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Environments predicting intermittent shortening access reduce operant performance but not home cage binge size in rats

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Abstract

When non-food-deprived rats are given brief access to vegetable shortening (a semi-solid fat used in baked products) on an intermittent basis (Monday, Wednesday, Friday), they consume significantly more and emit more operant responses for shortening than a separate group of rats given brief access to shortening every day. Since both groups are traditionally housed in the same room, it is possible that the environmental cues associated with placing shortening in the cages (e.g., investigator in room, cages opening and closing, etc.) provide predictable cues to the daily group, but unpredictable cues to the intermittent group. The present study examined the effects of providing predictable environmental cues to an isolated intermittent group in order to examine the independent contributions of intermittency and predictability on intake and operant performance. Two groups of rats were housed in the same room, with one group provided 30-min intermittent (INT) access and the second group provided 30-min daily access (D) to shortening. A third group (ISO) of rats was housed in a room by themselves in which all environmental cues associated with intermittent shortening availability were highly predictable. After five weeks of home cage shortening access, all rats were then exposed to several different operant schedules of reinforcement. The INT and ISO groups consumed significantly more shortening in the home cage than the D group. In contrast, the INT group earned significantly more reinforcers than both the ISO and D groups under all but one of the reinforcement schedules, while ISO and D did not differ. These data indicate that intermittent access will generate binge-type eating in the home cage independent of cue predictability. However, predictable cues in the home cage reduce operant responding independent of intermittent access.

Keywords

rats; binge eating; bulimia; predictability; uncertainty; operant

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1. INTRODUCTION

Intermittent access to a variety of substances promotes robust intake of those substances during the period that they are available. This phenomenon has been described in rodents for alcohol [1–6], nicotine [7], fatty or sugary foods [8–9], and in children for snack items [10]. Research from this laboratory and others using a limited access binge eating model has shown that brief periods of intermittent access to 100% vegetable shortening results in binge-type behavior in non-food deprived rats [11–21]. In this model, non-food deprived rats given brief access (20 min to 2-h) to vegetable shortening on Mondays, Wednesdays, and Fridays consume significantly more shortening during the access period than do rats given daily access for the same amount of time. While the above studies have elucidated various factors that contribute to bingeing, it remains unanswered as to what it is about intermittency per se that promotes bouts of excessive intake.

One possible explanation for why intermittency promotes binge-type behavior may relate to the uncertainty associated with eating opportunities, even if food is readily available [22]. For instance, adolescents who routinely eat dinner with the family have a lower risk of binge eating than adolescents who rarely eat dinner with the family [23–24]. Binge episodes often are not planned [25] and daily energy intake can vary widely even within individuals [26]. Furthermore, intolerance for uncertainty has been reported in subjects with bulimia nervosa [27], and chaotic/uncertain eating behavior has been reported among those with binge eating disorder [28]. In short, those who binge have a relatively low tolerance for uncertainty but often engage in uncertain/chaotic eating patterns within environments of food abundance. Interventions for the treatment of binge eating attempt to reduce uncertainty associated with eating and palatable food consumption by establishing regular eating patterns and incorporating “forbidden” foods back into the diet [29]. It is possible that uncertainty surrounding opportunities to consume palatable foods within environments of food abundance contributes to eating pathology.

In the limited access rat bingeing protocol, the intermittent groups are housed in the same colony room as the daily groups. As such, the intermittent groups are exposed to cues every day that are associated with shortening presentation (the presence of the experimenter entering and leaving the room, opening and closing of cages, placement and removal of jars from the jar clips, etc.), but shortening is only provided on 3 days each week. Stated otherwise, the cues associated with shortening availability do not reliably predict consummatory opportunities for the intermittent group, because shortening is not always provided. As a result, the food-cue associations become ambiguous/uncertain. This may be analogous to environments of food abundance in which a plethora of cues are associated with palatable food availability (e.g. sight and smell of baked goods), but may not predict an opportunity to actually consume those foods (e.g. money may be limited). While uncertainty appears to be associated with binge-type consumption of palatable foods, its causal relationship to bingeing has not been determined. Since the factors/variables constituting uncertainty are numerous and ill-defined, the present study reduced uncertainty by making intermittent presentation of vegetable shortening certain and predictable in one group of rats. Home cage intake and operant performance using several different schedules of reinforcement in this group were then compared to that of rats housed under our standard conditions described above.

