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ORAL SELF-ADMINISTRATION OF PENTOBARBITAL BY RHESUS MONKEYS: RELATIVE REINFORCING EFFECTS UNDER CONCURRENT FIXED-RATIO SCHEDULES

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During daily 3-hr sessions, orally delivered pentobarbital solutions and water, or two separate pentobarbital solutions, were concurrently available to rhesus monkeys according to fixed-ratio schedules of mouth contacts with a spout. First water, and then each of four "comparison-concentration" pentobarbital solutions (0.0625, 0.25, 1, and 4 mg/mL), was successively available from one spout for a block of sessions under a fixed-ratio-64 (three monkeys) or fixed-ratio-16 (one monkey) schedule. Under an identically sized fixed-ratio schedule, deliveries of a "standard-concentration" pentobarbital solution were concurrently available from a second spout. The concentration of the standard solution remained unchanged throughout testing of the series of comparison solutions. Each of three pentobarbital concentrations (4, 1, and 0.25 mg/mL) in turn served as the standard concentration. Within each pair of concurrently available solutions, the higher drug concentration maintained more behavior than the lower concentration. Thus when monkeys were provided with concurrent access to different pentobarbital concentrations, relative reinforcing effects were directly related to drug concentration. Further, the amount of behavior maintained by a particular drug concentration was dependent on the concentration of the concurrently available drug solution. Thus, the relative effectiveness of a reinforcer in maintaining behavior is a function of both the reinforcer's magnitude and the availability of alternative reinforcers in the environment.

Key words: drug reinforcement, drug self-administration, relative reinforcing effects, preference, concurrent fixed-ratio schedules, pentobarbital, oral route, mouth-contact responses, rhesus monkeys

Reinforcer magnitude is an important variable affecting behavior. The relation between reinforcer magnitude and effectiveness in maintaining behavior has been extensively investigated with a variety of reinforcers, including food (Keesey & Kling, 1961), water (Logan, 1964), sucrose (Conrad & Sidman, 1956), and intracranial electrical stimulation (Wauquier, Niemegeers, & Geivers, 1972). There also has been considerable interest in assessing the reinforcing effects of drugs (for a recent discussion, see Schuster, 1986). Aside from a few specially developed methods, many of the same paradigms employed to study nondrug reinforcers are used to analyze drug reinforcers.

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Results have not systematically differed between studies that have employed drug or nondrug reinforcers, but have differed considerably between studies employing different reinforcement schedules and schedule values: Larger reinforcer amounts usually maintain more behavior than smaller amounts under progressive-ratio schedules (e.g., Griffiths, Brady, & Snell, 1978; Hodos & Kalman, 1963; Hoffmeister, 1979; Yanagita, 1975). Under fixed-ratio (FR) schedules, behavior either has (Kliner, Lemaire, & Meisch, 1988; Lemaire & Meisch, 1984) or has not (Pickens, Muchow, & DeNoble, 1981) been directly related to reinforcer amount, depending on the parameter values used and the dependent measures examined (for a reconciliation of these different outcomes, see Kliner et al., 1988). Choices of parameter values can also determine whether responding will (Meltzer & Brahlek, 1970) or will not (Goldberg & Kelleher, 1976) be directly related to reinforcer amount under fixed-interval (FI) schedules. Finally, the functional relation between response rate and reinforcer magnitude when variable-interval (VI) schedules are used can

be direct (Keesey & Kling, 1961), inverted U-shaped (Conrad & Sidman, 1956), or relatively flat (Catania, 1963), depending on the parameter values studied, other experimental variables, and how measurements are taken.

In the studies cited above, as well as in many others, reinforcer deliveries were contingent upon responding under a single reinforcement schedule; reinforcer magnitude was varied across sessions, and comparisons of behavior maintained by different reinforcer magnitudes were therefore also made across sessions. Another body of experimental work concerns behavior maintained by concurrently available reinforcers differing in magnitude. Within-session concurrent scheduling permits a more direct comparison between the reinforcing effects of stimuli than does across-session comparisons. Discrete-trial choice procedures have occasionally been used to study both drug and nondrug reinforcers (e.g., Griffiths, Bigelow, Liebson, & Kaliszak, 1980; Young, 1981). A procedure that has more often been used is the concurrent-chains paradigm. Typically, different reinforcement conditions are programmed in the second components of two concurrently operating chained schedules, and response rates in the two identical first-component schedules (usually VI schedules) are compared. When reinforcer magnitudes differ in the second components, higher response rates are maintained in the first component by the VI schedule leading to the larger reinforcer magnitude (see de Villiers, 1977). Another widely used paradigm for studying behavior maintained simultaneously by two reinforcers is the concurrent VI-VI paradigm. In this experimental design, responding usually is maintained by both schedules, but a higher response rate is maintained under the VI schedule delivering the larger reinforcer magnitude (see Davison & McCarthy, 1988).

