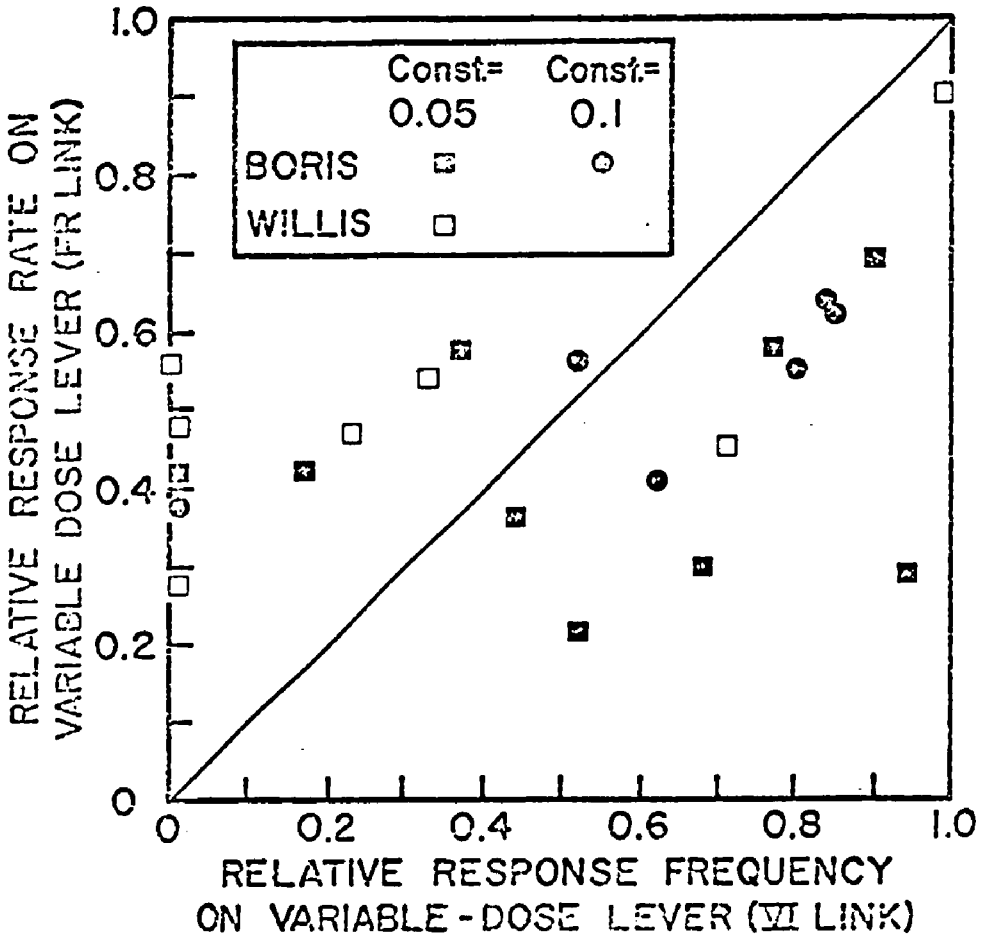

Const.= 0.05
Const.= 0.1
BORIS
WILLIS
RELATIVE RESPONSE RATE ON VARIABLE DOSE LEVER (FR LINK)
RELATIVE RESPONSE FREQUENCY ON VARIABLE-DOSE LEVER (VI LINK)
0
0.2
0.4
0.6
0.8
1.0

Figure 6

responding in both links, points would have fallen along 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 (in seconds) to respond on the center lever at the termination of the timeout period were computed separately for center-lever responses following each of the two doses. Table 3 presents the criterion-session latencies for each determination; for comparisons in which all reinforcements were obtained on one lever in the final session, only one latency could be calculated. Effects of the preceding dose are not apparent except after the higher doses, where longer average latencies occasionally occurred.

Table 3. Average latency to respond on the center lever at the end of the timeout period following different doses. 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, the animal did not receive the dose so indicated in the criterion session of the determination.