2. MATERIALS AND METHODS

2.1 Animals

Thirty-six male Sprague Dawley rats (Harlan, Indianapolis, IN), 60 days of age and weighing 251–285g (268.4 $\pm$ 1.2 g) at the start of the study, were individually housed in

hanging stainless steel wire cages in a temperature- and humidity-controlled environment on a 12:12 light:dark cycle. All rats had continuous access to tap water and to a nutritionally complete commercially available pelleted rodent diet (Laboratory Rodent Diet 5001, PMI Feeds, Richmond IN; percent of calories as protein: 28.05%, fat: 12.14%, carbohydrate: 59.81%; 3.3 kcal/g) placed in hanging metal food hoppers at the front of the cage.

After five days of adaptation to the vivarium, daily chow intake was recorded for 3 consecutive days (days 6 through 8), body weights were recorded (day 8) and vegetable shortening (Crisco® All-Vegetable shortening, J.M Smucker Co., Orrville, OH) was provided during a single overnight period (day 8 to 9). Three groups of 12 rats each were then matched by the 3-day average chow intake, body weight and the amount of overnight shortening consumed [ps NS, $F < 1.0$ for all three measures]. All procedures were approved by the Pennsylvania State University Institutional Animal Care and Use Committee.

2.2 Bingeing Procedure (Home Cage Protocol)

For the next five weeks, chow and water were available ad libitum to all groups. In addition, shortening was provided in glass jars clipped to the front of the home cage starting 2 hours prior to the start of the dark cycle. A fading procedure to establish shortening consumption during a 30-min period of time was used over the first three of these five weeks in order to equalize length of home cage shortening access to operant session length. During the fading procedure, the shortening was provided for 1h during the first week, for 45 min during the second week, and for 30 min for the duration of the study. A recent study has shown that this fading procedure will establish bingeing when the final access period is only 20 min [11]. For one group of rats shortening was provided on an intermittent (INT) basis (Mondays, Wednesdays, and Fridays), and for another group shortening was provided on a daily (D) basis.

These two groups were housed in the same colony room where other studies were also being conducted. Each group was housed in the top twelve cages of a 15-cage rack. The racks were arranged such that the INT and D groups for each study faced one another, i.e., the INT group could see the D group. Furthermore, the back of the D group rack for one study abutted the back side of a rack of cages for another study, i.e., the INT and D groups in the second study could not see the rats in the first study. In this way, the colony was able to accommodate 3 concurrent studies in which the INT and D groups faced one another and were visually isolated from the groups of other studies by creating 3 “rows” of studies. The colony was also arranged such that the testing for each group was staggered, e.g., the study at the front of the room was conducted first while the studies at the back of the room were conducted last. Once rats acclimated to the colony, they continued to sleep while other studies were conducted until the cages in their particular row began to be opened and closed.

The third group of rats (ISO) was provided shortening on the same days and at the same time relative to lights out as the first intermittent group. However, the presentation of shortening was made predictable by housing these animals in a separate isolated colony room with no other animals present. This colony room was located in a side hallway away from the “normal traffic” of the vivarium, and the room was entered only on days in which shortening was provided. A glass window in the door to the room provided visual inspection of the animals without entering. All animal care functions, i.e., weighing rats, filling food hoppers, changing water bottles and changing dropping pads, were performed on the three days that shortening was provided.

2.3 Apparatus

Twelve identical operant chambers (Model H10-11R-TC; Coulbourn Instruments, Allentown, PA) located in a room adjacent to the animal rooms were used for the operant testing. Experimental contingencies were programmed with Graphic State 2™ state notation. The back wall of each chamber contained a house light (Model H11-01R) located in the middle panel at the top of the chamber. The front wall of each chamber contained a retractable response lever (Model H23-17R) located in the middle panel and a triple cue lamp (H11-02R) located above the response lever. Whipped vegetable shortening was used as the reinforcer for lever pressing. It was delivered in 0.1 g units from a 20 mL glass syringe (Popper & Sons, New Hyde Park, NY) driven by an infusion pump (Model E73-01-3.3 rpm) into a receptacle located on the right panel adjacent and parallel to the response lever. A triple cue lamp located directly above the shortening receptacle was used to signal shortening delivery. Care was taken when packing the shortening into the 20 mL syringe to minimize any air pockets that would affect the amount delivered during each reinforcer delivery.