Although response rates under concurrent VI-VI schedules have often been used to evaluate reinforcing effects, concurrent FR-FR schedules have several advantages for examining the relative reinforcing effects of two consequent events. First, under concurrent FR-FR conditions, schedule influences affect both reinforcers identically throughout sessions and intrude minimally to differentially favor one or the other reinforcer at different times. In contrast, when concurrent interval schedules are used the two schedules themselves are important independent variables that can act to increase temporarily the reinforcing effectiveness of one event over another (cf. Davison & McCarthy, 1988, p. 84). Second, subjects' response rates under ratio schedules directly affect reinforcer delivery rates, and the time course of reinforcer deliveries is therefore controlled to a greater extent by the subject than is the case under concurrent VI schedules. This may be a critical advantage when studying stimuli whose reinforcing effects can depend on a relatively massed sequence of deliveries (e.g., electrical stimulation of the brain; see Valenstein, 1964) or on a cumulative number of deliveries (as may be the case under some conditions in which drugs are self-administered). Ratio schedules may also enjoy a third advantage in studies of the relation of behavior to reinforcer magnitude because differences in the time required to consume reinforcers of small and large magnitude do not affect scheduling of subsequent reinforcer deliveries under ratio schedules, whereas they may under interval scheduling procedures. Despite these favorable characteristics for studying relative reinforcing effects in a simple and direct manner, little work has been done using concurrent ratio schedules (see reviews by Catania, 1966; Davison & McCarthy, 1988; de Villiers, 1977). When concurrent ratio schedules have been used, the experiments have usually been designed to study the effects of schedule size as an independent variable; in these studies, responding has tended to be maintained fairly exclusively by the smaller of two FR (Herrnstein, 1958) or VR (Herrnstein & Loveland, 1975) schedules.

One study specifically varied reinforcer magnitude under concurrent FR-30 FR-30 schedules, but reinforcer magnitude per se was not the independent variable of interest: Pigeons had access to a feeder for either a fixed time (5 s) or for a time that varied, but whose average was equal to the fixed reinforcer time; responding was better maintained by the variable-duration reinforcer (Essock & Reese, 1974). In a study with rats in which reinforcer magnitude was of primary interest, 18 subjects received deliveries of 8% versus 16%, 8% versus 32%, or 16% versus 32% sucrose solutions under concurrent FR-5 FR-5 schedules (Collier & Rega, 1971). As a group, 60%, 93%, and

57% of responding, respectively, occurred on the lever delivering the higher concentration. Although each of these percentages differed significantly from chance results, the percentage of behavior maintained by the larger concentration was substantially less than 100% in two of the three conditions; not suprisingly, the greatest difference between levels of responding under the two concurrent schedules occurred when the greatest disparity between reinforcer magnitudes was present.

The drug self-administration literature reflects a similar sparsity of studies using concurrent ratio schedules. In studies in which different drug amounts have been concurrently available, response rates maintained under concurrently operating VI schedules have typically been a major dependent variable. In one series of studies, for example, different doses of intravenously delivered cocaine were examined (Iglauer, Llewellyn, & Woods, 1975; Iglauer & Woods, 1974; Llewellyn, Iglauer, & Woods, 1976). Generally, high drug doses maintained more responding than lower ones. One series of studies was conducted with concurrent FR schedules (Johanson & Aigner, 1981; Johanson & Schuster, 1975; Woolverton & Johanson, 1984). In these studies, a variation of Findley's (1958) concurrent scheduling procedure was used, whereby rhesus monkeys switched between FR schedules with their correlated discriminative stimuli by pressing a "switching" lever. Intravenous delivery of cocaine, methylphenidate, *d,l*-cathinone, and procaine was examined. In general, higher doses of each drug were preferred to lower ones, and several doses of cocaine maintained behavior better than higher doses of concurrently available procaine.

A few studies have examined behavior maintained under concurrent FR schedules by a drug and a nondrug reinforcer (Carroll, 1985; Samson & Grant, 1985). However, to our knowledge only one study has made different amounts of the same drug available under standard concurrent fixed-ratio schedules, as was done in the present experiment. In that study, under concurrent FR-16 FR-16 schedules monkeys were presented with oral deliveries of phencyclidine (PCP) solutions differing in concentration (Carroll, 1987). One PCP concentration (0.25 mg/mL) was used as a standard against which other concurrently available PCP concentrations were compared. Higher PCP concentrations usually, although not always, maintained more behavior than lower ones.

