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Effect of response-independent candy on responding maintained by candy using a novel model of commodity acquisition and consumption in nonhuman primates

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Abstract

Ingestive behavior consists of appetitive or foraging behavior, i.e., “acquisition,” followed by consummatory behavior. Responding of six adult rhesus monkeys, living in three-chambered enclosures, was studied under an operant chain schedule that simulated commodity acquisition and commodity consumption. Responding during the initial acquisition component was reinforced by stimuli paired with that commodity, while responding during the following consumption component was reinforced with that commodity. Throughout the 10-h experimental day, monkeys experienced multiple candy (plain M & Ms) and fruit-drink (Kool-Aid) sessions in different end chambers. The effects of response-independent candy reinforcement, in the context of extinction, were examined when monkeys received a daily food ration of 8 or 20 chow. Response-independent candy increased responding during the acquisition components of candy sessions when monkeys received a daily food ration of 8 chow but not when the food ration was 20 chow. Furthermore, response-independent candy increased candy choice over fruit-drink during choice opportunities and increased the length of time spent in the candy chamber when the candy stimulus lights were illuminated under both food ration conditions, i.e., location preference. The present procedure, which combines operant and place preference measures of commodity acquisition, when used in combination with methods of studying reinstatement of responding, may prove useful in analyzing factors affecting relapse. © 2002 Elsevier Science Inc. All rights reserved.

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1. Introduction

In natural ecology, ingestive behavior consists of periods of commodity seeking or acquisition followed by, or interspersed with, periods of consumption (Owen, 1980; Rodman and Cant, 1984). For example, the actual inhalation of smoked cocaine, which may take only seconds, is a small part of a cocaine users’ daily behavior. Much more time is spent in the seeking and preparation of cocaine, i.e., acquisition, than in cocaine smoking, i.e., consumption. Recent studies from this laboratory have focused upon the development of a new model of commodity acquisition and consumption behavior in nonhuman primates. Each rhesus monkey lives in a multichambered enclosure. Operant responding is reinforced with one type of commodity self-administration in one chamber, while operant responding is reinforced with another commodity in another chamber, or no alternative commodity is available in another chamber. Responding is reinforced under a two-component chain schedule of reinforcement: responding during the first component is maintained by the brief presentation of the stimuli associated with reinforcement, while responding during the second component is maintained by delivery of the reinforcer and the associated stimuli. Responding during the first component, which does not result in primary reinforcement, provides one measure of commodity acquisition. Responding during the second component provides the measure of commodity consumption. In some studies, monkeys also have choice trials each day when they can choose to work for either commodity. Thus, choice behavior provides a second measure of commodity acquisition. Because of the unique

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multichambered living arrangement, it is possible to record where monkeys spend their time during the experimental day. The length of time monkeys spend in the chamber associated with each commodity can be used to measure each monkey's location preference. This location preference provides a third measure of commodity acquisition.

Under these experimental conditions, rhesus monkeys developed a location preference for orally self-administered cocaine when food was also available (Foltin and Evans, 1997), food when fruit-drink was also available (Evans and Foltin, 1997) and smoked heroin when no other commodity was available (Foltin and Evans, 2001) or when fruit-drink was also available (Evans et al., submitted for publication). The amount of responding during acquisition components and choice behavior paralleled the location preference data. These three measures of commodity acquisition behavior do not, however, always provide isomorphic results. The administration of D-amphetamine prior to sessions when food and fruit-drink were available significantly decreased both acquisition and consumption of both commodities. Amphetamine did not affect choice behavior but *increased* the location preference for the food chamber (Evans and Foltin, 1997). A similar pattern of results was also obtained when the fruit-drink contained cocaine (Foltin and Evans, 1999). The first purpose of this experiment was to further develop the model of commodity acquisition behavior by examining responding reinforced by chocolate candy (M & Ms). Chocolate was used because (1) it is the most commonly reported food item craved by humans (Rozin et al., 1991; Weingarten and Elston, 1990); (2) like drugs of abuse, it is nonessential for life and (3) it is a preferred treat of nonhuman primates (Foltin and Fischman, 1990).

The delivery of response-independent reinforcement in the context of extinction of the behavior formerly maintained by that reinforcer characteristically produces short-term increases in responding (Schenk et al., 1996). Because responding is measured under extinction conditions, changes in responding following response-independent reinforcer delivery can be used as a measure of acquisition behavior for that commodity. Studies in which the commodity is a drug of abuse are commonly viewed as providing information about "relapse" to drug use (e.g., Carroll and Comer, 1996; de Wit, 1996; Spealman et al., 1999).

The prototypical reinstatement procedure involving laboratory animals has three phases (e.g., Gerber and Stretch, 1975): (1) animals are trained to self-administer a drug of abuse by the intravenous route, (2) saline is substituted for active drug, such that responding undergoes extinction and (3) response-independent drug is administered under extinction conditions. Increases in responding during the third phase are evidence for a drug-induced reinstatement of responding. It is important to note that the increase in responding following response-independent drug is not due to nonspecific arousal but is relatively drug specific (see Carroll and Comer, 1996 for review). For example, Gerber and Stretch (1975) reported that response-independent amphetamine or cocaine increased lever pressing of squirrel monkeys that was formerly maintained by amphetamine or cocaine, while response-independent chlorpromazine or pentobarbital did not.

Recently, several investigators have extended the operant model of reinstatement to procedures that provide a conditioned place preference (CPP) measure of reinforcement (Mueller and Stewart, 2000; Wang et al., 2000). In these procedures, rats that have a conditioning history that results in a CPP for a drug of abuse undergo repeated CPP extinction trials. The extinction trials are followed by the response-independent delivery of drug prior to a test session, which reinstates the CPP. The second purpose of this experiment was to the examine the effects of response-independent candy administration under extinction conditions using procedures that provide both operant and place preference measures of commodity acquisition.

