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HUMAN COFFEE DRINKING: MANIPULATION OF CONCENTRATION AND CAFFEINE DOSE

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In a residential research ward coffee drinking was studied in 9 volunteer human subjects with histories of heavy coffee drinking. A series of five experiments was undertaken to characterize ad-libitum coffee consumption and to investigate the effects of manipulating coffee concentration, caffeine dose per cup, and caffeine preloads prior to coffee drinking. Manipulations were double-blind and scheduled in randomized sequences across days. When cups of coffee were freely available, coffee drinking tended to be rather regularly spaced during the day with intercup intervals becoming progressively longer throughout the day; experimental manipulations showed that this lengthening of intercup intervals was not due to accumulating caffeine levels. Number of cups of coffee consumed was an inverted U-shaped function of both coffee concentration and caffeine dose per cup; however, coffee-concentration and dose-per-cup manipulations did not produce similar effects on other measures of coffee drinking (intercup interval, time to drink a cup, within-day distribution of cups). Caffeine preload produced dose-related decreases in number of cups consumed. As a whole, these experiments provide some limited evidence for both the suppressive and the reinforcing effects of caffeine on coffee consumption. Examination of total daily coffee and caffeine intake across experiments, however, provides no evidence for precise regulation (i.e., titration) of coffee or caffeine intake.

Key words: coffee, caffeine, drug self-administration, tremor, subjective effects, coffee drinking, humans

Caffeine is the world's most widely used behaviorally active drug, with one or more caffeine-containing beverages and foods consumed by most adults and children. Coffee and tea drinking account for 97% of caffeine consumption worldwide (Gilbert, 1984). In the United States, average daily caffeine intake per capita is approximately 200 mg (Gilbert, 1984; Graham, 1978). Although there is little apparent health risk associated with consumption of low amounts of caffeine (Dews, 1982; Ernster, 1984), several investigators have argued that significant health risk may begin to emerge at 500 to 600 mg of caffeine per day (Gilbert, 1976; Greden, 1981). Various North American surveys suggest that as many as 10 to 30% of adults consume more than 500 mg of caffeine per day (Greden, 1981); it is plausible, therefore, that a significant proportion of the population may be at health risk from excessive caffeine consumption.

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Because of the high prevalence of caffeine consumption, interest in possible performance-enhancing effects of caffeine, and increasing concern over health risks related to caffeine use, the effects of caffeine have been, and are continuing to be, extensively studied (Dews, 1982; Gilbert, 1976; G. A. Spiller, 1984; Weiss & Laties, 1962). Surprisingly, although coffee drinking is recognized as the major vehicle of caffeine consumption, only a few studies have experimentally addressed the determinants of such behavior (Bernard, Dennehy, & Keefauver, 1981; Foxx & Rubinoff, 1979; James, Stirling, & Hampton, 1985; Kozlowski, 1976). Even though it is widely believed and there is much circumstantial evidence suggesting that caffeine is the primary pharmacological constituent in coffee that is responsible for maintaining chronic, high-volume coffee consumption (Gilbert, 1976; Greden, 1981), an unequivocal experimental demonstration of the reinforcing effects of caffeine in coffee apparently has not been published. The lack of research on coffee drinking as an instance of drug self-administration is all the more surprising because methodologies for conducting human drug self-administration studies have been well established and

Table 1

Subject characteristics and sequence of experiments.

Subject	Age (years)	Weight (kg)	Education: Grade level completed	Years of coffee drinking	Self-reported cups coffee per day	Self-reported cigarettes per day	History of drug abuse	History of alcohol abuse	Sequence of exposure to experiments
S-CI	26	68	12	10	18	40	Yes	No	1, 2, 3
S-PO	47	75	12+	32	9	40	No	No	1, 2, 3
S-WA	43	83	5	34	24	50	No	Yes	1, 2, 3
S-DA	48	82	12	29	14	55	No	Yes	1, 4
S-HA	37	66	8	22	25	25	No	Yes	1, 4
S-LE	49	68	12+	31	15	35	No	Yes	1, 4, 5
S-KA	49	84	12	36	12	35	Yes	Yes	1, 5
S-TO	39	86	10	10	15	70	No	Yes	1, 5
S-JO	29	70	12+	15	15	50	No	No	1

have been previously used to evaluate a wide variety of compounds such as ethanol, marihuana, heroin, sedatives, and tobacco (Griffiths, Bigelow, & Henningfield, 1980).

The present studies were undertaken to begin to investigate coffee drinking as drug self-administration. Volunteers with histories of heavy coffee drinking were paid to live in a residential research ward where access to coffee and other dietary sources of caffeine could be experimentally controlled and manipulated. The basic strategy was similar to that employed previously in this laboratory to investigate the self-administration of ethanol (Bigelow, Griffiths, & Liebson, 1975), sedatives (Griffiths, Bigelow, & Liebson, 1976), and tobacco (Griffiths, Henningfield, & Bigelow, 1982). The primary objectives of these studies were to determine the feasibility of using an intensive within-subject design to investigate coffee drinking and to begin to explore the control of coffee drinking by coffee concentration and caffeine.

GENERAL METHODS

Subjects

Nine healthy male volunteers with histories of heavy coffee drinking participated. Table 1 shows individual subject characteristics. All but two of the volunteers had histories of problem alcohol drinking and/or drug abuse. Subjects reported consuming an average of 9 to 25 cups of coffee per day. Caffeine intake from sources other than coffee (e.g., cola, tea, chocolate, medications) was relatively low. Given the rough estimate of 85 mg per cup of coffee (Bunker & McWilliams, 1979; Gilbert, Marshman, Schwieder, & Berg, 1976), estimated daily caffeine intake ranged between 10 to 32 mg/kg. This level of caffeine consumption is in the 99th percentile of adults in the United States (Graham, 1978). Details of subject screening, financial compensation, and informed consent were similar to those described previously (Griffiths et al., 1982). Briefly, on the basis of physical examination, history, routine laboratory chemistries, and chest X-ray, participants were found to be without significant medical or psychiatric disturbance other than their drug/alcohol abuse. Volunteers were recruited from the local community and paid for their participation at the rate of approximately $80.00 per week; none was institutionalized or under legal pressure to enroll. Before research participation, subjects gave their sober, informed, written consent to the research procedure.

Setting

Subjects participated while residing in an eight-bed behavioral pharmacology research ward that provided continuous access to various recreational, reading, and craft activities. Cooperation with research procedures and ward routines was maintained via an earnings system in which points, which were convertible to money, were earned by engaging in various personal and ward-maintenance activities; these earnings could be spent on minor ward privileges and could be sacrificed as consequence of rule violations.

General Procedures

After admission to the research ward, subjects were observed for a period of 2 to 6 days before the initiation of the experiments. The subjects participated in this research singly rather than in groups, a procedure that increases the independence of each subject's data. The number of other residents in the research ward varied unsystematically between two and seven. These other residents participated in different behavioral pharmacology experiments that sometimes involved the administration of opioids, ethanol, barbiturates, or benzodiazepines.

Other than a general explanation of experimental purpose (described below), subjects were given no instruction as to what they were "supposed" to do or of what outcomes might be expected. To reduce the possibility that subjects would receive instructions or explanations that might confound the results, ward staff were explicitly instructed to refrain from discussing experiments with subjects, except to provide an objective description of the routines and procedures that a subject must follow. Subjects received explicit instructions concerning details of the daily research procedures and concerning the residential ward rules, including the fact that they should remain in the ward dayroom area from 7:15 a.m. to 5:00 p.m. daily except for necessary brief visits to the bathroom.