The use of different methods for examining reinforcing effects permits comparison of results obtained in one paradigm with those obtained in another. For example, different paradigms yield reinforcing-effectiveness rankings of various psychomotor-stimulant drugs that accord well with each other (Griffiths, Brady, & Bradford, 1979). Consistent conclusions are also reached when studies are examined in which primates self-administered drugs by the intravenous or oral routes, and either sequential (e.g., Griffiths, Findley, Brady, Dolan-Gutcher, & Robinson, 1975; Lemaire & Meisch, 1984, 1985; Winger, Stitzer, & Woods, 1975) or simultaneous (e.g., Iglauer & Woods, 1974; Johanson & Schuster, 1975; Woolverton & Johanson, 1984) comparisons were made between different drug amounts; both sequential and simultaneous procedures indicate that self-administration behavior is generally better maintained by larger amounts of a drug than by smaller amounts. The present study was designed to test the generality of previous findings of a positive relationship between pentobarbital amount and relative effectiveness in maintaining behavior when different drug amounts were available sequentially (Lemaire & Meisch, 1984, 1985). In the present study, concurrent FR schedules were used to make two pentobarbital solutions simultaneously available, and the amount of drug in one of the solutions was systematically varied.

METHOD

Subjects

Subjects were 4 rhesus monkeys (M-G2, M-P, M-P1, and M-W) with histories of oral drug self-administration. Monkey M-G2 was a subject in two earlier studies of pentobarbital self-administration (DeNoble, Svikis, & Meisch, 1982; Lemaire & Meisch, 1984). The other subjects had served in two previous studies of pentobarbital self-administration (Kliner & Meisch, 1982; Meisch, Kliner, & Henningfield, 1981). Thus all subjects had at least a partially similar experimental history. Two subjects had also participated in previous studies of ethanol self-administration (M-P: Hen-

ningfield & Meisch, 1976b; Meisch, Henningfield, & Thompson, 1975; M-W: Henningfield & Meisch, 1979), and two (M-P1 and M-W) were previously in an experiment involving methohexital self-administration (Carroll, Stotz, Kliner, & Meisch, 1984). Self-administration of pentobarbital and many other drugs is increased in subjects maintained at reduced weights (for a review, see Carroll & Meisch, 1984). Mean body weights were: M-G2, 9.3; M-P, 8.4; M-W, 8.1; and M-P1, 6.7 kg; these weights were 75%, 70%, 72%, and 83% of subjects' free-feeding weights, respectively. As noted previously (Lemaire & Meisch, 1985), expressing subjects' maintenance weights as percentages of their free-feeding weights can be misleading for some subjects. Providing monkeys unlimited access to food in the single-housing, caged conditions of our laboratory produces mild to severe obesity in some animals; free-feeding weights under these conditions, therefore, are not necessarily representative of "free-feeding" weights under more natural conditions. The maintenance weights in the present experiments do not reflect a marked degree of food deprivation, and the monkeys' health and appearance were good during the experiments. The monkeys' health was monitored daily by veterinary-care staff.

Apparatus

Subjects in each experiment were housed singly in stainless-steel cages (77 by 76 by 100 cm) 24 hr per day; 12 cages were located together in the same room. The fronts of the cages were barred. A liquid-delivery apparatus panel was attached to the outside of one side wall; elements fastened to the panel protruded into the cage through holes cut in that wall. Attached to the back of the apparatus panel was a T-shaped bar, on each limb of which was fastened a stainless-steel reservoir covered with a lid. Liquids contained in each reservoir passed via polyethylene tubing to a solenoid-operated valve at the rear of one of two brass spouts. These spouts (1.2 cm outside diameter, 0.2 cm inside diameter) protruded 2 cm into the cage, 64 cm above the floor and 15.5 cm either side of midline. The spouts served as manipulanda for operant responses (mouth contacts with either spout). At each liquid delivery, the solenoid at the rear of a spout was activated for a maximum of 150 ms, allowing approximately 0.64 mL of liquid to pass through the spout and into the monkey's mouth. To minimize spillage, solenoid activation was terminated short of 150 ms if mouth contact with the spout was broken before this interval had elapsed. The liquid-delivery apparatus has been described more extensively by Henningfield and Meisch (1976a).

Spouts were embedded in Plexiglas disks that covered the 7-cm-diameter holes in the cage wall through which the spouts entered. At each spout, two 1.1-W lights, one located 2.5 cm on either side of the spout and visible through the Plexiglas, were aligned diagonally; these lights were capped with green translucent lenses. Another two 1.1-W lights, one located 2.5 cm on either side of the spout, were aligned on the opposite diagonal, and were capped with white translucent lenses. Thus each spout was in the center of a square pattern of four lights, two green and two white. Within sessions, a spout's green lights were illuminated for the duration of each mouth-contact response with that spout. Between sessions, when water was available at a spout (see below) its white pair of lights remained illuminated for the duration of each mouth contact, and mouth contacts with the opposite spout had no programmed consequences. A green jewel-covered, 2.8-W discriminative-stimulus light was located 12 cm directly above each spout and extended 2 cm into the cage. Throughout sessions, these two jewel-covered lights flickered at a rate of 10 Hz; between sessions, the jewel-covered light above the spout at which water was available was continuously illuminated, and the light above the other spout was dark. Experiments were controlled and monitored with solid-state programming (Coulbourn Instruments, Inc.) and recording equipment located in an adjacent room.