2.4 Operant Procedures

2.4.1 General Procedures—Previous studies have assessed operant performance in intermittent and daily groups after lever pressing had been established using the method of hand shaping by successive approximations [18,21]. The current study used an autoshaping procedure instead of hand shaping. This was done in order to assess possible differences among the three groups in the time required to acquire lever pressing. If lever pressing was not established under the autoshaping parameters, hand shaping was then used. Once lever pressing was established, operant performance was assessed in all three groups using the following schedules of reinforcement: fixed ratio, progressive ratio (PR), and fixed ratio (FR) with periods of signaled reinforcer availability (SA) alternating with periods of signaled nonavailability (SNA) [17, 30]. The ISO group remained isolated from the other two groups during operant training and testing, i.e., the experimenter only entered the ISO room on Mondays, Wednesdays, and Fridays in order to take care of animal husbandry, to provide shortening or to transfer the rats to and from the operant chambers.

All operant sessions were conducted on Mondays, Wednesdays, and Fridays for 30 min starting about 2 h prior to the start of the dark cycle. The light cycles in the two rooms where the rats were housed were staggered to accommodate the start time of the sessions. Supplemental shortening was provided for 30 min in the home cages, 20–30 min after an operant session. Except for the autoshaping sessions, the rats were overnight food-deprived prior to reinforcer delivery training (analogous to food magazine training) and prior to the first session when a change in the reinforcement contingencies was programmed. All other sessions were conducted under non-food-deprived conditions. For all sessions, rats were placed into the operant chamber with the lever retracted. The lever was inserted into the chamber at the start of the session, retracted at the start of and during shortening delivery, reinserted after shortening delivery, and retracted at the end of the session. The triple cue lights above the lever were constantly on while the schedule was in effect, turned off during shortening delivery, and turned back on after shortening delivery when the lever was reinserted into the chamber. When shortening was scheduled to be delivered, all three cue lamps above the shortening receptacle flashed on and off every 0.5 sec for 2 sec prior to the start of the shortening delivery, during shortening delivery, and for 1 sec after delivery. Table 1 summarizes the sequence of exposure to the home cage protocol and operant sessions.

2.4.2 Shortening delivery training—After the fifth week of the bingeing procedure (home cage protocol) rats were overnight food-deprived, allowed a ½ hr acclimation period

to the operant chamber with the lever retracted, and given 5 g of rat chow in their home cages after the session. During the next session, all animals were trained to receive shortening deliveries. Every 25 sec, the triple cue lamps above the shortening receptacle signaled shortening delivery, 0.1 g of shortening was delivered, and 1 sec later the triple cue lights were turned off until the next scheduled shortening delivery 55 sec later. All rats were then returned to ad libitum chow for 3 days.

2.4.3 Autoshaping—After the initial shortening delivery training (above), an autoshaping procedure was in effect for the next 9 sessions. The rats were not food-deprived for these sessions. At the beginning of the session a fixed-ratio one schedule of reinforcement was in effect for 30 sec. If the rat failed to lever press, the lights above the lever were turned off, the lever was retracted and 0.1 g of shortening was delivered. An intertrial interval was in effect for 55 sec with the lever retracted, after which the cycle was restarted. If the rat pressed the lever, shortening was immediately delivered, the intertrial interval with the lever retracted was in effect for 55 sec, after which the cycle was restarted. Criterion for achieving autoshaping was met if a rat completed 3-FR1s during an autoshaping session, after which a FR1 schedule was in effect for the remainder of the session, absent the autoshaping segments and intertrial interval. For rats that met the autoshaping criterion (completed 3 FR1s during an autoshaping session), the following conditions were in place during the next session: FR1 schedule of reinforcement for 3 reinforcer deliveries, followed by FR2 schedule for 3 reinforcers, and then FR3 for the remainder of the session. Rats that failed to acquire lever pressing after the ninth autoshaping session were food-deprived and hand-shaped to lever press. Autoshaping was ended after nine sessions to avoid extended reinforcement of the “not-R” class of behavior [31–32], which may have made training rats to switch to the “R” class (lever pressing) more difficult.