TABLE 3

Dose (mg/kg/inj)		Latency (sec)	
Var.	Const.	After Var. Dose	After Const. Dose
BERNADETTE			
0.025	0.1 (1)	25	8
0.05	0.1 (1)	18	20
0.05	0.1 (2)	20	20
0.1	0.1 (1)	21	16
0.1	0.1 (2)	17	18
0.2	0.1 (1)	5	13
0.2	0.1 (2)	5	--
0.4	0.1 (1)	18	--
0.4	0.1 (2)	72	--
RICO			
0.025	0.1 (2)	--	12
0.05	0.1 (1)	--	9
0.05	0.1 (2)	8	9
0.067	0.1 (2)	9	11
0.1	0.1 (1)	12	12
0.1	0.1 (2)	15	13
0.2	0.1 (1)	8	6
0.2	0.1 (2)	3	--
0.2	0.1 (2)	3	--
0.4	0.1 (1)	5	--
0.4	0.1 (2)	4	--

Dose (mg/kg/inj)		Latency (sec)	
Var.	Const.	After Var. Dose	After Const. Dose
BORIS			
0.025	0.1 (2)	2	2
0.05	0.1 (1)	--	4
0.1	0.1 (1)	1	1
0.1	0.1 (2)	3	4
0.2	0.1 (2)	2	2
0.2	0.1 (2)	13	8
0.4	0.1 (1)	3	2
0.4	0.1 (2)	262	--
0.8	0.1 (1)	145	--
0.025	0.05(1)	2	11
0.025	0.05(2)	10	7
0.05	0.05(1)	10	12
0.05	0.05(1)	6	8
0.05	0.05(2)	9	13
0.1	0.05(1)	2	2
0.1	0.05(2)	2	3
0.2	0.05(1)	7	10
0.2	0.05(2)	22	7
WILLIS			
0.013	0.05(1)	24	16
0.025	0.05(1)	4	5
0.033	0.05(1)	8	7
0.05	0.05(1)	5	6
0.05	0.05(1)	13	11
0.05	0.05(1)	14	15
0.075	0.05(1)	18	19
0.1	0.05(1)	11	--
0.2	0.05(1)	52	--
0.4	0.05(1)	34	--

DISCUSSION

All monkeys in the present experiment consistently preferred the larger of two doses of cocaine presented for comparison. They also all demonstrated quite close matching between relative response frequency (the measure of preference) and relative drug intake (the measure of relative reinforcement magnitude). And when dose was varied on one lever, changes in all monkeys' preferences were found to reflect changes in their absolute response rates on both levers. These data, then, extend the generality of relationships previously found with other, non-drug reinforcers under concurrent scheduling procedures 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. The occurrence of such strong preferences, even with small differences in dose size, can be considered to be an indicator of the responsiveness of behavior under both procedures to manipulations of reinforcer magnitude. However, because preference was frequently exclusive for the larger of two doses, regardless of the difference in dose size, 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 which they maintained when compared to the same constant dose, was generally not attained. By a relative response frequency criterion, doses lower than the constant dose could always be said to be less effective reinforcers than the constant dose, while doses higher than the constant dose could always be said to be more effective reinforcers than this dose, or lower doses. However, whether doses on the same side of the constant dose, which were not directly compared, were equal, or different, in their reinforcing efficacy usually could not be ascertained.

In the matching functions in Figure 4 (p. 33), data points from exclusive preferences are clustered in the lower left-hand and upper right-hand corners of the individual graphs. Although relative intake at these points deviates widely from relative dose (relative scheduled reinforcement), 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). However, as Herrnstein (1970) has pointed out, 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. These conditions did not always obtain in the present experiment. When exclusive preferences occurred for the highest doses, and overall response rates were low, response-to-reinforcer ratios sometimes fell as low as 3 or 4 to 1; and more generally, extreme distributions of responses clearly had a profound influence on the relative reinforcement obtained. The finding of approximate equality between relative response frequencies and relative intake at extreme

relative intake values is thus somewhat vacuous. Since a major portion of the matching which occurred when unequal doses were available involved exclusive preferences, the replication of the matching relationship seen in the present data should not be overemphasized.