Coffee Availability

Subjects were told that the general purpose of the research was to investigate the effects of different kinds and strengths of coffee "upon how you feel, upon your behavior, and upon the physiological response of your body." They were told that during their research participation the brand, strength, and caffeine content of the coffee might be changed from day to day, but the coffee would never be changed within the day. With respect to caffeine, subjects were told that the caffeine content of the coffee "may be varied from no caffeine at all to a high dose of caffeine (as much as 10 times greater than a normal cup of coffee)." It was emphasized to subjects that they were free to drink as much or as little coffee as they desired.

During the experiments subjects were allowed to drink only coffee prepared by staff. Other sources of caffeine (e.g., cola, tea, chocolate, etc.) were monitored and forbidden. Each day staff members were given 20 or more premeasured individual doses of coffee, marked only with that day's date, for dispensing to the 1 subject who was residing in the research ward at that time. Neither staff nor subjects were informed of the coffee brand, amount of coffee, or the caffeine content of the premeasured doses. Throughout the studies Taster's Choice® freeze-dried caffeinated or decaffeinated coffee was used. Except in Experiments 2 and 3, which involved manipulation of coffee concentration, coffee was prepared at the manufacturer's recommended concentration of 2 g freeze-dried coffee (approximately 1 rounded teaspoon) per cup. This amount of caffeinated and decaffeinated Taster's Choice® coffee has approximately 52 and 2 mg caffeine, respectively ("Instant Coffees," 1979). When a subject wanted coffee, he informed the staff. Staff poured the coffee dose in a cup, added preheated water (approximately 70 °C) to a volume of 180 mL, gave the cup to the subject, recorded the time the cup was dispensed, and began a timer to measure the time to consume the coffee. Subjects were allowed to add premeasured portions of cream and/or sugar if they desired; however they were not allowed to change these amounts during the course of their experimental participation. To facilitate staff monitoring of coffee drinking, subjects were required to drink their coffee while sitting in a designated chair near the nurses' station. In Experiment 1, coffee was available 24 hr a day; in all subsequent experiments, coffee was not available during the period from 12 midnight until the morning protocol began. The restriction of coffee overnight was implemented in order to eliminate the possible sleep-disrupting effects of consuming coffee at night. Although this change in coffee availability means that unambiguous comparisons between the results of Experiment 1 and subsequent experiments cannot be made, there appeared to be only a negligible effect on total cups of coffee consumed and average intercup interval.

Sequences of Experiments

The right-hand column of Table 1 shows the experiments in which each subject participated as well as the sequence of exposure to individual experiments for each subject. All subjects participated in the characterization of

Table 2

Characterization of ad-libitum coffee drinking in 9 subjects during each subject's last 6 days in Experiment 1. Cups per day and cup durations in minutes are expressed as means, with SE_M in parentheses; intercup intervals in minutes are expressed as medians with interquartile ranges in parentheses.

Subject	Cups per day	Cup duration (min)	Intercup interval (min)
S-CI	17.00 (0.63)	18.95 (0.97)	41 (23-67)
S-PO	14.67 (0.42)	11.85 (0.19)	61 (53-83)
S-WA	18.33 (0.99)	3.86 (0.18)	50 (34-73)
S-DA	15.17 (0.48)	30.73 (1.17)	61 (43-100)
S-HA	17.83 (0.31)	18.70 (0.36)	45 (37-55)
S-LE	17.00 (0.82)	14.75 (0.75)	52 (25-82)
S-KA	13.17 (0.31)	12.85 (0.51)	60 (38-98)
S-TO	13.33 (0.84)	22.27 (0.92)	55 (36-112)
S-JO	10.50 (0.76)	11.44 (0.60)	93 (55-130)

ad-libitum coffee drinking (Experiment 1). Three subjects each participated in Experiments 2 to 5, which were conducted in sequential order. Because at any given time only 1 subject participated in research on coffee drinking, subjects were arbitrarily assigned to experiments in the order in which they participated in the research. Differences among subjects in the number of experiments completed reflect differences in the length of time subjects agreed to participate in the inpatient research.

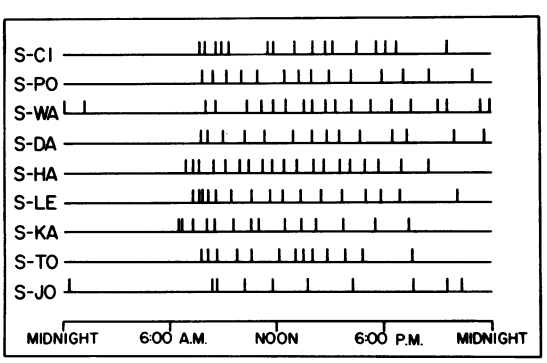


Fig. 1. Distributions of ad-libitum coffee drinking for the 9 subjects in Experiment 1. Times at which individual cups of coffee were dispensed are represented by vertical hatch marks. For each subject, data are from a 24-hr period during the last 6 days of the experiment. The 24-hr period was selected for each subject such that the number of cups consumed approximated the mean consumed during the last 6 days.

EXPERIMENT 1: CHARACTERIZATION OF AD-LIBITUM COFFEE DRINKING

The objective of the initial experiment in this series was simply to describe patterns of 24-hr ad-libitum coffee intake in subjects with histories of heavy coffee drinking.

METHOD

Nine subjects with histories of heavy coffee drinking participated (Table 1). Using the general methods described previously, caffeinated coffee was freely available 24 hr a day. Each cup of coffee was prepared from 2 g of freeze-dried caffeinated coffee. The experiment was continued at least 6 days and until there were no trends over the last 6 days in number of cups per day. For purposes of data analysis, cup duration was defined as the time from dispensing a cup of coffee to the time the subject returned the empty cup. Intercup interval was defined as the time between dispensing sequential cups of coffee.

RESULTS

Stable patterns of coffee drinking emerged when subjects were given free access to coffee for 6 to 10 days (mean: 7.5 days). Average number of cups per day, cup duration, and intercup interval over the last 6 days are presented in Table 2 for each of the 9 subjects. Although there were between-subject differences, these measures were relatively stable within subjects as suggested by the measures of variability. Representative within-day distributions of coffee drinking for all 9 subjects are presented in Figure 1. As shown in the figure, during normal waking hours coffee drinking tended to be rather regularly spaced, with a tendency for intercup intervals to become progressively longer throughout the day. Coffee drinking was erratic during mid-evening and early-morning hours when subjects typically slept. Over the 6-day period, 6 of the 9 subjects drank some coffee between midnight and 6:00 a.m. (range of the means was 0.33 to 1.66 cups/night for the 6 subjects).

Figure 2 presents average intercup interval and cup duration as a function of sequential cups of the day. Intercup interval showed a progressive increase from approximately 20 to 80 min over successive cups. Cup duration, in contrast, showed a modest increase from the

first to the second cup of the day and remained relatively stable over subsequent cups.

EXPERIMENT 2: MANIPULATION OF COFFEE CONCENTRATION

Experiment 1 showed that orderly within-day and stable across-day patterns of coffee drinking occur when subjects are given free access to coffee. Experiment 2 was undertaken to examine the sensitivity of coffee drinking to changes in coffee concentration.