2.4.4 Home Cage Protocol—Following the autoshaping sessions and periodically throughout the study, all rats were placed on the home cage protocol for a week to verify that differences in home cage shortening intake among the groups still existed.

2.4.5 Reinforcement schedules—The first FR3 (FR3 #1) sessions assessed how long rats would work for shortening deliveries within the 30-min sessions and how much shortening would be earned; the second FR3 series (FR3 #2) assessed replicability of results obtained in the first series. In contrast to the FR3 schedules, the PR schedules assessed how hard the rats would work for shortening deliveries. PR schedules avoid confounds associated with ceiling effects on intake during the tests; therefore PR performance is considered a better measure of reinforcing efficacy than home cage intake or FR performance [33]. PR responding successfully distinguished INT from D rats in a previous report [21]. Two different PR schedules that previously were used by our group were used here, one in which the response cost increased by one lever press after the receipt of each reinforcer (PR1) and another in which the response cost increased by 3 lever presses after receipt of each reinforcer (PR3).

Each of the signaled reinforcer availability (SA) and signaled nonavailability (SNA) schedules (FR1 and FR3) assessed whether rats would attend to cues signaling whether or not reinforcers could be earned [17,30]. These contingency arrangements were originally developed in rats to model the inability to control drug intake that is one criterion of substance dependence in humans [25, 30]. Responding during the SNA period was highly correlated with the propensity to reinstate cocaine-reinforced responding in that report, supporting the validity of the approach [30]. We modified the procedure here, in an attempt to model the “loss of control” that is a defining characteristic of human binge eating episodes [25].

Each component alternated throughout the session to avoid extinction during repeated SNA components. Each session started with the signaled available (SA) component and alternated with the signaled non-available component. During the SA component, the lever was inserted into the chamber and the cue lights above the lever were turned on for 20 sec. If a lever press was emitted, the lights above the lever were turned off, the lever was retracted, and 0.1 g of shortening was delivered. After shortening delivery, a 5-sec intertrial interval ensued which was then followed by the signaled non-available component (SNA). If a lever press was not emitted during the SA component, the lever was retracted, a 5-sec intertrial interval ensued and the SNA component followed. During the SNA component, the lever was inserted into the chamber for 20 sec, but the cue lights above the lever remained off. Lever presses during this component had no experimenter-scheduled consequences. After the 20-sec SNA component, the lever was retracted, a 5-sec intertrial interval was in effect, and then the SA component started again. Responding early in the SA component shortened the time for that component, which resulted in more SA/SNA cycles and more opportunities to earn reinforcers.

2.5 Statistics

The design of this study and the statistical analysis of results were intended to determine the independent contributions of predictability and intermittency to binge-type behavior. If predictability plays a critical role, then the intake and operant performance of the ISO group should be similar to that of the D group. Alternatively, if intermittency is critical, then the intake and operant performance of ISO should be similar to INT. In short, we wanted to determine if intermittency would induce binge-type behavior independent of predictability or if predictability would reduce binge-type behavior independent of intermittency.

SAS v.9.2 (SAS Institute, Cary, NC) was used for all analyses. Data from the last 4 sessions of each schedule were averaged except for the PR3 schedule, where the last 3 sessions were used. There were no within-group differences among the sessions that were used to generate the group averages. 1-way analysis of variance (ANOVA) was used to determine if differences among groups existed for each measure. Significant results were followed by Tukey's Studentized Range (HSD) Test to determine specific differences among the groups. A Duncan's Multiple Range Test was used instead of Tukey's HSD under the FR 3#1 for the number of reinforcers earned, as a significant main effect was reported after ANOVA, but Tukey's HSD did not reveal differences among the groups.

A 2-way ANOVA (group $\times$ 3' bin [time]) using combined data of FR3#1 and FR3#2 was used to analyze the number of reinforcers earned within 3-min bins during the sessions. For this analysis, group was the between group factor, and bin was the within group (repeated) factor. Significant results within each bin were further analyzed by Tukey's HSD to determine differences among groups.

