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Anorectic Specificity as Measured in a Choice Paradigm in Rhesus Monkeys

REBECCA L. CORWIN[1] AND CHARLES R. SCHUSTER[2]

The Drug Abuse Research Center, Department of Psychiatry, The University of Chicago, Chicago, IL, 60637

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CORWIN, R. L. AND C. R. SCHUSTER. *Anorectic specificity as measured in a choice paradigm in rhesus monkeys.* PHARMACOL BIOCHEM BEHAV 45(1) 131–141, 1993.—The present report describes a new procedure for assessing anorectic specificity. Two rhesus monkeys (*Macaca mulatta*) surgically prepared with indwelling intragastric catheters were trained in a discrete trial choice paradigm to respond for either food or visual access to a room containing other monkeys. Our hypothesis was that a specific anorectic would reduce only food-maintained responding; responding to open a window would either not be affected or would increase. Caloric preloads, *d*-amphetamine, (*d,l*)-fenfluramine, and cholecystokinin octapeptide all decreased food-maintained responding and had no effect on or increased responding maintained by window opening. These results demonstrate that choice procedures are useful for assessing anorectic specificity.

Amphetamine Anorectics Cholecystokinin Feeding Food Fenfluramine Monkeys Self-administration Visual reinforcement

DRUGS that reduce food intake may do so for a variety of reasons, some of which are specific to food intake and some of which are not. One way to separate specific from nonspecific effects on food-maintained behaviors is to compare the drug's effect on responding for food and for nonfood reinforcers. A drug that acts specifically to suppress food intake should only decrease food-maintained behaviors; responding for other reinforcers should not be affected or should increase. A method commonly used to examine anorectic specificity is to compare the effects of drugs on food and water intake in separate tests. The satiety peptide cholecystokinin (CCK) and two anorectics, *d*-amphetamine (AMPH) and fenfluramine (FEN), have been studied in this way. These compounds have no effect on water intake at doses that reduce feeding, providing strong evidence that their effects on food intake are behaviorally specific (13,17,18,28,39). Although this type of analysis is compelling, separate tests of food and water intake are required. Choice paradigms, on the other hand, allow the simultaneous determination of a drug's effect on responding for more than one reinforcer and thus seem ideal for assessing anorectic specificity. The first purpose of the present study was to use a choice paradigm to extend previous reports of the anorectic specificity of AMPH, FEN, and CCK.

When deciding which reinforcers to use in a choice paradigm for assessing anorectic specificity, several factors should be considered. Food must be one of the reinforcers to measure a drug's effect on food-maintained behavior. The other reinforcer(s) should ideally be unrelated to the ingestion of food. Water, for instance, would not be useful in this type of study if the subject were primarily a prandial drinker. If a drug decreased responding for food, responding for water within the same session would probably also decrease, making differential drug effects impossible to discern. It has been suggested that visual reinforcement in monkeys could prove useful in pharmacological studies and eliminate confounds produced by drug effects on responding maintained by food and water (20,26). It has been known for some time that monkeys will respond to view a variety of stimuli (3,4,7,8,9,20,31) and that the opportunity to see or hear other monkeys will maintain a higher frequency of behaviors than the opportunity to see or hear other animals or objects (3–5,7,8,21). Visual reinforcement has been used in one study to reveal specific effects of drugs. When food and visual access were made available on a concurrent fixed ratio (FR) 10 schedule of reinforcement, differential effects of morphine were seen (31). The above reports suggest that the opportunity for rhesus monkeys to view other monkeys would function well as a nonfood reinforcer in a choice paradigm. The second purpose of the present study was to extend these previous reports regarding the usefulness of visual reinforcement in pharmacological studies.

In the present experiment, rhesus monkeys (*Macaca mulatta*) were trained to choose between a food reinforcer (1-g banana-flavored Noyes pellet) and a nonfood reinforcer (5 s

[1] To whom requests for reprints should be sent at her current address: National Institute of Mental Health, Building 10, Room 4N214, Bethesda MD 20892.
[2] Current address: National Institute on Drug Abuse, Addiction Research Center, P.O. Box 5180, Baltimore MD 21224.

of open window, allowing visual access to a room containing other caged rhesus monkeys) in a discrete trial choice paradigm. The hypothesis was that caloric preloads, AMPH, FEN, and CCK would only reduce responding maintained by food; responding maintained by opening the window would either be unaffected or would increase. Chlorpromazine (CPZ), on the other hand, would reduce both food-maintained responding and responding maintained by window-opening because previous work in this laboratory has shown reductions not only in food-maintained behavior but also in other behaviors suggestive of nonspecific CNS depression in monkeys after pretreatment with CPZ (35,36). Diazepam (DZ), known for its ability to increase food intake in a variety of species (15,37), was hypothesized to increase food-maintained responding and either decrease or have no effect on responding maintained by opening the window.

METHOD

Animals

One male (6099, 10.4 kg) and one female (0036, 8.6 kg) rhesus monkey (*Macaca mulatta*) were used. Both monkeys had participated in other experiments, including drug self-administration studies (6099) and experiments that assessed the effects of drugs on schedule-controlled behavior (0036). Each monkey was fitted with a stainless steel restraint harness and spring arm that attached to the rear of the experimental cubicle (86 × 74 × 89 cm). This arrangement gave the animals relatively free movement about the cubicle. Water was available ad lib. In addition to the food pellets earned during the experimental sessions, Noyes 1-g banana-flavored pellets (Lancaster, NH) were provided several hours after each session. Enough food was provided to maintain the animals' health and to maintain food-reinforced responding during the experimental sessions to as close to 50% of total choices as possible. A vitamin supplement in the form of a chewable multiple-vitamin tablet was provided 3 days/week.