METHOD

Three subjects with histories of heavy coffee drinking participated (Table 1). Using the general methods described previously, freeze-dried caffeinated coffee was made available daily from 7:00 a.m. until 12:00 midnight. Subjects were told that the brand, strength, and caffeine content of the coffee might be changed from day to day but the coffee would never be changed within the day. Coffee concentration was manipulated by varying the amount of caffeinated freeze-dried coffee from which each 180-mL cup of coffee was made. Six concentrations corresponding to 0.5, 1, 2, 4, 8, and 16 g of caffeinated coffee per cup were examined; concentrations were examined in a block randomized sequence across days (a single concentration was examined on a given day and the order of concentrations was random, with the constraint that all concentrations occurred once before any concentration was repeated). Each block was repeated four times. Although subjects were not explicitly informed of the nature of the change in their coffee from day to day, gross differences across the 32-fold concentration range were readily apparent to subjects by visual inspection of a prepared cup of coffee. At 5:00 p.m. each day, subjects rated the "strength" (7-point scale from "very weak" to "very strong"), "bitterness" (7-point scale from "not at all bitter" to "very bitter"), and their "overall liking" (5-point scale from "I dislike it" to "I like it very much") of the coffee they received that day.

RESULTS

As shown in Figure 3, there were orderly concentration-related effects on all of the major dependent variables. As coffee concentration was increased, cups consumed varied as an inverted U-shaped function, while intercup interval was a U-shaped function. Average cup duration showed concentration-related increases at the highest concentrations. Total coffee consumed was an increasing function of concentration except for the highest concentrations, at which it decreased somewhat. Subject ratings of coffee "strength" (not shown) and "bitterness" were monotonically increasing functions of concentration, while "liking" was an inverted U-shaped function.

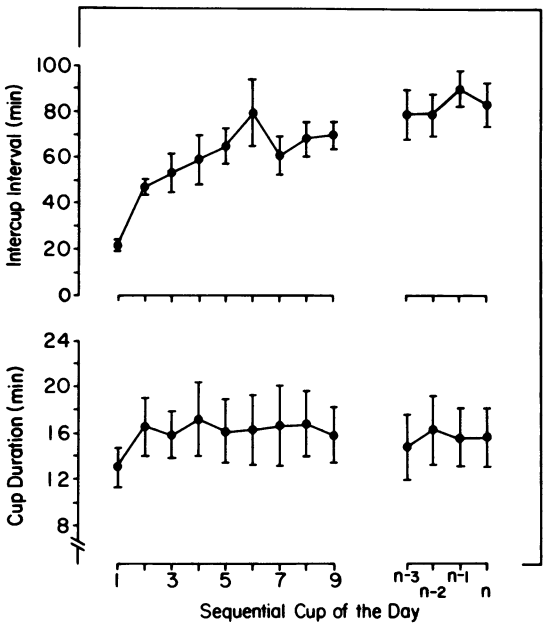
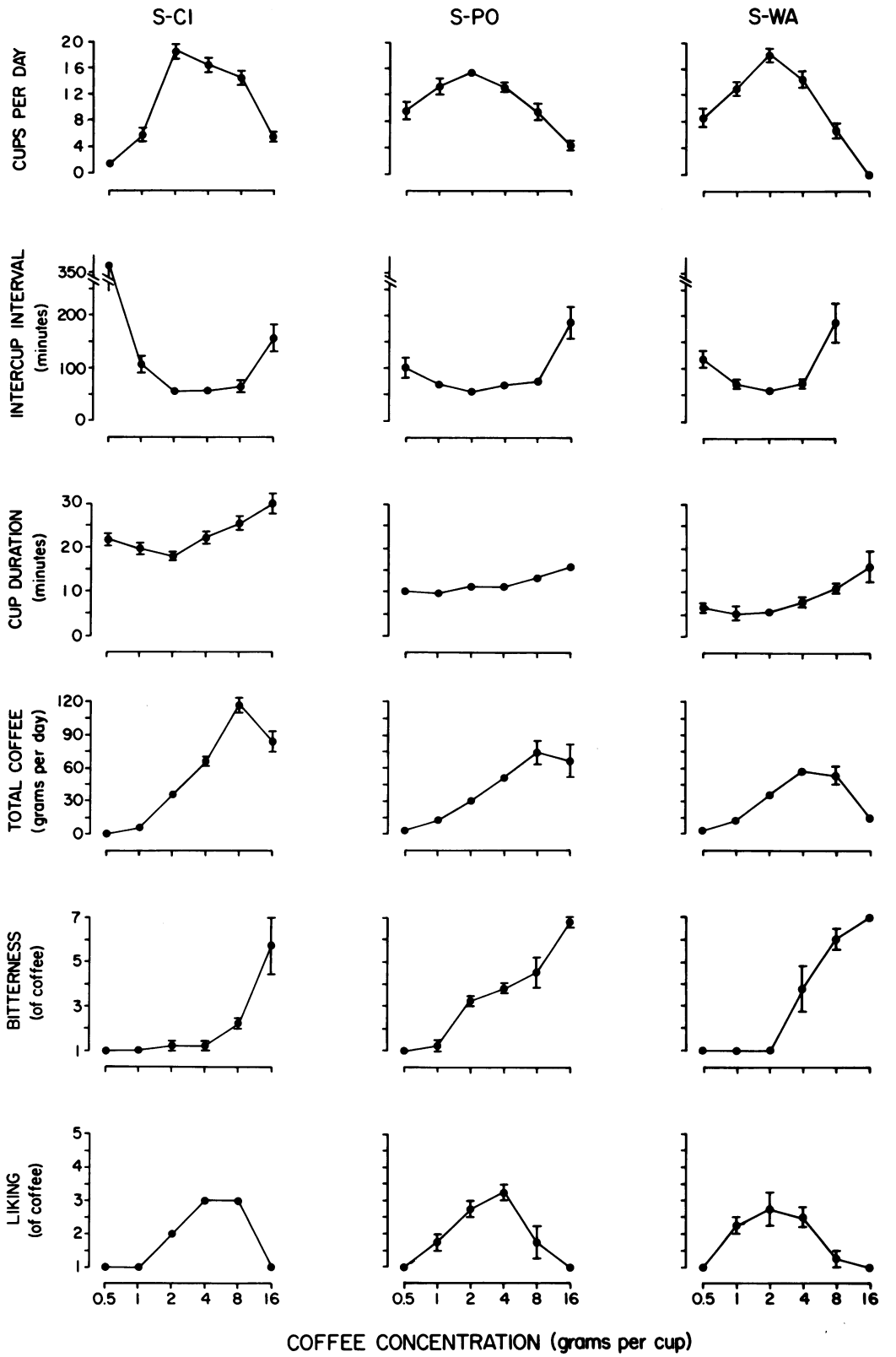


Fig. 2. Average intercup interval and cup duration as a function of sequential cup of the day in Experiment 1. *y* axes: intercup interval and cup duration in minutes; *x* axes: sequential cup of the day. The first cup to occur after 6:00 a.m. was considered the first cup of the day; *n* indicates the last cup of the day. Data points and brackets indicate means ± 1 SE_M for 9 subjects (N = 9), based upon the individuals' median intercup intervals and mean cup durations during the last 6 days in Experiment 1.

Representative within-day distributions of coffee drinking across the six concentrations in all 3 subjects are presented in Figure 4. As suggested by this figure, number of cups per day was an inverted U-shaped function of concentration and intercup interval was a U-shaped function of concentration (cf. Figure 3). As in Experiment 1, analysis of sequential intercup intervals generally showed increases over successive cups of the day.