It is well known that food restriction and/or weight reduction significantly increases drug self-administration by laboratory animals (e.g., Carroll et al., 1984; Meisch and Thompson, 1973). Because food and/or weight restriction is commonly used in other studies on the reinstatement of commodity acquisition behavior, the third purpose of this experiment was to determine what effect the daily food ration had on the effects of response-independent reinforcement.

2. Method

2.1. Animals

Six adult male rhesus monkeys (*Macaca mulatta*, purchased from Laboratory Animal Breeders and Services, Yemassee, SC) lived in customized, stainless steel, squeeze-capable, rack-mounted, nonhuman primate cages (Hazleton Systems, Aberdeen, MD) in the animal care facility of The New York State Psychiatric Institute. Each monkey had access to three identically sized chambers (61.5 cm wide × 66.5 cm deep × 88 cm high) connected by 40 × 40-cm openings. Monkeys had participated in previous studies examining responding maintained by fruit-drink, with and without cocaine, and banana-flavored pellets under schedule conditions similar to those used here (Evans and Foltin, 1997; Foltin and Evans, 1997). In these studies, no supplemental food had been given. Thus, the first experimental condition in this study was the first time that these monkeys had ad libitum access to chow in 3 years. The daily food rations (High protein monkey diet #5047, 3.37 kcal/g; LabDiets, PMI Feeds, St. Louis, MO), as described below, were given in the middle chamber. Any uneaten chow from the previous day was removed and counted prior to giving the ration for that day. Water was freely available from spouts located on the back wall of all three chambers. Daily room cleaning began at 0730, and cages were washed weekly on Friday after the daily sessions. Each monkey received chewable vitamins and a piece of fruit before the session each day and occasional treats (e.g., cookies were given the weekend after Thanksgiving and candy canes were given during the week of Christmas). The room lights were illuminated from 0730 to 2000.

2.2. Apparatus

Response panels (38 cm wide × 54 cm high, 3-mm thick aluminum) were located on the front wall of each of the chambers. For three of the monkeys, fruit-drink self-administration occurred in the left chamber and candy self-administration occurred in the right chamber. These locations were reversed for the other three monkeys. No self-administered commodities were available in the middle chamber that separated the other two chambers. Three white lights (all lights were 28 V, 0.1 A lamps) were located in the upper left corner (from the monkey's perspective) and one white session light was located in the other three corners. Two Lindsley operanda were mounted 19.5 cm from the bottom of each panel. The left "acquisition" operandum was centered 15 cm from the left edge and the right "consumption" operandum was centered 10 cm from the right edge (these distances were chosen so levers fit between existing cage bars). An infrared heat and motion detector (Motion Sensor, Radio Shack, Fort Worth, TX) was mounted to the upper left corner of each monkey's left chamber and to the upper right corner of each monkey's right chamber. Detectors were mounted on an L-shaped Plexiglas holder 10 cm back from the front of the cage and 30 cm up from the top of the panel. When a monkey was in one of the end chambers, the detector for that chamber was activated.

On the candy and fruit-drink response panels, a yellow stimulus light was located above the left acquisition operandum and an amber stimulus light was located above the right consumption operandum. The candy response panel also had a food hopper centered at the bottom of the panel, a pair of green lights 6 cm apart and 1.5 cm above the candy hopper and a pellet dispenser (BRS-LVE model PDC-005, Beltsville, MD) mounted on the outside. The fruit-drink response panel had a spout for fluid delivery 17 cm down and 6 cm in from the right side, a red light 5 cm over and a red light 5 cm beneath the spout, a peristaltic pump (7543-06 with pump head 7016; flow rate of 10 ml/min; Cole Parmer, Chicago, IL) and a fluid source mounted on the outside. The panel for the middle chamber only contained two response operanda and the white lights.

All activity was monitored, and schedule contingencies were controlled by customized software (Eureka Software, Cary, NC) running on two Macintosh (Cupertino, CA) 610 computers located in an adjacent area.

2.3. Procedure

Responding was maintained by candy or fruit-drink under a two-component heterogenous chain schedule of reinforcement: responding during each component occurred on a separate operandum. The first component, indicated by a yellow light over the left operandum, was a second-order fixed interval (FI) 10-min schedule, with a fixed ratio (FR) 40 contingency [FI 10′ (FR 40:S)]. Thus, every 40th response produced the stimuli paired with fruit-drink (a steady red light over and below the fruit-drink spout) or candy (two green flashing lights over the candy hopper) delivery for 10 s followed by a 30-s timeout. This component provided a measure of candy or fruit-drink acquisition. Responding either during stimulus presentation or during the timeout did not count towards completion of the next ratio. The first FR 40 completed after 10 min resulted, after the presentation of the paired stimuli and the timeout, in the light over the left operandum being extinguished and the amber light over the right operandum being illuminated, which began the second component of the chain schedule. In the second component, which lasted 10 min, candy or fruit-drink was available under a FR 20 schedule; a 30-s timeout, when responding had no programmed consequences, followed reinforcer delivery [FR 20 (TO 30)]. This component provided a measure of candy or fruit-drink consumption. Responding in the candy chamber was maintained by the delivery of one plain chocolate M & Ms (Mars, Hackettstown, NJ; about 4.5 kcal: 0.6-g carbohydrate, 0.2-g fat, 0.1-g protein). Responding in the fruit-drink chamber was maintained by 5 ml of fruit-drink (two 15-s deliveries of 2.5 ml each, separated by a 5-s pause; about 1.25 kcal). The fruit-drink consisted of a 0.25-kcal/ml dilute strawberry–raspberry-flavored solution [260-g glucose (3.85 kcal/g, Sigma, St. Louis, MO) dissolved in 4000-ml tap water with one packet of Incrediberry Kool-Aid (Kraft General Foods, White Plains, NY)].