Procedure

Daily 3-hr sessions were conducted from 10:00 a.m. to 1:00 p.m. A timeout (TO) was in effect for an hour before sessions; during this period, intersession water-drinking values were recorded, and liquids appropriate for the session were placed in monkeys' reservoirs. Some of each side's solution was drained through the respective tubing leading from the reservoir to the solenoid-operated spout to displace water remaining in the tubing from the intersession period or to displace solution re-

maining from the previous day's session. This ensured that the appropriate solution was present on the very first reinforcer delivery of the session; liquids were remeasured after this "flushing" procedure to obtain the exact volume in the reservoirs at the outset of each session. Timeout periods were also in effect for the hour after the session and for the third hour after the session. During the first of these, data from the session were collected, and water was placed in one of each monkey's reservoirs and flushed through the tubing to the spout. The spout from which water was available between sessions alternated from day to day. During the second postsession TO, subjects were fed their daily food rations of Purina Monkey Chow. Between sessions, water was available under an FR-1 schedule from one spout when TO periods were not in effect (i.e., during the second hour after each session and from 4:00 p.m. until 9:00 a.m. the next morning).

During sessions, two liquid solutions were available to subjects under concurrently operating, equal-sized fixed-ratio schedules (FR 64 for M-G2, M-P1, and M-W; FR 16 for M-P). Monkey M-P was tested at FR 16 because a range of pentobarbital concentrations had earlier maintained behavior well at that FR size, but had not at FR 64. The concentration of the solution available from one spout (the "comparison" solution) was changed across blocks of sessions (between water and 0.0625, 0.25, 1, and 4 mg/mL pentobarbital), while the concentration of the solution available from the second spout (the "standard" solution) remained the same across the series of comparison concentrations tested. The side positions of the standard and comparison solutions were reversed daily.

Water and then each of four pentobarbital concentrations was tested as the comparison concentration in the following ascending-descending sequence to balance for order effects: water, 0.0625, 0.25, 1, 4, 1, 0.25, and 0.0625 mg/mL pentobarbital, and finally water again. The concurrently available standard concentration was a 4-mg/mL pentobarbital solution. At each pair of concentrations, six sessions of stable self-administration behavior were obtained. Stability was defined as no appreciable increasing or decreasing trend in the number of deliveries per session of either available liquid.

Table 1

Number of sessions required to meet six-session stability criterion.[a]

Monkey	4[b] vs. water	4 vs. 0.0625	4 vs. 0.25	4 vs. 1	4 vs. 4
M-G2	8, 9[c]	7, 6	8, 7	7, 7	6
M-P	7, 6	7, 6	6, 11	6, 6	6
M-P1	16, 8	7, 6	17, 9	7, 12	9
M-W	6, 6	6, 6	7, 6	6, 6	6
	1 vs. water	1 vs. 0.0625	1 vs. 0.25	1 vs. 1	1 vs. 4
M-G2	6, 6	12, 8	10, 7	10, 11	7
M-P	7, 6	7, 6	12, 10	10, 6	9
M-P1	8, 14	17, 6	8, 8	6, 7	15
M-W	13, 6	6, 6	7, 6	6, 7	14
	0.25 vs. water	0.25 vs. 0.0625	0.25 vs. 0.25	0.25 vs. 1	0.25 vs. 4
M-P	12, 14	13, 22	6, 11	10, 8	8
M-W	7, 8	7, 6	7, 6	8, 8	8

[a] Schedules throughout the experiment were M-G2, M-P1, and M-W, FR 64; M-P, FR 16.

[b] Columns headings refer to pentobarbital concentrations (mg/mL).

[c] The first number at each condition refers to the ascending comparison-concentration series, and the second number refers to the retest during the descending comparison-concentration series.

Following completion of testing the series of comparison concentrations with 4 mg/mL concurrently present, a 1-mg/mL pentobarbital solution was made the standard-concentration solution, and the entire series of comparison concentrations was tested anew, according to the order and procedure described for the 4-mg/mL standard series. Finally, following completion of the comparison series with 1 mg/mL concurrently available, a 0.25-mg/mL pentobarbital solution became the standard-concentration solution for 2 subjects (M-P and M-W), and the entire series of comparison concentrations was once again repeated. The 0.25-mg/mL solution did not maintain M-G2 or M-P1's behavior well when initially available with water at FR 64, so comparison-concentration solutions were not tested with these subjects with 0.25 mg/mL as a standard concentration. Table 1 lists the number of sessions each subject required to achieve the six-session stability criterion at each condition of the experiment.

The highest pentobarbital concentration used as a "standard" drug solution was 4 mg/mL because higher concentrations potentially

Table 2

Six-session mean liquid deliveries per 3-hr session (± *SEM*).