Monkey 6099 entered this experiment equipped with an intragastric (IG) catheter. After adaptation to the cubicle and restraint system, monkey 0036 was also surgically implanted with an intragastric catheter. This made the administration of drugs and/or caloric preloads possible without opening the cubicle door, thus maintaining the presession visual deprivation period (6). The surgical procedure for catheter implantation has been described previously (38). Briefly, each animal was injected with a combination of phencyclidine HCl (1.0 mg/kg, IM) and atropine sulfate (0.04 mg/kg, IM). When the animal was sedated, it was removed from the cubicle and pentobarbital anesthesia (10–20 mg/kg, IV) was initiated. When anesthesia was adequate, a silicone catheter (0.063 in inside diameter, Ronsil Rubber Products, Belle Mead, NJ) was surgically implanted into the stomach. After surgery, the monkey was returned to the experimental chamber and the catheter was threaded through the spring arm, out the back of the cubicle, and connected to a syringe. Monkey 0036's catheter became nonfunctional during the experiment and a new catheter was implanted as before after a 1- to 2-week period.

Apparatus

Each monkey was housed continuously in the experimental chamber. Two response levers (BRS/LVE, PRL-001, Beltsville, MD) were mounted on the inside front of each door 20 cm above the grid floor. Two jeweled stimulus lights, one green and one red, were mounted directly above each lever. In addition, red and white houselights were mounted on the ceiling of the cubicle and were covered with translucent Plexiglas. Each cubicle had a Plexiglas window on the front that allowed the monkey visual access to the laboratory (a room housing other rhesus monkeys). Lighting was maintained on a 8 D : 16 L (light 2200–0600 h) cycle. All programming and recording of experimental events were accomplished using AIM 65 computers.

Procedure

Animals were trained in a discrete trial choice paradigm similar to that described previously (22) to respond for either food (1-g, banana-flavored pellet, Noyes) or visual access to a room containing other caged rhesus monkeys (5 s of open window) (see Fig. 1). Experimental sessions were started at approximately 1100 h each day, Monday–Friday, and lasted either 6 h or until the monkey completed 100 trials, whichever came first. Sessions were not run on the weekends because activity levels in the laboratory were not the same as during the week. At the beginning of each trial, the red houselight was illuminated, as well as a green light over one lever and a red light over the other lever. Pressing the lever with the green light over it resulted in delivery of a food pellet, whereas pressing the lever with the red light over it caused a sliding door covering the window of the cubicle to open for 5 s. To avoid the development of position preferences, the lever associated with red or green was randomly varied such that the monkey had to follow one color for one reinforcer and the other color for the other reinforcer. The first lever response of each trial caused the light over the opposite lever to go out. Responding on the nonilluminated lever had no further consequences during the trial, that is, the first response of each trial "locked in" that choice. Completing 15 responses (fixed-ratio 15, FR 15) on the chosen lever resulted in delivery of the

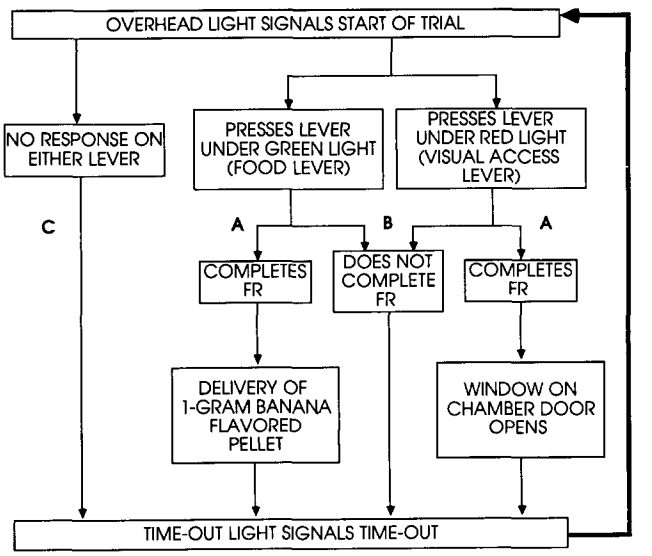

FIG. 1. Choice procedure flowchart. Points A, B, and C represent the three possible outcomes once a trial has begun. (A) The monkey chooses either the window-open lever or the food lever, completes the FR, and receives the appropriate reinforcer. (B) The monkey chooses one of the levers but does not complete the FR. (C) The monkey does not choose either lever.

associated reinforcer and the end of the trial. If the monkey failed to complete the FR within the allotted trial time (500 s), then the trial ended with no reinforcer delivery. At the end of each trial, the white houselight was illuminated and a 60-s time-out began. At the end of the time-out, the white houselight was extinguished, the red houselight was illuminated, and the lever lights were again presented, signaling the start of another trial.

When responding stabilized (no more than 30% variability in responding between the 2 days immediately prior to testing), sessions were conducted in which various pretreatments known to affect food intake were administered. In the first series of tests, 200 ml tapwater (vehicle), as well as 200 ml caloric preloads, were given IG. Sessions were started 15 min after delivery of the water and the 20 and 40% preloads and immediately after delivery of the 60% preload. Rate of gastric emptying in monkeys is an inverse function of the caloric density of the stomach load (24); thus, in the present study the volume of preload in the stomach and intestine at any given point in time varied with the caloric density of the different preloads. It is possible, then, that results obtained with caloric preloads could be a function of volume and not the nutrients in the preload. For this reason, another series of tests were conducted in which 3 volumes of tapwater (200, 400, or 600 ml) were given IG immediately before starting the session. Because a noncaloric solution has been shown to empty rapidly from the stomach in monkeys (24,30), time of infusion was not held constant. Rather, the water was infused as quickly as possible, and the session started immediately. Infusions were given at the rate of approximately 22 ml/min.