S-CI
S-PO
S-WA
CUPS PER DAY
INTERCUP INTERVAL (minutes)
CUP DURATION (minutes)
TOTAL COFFEE (grams per day)
BITTERNESS (of coffee)
LIKING (of coffee)
0.5 1 2 4 8 16
COFFEE CONCENTRATION (grams per cup)

EXPERIMENT 3: MANIPULATION OF COFFEE CONCENTRATION AND CAFFEINE DOSE

Experiment 2 showed that coffee drinking was an orderly function of coffee concentration. The inverted U-shaped function relating cups per day to coffee concentration suggested that intermediate coffee concentrations were reinforcing in that these concentrations reliably maintained coffee drinking at rates exceeding the lowest (vehicle-like) concentration. The experiment also demonstrated the feasibility of conducting coffee-drinking experiments by manipulating the coffee contents on an across-day basis. In Experiment 2, the manipulation of coffee concentration and caffeine concentration covaried (i.e., coffee and caffeine concentration were purposely confounded). Experiment 3 was undertaken to begin to provide more information about the role of caffeine in coffee drinking by manipulating coffee concentration and caffeine dose independently.

METHOD

Three subjects with histories of heavy coffee drinking participated (Table 1). Using the general methods described previously, coffee was made available daily from 7:00 a.m. until 12:00 midnight. Subjects were told that the brand, strength, and caffeine content of the coffee might be changed from day to day but the coffee would never be changed within the day. Coffee concentration was manipulated over a four-fold range by varying the amount of decaffeinated freeze-dried coffee from which each cup was made; three concentrations corresponding to 2, 4, and 8 g of decaffeinated coffee per cup were examined. Caffeine dose was manipulated over two levels by using either decaffeinated coffee to which caffeine had been added in the ratio of 100 mg caffeine anhydrous (USP) per 2 g freeze-dried coffee, or by using decaffeinated coffee to which powdered lactose had been added in a ratio similar to caffeine. The ratio of caffeine to powdered decaffeinated coffee was chosen such that at the manufacturer's recommended coffee concentration (2 g per cup) each cup would contain 100 mg caffeine. Although this caffeine amount is higher than the equivalent brand of caffeinated freeze-dried coffee—52 mg/cup ("Instant Coffees," 1979), it is in the mid-range of caffeine doses that normally occur in cups of brewed coffee (Bunker & McWilliams, 1979; Gilbert et al., 1976). Lactose was used in the decaffeinated conditions in amounts similar to caffeine in the caffeinated conditions in order to match the appearance of the unprepared coffee in the two conditions. A previous study by Goldstein (1964) and preliminary trials at the 2-g concentration (Griffiths, unpublished observations) sug-

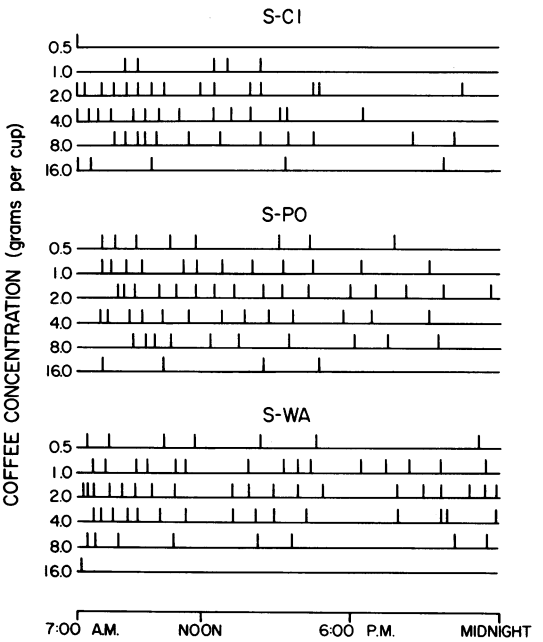


Fig. 4. Representative distributions of coffee drinking for each of the 3 subjects in Experiment 2. Times at which individual cups of coffee were dispensed are represented by vertical hatch marks. Coffee concentration was varied across days; data are from 1 of the 4 days at each concentration. Selection of data for presentation was quasi-random.

←

Fig. 3. Effects of coffee concentration on coffee drinking and subjective ratings shown separately for the 3 subjects in Experiment 2. y axes: number of cups per day, intercup interval in minutes, cup duration in minutes, total coffee per day in grams, coffee bitterness, and coffee liking; x axes: coffee concentration in grams per cup, log scale. Each data point and bracket indicates mean ± 1 SE_M for 4 days ($N = 4$). Absence of bracket indicates radius of data point is greater than 1 SE_M; the upper bracket for Subject S-CI's intercup interval at the 0.5-g concentration has been deleted for clarity.

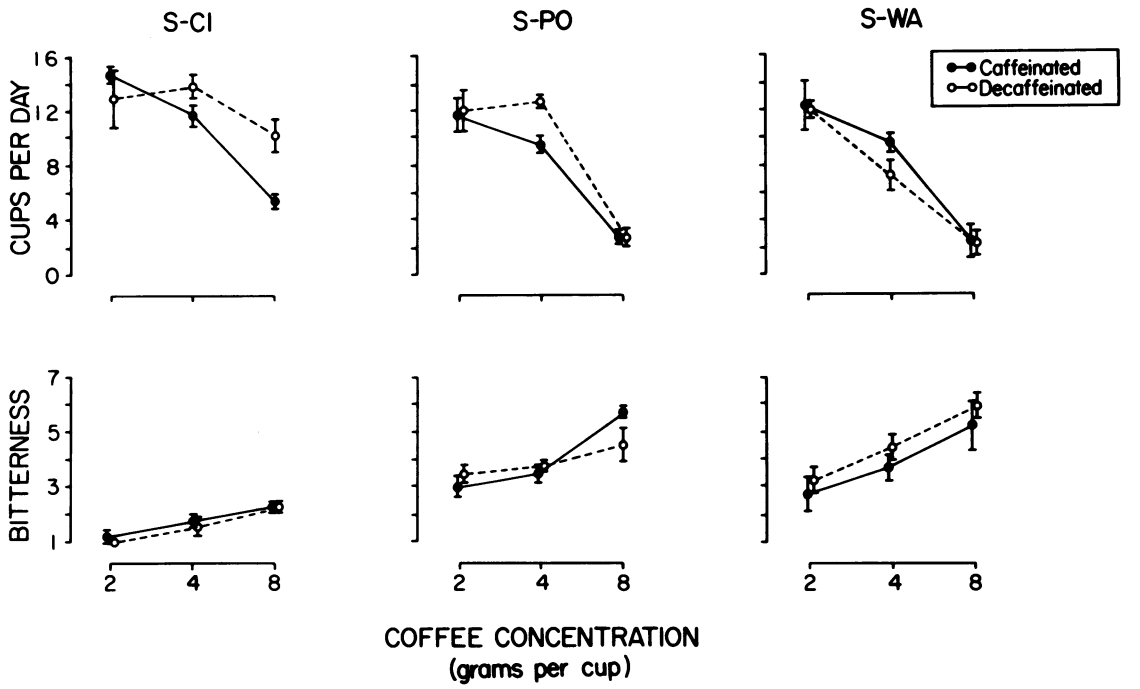


Fig. 5. Effects of coffee concentration and caffeine dose on coffee drinking and subjective ratings, for each of the 3 subjects in Experiment 3. y axes: number of cups per day and coffee bitterness; x axes: coffee concentration in grams per cup, log scale. Filled and unfilled data points indicate caffeinated and decaffeinated conditions, respectively. Each data point and bracket indicates mean ± 1 SE_M for 4 days (N = 4). Absence of a bracket indicates that the radius of the data point is greater than 1 SE_M.

gested that the decaffeinated coffee plus lactose and the decaffeinated coffee plus caffeine (100 or 150 mg per cup) could not be reliably differentiated on the basis of taste or appearance. The six experimental conditions (2, 4, and 8 g of decaffeinated coffee and 2, 4, and 8 g of caffeinated coffee) were examined in a block randomized sequence across days and each block was repeated four times. As in Experiment 2, at 5:00 p.m. subjects rated "strength," "bitterness," and their "liking" of the coffee available that day.