	4 vs. water		4 vs. 0.0625		4 vs. 0.25	
M-G2	90.0 (2.6)	0.7 (0.3)	91.5 (2.4)	1.2 (0.5)	89.0 (2.2)	0.7 (0.3)
	101.2 (1.2)	0.8 (0.2)	97.2 (2.5)	1.0 (0.4)	97.2 (2.5)	0.5 (0.2)
M-P	119.7 (6.7)	2.8 (2.3)	130.0 (8.0)	3.8 (2.7)	125.7 (7.5)	3.7 (0.7)
	150.3 (5.8)	4.3 (0.6)	140.0 (4.8)	4.7 (1.1)	126.7 (3.2)	5.7 (1.5)
M-P1	70.0 (3.3)	9.5 (1.4)	60.0 (3.4)	10.7 (2.2)	66.2 (3.8)	4.7 (0.9)
	84.0 (2.5)	7.7 (2.0)	70.3 (2.7)	12.0 (3.4)	73.8 (3.2)	12.3 (3.6)
M-W	86.0 (3.1)	1.2 (0.4)	88.5 (1.1)	0.7 (0.3)	87.7 (2.9)	1.2 (0.4)
	92.5 (2.0)	1.3 (0.2)	91.5 (3.2)	1.2 (0.4)	96.7 (1.4)	1.5 (0.4)
	1 vs. water		1 vs. 0.0625		1 vs. 0.25	
M-G2	146.8 (6.2)	1.8 (1.1)	100.8 (4.7)	0.5 (0.2)	92.7 (5.5)	0.7 (0.2)
	91.0 (3.8)	0.7 (0.3)	85.2 (2.3)	0.7 (0.4)	96.0 (4.1)	0.5 (0.3)
M-P	239.2 (7.5)	2.7 (0.4)	252.0 (7.3)	2.7 (0.4)	294.0 (15.2)	3.5 (1.2)
	354.5 (9.2)	3.5 (0.4)	328.5 (17.0)	4.0 (0.6)	296.3 (9.8)	5.7 (1.4)
M-P1	101.2 (7.2)	5.3 (1.1)	84.0 (14.3)	12.3 (6.0)	66.8 (10.5)	22.2 (9.2)
	61.0 (6.2)	2.7 (0.6)	88.7 (7.1)	7.8 (2.3)	78.2 (10.8)	11.5 (2.2)
M-W	174.7 (6.8)	1.7 (0.3)	159.2 (3.9)	1.5 (0.4)	173.7 (7.8)	1.3 (0.3)
	154.5 (5.1)	1.7 (0.3)	145.7 (7.6)	2.0 (0.4)	173.0 (6.3)	3.2 (1.0)
	0.25 vs. water		0.25 vs. 0.0625		0.25 (stand.) vs. 0.25 (comp.)	
M-P	171.2 (29.8)	4.2 (0.8)	148.3 (12.4)	15.7 (11.7)	91.8 (18.6)	107.5 (31.7)
	161.3 (18.5)	2.7 (0.6)	106.7 (19.5)	5.8 (2.2)	132.2 (27.1)	132.2 (30.7)
M-W	168.0 (13.8)	1.5 (0.4)	145.5 (6.7)	1.7 (0.2)	92.2 (21.9)	59.3 (20.2)
	121.2 (10.0)	2.8 (0.3)	151.3 (8.6)	4.2 (0.6)	73.3 (10.8)	75.3 (12.3)

Note. Column headings are pentobarbital concentrations (mg/mL). At each condition, values in the first and second lines were obtained during the ascending and descending comparison-concentration series, respectively. Monkey M-P received deliveries according to an FR-16 schedule; the other 3 subjects received deliveries according to FR-64 schedules.

could lead to drug overdosing at FR 16, the schedule value at which M-P received drug deliveries. The lowest standard drug concentration used was 0.25 mg/mL because 0.0625 mg/mL was too low to maintain behavior well at FR 64.

When the same concentration was available as both the standard and comparison solution (viz., when 4 vs. 4, 1 vs. 1, and 0.25 vs. 0.25 mg/mL were available), it was not possible to alternate side positions, because the same concentration was present on both sides. Therefore, the mean number of deliveries obtained on alternating sides over the six successive stable sessions was arbitrarily designated as the mean number of "comparison-solution" deliveries. For 2 subjects (M-G2 and M-P1), the side designated as the "comparison solution" across the six sessions was: left (L), right (R), L, R, L, and R. For the other 2 subjects (M-P and M-W), the same procedure was followed, but data were averaged across the six sessions beginning with the right side on the first day (i.e., R, L, R, L, R, and L). The number of drug deliveries designated as the "standard-solution" value was the mean of the number of drug deliveries on alternating sides that had not been used in calculating the "comparison-solution" mean. This method for presenting results was used so that data analysis was comparable across all conditions.

Drug

A concentrated sodium pentobarbital stock solution (6.25 mg/mL) was prepared weekly and stored at 3°C. Monkeys' daily solutions were prepared approximately 2 hr prior to each session. Solutions were at room temperature at the start of sessions. Drug concentrations are expressed in terms of the sodium salt.