As shown in Table 1, the daily 10-h experimental day (7 days/week), which began at 0900, consisted of six consecutive 1-h and 40-min cycles of experimental sessions. Five different 20-min sessions made up each cycle. During three of the five sessions, a commodity was available for

Table 1
Schedule for the experimental day

Time	Event
0900	Cycle 1 begins
1040	Cycle 2 begins
1220	Cycle 3 begins
1400	Cycle 4 begins
1540	Cycle 5 begins
1720	Cycle 6 begins
1900	Experimental day ends

Session types within each cycle[a]
20-min candy self-administration session
20-min fruit-drink self-administration session
20-min choice between candy and fruit-drink self-administration session
20-min no-commodity session
20-min no-cue session

[a] Session order within each cycle varied between animals and between days.

self-administration. There was one candy self-administration session, indicated by the illumination of the white stimulus lights in the candy chamber, and one fruit-drink self-administration session, indicated by the illumination of the white stimulus lights in the fruit-drink chamber. Due to timing constraints, i.e., fruit-drink delivery took longer than candy delivery, the maximum number of deliveries during the FR components of fruit-drink and candy sessions was 8 and 13. There was one candy/fruit-drink choice session during each cycle. During choice sessions, session lights and left operandum lights in both the candy and the fruit-drink chambers were illuminated. The first response on left operandum terminated the schedule opportunity in the alternate chamber and initiated the acquisition component for the chosen commodity. So that an equal number of candy and fruit-drink deliveries was available during choice sessions, the timeout following candy delivery was 65 s during choice sessions. During one session (no-commodity session) of each cycle, session stimulus lights were illuminated in the middle chamber, and responding was recorded but had no programmed consequences. These sessions were used to determine the amount of nonspecific responding. Finally, during one session (no-cue session) of each cycle, no stimulus lights were illuminated. Session order within each cycle was systematically varied, with the exception that a choice session could not follow a candy or fruit-drink session. Session order was varied such that the pattern of the experimental day changed from day to day and was different across monkeys each day to minimize the likelihood that the monkeys would learn the order of sessions.

The effects of candy extinction and response-independent reinforcement in the context of extinction were studied when monkeys received 8 and 20 chow each day. Initially, the daily food ration was 20 chow: 10 chow were given to the monkeys at 0800, and 10 chow were given to the monkeys at 1300. After responding for candy and fruit-drink stabilized (no upward or downward trends in the daily total number of responses in both schedule components of fruit-drink and candy sessions, based on visual inspection of the data), extinction was initiated for candy. During extinction, candy was not delivered during the consumption component but the *stimuli paired with candy delivery continued to be presented* during the acquisition and consumption components of the chain schedule. During extinction, each of the six daily cycles began with a different session: (1) candy/fruit-drink choice, (2) candy, (3) fruit-drink, (4) no-commodity, (5) only stimulus light over left operandum illuminated in candy chamber and (6) only stimulus light over left operandum in fruit-drink chamber. All cycles ended with a no-cue session. The response-independent delivery day occurred after the daily total number of responses emitted during *consumption* components decreased to 10–15% of baseline. Response-independent reinforcement occurred immediately prior to the start of the first cycle of the experimental day and again at the end of the no-commodity session before the second, third and fourth cycles (there were no response-independent reinforcers delivered before the fifth and sixth cycles). Response-independent candy delivery involved dropping 10 M & Ms in the catch cup of the dispenser. Two additional days of extinction occurred after the single day of response-independent delivery. Candy and fruit-drink were then made available for 7–10 days before testing when the daily food ration was 8 chow. Under this maintenance condition, all 8 chow were given to the monkeys at 0800.

2.4. Data analysis

The number of responses during each acquisition and consumption component was summarized for candy and fruit-drink sessions, and the number of candy choices was summarized for each experimental day. Location of each monkey was recorded every 30 s throughout the day. The location system categorized monkeys that were moving amongst chambers and monkeys that were perched partly in the middle and in an end chamber as being in the middle no-commodity chamber. Finally, if a monkey was "lost" to the location detector, he was classified as being in the middle chamber. Thus, time spent in the candy and fruit-drink chambers was estimated conservatively, and the middle chamber was the default location. The length of time that monkeys spent in each chamber was summarized for four stimulus conditions: (1) daily total during the 10-h session, (2) candy or candy-choice sessions (candy available), (3) fruit-drink or fruit-drink-choice sessions (fruit-drink available) and (4) neither candy nor fruit-drink were available (no illuminated stimulus lights).

Data describing responding during candy and fruit-drink sessions were analyzed using repeated-measures analyses of variance with three within-participant factors. Because monkeys rarely made any responses during no-commodity or no-cue sessions, data from these sessions were not analyzed. The first factor was cycle number (mean data collected during Cycles 1–4, i.e., cycles that followed response-independent reinforcement, and mean data collected during Cycles 5 and 6, i.e., cycles that did not follow response-independent reinforcement). The second factor was experimental phase [mean data collected during 4 days of reinforced responding (baseline), mean data collected the 2 days before the day of response-independent reinforcement (extinction before), data collected the day of response-independent reinforcement (response-independent), mean data collected the 2 days after the day of response-independent reinforcement (extinction after) and mean data collected during 4 days after responding was again reinforced (recovery)]. The number of fruit-drink and candy choices each day was analyzed using only the second and third factors. Three planned comparisons were conducted on the experimental phase factor: (1) data obtained during the 2 days before the day of response-independent reinforcement were compared with baseline, (2) data collected the day of response-independent reinforcement were compared with the data obtained the 2 days before response-independent reinforcement and (3) data obtained during baseline were compared to data obtained when responding was again reinforced following the extinction phase. Analyses of the location data were as described for the above data, except data were summarized across all six cycles, i.e., there was no cycle factor. Results for all analyses were considered statistically significant at $P < .05$, using Huynh–Feldt corrections, where appropriate. Separate analyses were accomplished for each maintenance condition.