3. RESULTS

3.1 Home Cage Protocol

During the five periods of exposure to the home cage protocol there were significant differences in shortening intake among the ISO, INT and D groups (Fig. 1, top panel; see Table 2A for F- and p-values). Specifically, the ISO and INT groups consumed significantly more shortening than the D group during the 30-min access period each time the home cage protocol was in effect (Tukey's HSD p s <0.05), but intakes did not differ between the ISO and INT groups.

3.2 Autoshaping

Nine autoshaping sessions were conducted, with acquisition determined by the number of sessions required to complete three FR1s. Thus, a rat that completed three FR1s during the 4th session was assigned the number 4; those rats that did not lever press by the last session were assigned the number 10. Eight INT rats, 7 ISO rats, and 5 D rats learned to lever press. However, there were no statistically significant differences among the groups in the number of sessions required to meet the autoshaping criterion ($F[2,35] = 2.17$, p NS). The average number of days required for each group to meet criterion was INT (6.7 ± 0.8), ISO (7.7 ± 0.8), and D (8.8 ± 0.6).

3.3 Schedules of Reinforcement

For each of the schedules of reinforcement, except PR3, there were significant differences among the groups with respect to the number of reinforcers earned (Fig 1, bottom panel; see Table 2B for F - and p -values). In contrast to the home cage results, the INT group earned significantly more reinforcers than either the ISO or the D group for every schedule tested except PR3 (Tukey's HSD or Duncan's Multiple Range: $p < 0.05$). Furthermore, there were no differences in the number of reinforcers earned between the ISO and D groups for any of the schedules (p s NS).

3.4 Signaled Availability and Signaled Non-Availability

As indicated by the number of earned reinforcers (Figure 1, bottom panel), the INT group emitted significantly more responses during the SA components than did the D group. However, the number of responses during the SNA components of the FR1 SA/SNA sessions and the FR3 SA/SNA sessions did not differ among the groups when expressed either as the average responses emitted or as a percentage of total responding (not shown). Although there were no differences among the groups for the SNA component, the rats did learn the procedure. This is evidenced by significant declines in the percentage of responses emitted during the SNA component during the first twelve SA/SNA sessions to which the rats were exposed [2-way ANOVA for FR1 SA/SNA, main effect of sessions $F(11,363) = 28.34$, $p < 0.0001$; no main effect of group; no session by group interaction].

3.5 Distributions of reinforcers throughout session

The temporal distribution of reinforcers earned throughout the sessions for all schedules of reinforcement was also examined in 3-min bins. Data from each bin of the last 4 sessions of each schedule (last 3 for PR3) were analyzed as: 1) average reinforcers earned, and 2) percentage of total reinforcers earned. Despite the constraints on responding by each of the schedules of reinforcement, the results of these analyses were generally similar, i.e. more reinforcers were earned during the initial bins than in later bins and group differences were present, particularly in the earlier bins (Table 3A & B). Therefore, to simplify presentation, data from the last 4 sessions of FR3 #1 and FR3 #2 were combined and are presented in Fig. 2. We used the combined FR 3 distributions in that there were no within group differences between the first and second exposure to the schedule. Using the data from both exposures allowed for a greater number of sessions to be included in the analysis.

For the average number of reinforcers earned, there were main effects of group [$F(2,33) = 8.99$, $p < 0.0008$] and bin [$F(9,297) = 132.82$, $p < 0.0001$], and a group X bin interaction [$F(18,297) = 10.34$, $p < 0.0001$]. The INT group earned significantly more reinforcers than the ISO group during each of the first four bins (min 0–12; p s < 0.05), and more than the D group during the first six bins (min 0–18, p s < 0.05 ; Fig. 2, top panel). The ISO group, in contrast, earned fewer reinforcers than the D group during the first 2 bins (p s < 0.05), and did not differ from D during the remaining bins (Fig. 2, top panel).