RESULTS

Table 2 shows that for each condition, for each subject, the larger of two pentobarbital concentrations maintained more self-administration behavior than the smaller one. Results from the ascending and descending com-

Table 2 (*Continued*)

4 vs. 1		4 (stand.) vs. 4 (comp.)	
94.3 (2.2)	0.7 (0.3)	44.2 (19.9)	48.3 (21.6)
91.3 (6.2)	14.3 (12.9)		
125.3 (4.9)	2.3 (0.8)	59.7 (22.8)	83.3 (27.7)
131.2 (6.9)	7.0 (0.8)		
51.3 (2.7)	25.8 (3.9)	41.8 (6.3)	31.2 (8.2)
71.2 (1.8)	16.0 (4.9)		
89.5 (0.8)	1.5 (0.8)	74.0 (12.8)	20.0 (13.3)
96.5 (2.7)	2.8 (0.7)		
1 (stand.) vs. 1 (comp.)		1 vs. 4	
68.3 (16.5)	16.8 (10.7)	2.7 (1.0)	67.2 (2.1)
48.5 (20.1)	43.2 (20.0)		
153.0 (48.7)	192.8 (46.1)	12.3 (3.9)	171.8 (6.9)
169.0 (21.9)	118.2 (34.6)		
47.2 (19.8)	42.3 (19.0)	17.3 (2.6)	60.3 (2.1)
61.8 (7.5)	45.0 (9.2)		
116.2 (28.4)	64.7 (24.6)	2.8 (1.1)	90.8 (3.3)
59.7 (19.0)	124.7 (19.7)		
0.25 vs. 1		0.25 vs. 4	
5.0 (1.2)	300.7 (17.7)	4.5 (0.8)	154.2 (4.9)
7.2 (2.9)	259.3 (7.3)		
17.0 (7.3)	139.0 (7.9)	2.2 (0.9)	80.0 (1.2)
7.3 (3.2)	138.5 (7.4)		

parison-concentration series were similar. At conditions in which the same concentration was available as both the standard and comparison concentrations (4 vs. 4, 1 vs. 1, and 0.25 vs. 0.25 mg/mL), responding was well maintained by both the comparison and the standard solutions, and neither solution systematically maintained more behavior than the other. Table 3 lists mean drug intakes (mg of pentobarbital per kg of body weight per session) when each standard concentration was concurrently available with water. As in a previous study (Lemaire & Meisch, 1984), oral intake of pentobarbital was directly related to drug concentration.

Figure 1 shows the mean number of comparison-solution deliveries as a percentage of the total number of deliveries at each condition (i.e., comparison deliveries divided by the sum of comparison and standard deliveries, then multiplied by 100). If responding were evenly divided between the schedules delivering the comparison and standard solutions (i.e., indifference between the two solutions), this would result in a bar reaching to the 50% level. Results are shown for both the ascending (left bar) and descending (right bar) comparison series at each standard concentration. Only one bar appears at conditions in which 4 mg/mL was tested as the comparison concentration; such conditions were tested only once, because 4 mg/mL was at the apex of the ascending and descending series of comparison concentrations. At each condition in which the concentration of the comparison solution was less than that of the standard solution, the number of comparison-solution deliveries was a small percentage of total deliveries. When the concentration of the comparison solution was greater than that of the standard solution, comparison-solution deliveries were a large percentage of total deliveries. When the same concentration was available as both the standard and the comparison concentrations (4 vs. 4, 1 vs. 1, and 0.25 vs. 0.25 mg/mL), comparison-solution deliveries usually hovered around 50%, which indicates that subjects' responding was maintained about equally well by the identical-concentration comparison and standard solutions.

Table 3

Mean drug intake (mg of pentobarbital/kg of body weight/3-hr session).[a]

Monkey	4[b] vs. water	1 vs. water	0.25 vs. water
M-G2	27.8	8.1	
M-P	35.5	19.4	2.9
M-P1	29.0	7.5	
M-W	27.8	13.3	3.0

[a] Means of values during the ascending and descending comparison-concentration series.

[b] Column headings refer to pentobarbital concentrations (mg/mL).

DISCUSSION

Results of the present experiment are relevant both to the specific area of drug-reinforced behavior and to the wider study of choice situations involving multiple reinforcers. Issues pertaining to the experiment's specific data will be discussed first, followed by consideration of several broader topics.

In the present experiment different pentobarbital concentrations were simultaneously available under FR schedules, and relative