Exclusive preferences have not typically been reported in other studies where reinforcement magnitude has been varied under equal-valued concurrent variable-interval schedules, or where terminal-link reinforcement parameters have been varied under concurrent-chain procedures employing equal-valued variable-interval schedules in the initial links (e.g., Catania, 1963a; Fantino and Herrnstein, 1968; Herrnstein, 1964; Pliskoff and Hawkins, 1967). The difference in findings between the present study and these others may relate to the extent to which responding has influenced reinforcement in the different experiments. In the present study, overall variable-interval rates were generally lower than those which have been reported in other, comparable concurrent and concurrent-chain experiments. Catania (1963a), for example, found pigeons' overall rates under concurrent VI 2-min VI 2-min to average about 1.3 resp/sec, while Pliskoff and Hawkins (1967), employing a concurrent-chains procedure, reported rats' overall rates under initial-link concurrent VI 1-min VI 1-min schedules to be between 1 and 2.5 resp/sec. By comparison, for all monkeys except Bernadette, overall rates were consistently below 0.8 resp/sec; often, they were much lower. These low rates increased the likelihood that the distribution of responses between the two levers would affect the distribution of reinforcers, since when responding on the non-preferred lever occurred infrequently with respect to time, it became more probable that reinforcers scheduled for this lever would be held

through a number of cycles, instead of being collected as soon as they became available. An inequality in the number of reinforcers received on the two levers would then be expected.

Once responding has influenced the relative reinforcement obtained, it seems reasonable to assume, as Killeen (1972) has argued, that reinforcement actually obtained, rather than that which was scheduled, will influence subsequent behavior. Preference for the lever on which the larger dose was available might then be expected to increase, thereby further increasing the relative number of reinforcements collected on this lever, and so on, until most or all responding and reinforcement occurred on one lever.

Fantino, Squires, Delbrück, and Peterson (1972) have reported a study which lends support to this somewhat speculative line of argument. These experimenters held scheduled relative magnitude of food reinforcement constant at 0.80, reinforcing pigeons' responding with either 1.5 sec or 6 sec of access to grain under equal concurrent variable-interval schedules. Three variable-interval values--600 sec, 60 sec, and 10 sec--were examined, all with a COD of 1.5 sec. Under concurrent VI 600-sec VI 600-sec and concurrent VI 60-sec VI 60-sec, response rates were about 1.5/sec, and the relative number of reinforcements obtained on each key was close to 0.50. Relative total access to reinforcement therefore approximated closely scheduled relative magnitude (duration). Under concurrent VI 10-sec VI 10-sec, however, while overall rates remained high, preferences were close to exclusive by either criterion of the present study: Relative response frequencies on the 6-sec key averaged 0.93, and relative total access to reinforcement averaged 0.97.

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. Under small variable-interval values, even with high response rates, relatively infrequent responding on one key will result in reinforcements for that key being held through a number of variable-interval periods, with a consequent lowering in the relative number of reinforcers obtained on that key to below 0.50. When the COD is relatively long in comparison to the variable-interval values, the effect of the distribution of responses on the distribution of reinforcements will be still greater. Thus, the circular process which may account for the development of exclusive preferences in the present study could also account for the near-exclusive preferences in Fantino et al.'s study. This analysis suggests that in a replication of the present experiment, increasing the value of the variable-interval schedules would abolish, or reduce in frequency, the occurrence of exclusive preferences.

Methodologically, both Procedure A and Procedure B differed in some respects from concurrent and concurrent-chain studies reported with other reinforcers, as well as from other reported experiments utilizing cocaine as a reinforcer. The 5-min timeout after reinforcement and the requirement of a single center-lever response to initiate the variable-interval link were instated for both procedures after preliminary observations indicated that overall variable-interval rates were very low (i.e., consistently under 0.20 resp/sec) when the variable-interval period began immediately after reinforcement. Since data from other cocaine experiments suggested that the low rates resulted from response-disrupting drug effects immediately following

infusion, two delays between reinforcement and the variable-interval period were imposed. One, the timeout, was of a fixed duration; the other, the latency to respond on the center lever, was of a duration determined by the behavior of the animal. To the extent that these techniques succeeded in averting rate-decreasing 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 highest doses, while center-lever latencies were also unrelated to the preceding dose except at the higher values. Latencies following the highest doses were often 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. This finding, together with the finding that variable-interval rates at all comparison-dose values and under both constant-dose conditions were usually considerably lower than in comparable concurrent-schedule studies employing other reinforcers, suggests that the two delays never entirely prevented response-disrupting drug effects from decreasing overall variable-interval rates.