3. Results

3.1. Responding reinforced with candy

Fig. 1 compares the mean number of responses emitted during each 10-min acquisition and consumption component of candy sessions when the daily food ration was 8 and 20 chow. As shown in the top panels, monkeys responded more during the first four acquisition cycles [8 chow: $F(1,5) = 16.1$; 20 chow: $F(1,5) = 28.4$] compared to the last two cycles. The baseline number of acquisition responses for candy during the first four cycles was similar when the daily chow ration was 8 (160 responses per session) and when the daily chow ration was 20 (175 responses per session). As shown in the bottom panels, monkeys responded more during the first four consumption cycles [8 chow: $F(1,5) = 26.6$; 20 chow: $F(1,5) = 60.3$] compared to the last two cycles. The baseline number of consumption responses for candy during the first four cycles was similar when the daily chow ration was 8 (270 responses per session) and when the daily chow ration was 20 (260 responses per session).

Under the 8-chow maintenance condition, when candy was no longer delivered during the consumption components, responding decreased to about 10% of baseline levels in 3 days [$F(1,20) = 90.9$]. By contrast, though the number of responses was lower during acquisition components when candy was not delivered during consumption components, this decrease in responding during acquisition components

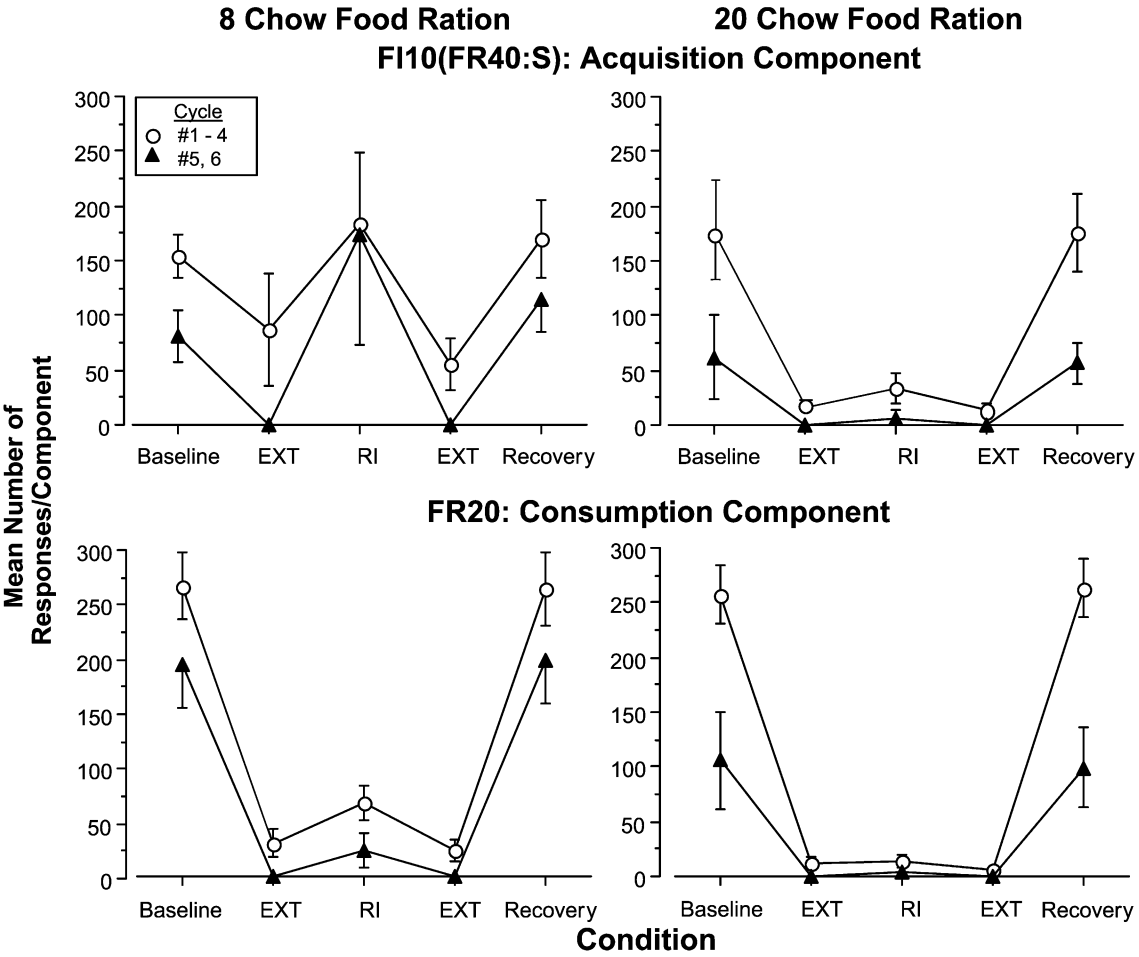

Fig. 1. Mean number of responses emitted during the acquisition [FI 10 min (FR 40:S); top panels] and consumption [FR 20; bottom panels] components of candy sessions as a function of cycle number and experimental phase when the daily food ration was 8 chow (left panels) and 20 chow (right panels). Data presented were obtained during (1) the last 4 days of baseline (Baseline), (2) the 2 days before and after the day of response-independent reinforcement (EXT), (3) the day of response-independent reinforcement prior to the first four cycles (RI), and (4) the 4 days after responding was again reinforced (Recovery). Error bars represent ± 1S.E.M.

was not significant ($P < .10$). The monkeys first experienced candy extinction under the 20-chow maintenance condition and responding during consumption components decreased to about 10–15% of baseline in 8 days (Fig. 1 only presents mean data for the last 2 days of extinction to facilitate comparisons across conditions). When candy was no longer delivered during the consumption components, responding decreased during both acquisition [$F(1,20) = 24.4$] and consumption [$F(1,20) = 60.6$] components.