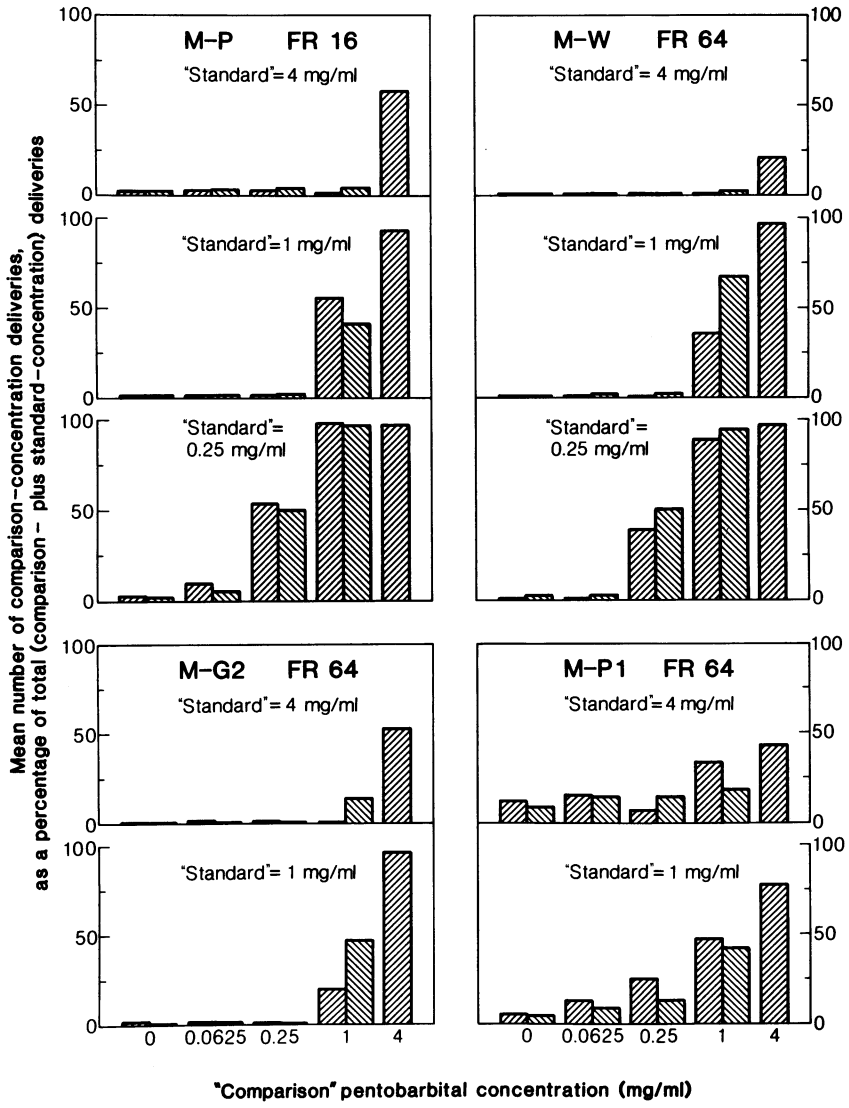

Fig. 1. Mean number of comparison-solution deliveries per session at each condition, as a percentage of the mean total (comparison plus standard solution) number of deliveries per session. Left and right bars at a condition represent tests during the ascending and descending series of comparison concentrations, respectively. In general, large differences between test and retest conditions occurred only when the standard and comparison concentrations were the same (e.g., M-W at 1 mg/mL vs. 1 mg/mL).

reinforcing effects were directly related to drug concentration. Findings were consistent across the three separate concentration-choice series: Higher pentobarbital concentrations were consistently preferred to lower ones. (By a concentration being preferred, we mean that a solution of that concentration maintained higher response rates, and was consumed in larger volumes, than the concurrently available solution.) These results systematically replicate the findings of a previous experiment in which different pentobarbital concentrations were sequentially available at each of several FR sizes and the principal dependent variable was the percentage decrease in reinforcer deliveries from baseline as FR size was increased (Lemaire & Meisch, 1984). In both the present and the earlier study, relative reinforcing effects were directly related to drug concentration. Thus the findings of the two

studies complement one another and demonstrate that concurrent and sequential procedures can yield equivalent results.

The results of the present experiment were not attributable to the sequence in which either the standard or the comparison concentrations were presented. The series tested with 1 and with 0.25 mg/mL as the standard concentrations replicated the relationship between drug concentration and self-administration behavior seen with the 4-mg/mL concentration: Each standard concentration (4, 1, and 0.25 mg/mL) always maintained more behavior than concurrently available solutions lower in concentration than itself and less behavior than concurrently available solutions of higher concentrations (Table 2; Figure 1). Results were similar during the ascending and descending series of comparison concentrations (Figure 1), and thus the results cannot be due to the order in which comparison concentrations were presented. Finally, at several points during series with 1 or 0.25 mg/mL as the standard concentration, there were replications of conditions previously tested during the 4-mg/mL standard-concentration series (Table 2). This replication of conditions in which the 4-mg/mL concentration was tested controlled for possible historical factors that might have affected behavior across conditions. The results of these replicated conditions were similar to those at the respective like conditions in the first (4 mg/mL) standard-concentration series. Thus self-administration behavior was a function of pentobarbital concentration rather than of the order in which standard or comparison concentrations were tested.