Results

In general, variation of coffee concentration produced orderly effects consistent with those in Experiment 2; surprisingly, there were no consistent differences between the caffeinated versus decaffeinated conditions on the behavioral and subjective measures.

As shown in Figure 5, cups of caffeinated coffee consumed decreased monotonically with concentration, an effect similar to that observed at similar concentrations in Experiment 3 (cf. Figure 3). Cups of decaffeinated coffee consumed also decreased with concentration. There were no consistent differences across the 3 subjects between caffeinated versus decaffeinated conditions in number of cups consumed. Subject ratings of "bitterness" (Figure 5), "strength," and "liking" were similar to the results in Experiment 2 at these same coffee concentrations. Again, there were no consistent differences between the caffeinated versus decaffeinated conditions on these ratings (e.g., bitterness in Figure 5).

EXPERIMENT 4: MANIPULATION OF CAFFEINE DOSE

Experiment 3 began to explore the role of caffeine in coffee drinking by comparing the self-administration of caffeinated versus decaffeinated coffee at three different coffee concentrations. No consistent differences between the caffeinated and decaffeinated conditions were found. Experiment 4 was undertaken to explore further the role of caffeine in coffee

drinking by systematically manipulating caffeine dose over a wide range.

Method

Three subjects with histories of heavy coffee drinking participated (Table 1). With the exception of some changes in coffee availability and testing at the beginning of the day, the general methods were similar to those used in Experiments 2 and 3. As before, subjects were told that the brand, strength, and caffeine content of the coffee might be changed from day to day but the coffee would never be changed within the day. Unlike previous experiments, subjects were required to start their first cup of coffee for the day at 7:30 a.m. and they were permitted no additional coffee until 8:45 a.m. At 8:30 a.m. arm tremor was assessed as described below. From 8:45 a.m. until 12:00 midnight subjects were given free access to coffee as in Experiments 2 and 3. The primary rationale of the 7:30 a.m. "sample" cup and the delayed availability of subsequent coffee was to attempt to reduce the likelihood of inadvertent caffeine overdose; inasmuch as caffeine content was to be varied over a wide range from day to day, it was reasoned that the sample cup and delay interval would allow subjects the opportunity to experience fully the effects of the coffee before the beginning of the period of free availability.

Caffeine dose was manipulated by varying the amount of caffeine added to a standard concentration of decaffeinated coffee. All cups of coffee were made from 2 g freeze-dried decaffeinated coffee (the manufacturer's recommended concentration) to which caffeine anhydrous (USP) and/or powdered lactose had been added. In order to match the appearance of the unprepared coffee across conditions, the amount of caffeine, lactose, or caffeine/lactose combination was held constant across conditions. Five or six dose conditions involving 0, 25, 50, 100, 200, and 400 mg caffeine anhydrous per cup were examined; conditions were studied in a block randomized sequence across days and each block was repeated five times. Subject-DA was studied at all six caffeine doses. Because at the beginning of the experiment S-HA and S-LE sometimes reported symptoms suggesting caffeine toxicity (e.g., having an upset stomach, feeling jittery), the 400-mg condition was not studied in S-HA and was examined on only 1 day in S-LE. As in Experiments 2 and 3, at 5:00 p.m. subjects rated "strength," "bitterness," and their "liking" of the coffee available that day.

Arm Tremor

At 8:30 a.m., 1 hr after receiving the "sample" cup of coffee, subjects participated in an arm-tremor task on which dose-related sensitivity to caffeine has previously been reported (Chait & Griffiths, 1983). A pretreatment interval of 60 min between dosing and testing is appropriate because caffeine is rapidly absorbed and distributed (Gilbert, 1976) and has been shown to produce reliable effects on verbal self-reports with this pretreatment interval (Chait & Griffiths, 1983). For this task, the subject held a metal stylus (2 mm in diameter, approximately 30 cm long) in the preferred hand. With the arm fully extended, the subject inserted the stylus into a 6-mm diameter hole in a metal plate. The metal plate was mounted vertically, facing the subject, on a rack at about shoulder level. The subject was instructed to hold the stylus as steadily as possible without touching the sides of the hole. After the subject inserted the stylus into the hole, a timer was started and the number of contacts in a 20-s period was automatically recorded.

Results

Figure 6 presents the major results of manipulating caffeine dose. For all 3 subjects, cups consumed increased slightly from 0 to 25 or 50 mg caffeine, thus providing some limited evidence for the reinforcing effects of caffeine in coffee (maximum effect for decaffeinated vs. caffeinated conditions, respectively: 11.8 ± 0.8 vs. 15.8 ± 1.6 cups in S-DA; 15.2 ± 0.3 vs. 16.6 ± 0.2 cups in S-HA; and 9.6 ± 1.1 vs. 13.4 ± 1.3 cups in S-LE). For all 3 subjects, higher caffeine doses (50 to 400 mg) produced an orderly dose-related suppression in cups consumed. Total caffeine consumed (including 2 mg caffeine per 2 g of decaffeinated coffee) increased monotonically with dose except at the highest dose tested in 2 subjects (S-DA and S-HA) at which it decreased slightly. The intercup-interval function of dose and the cup-duration function of dose did not vary consistently across subjects (not shown). Subject ratings of "bitterness" showed clear dose-related increases in S-DA, but only relatively small elevations at the highest dose