Under the 8-chow maintenance condition, delivery of response-independent candy prior to the first four cycles significantly increased responding during the acquisition components [$F(1,20) = 11.7$] but *not* the consumption components of all six cycles. By contrast, under the 20-chow maintenance condition, delivery of response-independent candy prior to the first four cycles did *not* alter responding during acquisition or consumption components. When responding during the consumption components was again reinforced by candy, responding rapidly returned to baseline levels during both acquisition and consumption components of candy sessions under both chow maintenance conditions.

3.2. Responding reinforced with fruit-drink

Fig. 2 compares the mean number of responses emitted during each 10-min acquisition and consumption component of fruit-drink sessions when the daily food ration was 8 and 20 chow. As shown in the top panels, the baseline number of acquisition responses for fruit-drink during the first four cycles was similar when the daily chow ration was 8 (75 responses per session) and when the daily chow ration was 20 (70 responses per session). As shown in the bottom panels, the baseline number of consumption responses for fruit-drink during the first four cycles was similar when the daily chow ration was 8 (80 responses per session) and when the daily chow ration was 20 (90 responses per session).

When candy was no longer delivered during candy sessions under the 8-chow maintenance condition, responding increased during acquisition [$F(1,20) = 16.9$] and consumption [$F(1,20) = 43.1$] components of fruit-drink sessions. Candy extinction did not alter, however, responding reinforced with fruit-drink under the 20-chow maintenance condition. Delivery of response-independent candy prior to

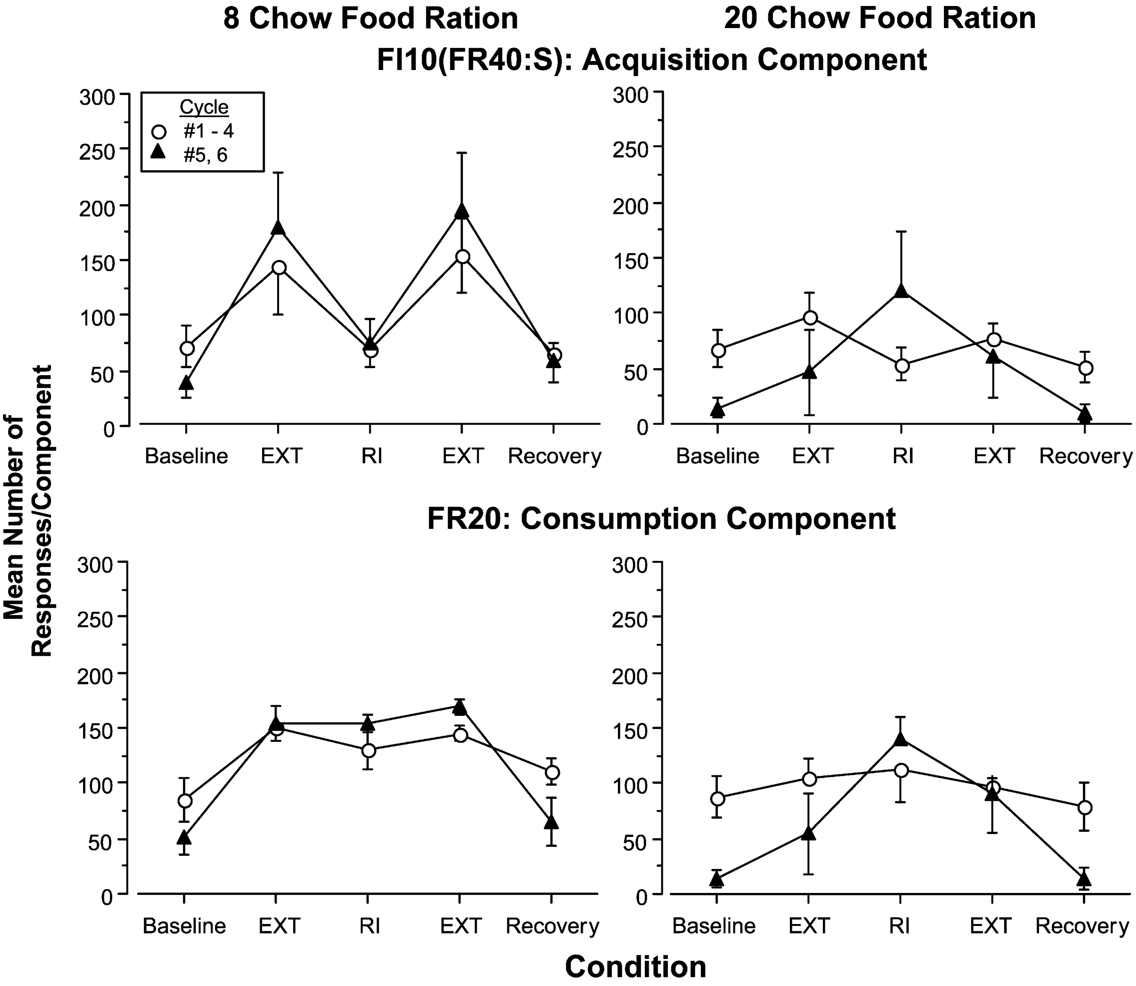

Fig. 2. Mean number of responses emitted during the acquisition [FI 10 min (FR 40:S); top panels] and consumption [FR 20; bottom panels] components of fruit-drink sessions as a function of cycle number and experimental phase when the daily food ration was 8 chow (left panels) and when the daily food ration was 20 chow (right panels). See Fig. 1 for details.

the first four cycles significantly decreased responding during the acquisition components of all six cycles of fruit-drink sessions [*F*(1,20) = 11.9] under the 8-chow maintenance condition and significantly increased responding during the consumption components of all six cycles of fruit-drink sessions [*F*(1,20) = 6.9] under the 20-chow maintenance condition. When responding during the consumption components of candy sessions was again reinforced by candy, responding during fruit-drink sessions rapidly returned to baseline levels during both acquisition and consumption components.