Separate tests were also conducted in which no gastric preloads were given. Instead, pharmacological agents known to

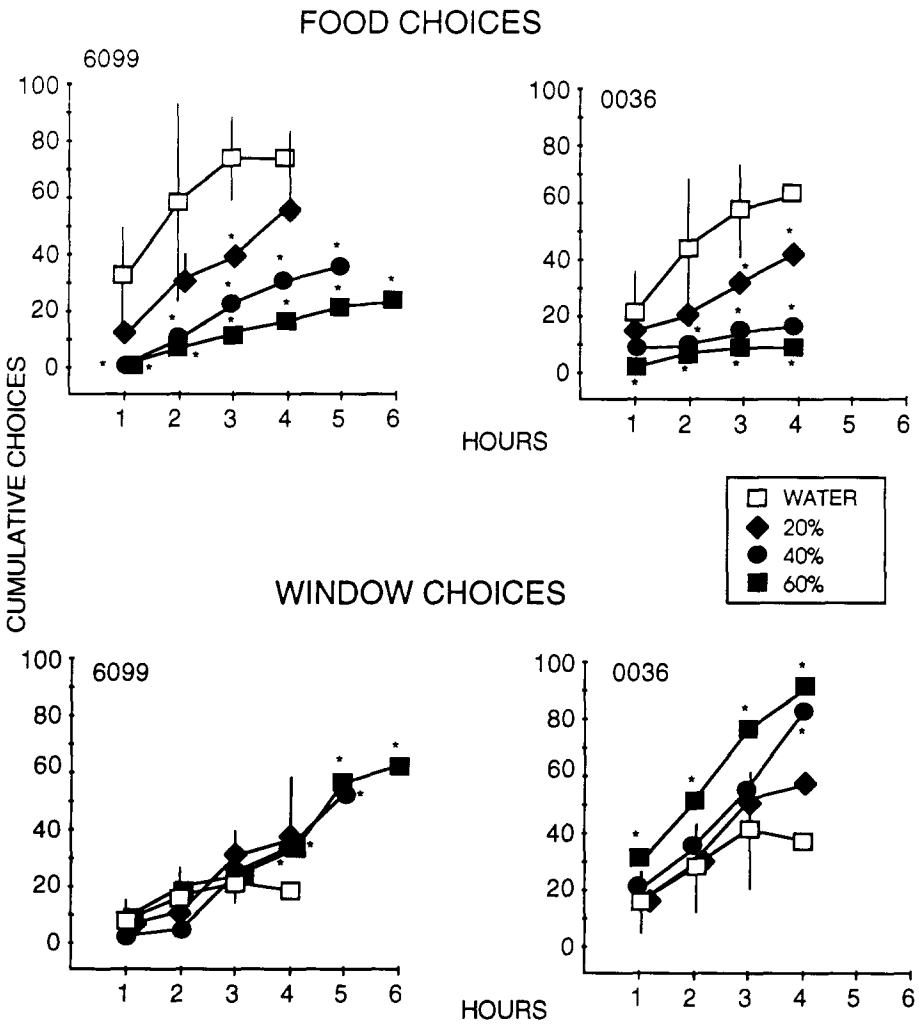

FIG. 2. Cumulative choices after administration of caloric preloads (% of total daily ration given IG, 15 min before the session, in a 200-ml tapwater vehicle). Hours are represented along the abscissa and cumulative choices along the ordinate. The top two graphs show the cumulative food choices; the bottom two graphs show the cumulative window choices. Open symbols represent the mean of vehicle tapwater pretreatments. Closed symbols represent the caloric preload pretreatments. Diamonds = 20% of daily caloric ration; circles = 40% of daily caloric ration; squares = 60% of daily caloric ration. Vertical bars represent 2 SD from the mean. Asterisks indicate different from tapwater mean ± 2 SD.

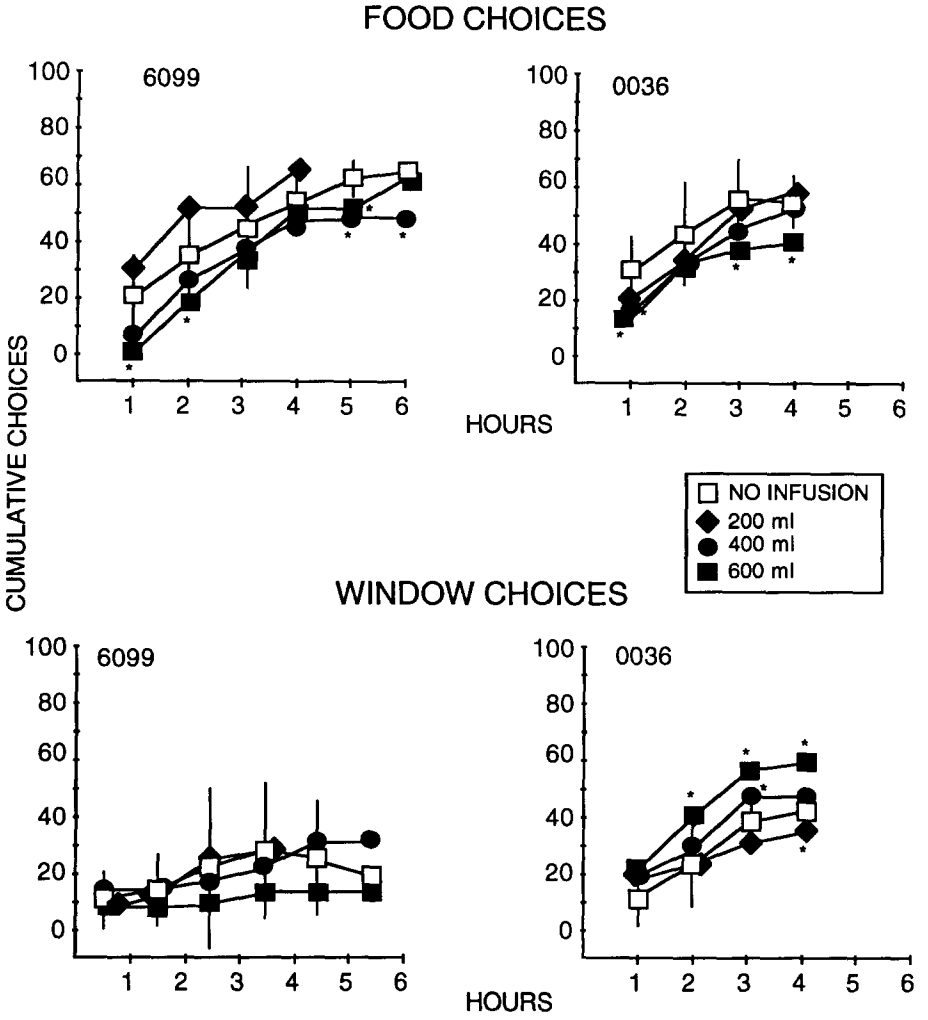

FIG. 3. Cumulative choices after administration of tapwater preloads (total ml given IG, immediately before the session). Hours are represented along the abscissa and cumulative choices along the ordinate. The top two graphs show the cumulative food choices; the bottom two graphs show the cumulative window choices. Open symbols represent the mean of baseline days (see the Method section). Closed symbols represent the water preload pretreatments. Diamonds = 200 ml; circles = 400 ml; squares = 600 ml. Vertical bars represent 2 SD from the mean. Asterisks indicate different from baseline mean ± 2 SD.