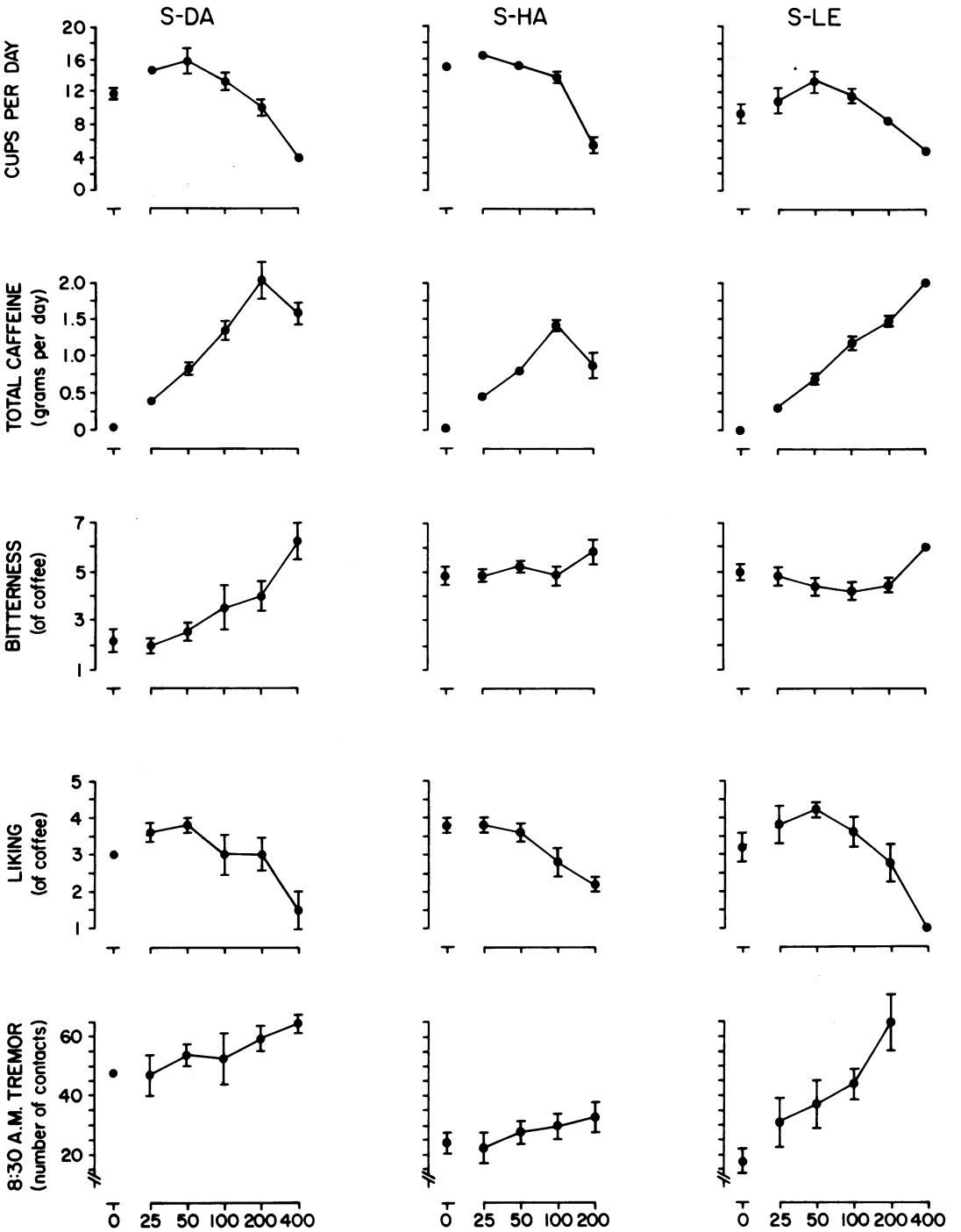


Fig. 6. Effects of caffeine dose on coffee drinking, subjective ratings, and arm tremor, for each of the 3 subjects in Experiment 4. *y* axes: number of cups per day, total caffeine per day in grams, coffee bitterness, coffee liking, and number of stylus contacts from the 8:30 a.m. tremor measure; *x* axes: caffeine dose in milligrams of caffeine added to each cup of decaffeinated coffee. Each data point and bracket indicates mean ± 1 SE_M for 5 days ($N = 5$) except for S-LE at 400 mg, at which $N = 1$. Absence of a bracket indicates that the radius of the data point is greater than 1 SE_M. Due to an equipment malfunction, tremor data were not collected for Subject S-LE at 400 mg.

tested in S-HA and S-LE. Ratings of coffee "strength" (not shown) were not sensitive to caffeine-dose manipulations. Subject ratings of "liking" were generally similar to cups consumed, showing dose-related decreases as dose was increased from intermediate to high levels (50 to 400 mg). Finally, the 8:30 a.m. measure of arm tremor (1 hr after the sample cup) showed dose-related increases in all 3 subjects.

Representative within-day distributions of coffee drinking across the doses examined are presented in Figure 7. As suggested by this figure, average number of cups was an inverted U-shaped function of caffeine dose (cf. Figure 6). Figure 7 also shows that at the highest caffeine doses (200 and 400 mg), subjects sometimes abruptly stopped drinking coffee relatively early during the coffee-drinking day. This effect occurred occasionally in each of the 3 subjects. As a consequence, the intercup interval function of dose tended to be erratic both within and across subjects. As in previous experiments, analysis of sequential intercup intervals showed increases over successive cups of the day.

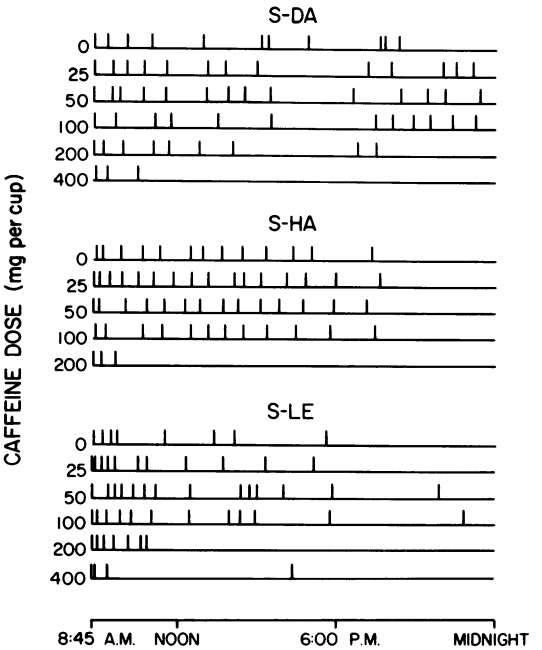


Fig. 7. Representative distributions of the 3 subjects' coffee drinking in Experiment 4. Times at which individual cups of coffee were dispensed are represented by vertical hatch marks. Caffeine doses indicate milligrams of caffeine added to each cup of decaffeinated coffee. Dose was varied across days; data are from 1 of the 5 days at each dose, except that S-LE was exposed to 400 mg for only 1 day. Selection of the data for presentation was quasi-random.