3.3. Choice

When given a choice between responding for candy or fruit-drink under baseline conditions, monkeys chose to

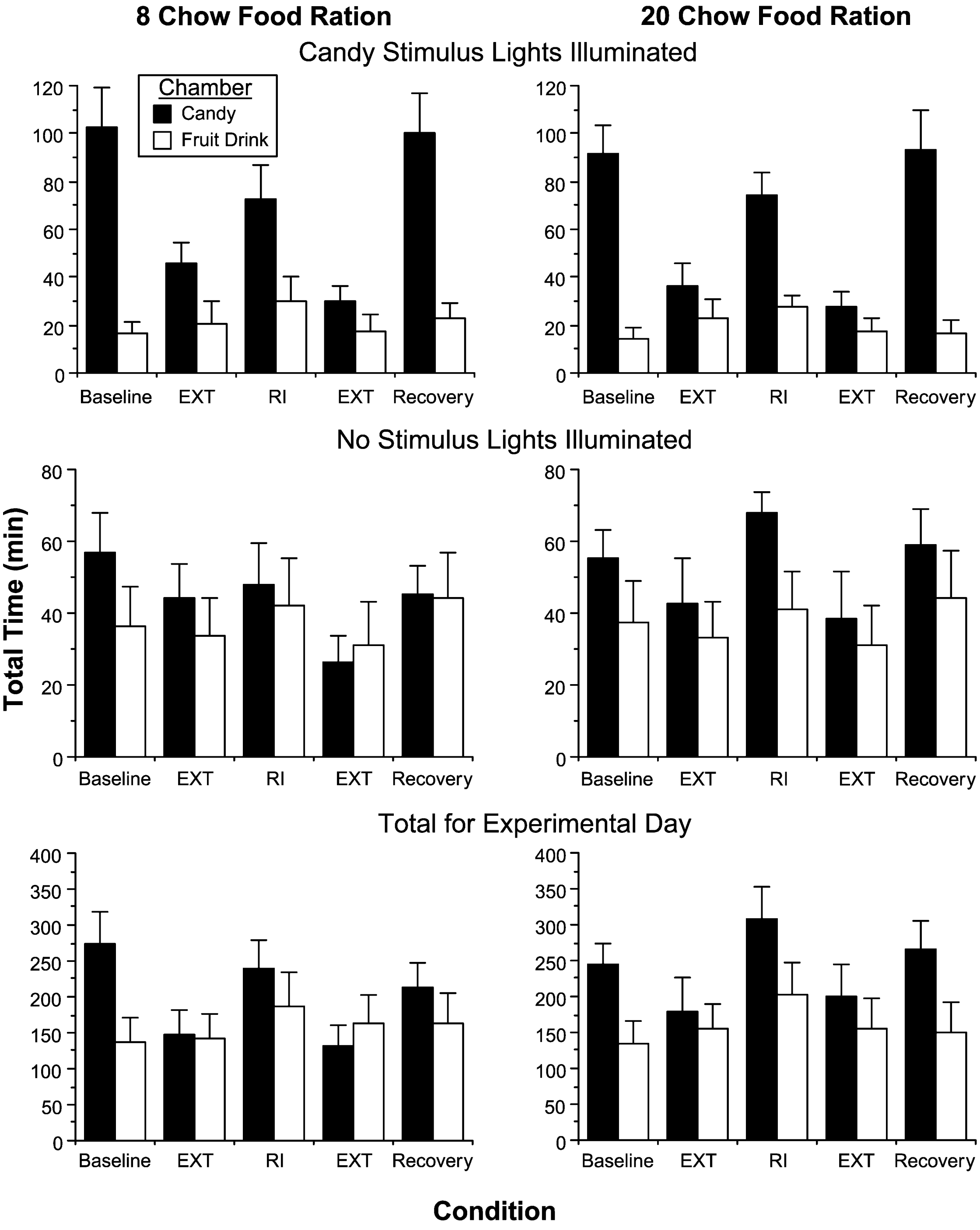

Fig. 3. Mean length of time spent in the candy and fruit-drink chambers when the candy stimulus lights were illuminated (top panels), no stimulus lights were illuminated (middle panels) and over the entire experimental day (bottom panels) when the daily food ration was 8 chow (left panels) and when the daily food ration was 20 chow (right panels). See Fig. 1 for details.

work for candy 3.2 ± 0.4 times (mean ± S.E.M.) during the first four cycles under both chow maintenance conditions, 1.3 ± 0.1 times during the last two cycles under the 8-chow maintenance condition and 0.5 ± 0.2 times during the last two cycles under the 20-chow maintenance condition. Under candy extinction conditions, the number of candy choices significantly decreased to 1.7 ± 0.4 and 0.2 ± 0.1 during the first four and last two cycles [$F(1,20) = 22.2$] under the 8-chow maintenance condition and decreased to 1.4 ± 0.4 and 0.2 ± 0.2 during the first four and last two cycles [$F(1,20) = 12.6$] under the 20-chow maintenance condition. Response-independent candy significantly increased the number of candy choices to 3.1 ± 0.2 and 0.8 ± 0.4 during the first four and last two cycles [$F(1,20) = 14.5$] under the 8-chow maintenance condition and increased the number of candy choices to 2.5 ± 0.4 and 0.7 ± 0.4 during the first four and last two cycles [$F(1,20) = 6.6$] under the 20-chow maintenance condition. The number of candy choices returned to baseline levels when candy was again delivered during consumption components.