affect food intake were administered. Fenfluramine (0.5–4.0 mg/kg), *d*-amphetamine (0.06–1.0 mg/kg), CPZ (1–17.6 mg/kg), and DZ (0.01–0.3 mg/kg) were administered, IG, 1 h before the session via the intragastric catheter. CCK (1–10 μg/kg, IM) was administered 15 min before the session. At least three doses of each compound were tested in a mixed order and the order of testing was varied between monkeys. Single determinations of each dose were usually done. Drug doses were chosen based upon previous research in this laboratory as well as other literature regarding their behavioral effects (15,16,27,35,36). Testing of one drug was completed before testing of another began.

Tests were conducted once a week. At least 2 days of stable responding were required before a dose was tested. The appropriate vehicle for the compound being tested was generally given the day before a test. For the separate tapwater test series, the previous day's data, in which no treatments were given, served as the baseline. Testing of different compounds was separated by at least 1 week.

Data Analysis

Cumulative choices following vehicle and drug or preload treatments were plotted for each monkey. Each treatment was compared to its respective vehicle baseline. Vehicle was generally administered via the appropriate route of administration the day immediately preceding a drug test. Thus, if four doses of a drug were tested the vehicle baseline was the mean responding on the four vehicle days. Any treatment that produced responding exceeding the mean ± 2 SD under vehicle conditions was considered to have had an effect. If a monkey received a given dose on two or more occasions, then the

mean ± 2 SD of the tests was plotted. To be considered effective, the 2 SD of the test could not overlap with the 2 SD of the baseline.

Drugs and Preloads

The drug solutions used were as follows: *d*-amphetamine sulfate (National Institute on Drug Abuse); fenfluramine HCl (A.H. Robbins Co., Richmond, VA); cholecystokinin (Sigma Chemical Co., St. Louis, MO, Behring Diagnostics, San Diego, CA, and Peninsula Laboratories, Belmont, CA, as the sulfated COOH-terminal octapeptide ([Tyr-SO_3H^{27}]-cholecystokinin fragment 26-33 amide); diazepam (Hoffman-La Roche, Nutley, NJ); and chlorpromazine HCl (Elkins-Sinn Pharmaceutical, Cherry Hill, NJ). CCK was mixed with 0.9% saline at room temperature and then stored below freezing in aliquots that were thawed immediately before injecting. All other drugs except diazepam were dissolved in 0.9% saline and doses are expressed as the salt. Diazepam was mixed in a 1:1 stock solution of emulphor (GAF Corporation, New York) and alcohol and then diluted with saline as needed. Doses of diazepam are expressed in terms of the base.

Caloric preload stock solutions were made by mixing 120 ml Polycose liquid (Ross Laboratories, Columbus, OH) with 1 envelope of Carnation Instant Breakfast and 42 g glucose. The caloric content of the preload was based upon each animal's daily ration. Four preloads were given: 0 (tapwater), 20, 40, and 60% of the daily ration. For each preload, the appropriate amount of the stock solution was mixed with water to bring the total volume up to 200 ml. For the separate series of tapwater tests, water preloads were given in volumes of 200, 400, and 600 ml.

RESULTS

Caloric preloads, FEN, CCK, and intermediate doses of AMPH all decreased food-maintained responding and had no effect on or increased responding maintained by opening the