In the present experiment there were no differences between exteroceptive stimuli that accompanied drug solutions. Discriminations between two available solutions, therefore, had to be based either on taste, pharmacological effects following consumption of a solution, or both. Subjects readily discriminated between solutions (Table 2), and the time course of responding suggests that taste, rather than pharmacological effect, was the basis of the discrimination. Subjects typically obtained one or a few deliveries of each available liquid at the outset of sessions, and then responding was restricted to the spout delivering the greater concentration solution. Although discriminations between solutions seemed based on taste, the taste of the solutions was not the reinforcing stimulus ultimately maintaining behavior. A previous study showed that with the concentration of a drug solution (and therefore the taste) held constant, maintenance of monkeys' behavior is directly related to the quantity of drug delivered (Lemaire & Meisch, 1985). Further, unpublished data from this laboratory of drug probes with naive monkeys have shown that a 0.5- or 1-mg/mL pentobarbital solution will not function as an orally delivered reinforcer without a history of exposure to gradually increasing pentobarbital concentrations. Thus the taste of the solutions may serve as a discriminative stimulus (and possibly a conditioned reinforcing stimulus) for subjects having histories in which the taste of drug solutions has been highly correlated with pentobarbital's pharmacological effects.

Switching between schedules is not differentially reinforced under concurrent FR schedules; however, switching between schedules can be intermittently reinforced when events are arranged concurrently under interval schedules. In the present study, most subjects' nearly exclusive responding on the schedule delivering the greater concentration reinforcer indicates that presenting two reinforcers under concurrent FR-FR schedules can be a sensitive technique for detecting differences in relative reinforcing effects.

In one other experiment in which monkeys orally self-administered drug solutions under concurrent FR-FR schedules, responding was maintained less exclusively than in the present study by drug solutions of greater concentration (Carroll, 1987). This difference in results may be the result of the different schedule values used in the two experiments. Carroll's experiment was conducted with concurrent FR-16 schedules, whereas the present experiment used FR-64 schedules for 3 of the 4 subjects. It is possible that under concurrent FR-FR conditions, testing at higher schedule sizes may reveal differences in reinforcing effects that are not evident at low schedule sizes. In a previous study in which a nonconcurrent procedure was used, monkeys orally self-administered an 8% ethanol solution or water, across sessions, first under an FR-1 schedule and then under an FR-16 schedule; although differences in reinforcing effects between ethanol and water were not demonstrated at FR 1, the ethanol solution produced unequivocally greater reinforcing effects under FR-16 con-

ditions (Henningfield & Meisch, 1976b). Analogous results were obtained when rats intravenously self-administered different methohexital doses at several FR values (Pickens et al., 1981). Thus, whether differences between the reinforcing effects of different consequent events will be evident may critically depend on the FR size at which behavior is maintained.

Experimental conditions that are sufficient to demonstrate reinforcing effects (i.e., to demonstrate that an event will maintain behavior) are not always sufficient to demonstrate relative reinforcing effects. Thus, use of simple reinforcement schedules may be adequate to demonstrate that a particular stimulus event can function as a reinforcer. However, differences among consequent stimuli in their reinforcing effects may not be evident under simple schedules. For instance, under many simple reinforcement schedules there is an inverted U-shaped relation between drug quantity (drug concentration, volume, or dose) and the number of drug deliveries obtained. Thus similar rates of behavior may be maintained by a low and a high drug amount. Under such conditions, however, the relative reinforcing effects of the two drug amounts are probably obscured by the disruptive effects of high drug intake that occur at the higher concentration (cf. Griffiths et al., 1979). In characterizing the relative reinforcing effects of different drug amounts, absolute response rates maintained by their delivery may therefore be misleading. Analogous problems arise when absolute response rates are relied upon to reveal differences among nondrug reinforcers (see Kliner et al., 1988). However, it is possible to obtain more consistent findings through the use of alternative measures, such as the percent-choice measure used in the present study or percentage changes in behavior maintained by reinforcers across experimental conditions (Kliner et al., 1988; Lemaire & Meisch, 1984, 1985; Nevin, 1974).

An important finding of the present experiment, which has been demonstrated in previous studies (e.g., Carroll, 1985; Catania, 1963), is the remarkable extent to which the concurrent availability of alternative reinforcers can alter the amount of behavior that a particular reinforcer will maintain: Each of the standard pentobarbital concentrations (4, 1, and 0.25 mg/mL—a high, an intermediate, and a relatively low concentration) maintained behavior well when it was available concurrently with water, the drug vehicle; water was a minimally effective reinforcer under the concurrent FR-FR conditions of this experiment (Table 2). It is especially interesting that when concurrently available with water, the low (0.25 mg/mL) and intermediate (1 mg/mL) pentobarbital concentrations generally maintained higher rates of responding than did the highest concentration (4 mg/mL). With most subjects, however, the same low and intermediate drug concentrations maintained negligible levels of behavior when concurrently available with the 4-mg/mL concentration (Table 2). A related finding is that intermediate pentobarbital concentrations can maintain much behavior leading to their presentation when available in the company of lower pentobarbital concentrations, yet maintain hardly any behavior when available with higher concentrations (Table 2). Thus the behavior-maintaining effects of particular stimulus events are not fixed and immutable, but may vary with the availability of other reinforcers.

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