3.4. Location preference

Fig. 3 compares the length of time that monkeys spent in each chamber under several stimulus conditions when the daily food ration was 8 and 20 chow. As shown in the upper panels, when the stimulus lights indicating candy availability were illuminated, monkeys spent about five times as much time in the candy chamber as in the fruit-drink chamber at baseline. Under candy extinction, monkeys spent significantly less time in the candy chamber [8 chow: $F(1,20) = 25.7$; 20 chow: $F(1,20) = 47.9$], and response-independent candy significantly increased the length of time monkeys spent in the candy chamber when the candy stimulus lights were illuminated [8 chow: $F(1,20) = 5.8$; 20 chow: $F(1,20) = 22.7$]. Time spent in each chamber returned to baseline when candy was again delivered during consumption components.

As shown in the middle panels, when no commodities were available (i.e., no stimulus lights illuminated), monkeys spent 50% more time in the candy chamber than the fruit-drink chamber at baseline. This preference for the candy chamber when no commodities were available was not affected by either candy extinction or response-independent candy. Data describing the length of time monkeys spent in each chamber over the entire experimental day (bottom panels) parallel the data described in the top panels.

3.5. Weights and chow intake

Table 2 summarizes body weight and chow intake under each maintenance condition. Monkeys consumed nearly all of their 20-chow ration during the initial 7 weeks of the study and consumed nearly all of their 8-chow ration over the last 4 weeks of the study. Monkeys gained an average of 1 kg over the initial 7 weeks of the study when they received 20 chow/day and lost an average of 0.4 kg over the 4 weeks of the study when they received 8 chow/day.

Table 2
Amount of chow ration consumed and body weight under both maintenance conditions

	Number of chow consumed (range)	
Monkey	20 Chow	8 Chow
1	18–20	8
2	14–20	8
3	12–20	7–8
4	16–20	8
5	17–20	8
6	19–20	8

	Body weight (kg)		
Monkey	Initial	End 20 chow	End 8 chow
1	9.9	11.7	11.6
2	7.5	8.6	7.7
3	9.7	9.8	9.4
4	5.9	6.3	6.4
5	6.1	6.8	6.4
6	9.6	11.1	10.9
Mean	8.1	9.1	8.7
S.D.	1.9	2.2	2.3

4. Discussion

The current procedure provided three measures of commodity acquisition: responding during acquisition components, choice and location preference. Previous studies from this laboratory have reported greater commodity acquisition behavior for (1) orally self-administered cocaine when food was also available (Foltin and Evans, 1997), (2) food when fruit-drink was also available (Evans and Foltin, 1997) and (3) smoked heroin when fruit-drink was also available (Evans et al., submitted for publication). The results of the present study clearly demonstrate that rhesus monkeys responded more during acquisition components of candy sessions than fruit-drink sessions, chose to work for candy more often than fruit-drink and developed a location preference for the chamber associated with candy. The present findings extend the utility of this procedure in demonstrating greater acquisition behavior related to candy when fruit-drink was also available.

The second purpose of this study was to determine the effects of response-independent reinforcement under extinction conditions on the three measures of commodity acquisition. The results of the present study clearly demonstrate that response-independent candy increased acquisition behavior as evidenced by increases in responding during acquisition components, increased candy choice and increased time spent in the candy chamber under the 8-chow maintenance condition. The vast majority of studies that have used the reinstatement procedure to model relapse to commodity acquisition have been accomplished with rats responding under a FR 1 (CRF) schedule of reinforcement (see reviews by Carroll and Comer, 1996; de Wit, 1996; Spealman et al., 1999). With the exception of several studies using squirrel monkeys (Barrett-Larimore and Spealman, 1996, described in Spealman et al., 1999; Gerber and Stretch, 1975; Khroyan et al., 2000; Stretch and Gerber, 1973; Stretch et al., 1971), two studies using rhesus monkeys (Slikker and Killam, 1979; Slikker et al., 1984) and one study using baboons (Kautz and Ator, 1995), little is known about the effects of noncontingent stimulus delivery on responding by nonhuman primates. The present results extend the findings of these earlier studies to a complicated reinforcement schedule in nonhuman primates. Also, previous studies on reinstatement emphasize the short-term effects of the response-independent reinforcer by measuring responding immediately following the stimulus presentation. In the present study, response-independent reinforcer delivery increased acquisition responding during the last two cycles of the session: cycles that did not follow response-independent reinforcer delivery. These results show that the procedure provides measures of the immediate and longer-term consequence of response-independent reinforcer delivery.

Several studies, however, have examined the effects of response-independent commodity delivery on reinstatement of behavior using second-order schedules of reinforcement. For example, Arroyo et al. (1998) reported that presentation of cocaine-paired cues increased responding that had previously been reinforced with intravenous cocaine. Unfortunately, that study did not examine the effects of response-independent cocaine under extinction conditions. Barrett-Larimore and Spealman (1996, described in Spealman et al., 1999) and Khroyan et al. (2000) reported that presentation of cocaine-paired cues *plus* cocaine increased responding of squirrel monkeys under a second-order schedule that had previously been reinforced with intravenous cocaine to a greater extent than response-independent cocaine or cocaine cues alone.