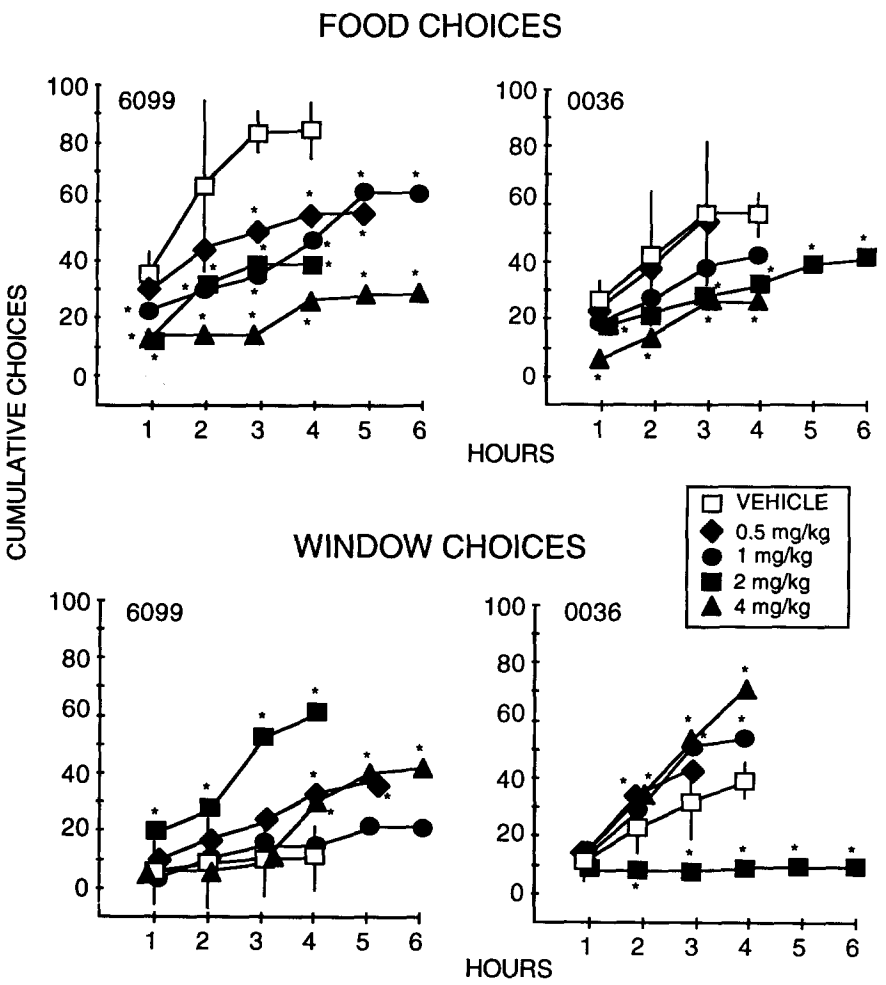

FIG. 4. Cumulative choices after administration of fenfluramine (FEN) (mg/kg given IG, 1 h before the session). Hours are represented along the abscissa and cumulative choices along the ordinate. The top two graphs show the cumulative food choices; the bottom two graphs show the cumulative window choices. Open symbols represent the mean of vehicle pretreatments. Closed symbols represent the FEN pretreatments. Diamonds = 0.5 mg/kg; circles = 1.0 mg/kg; squares = 2.0 mg/kg; triangles = 4.0 mg/kg. Vertical bars represent 2 SD from the mean. Asterisks indicate different from vehicle mean ± 2 SD.

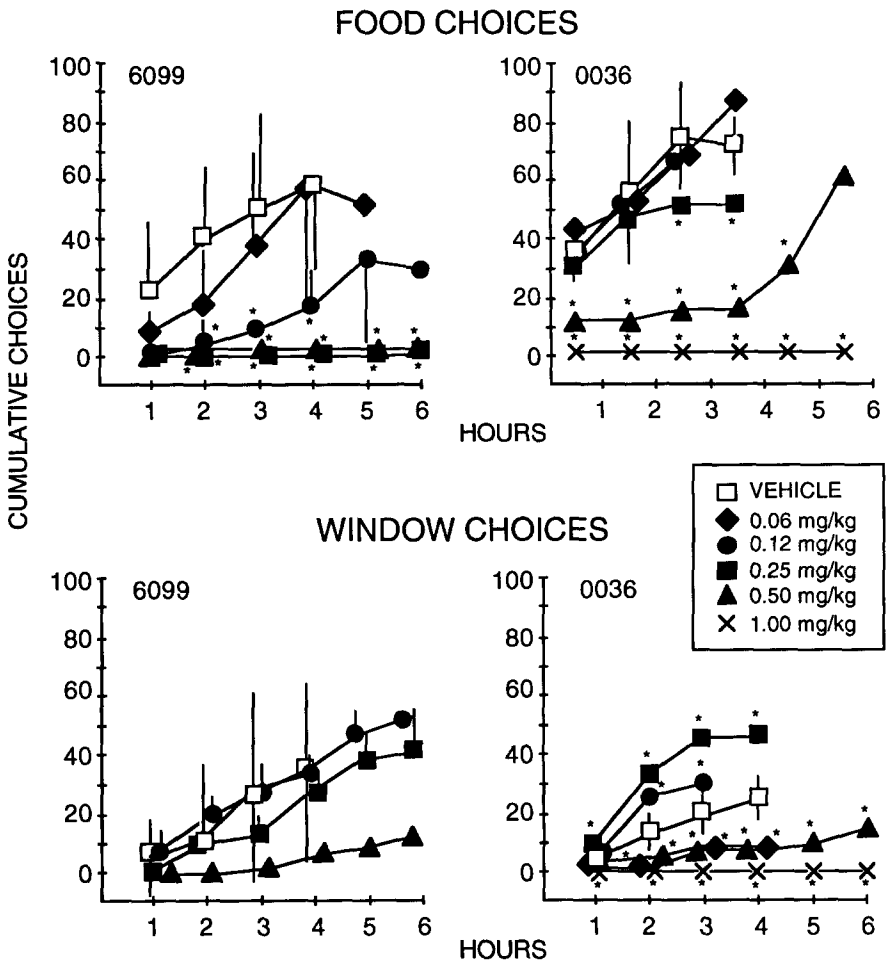

FIG. 5. Cumulative choices after administration of amphetamine (AMPH) (mg/kg given IG, 1 h before the session). Hours are represented along the abscissa and cumulative choices along the ordinate. The top two graphs show the cumulative food choices; the bottom two graphs show the cumulative window choices. Open symbols represent the mean of vehicle pretreatments. Closed symbols represent the AMPH pretreatments. Diamonds = 0.06 mg/kg; circles = 0.12 mg/kg; squares = 0.25 mg/kg; triangles = 0.5 mg/kg; × = 1.0 mg/kg. Vertical bars represent 2 SD from the mean. Asterisks indicate different from vehicle mean ± 2 SD.

window. Thus, food choices were decreased in a behaviorally specific manner by these compounds.

Cumulative choices made after caloric preloads are shown in Fig. 2. Total food choices decreased and window choices increased as a function of the caloric density of the preload in both monkeys. No evidence of gastrointestinal distress was observed in either monkey. The effect on responding seen after water preloads was not nearly as pronounced as that seen after caloric preloads (Fig. 3), suggesting that the results obtained with caloric preloads cannot be accounted for by volume alone.

FEN decreased food choices and increased or had no effect on window choices at most doses in both monkeys (Fig. 4). In monkey 0036, 2 mg/kg FEN decreased both food and window choices but 4 mg/kg decreased only food choices. Higher doses of FEN were not given due to concerns regarding possible neurotoxic effects (32).

AMPH decreased food choices dose dependently in both monkeys for 4 h (Fig. 5). Window choice, however, was affected differentially depending upon the dose of AMPH. Lower doses of AMPH that decreased food intake either had no effect on (6099) or increased (0036) window choices, whereas higher doses suppressed window choices in monkey 0036 below 2 SD from the vehicle mean and in monkey 6099 below the minimum range of 4-h vehicle responding [vehicle minimum (6099) = 20 window choices in 4 h; 0.5 mg/kg AMPH = 7 window choices in 4 h].

CCK resembled caloric preloads, AMPH, and FEN (Fig. 6), with the effects of CCK being less pronounced than the other pretreatments. In the first hour in both monkeys, food-maintained responding decreased after CCK whereas responding maintained by opening the window either increased (0036) or was unaffected (6099). Because the half-life and disappearance half-time of CCK are short (23,34), there was concern that any nonspecific effects of CCK might have been obscured by analyzing the data in 1-h bins. For this reason, the results during the first hour after the largest CCK dose tested in each monkey were divided into six 10-min bins; there was no evi-

dence of general behavioral suppression at any time (data not shown).