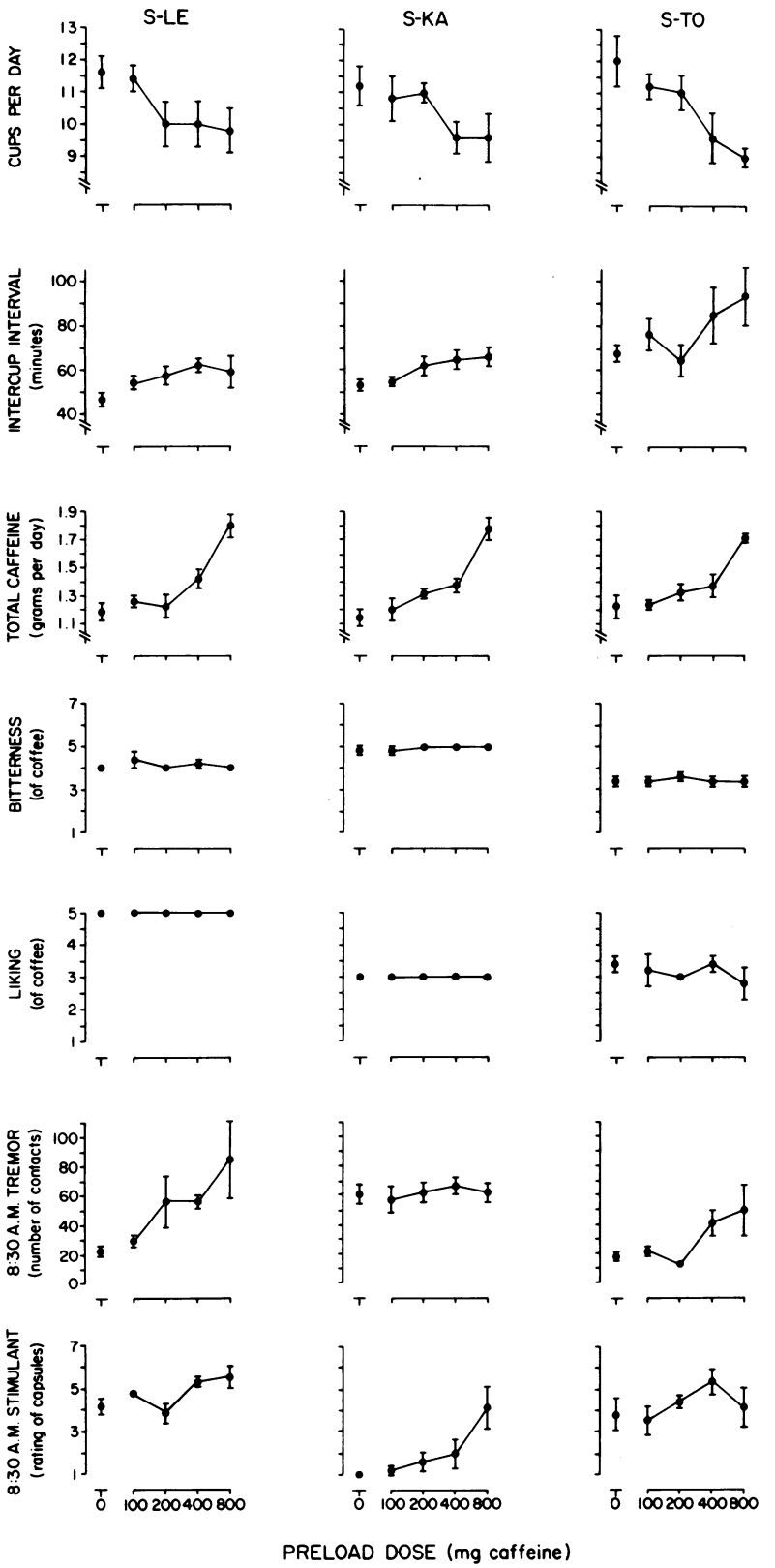
EXPERIMENT 5: EFFECTS OF CAFFEINE PRELOAD

In Experiment 4 the role of caffeine in coffee drinking was investigated by manipulating the caffeine dose in the coffee. The study demonstrated that high doses of caffeine (i.e., 200 or 400 mg/cup) suppressed coffee drinking. The study also provided some limited evidence for reinforcing properties of low doses of caffeine: Compared with the decaffeinated condition, low doses of caffeine (25 or 50 mg per cup) were correlated with a slightly higher number of cups consumed. Experiment 5 was undertaken to provide additional information on caffeine and coffee drinking, by exploring the effects on coffee drinking of preloading subjects with caffeine in capsules.

METHOD

Three subjects with histories of heavy coffee drinking participated (Table 1). The general methods were similar to those used previously and the daily procedure was similar to that in Experiment 4 except that subjects ingested capsules at 7:30 a.m. in place of ingesting a sample cup of coffee. Each day at 7:30 a.m. subjects ingested two opaque size 0 gelatin capsules with approximately 210 cc water. Subjects were informed that the capsules contained a placebo or one in a wide range of doses of caffeine. The capsules, which were administered under double-blind conditions (i.e., neither the subjects nor staff knew the contents), contained caffeine anhydrous and/or lactose. Five doses were examined, involving 0, 100, 200, 400, and 800 mg caffeine anhydrous; the conditions were studied in a block randomized sequence across days and each block was repeated five times.

At 8:30 a.m. arm tremor was assessed as described in Experiment 4 and subjects rated magnitude of the "stimulant effect" from the capsules on a 7-point scale from "no effect" to "very strong effect." As in Experiment 4, from 8:45 a.m. until 12:00 midnight subjects were given free access to coffee. As before, subjects were told that the brand, strength, and caffeine content of the coffee might be changed from day to day but the coffee would


S-LE
S-KA
S-TO
CUPS PER DAY
INTERCUP INTERVAL (minutes)
TOTAL CAFFEINE (grams per day)
BITTERNESS (of coffee)
LIKING (of coffee)
8:30 A.M. TREMOR (number of contacts)
8:30 A.M. STIMULANT (rating of capsules)
0 100 200 400 800
PRELOAD DOSE (mg caffeine)

never be changed within the day. In fact, coffee was not manipulated in this experiment; all cups of coffee were made from 2 g freeze-dried decaffeinated coffee (the manufacturer's recommended concentration) to which 100 mg caffeine anhydrous was added. This amount of caffeine is in the mid-range of caffeine doses that normally occur in cups of brewed coffee (Bunker & McWilliams, 1979; Gilbert et al., 1976) and the ratio of decaffeinated coffee to caffeine was identical to that used in Experiment 3. As in Experiments 2, 3, and 4, at 5:00 p.m. subjects rated "strength," "bitterness," and their "liking" of the coffee available that day.

Results

Figure 8 presents the major results of manipulating the caffeine preload dose. In all 3 subjects, as preload dose increased, cups consumed decreased, and intercup interval increased. Although the magnitude of these changes was modest (e.g., difference between 0- and 800-mg preload ranged between 1.6 and 3.0 cups per day across subjects), the preload effect was clearly dose-related. Despite the decreases in cups consumed, total caffeine consumed per day (preload dose plus 102 mg per cup of coffee) increased with increases in preload dose. Cup duration as a function of preload dose did not vary consistently across subjects (not shown). Subject ratings of coffee "strength" (not shown), "bitterness," and "liking" were insensitive to preload dose. Finally, with regard to the 8:30 a.m. measures of tremor and stimulant effect, each of the 3 subjects showed clear dose-related sensitivity to at least one of these two measures of the magnitude of the preload drug effect.

Inspection and analysis of within-day distributions of coffee drinking revealed no striking effects of preload dose. Intercup intervals increased over successive cups of the day under all preload doses in all 3 subjects (e.g., mean $\pm$ SE_M for first and last intercup interval, respectively, under the 0 preload condition were 22.2 $\pm$ 4.9 and 122.6 $\pm$ 11.1 for S-LE; 19.2 $\pm$ 4.1 and 86.2 $\pm$ 11.5 for S-KA; and 13.8 $\pm$ 2.3 and 89.8 $\pm$ 20.4 for S-TO). Although average intercup interval increased with increases in preload dose (cf. Figure 8), the latency to start the first cup of the day and the length of the initial intercup intervals of the day did not show dose-related increases with preload dose as would be expected if intercup interval were predominately controlled by prior caffeine intake.

DISCUSSION

The present set of studies has shown coffee drinking in heavy coffee-drinking subjects to be stable and orderly behavior. When cups of coffee were freely available, coffee drinking tended to be rather regularly spaced during the day with intercup intervals becoming progressively longer throughout the day. That caffeinated coffee was reinforcing at intermediate (i.e., usual) concentrations was suggested by the finding that intermediate concentrations reliably maintained higher numbers of cups per day than the lowest (vehicle-like) concentration (Figure 3).