The present study used a chain schedule of reinforcement with an initial second-order acquisition component and a final FR consumption component that allowed a differentiation of the effects of response-independent reinforcer delivery on acquisition and consumption. This contrasts with the above studies that did not use a chain schedule of reinforcement, i.e., the second-order schedule terminated with the delivery of the primary reinforcer. Furthermore, in the present study under extinction conditions, candy was not delivered, but the stimuli that had been previously paired with candy were delivered. In the above studies that also used second-order schedules of reinforcement, under extinction conditions, neither cocaine *nor* the stimuli paired with cocaine was delivered. Response-independent candy delivery in the present study only increased responding during the second-order acquisition component. These results, in combination with those of Barrett-Larimore and Spealman (1996, described in Spealman et al., 1999), Arroyo et al. (1998) and Khroyan et al. (2000), indicate the major role that stimuli paired with a commodity play in the reinstatement of acquisition of that commodity.

While second-order schedules, like the one used here, are commonly used to study the motivational effects of stimuli paired with reinforcement, and as models of commodity acquisition (Foltin, 2001; Markou et al., 1999), this is the first study to combine operant and place preference methodologies for studying factors modulating commodity acquisition. While candy extinction decreased the location preference for the candy chamber, there was still a significant location preference for the candy chamber when the effects of response-independent candy were determined. Mueller and Stewart (2000) reported reinstatement of cocaine-induced CPP when cocaine was given prior to a test session in rats that, prior to saline extinction trials, have shown a cocaine CPP. In the present study, there was an increase in time spent in the candy chamber during candy sessions under chow maintenance conditions, but no overall increase in location preference when no stimulus cues were illuminated. The increase in time spent in the candy chamber under the 8-chow maintenance condition may be accounted for, at least in part, by the amount of time necessary to make the additional acquisition responses that were also observed under this food maintenance condition. Increased time spent responding cannot account for the increase in time spent in the candy chamber observed under the 20-chow maintenance condition, because there was *no* significant increase in either acquisition or consumption responses during candy sessions. Thus, the increase most likely reflects an increase in the preference for the cues associated with candy reinforcement, an effect similar to that reported for CPP by Mueller and Stewart (2000) and Wang et al. (2000).

Finally, the present procedure is unusual in that two different reinforcers were available during daily sessions, and there was a choice measure of commodity acquisition. Response-independent candy had variable effects on responding maintained by fruit-drink. The variability in the changes in responding reinforced with fruit-drink is difficult to interpret and further parametric research is warranted. Response-independent candy increased the number of choices to work for candy during choice sessions. de Wit and Chutuape (1993) reported that response-independent ethanol increased ethanol choice by humans. These findings, in combination with the present results, indicate that choice is a useful measure of acquisition behavior.

The third purpose of this study was to determine if the effects of response-independent reinforcer delivery would be modulated by an environmental manipulation. Because food deprivation increases responding maintained by drugs (e.g., Carroll et al., 1984; Meisch and Thompson, 1973), food and flavored fluid (Sheffield and Roby, 1950), it was expected that monkeys would respond more for candy and fruit-drink when the daily food ration was 8 chow. The failure to increase candy and fruit-drink intake was probably due to the fact that providing 8 chow, each weighing 15–16 g

(120–128 g total), did not sufficiently decrease total daily food intake from the baseline pellet intake of these monkeys when given access to food pellets under similar conditions (100–140 g total) (Evans and Foltin, 1997; Foltin and Evans, 1997). Monkeys also only lost about 5% of their body weight while maintained on 8 chow, which is a much smaller reduction than the 10–20% reduction in body weight commonly used in drug self-administration studies.

The behavioral effects of response-independent candy delivery were determined, however, by the magnitude of the daily food ration. Response-independent candy increased responding during acquisition but not consumption components of candy sessions only when the daily ration was 8 chow. By contrast, under both food maintenance conditions, response-independent candy increased choice of candy sessions and the length of time monkeys spent in the candy chamber. Thus, the latter two measures may be more sensitive indicators of commodity acquisition than the number of responses during acquisition components.

Comer et al. (1995) examined the effects of feeding condition in rats trained to self-administer intravenous cocaine to response-independent cocaine under extinction conditions. Response-independent cocaine produced dose-dependent increases in responding, with significantly greater increases occurring when rats were fed their daily food ration after, compared to before the laboratory session. The present results, in combination with those of Comer (Carroll and Comer, 1996; Comer et al., 1995), argue that increasing the daily food ration decreases the ability of response-independent reinforcers to increase responding formerly maintained by that reinforcer. Given that the monkeys did not lose weight under the 8-chow maintenance condition, the reason for the increase in sensitivity to response-independent reinforcer delivery is probably related to the fact that fewer alternatives were available under the 8-chow maintenance condition. Numerous studies have shown that the presence of an alternative reinforcer affects responding reinforced by a commodity of interest (see review by Bickel et al., 1995). In this case, providing monkeys with a larger food ration outside of the session, or a larger food ration outside of the session in combination with fruit-drink within the session, decreased the effects of response-independent reinforcer delivery.

Unfortunately, there are some limitations imposed by the current methodology that may affect the generalizability of the findings. (1) The procedures were tested in the same order in all monkeys. (2) Only one size of response-independent reinforcement was assessed under both food maintenance conditions. (3) These observations were based on 10-h daily sessions, which have rarely been used in other studies. (4) The FR within the second-order acquisition component was 40, while FR within the consumption component was 20.

In summary, the present procedure combined operant and location preference measures of commodity acquisition. Candy increased acquisition responding, choice and location preference measures of commodity acquisition. The effects of response-independent candy, in the context of extinction of candy-maintained responding, varied across these measures and were influenced by the daily food maintenance conditions. Response-independent candy increased acquisition responding under the 8-chow maintenance condition only, while response-independent candy increased candy choice and time spent in the candy chamber when candy stimulus lights were illuminated under both daily food maintenance conditions. The present procedure, when used in combination with methods of studying reinstatement of responding, may prove useful in analyzing factors affecting relapse to commodity use.

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