In other reported cocaine self-administration experiments, time-outs after reinforcement have not been employed, so that only the behavior of the animal has restricted maximum hourly intake. Rate declines in these studies under CRF schedules have first been consistently observed as dose was increased from 0.05 to 0.1 mg/kg/injection. Intake at this latter dose, averaged across monkeys, reached about 3.3 mg/kg/hour (Goldberg et al., 1971) or 4.2 mg/kg/hour (Wilson et al., 1971; Woods and Schuster, 1968), and further decreases in

rate with increases in dose were accompanied by small additional increases in hourly intake. In the present study, on the other hand, timeout length severely restricted hourly drug intake in any dose comparison: Intake at a comparison dose of 0.4 mg/kg/injection varied from 2.2 to 3.7 mg/kg/hour, and at a comparison dose of 0.8 mg/kg/injection was 4.2 mg/kg/hour. That declines in rate with increases in comparison dose were not consistently observed in this experiment except at these high doses is therefore not surprising. On the basis of data from other studies, what is somewhat surprising is that these declines occasionally occurred at intakes below 1 mg/kg/hour (Willis, and Boris at a constant dose of 0.1 mg/kg/injection), and that there is some suggestion that drug effects depressed variable-interval rates at all intakes. However, since this experiment differed from other cocaine self-administration studies in the reinforcement schedule employed, as well as in the use of timeouts after reinforcement, it is difficult to make detailed comparisons among the studies of response rates at different intakes.

In Procedure B, which was basically a concurrent-chains procedure (Autor, 1960, 1969), equal fixed-ratio schedules were available in the terminal links on both levers. An early concern in the present experiment was to determine how terminal-link ratio value and dose size might jointly influence preference in the concurrent variable-interval link (cf. Schwartz, 1969). When investigation of this question was later postponed, the terminal links were retained, but with the ratio values for each animal kept constant and equal across all dose variations. The terminal-link schedules thus served no function pertinent to the primary purposes of the study. However, since a number of experiments

have demonstrated that under two-link concurrent-chain schedules preference in the concurrently available initial links is strongly influenced by terminal-link reinforcement parameters, while responding in the mutually exclusive terminal links (like responding under most single-schedule procedures) is not (e.g., Fantino and Herrnstein, 1968; Herrnstein, 1964; Pliskoff and Hawkins, 1967; Schwartz, 1969), the opportunity to make a similar comparison in the context of the present study was utilized. The finding that terminal-link responding was minimally affected by dose manipulations which profoundly affected concurrent variable-interval responding confirms the findings of other investigators, and extends their generality to include a different reinforcer.

An important objective in utilizing concurrent scheduling procedures in the present study was to minimize the influence of response-disrupting effects of cocaine on the evaluation of the reinforcing efficacy of different doses. Since the degree of preference demonstrated for the larger dose appeared, on inspection, unrelated to hourly drug intake or overall absolute response, the data could be interpreted as indicating that the relative response frequency measure was not significantly influenced by drug effects which appear to have decreased overall responding. However, since the unusually low response rates observed, coupled with the variable-interval values employed, may have occasioned the development of exclusive preferences, the eventual effects of dose manipulations on relative response frequencies seem dependent, to some extent, on the absolute rates of responding which the doses evaluated maintained: Had these rates been higher, the degree of preference demonstrated might have been different. The

present concurrent scheduling procedures cannot, therefore, be said to provide a measure of the reinforcing efficacy of different doses which is clearly impervious to their rate-decreasing effects. Over what ranges of absolute rates and variable-interval values preferences for different doses may in fact be invariant remains to be determined.

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