In contrast to the anorectic agents, DZ increased food choices (both monkeys) and either decreased (0036) or had no effect on (6099) window choices (Fig. 7).

There was a decrease in total responding for both reinforcers in monkey 0036 after 17.6 mg/kg CPZ (Fig. 8). Monkey 6099 was seen lying down during several observations made during the session after pretreatment with 17.6 mg/kg CPZ. When either the cubicle door or the window was opened to check on the monkey, he sat up and resumed lever pressing. Thus, responding would probably have been even lower except for the periodic interruptions. Monkey 0036 was seen smacking her lips and retching nonproductively within 4 min of drug administration after 17.6 mg/kg CPZ, but appeared normal during her session. CPZ (1 mg/kg) increased both food- and window-reinforced responding during the first 3 h in monkey 6099 only.

Results are summarized in Table 1. Caloric preloads decreased food-reinforced responding and increased responding reinforced by window opening. CCK, as well as two prototypic anorectics, FEN (0.5–4.0 mg/kg, IG) and AMPH (0.06–0.25 mg/kg, IG), produced responding like that seen after caloric preloads, suggesting that these drugs at these doses exerted a specific effect on food-maintained behavior. High doses of AMPH and CPZ decreased responding for both reinforcers in monkey 0036, demonstrating that at these doses AMPH and CPZ can exert a nonspecific effect on food-maintained responding. DZ increased food-reinforced responding and either decreased or had no effect on visually reinforced responding.

DISCUSSION

Caloric preloads, FEN (0.5–4.0 mg/kg), CCK (1.8–10.0 μg/kg), and low doses of AMPH (0.12–0.25 mg/kg) decreased food choices and either had no effect on or increased window choices in the present study. These results are consistent with

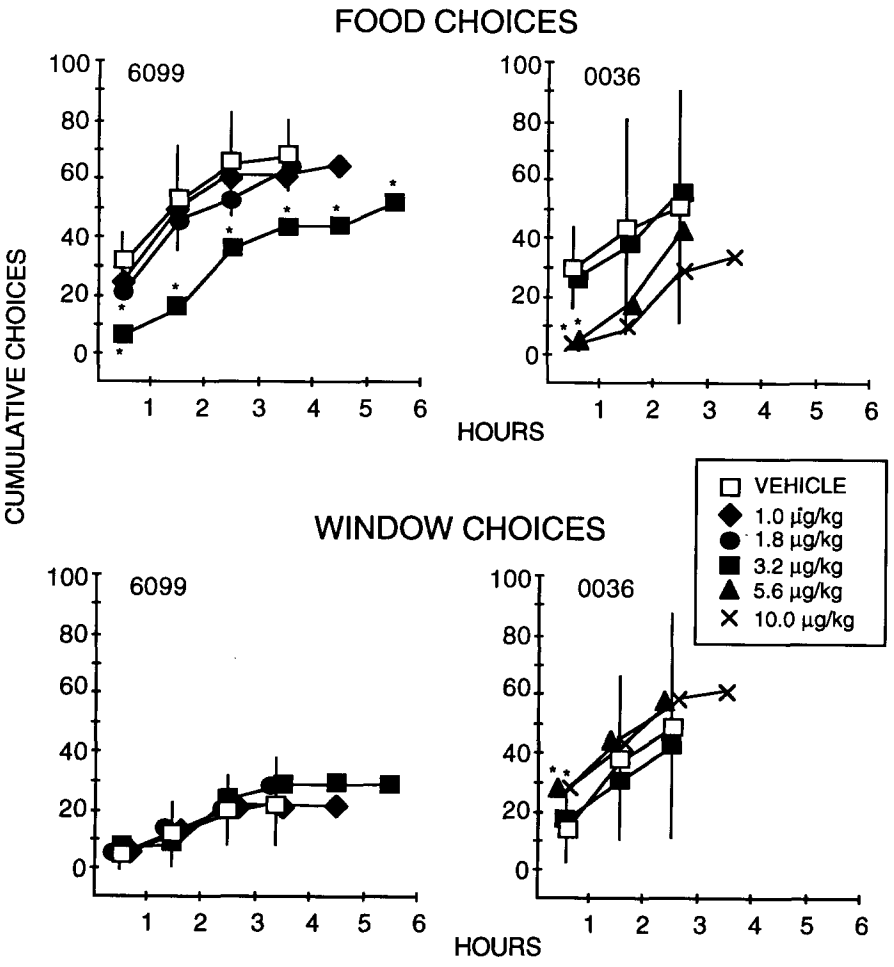

FIG. 6. Cumulative choices after administration of cholecystokinin (CCK) (μg/kg given IM, 15 min before the session). Hours are represented along the abscissa and cumulative choices along the ordinate. The top two graphs show the cumulative food choices; the bottom two graphs show the cumulative window choices. Open symbols represent the mean of vehicle pretreatments. Closed symbols represent the CCK pretreatments. Diamonds = 1.0 μg/kg; circles = 1.8 μg/kg; squares = 3.2 μg/kg; triangles = 5.6 μg/kg; × = 10.0 μg/kg. Vertical bars represent 2 SD from the mean. Asterisks indicate different from vehicle mean ± 2 SD.