The progressive increase in intercup interval over the initial cups of the day cannot be attributed solely to accumulating caffeine levels (e.g., a caffeine-satiation mechanism) because the effect occurred at a range of caffeine concentrations (Experiment 4) and because caffeine preloads did not influence initial intercup intervals of the day (Experiment 5).

Although coffee drinking was suppressed both by high caffeine doses per cup (Figure 6) and by high coffee concentrations (Figure 3), the bases for the caffeine-related versus concentration-related suppression may be different. Manipulation of coffee concentration produced orderly effects on intercup interval and cup duration (Figure 3) while caffeine dose manipulations had only erratic effects on these measures. Further, in contrast to the manipulations of coffee concentration, high caffeine doses sometimes produced abrupt cessations of coffee drinking (Figures 4 and 7).

←

Fig. 8. Effects of caffeine preload in capsules on 3 subjects' coffee drinking, subjective ratings, and arm tremor in Experiment 5. *y* axes: number of cups per day, intercup interval in minutes, total caffeine per day in grams, coffee bitterness, coffee liking, number of stylus contacts during the 8:30 a.m. tremor measure, and 8:30 a.m. stimulant rating of capsules; *x* axes: preload dose of caffeine in milligrams. Each data point and bracket indicates mean $\pm$ 1 SE_M for 5 days ($N = 5$). Absence of a bracket indicates that the radius of a given data point is greater than 1 SE_M.

The present studies provide some evidence that caffeine can suppress coffee drinking. In Experiment 4, high caffeine doses (200 and 400 mg per cup) consistently reduced the number of cups consumed below that observed in the decaffeinated, low, and intermediate caffeine-dose conditions. In Experiment 5, caffeine preloads consistently but modestly reduced the number of cups consumed in a dose-dependent fashion. These results extend those of Kozlowski (1976), who manipulated the caffeine content of coffee (25, 50, or 100 mg per cup) and found that fewer cups were consumed at the highest dose than at the lower doses.

The present studies provide very limited evidence for the reinforcing properties of caffeine. In Experiment 4, low caffeine doses (25 or 50 mg per cup) were correlated with a slightly higher number of cups consumed than in the decaffeinated condition. Although the magnitude of the effect was small, it occurred in all 3 subjects. It is unlikely that the effect is due to taste differences because ratings of "bitterness" and "strength" did not differentiate the caffeinated (25 and 50 mg per cup) from the decaffeinated doses and because previous taste comparisons (Goldstein, 1964; Griffiths, unpublished observations) suggested that caffeinated (100 or 150 mg per cup) and decaffeinated coffee cannot be differentiated reliably. Thus, these results suggest that low doses of caffeine in coffee may be reinforcing (i.e., may maintain self-administration above control levels).

The possible reinforcing properties of caffeine notwithstanding, it is noteworthy that, at usual concentrations, drinking of decaffeinated coffee was well maintained in the present studies. In fact, the numbers of cups consumed per day of normal-strength decaffeinated coffee did not differ greatly from the corresponding numbers for normal-strength caffeinated coffee (cf. conditions of 2 g per cup in Experiment 3; conditions of 0 and 100 mg per cup in Experiment 4). Although it is possible that decaffeinated-coffee drinking was maintained by caffeine-related conditioned reinforcers (e.g., taste and sensory stimuli), there are numerous substances in decaffeinated coffee that might have behavioral (including reinforcing) effects (Boublik, Quinn, Clements, Herington, Wynne, & Funder, 1983; Cohen & Booth, 1975; M. A. Spiller, 1984). Future studies should further investigate the maintenance of decaffeinated-coffee drinking by determining the extent to which intake is maintained over prolonged periods of continuous availability.

Although the number of cups consumed was responsive to manipulations of coffee concentration (Experiment 2), of caffeine dose (Experiment 4), and of caffeine preloads (Experiment 5), the present experiments did not provide evidence for precise regulation (i.e., titration) of coffee or caffeine intake. Through the intermediate portions of the concentration and caffeine dose-effect curves, there were substantial increases in total consumption of coffee (Figure 3) and caffeine (Figure 6). Further, caffeine preloads produced substantial increases in total caffeine consumed (Figure 7). This lack of precise regulation of coffee and caffeine intake is consistent with a variety of studies of drug self-administration in both humans and nonhumans, which have shown that dose manipulations are typically not accompanied by precise regulation of drug intake (cf. Griffiths, Bigelow, & Henningfield, 1980).

Although it is sometimes assumed that drug-produced euphoria and liking are determinants of drug self-administration, such assumptions can reasonably be questioned, and dissociations between such subjective measures and behavioral measures of drug reinforcement have been reported (Griffiths, Bigelow, Liebson, & Kaliszak, 1980; Schuster, Fischman, & Johanson, 1981). The results of the present studies provide an opportunity to examine the relationship between subject ratings of their liking of the coffee and corresponding rates of coffee self-administration. Examination of data from Experiments 2 and 4, which involved manipulation of coffee concentration and caffeine dose (Figures 3 and 6), indicates a generally close covariation between cups consumed and reported liking. However, the results of Experiment 5, which involved administration of caffeine preload doses, showed that caffeine preload decreased cups consumed without influencing subjects' reports of liking the coffee (Figure 8). Although there are undoubtedly several plausible explanations for this dissociation between cups consumed and reports of liking, the dissociation further emphasizes the fact that be-

havioral measures of drug self-administration need not always covary with verbal reports presumed to reflect reinforcing properties.

Because caffeine is a bitter alkaloid, subject ratings of coffee "bitterness" were used in the present study in an attempt to assess the extent to which subjects discriminated between different caffeine conditions on the basis of taste. High concentrations of caffeine produced elevations in bitterness ratings compared to decaffeinated conditions in all 3 subjects tested (Experiment 4, Figure 6). However, at a more "usual" caffeine concentration in coffee (i.e., 100 mg per cup), 5 of 6 subjects tested did not differentiate between caffeinated and decaffeinated conditions (2 g per cup conditions in Experiment 3 [Figure 5]; 0 and 100 mg per cup conditions in Experiment 4 [Figure 6]). This finding is consistent with the results of previous taste comparisons that suggested that decaffeinated coffee plus lactose (placebo) cannot be reliably differentiated from decaffeinated coffee plus 100 or 150 mg caffeine (Goldstein, 1964; Griffiths, unpublished observations). However, the sixth subject (S-DA, Figure 6) rated coffee containing 100 mg of caffeine as being slightly more bitter (3.6 ± 0.9) than the decaffeinated coffee (2.2 ± 0.4). The finding of differences among subjects with respect to their ability to detect caffeine at normal concentrations is consistent with the prediction of Hall, Bartoshuk, Cain, and Stevens (1975), who demonstrated population differences in taste sensitivity to caffeine. In conducting studies comparing "usual" concentrations of caffeinated versus decaffeinated coffee, investigators should not assume that all subjects will be unable to differentiate between conditions on the basis of taste.

The present set of studies has revealed coffee drinking to be a stable and orderly form of drug self-administration behavior that is readily amenable to experimental analysis using intensive within-subject experimental designs. One focus of this research was to begin to explore the role of caffeine in coffee drinking. Under the limited set of conditions examined, these studies provide some evidence for both the suppressive and the reinforcing effects of caffeine on coffee consumption. Valuable additional information about caffeine's role in coffee drinking will be provided by future studies in which caffeine is manipulated on a more chronic basis for periods of weeks, rather than on the acute, daily basis as was done in the present studies.

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