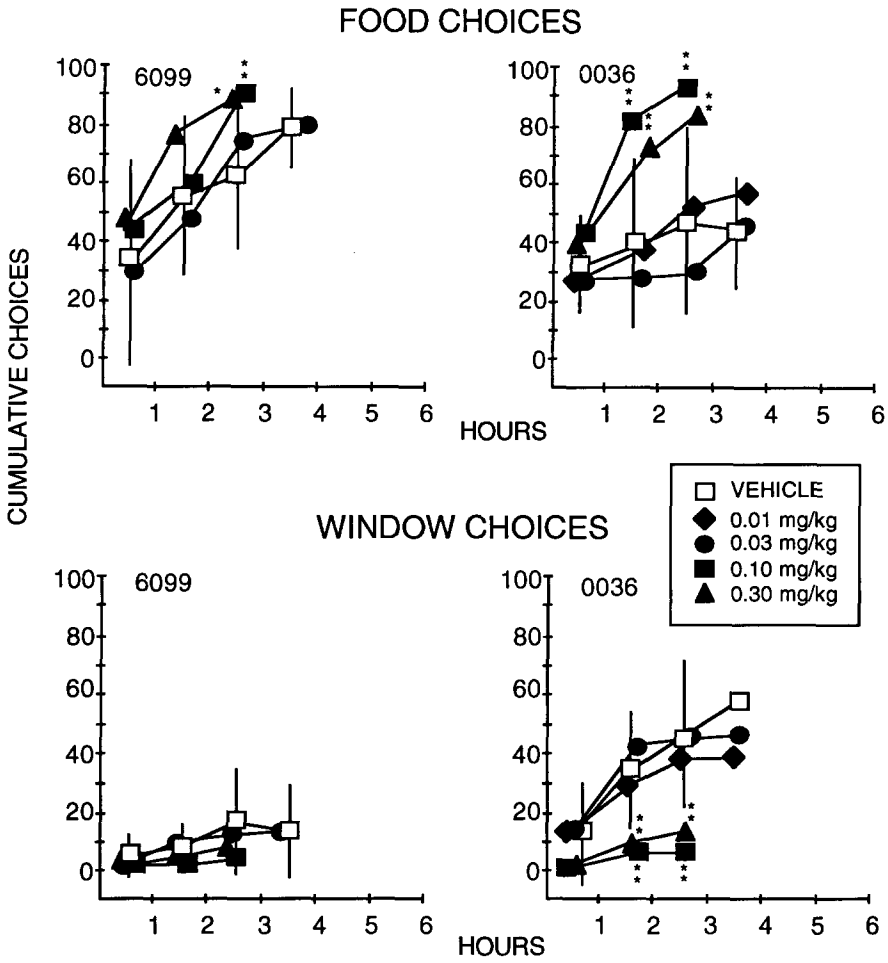

FIG. 7. Cumulative choices after administration of diazepam (DZ) (mg/kg given IG, 1 h before the session). Hours are represented along the abscissa and cumulative choices along the ordinate. The top two graphs show the cumulative food choices; the bottom two graphs show the cumulative window choices. Open symbols represent the mean of vehicle pretreatments. Closed symbols represent the DZ pretreatments. Diamonds = 0.01 mg/kg; circles = 0.03 mg/kg; squares = 0.1 mg/kg; triangles = 0.3 mg/kg. Vertical bars represent 2 SD from the mean. Asterisks indicate different from vehicle mean ± 2 SD: *different from cumulative choices at that time point; **different from total cumulative choices for the session.

the prediction for a specific suppression of food-maintained behavior and demonstrate that, at these doses, the decreases in food-maintained responding seen after FEN, AMPH, and CCK are not due to general behavioral suppression. These results, using a choice procedure, confirm previous reports using behavioral comparisons between sessions that appropriate doses of AMPH, FEN, and CCK can decrease food-maintained behavior in a specific manner (13,17,18,28,39).

One dose of FEN (2 mg/kg) in one monkey (0036) suppressed responding for both reinforcers (Fig. 4). Because this effect was not seen in both monkeys, no explanation can be made for these results. A larger dose of FEN (4 mg/kg) was tested in this monkey and suppressed only food intake. Window choices increased at this dose, suggesting that the general behavioral suppression seen at 2 mg/kg were not due to possible neurotoxic effects of FEN.

Cumulative food choices after IM CCK were decreased during the first hour of responding in both monkeys and for the entire session in monkey 6099. These results confirm a previous report of IV CCK suppressing total food intake for 3 h in rhesus monkeys (16). To understand how this could occur given the short half-life and disappearance half-time of CCK, Gibbs et al. (16) analyzed their data in 15-min bins. CCK reduced food intake in the first 15-min interval only. In subsequent intervals, the monkeys ate as much after CCK as after saline; they did not compensate for early intake suppression by eating more later in the session. Thus, cumulative intake remained low, as in our study. In the present study, CCK data were analyzed in 10-min bins, and intake remained low for the first 40 min in both monkeys at the highest doses tested (data not shown). The different routes of administration and size of the doses could explain why our early session effects lasted slightly longer than those reported by Gibbs et al. (16) In monkey 6099, a lower dose of CCK (1.8 μg/kg) suppressed intake in the first 10 min of the session only, a result similar to that reported by Gibbs et al. (16). Window

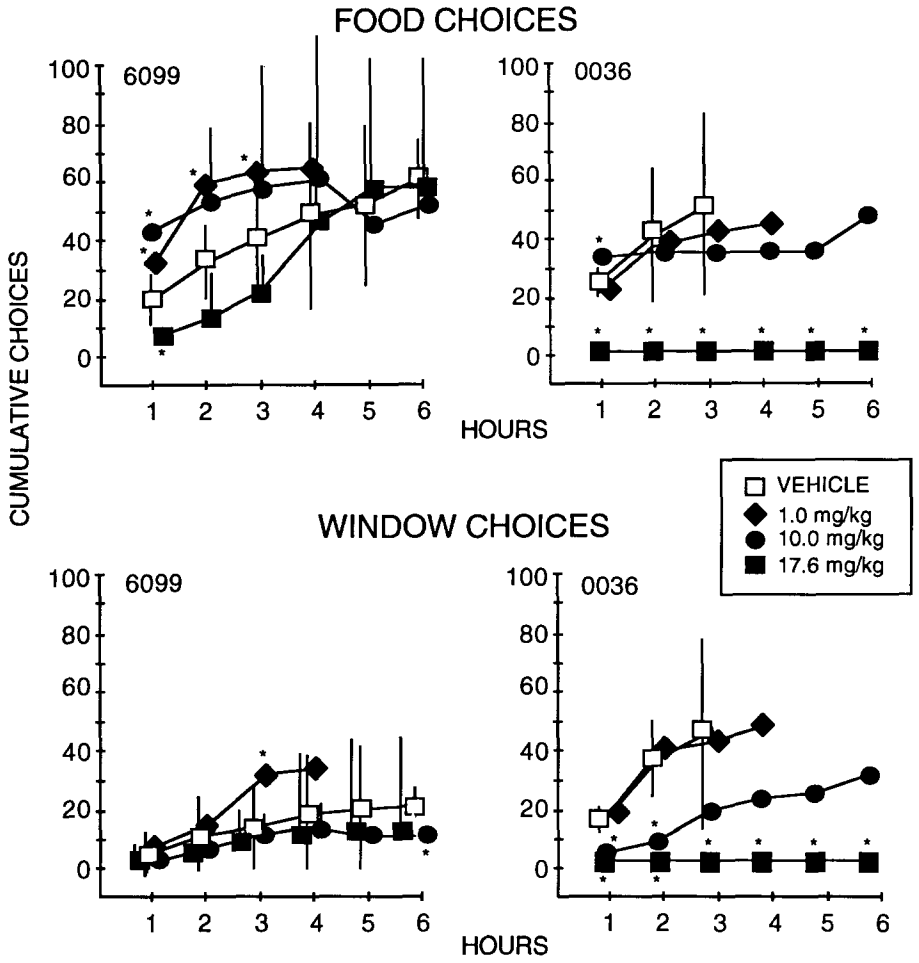

FIG. 8. Cumulative choices after administration of chlorpromazine (CPZ) (mg/kg given IG, 1 h before the session). Hours are represented along the abscissa and cumulative choices along the ordinate. The top two graphs show the cumulative food choices; the bottom two graphs show the cumulative window choices. Open symbols represent the mean of vehicle pretreatments. Closed symbols represent the CPZ pretreatments. Diamonds = 1.0 mg/kg; circles = 10.0 mg/kg; squares = 17.6 mg/kg. Vertical bars represent 2 SD from the mean. Asterisks indicate different from vehicle mean ± 2 SD.

responding was not suppressed in either monkey at these doses at any of these time points, demonstrating that the suppressive effect of CCK on food intake in this paradigm was behaviorally specific.

The pattern of responding seen at higher doses of AMPH and CPZ in monkey 0036 (decrease in both food and window choices) is consistent with the prediction for a nonspecific disruption of food-maintained behavior.

Gastric preloads, CCK, FEN, and AMPH have been reported to induce conditioned taste aversions and it has been suggested that reductions in food intake after any of these may be the result of illness (1,2,10–12,19,33). Although the present study cannot differentiate malaise from satiety, the fact that total window opening, in general, was either unaffected or increased after gastric preloads, CCK, FEN, and low doses of AMPH argues against illness and in favor of a more behaviorally selective effect. Additionally, the results clearly show that regardless of the interoceptive cues the food intake reductions after caloric preloads, CCK, FEN, and low doses of AMPH were not due to general behavioral suppression. Higher doses of AMPH (0.5–1.0 mg/kg) and CPZ (17.6 mg/kg) reduced responding for both reinforcers in monkey 0036, demonstrating that the present paradigm is sensitive to general behavioral suppression.

One confound in the present study is that the number of baseline food choices was almost always greater than the number of baseline window choices. Thus, the reductions in food choices and increases in window choices after drug administration might be due to rate-dependent effects. If this were true, AMPH might be expected to decrease the high-rate behavior (in this case food-reinforced responding) and increase the low-rate behavior (in this case responding reinforced by opening the window) as was found in the present study. A problem with this interpretation is that rate-dependency effects usually describe the effects of drugs on local response rates of a free operant and not on choice frequency [see (25) for a review]. In the present study, there were no systematic differences in the local response rates between food-maintained responding

TABLE 1

SUMMARY OF EFFECTS OF VARIOUS PRETREATMENTS ON CHOICE BETWEEN FOOD AND WINDOW OPENING IN RHESUS MONKEYS

	Food	Window
Caloric preloads	↓	↑
FEN	↓	↑
CCK	↓	↑ or ↔
AMPH (0.12, 0.25 mg/kg)	↓	↑ or ↔
AMPH (0.5, 1 mg/kg; 0036 only)	↓	↓
Chlorpromazine (0036 only)	↓	↓
Diazepam	↑	↔ or ↓

Arrows indicate whether choice was increased (↑), decreased (↓), or unaffected (↔).

and responding maintained by window opening, nor were there any reliable drug effects on these rates (data not shown). A more parsimonious explanation might be to invoke a "probability-dependency" concept (14,29). Evendon and Robbins (14) suggest that "According to this idea, responses occurring with a high probability (relative to other responses, rather than in time as in rate-dependency) are reduced by the drug, whereas responses occurring with a lower probability may be increased." Evenden and Robbins (14) present evidence in support of this concept in a study examining the effects of AMPH on switching behavior in the rat. Although the paradigm used by Evendon and Robbins (14) is different from the one employed in the present study, their concept is supported by the present data, that is, the high-probability behavior (food-reinforced responding) decreased after low doses of AMPH whereas the low-probability behavior (behavior reinforced by opening the window) increased or was unaffected. While it is possible that the present results are due to probability dependency, the fact that results after caloric preloads, CCK, FEN, and low doses of AMPH were all similar argues against this interpretation. It is more probable that selective anorectic effects are operating. Further studies are clearly required, however, to distinguish between these two interpretations.

Probability dependency cannot explain the DZ results. Food choices increased and window choices either decreased or were unaffected after DZ, the opposite of what was observed with caloric preloads, AMPH, FEN, and CCK. These results confirm previous reports that DZ can increase food intake in a variety of species (15,37) and demonstrate that this paradigm is sensitive to behaviorally specific increases in food intake.

In summary, caloric preloads, AMPH, FEN, and CCK all reduced responding for food and either increased or had no effect on responding for opening the window. None of the other compounds tested consistently had these effects in both monkeys. These results demonstrate that the food intake reductions produced by caloric preloads, CCK, FEN, and low doses of AMPH observed in this study are not the result of generalized behavioral suppressions. The present study supports the suggestion by Moon (26), Schuster and Estrada (31), and Haude and Ray (20) that visual reinforcement in rhesus monkeys can be a useful behavioral tool in pharmacological studies. Further, the present results demonstrate that within-session choice procedures can effectively differentiate specific reductions in food-maintained responding from nonspecific behavioral suppression.

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