When reinforcer deliveries in each bin were expressed as a percentage of total reinforcers, a different characterization emerges from the same data set. There was no main effect of group as data were expressed as a percentage of total reinforcers, i.e., all groups earned 100% of their reinforcers. However, there was a main effect of bin [$F(9,297) = 102.28$, $p < 0.0001$], as well as a group X bin interaction [$F(18,297) = 8.27$, $p < 0.0001$]. The D group earned a significantly greater percentage of their reinforcers during the first two bins (min 0–6) than the ISO group, but a lower percentage than the ISO group in later bins (Fig. 2, bottom panel). INT rats did not earn a greater percentage of reinforcers than D rats in any bin. What is particularly striking about both of these analyses is the small number and low percentage of reinforcers earned by the ISO group during the first bin of the session.

4. DISCUSSION

When environmental conditions reliably predicted opportunities to consume an optional fatty food, the behavioral characteristics of eating, i.e., amount of consumption and duration of time spent eating, depended upon the context in which that behavior occurred (intermittent v daily access and home cage v operant chamber). In the home cage context, intermittent 30-min access (M, W, & F) to shortening generated binge-type behavior compared to daily 30-min access regardless of whether the intermittent presentation of shortening was unpredictable (INT group) or predictable (ISO group). However, in the operant context more reinforcers were earned when shortening presentation was unpredictable in the home cage (INT group) compared to the other groups (ISO and Daily groups).

These results demonstrate that consummatory behavior in one context (e.g. home cage) does not predict appetitive behavior in another context (e.g. operant chamber). This principle has been demonstrated in another study [21] in which the reinforcing efficacy of shortening as assessed by progressive ratio responding depended upon the home cage context of shortening presentation (intermittent v daily), not the amount consumed in that context. In that study, the group of rats with intermittent access to shortening in the home cage had a higher breakpoint than the group with daily access to shortening in the home cage. Furthermore, when subgroups of individual rats in each group (intermittent v daily) were matched on the amount consumed in the home cage and the progressive ratio data were reanalyzed, the subgroup with intermittent home cage access still had a significantly higher break point than the subgroup with daily home cage access.

The results of the present study also parallel another study in which liquid sucrose [34] was used as the optional food. In that study, there were no intake differences between groups with intermittent or daily access to 3.2% and 10% solutions, when the response cost for drinking was low (amount of liquid sucrose per lick). However, when the response cost was increased (less sucrose per lick) by changing to a different sipper tube, the intermittent groups consumed significantly more sucrose than the daily groups. In the present study, shortening intake did not differ between the intermittent unpredictable (INT) and predictable (ISO) groups in the home cage context. In the home cage, the response cost was low (i.e., eat shortening from a jar), and the topography of eating was not defined by the experimenter. There is considerable variability in how different rats consume shortening in the home cage. Some rats will scoop shortening in their paws, some will lick the shortening, while others will (for a lack of better term) “nose dive” into the shortening. In contrast to the home cage, the number of reinforcer deliveries (intake) did differ between the intermittent unpredictable (INT) and predictable (ISO) groups in the operant context. In this context, the response cost for consuming shortening was greater than that of the home cage, i.e. responding on different schedules of reinforcement was required. Furthermore, the response requirement, the amount of shortening (0.1 g) per delivery, and the response topography

(licking from the slip neck of the syringe) were all defined by the experimenter rather than the rat.

The results of the PR1 and PR3 schedules replicate previous findings [21] showing that the PR1 schedule was able to differentiate between intermittent and daily access groups, but the PR3 schedule did not. It is possible that other PR schedules with smaller ratio increments would also be effective, such as increasing the response requirement by one after every even-numbered reinforcer delivery, but this remains to be tested. Regardless, the present results indicate that PR schedules with relatively large slopes (steep ratio increments) are ineffective in differentiating groups when examining food-reinforced behavior in non-food deprived animals.

Other reports support this idea. For instance, exponential PR schedules, which have been used to study cocaine self-administration [33], failed to distinguish intermittent and daily groups of non-deprived rats responding for 10% sucrose [35] or 100% shortening reinforcers [18]. Naleid et al., [36], also used an exponential PR schedule and reported a concentration dependent increase in sucrose reinforcers earned, but not in oil reinforcers earned. Taken together, the present results suggest that there may be an optimal PR slope (incremental ratio increase) that differentiates groups of non-food-deprived rats responding for fat and perhaps sucrose, as well. These results confirm the statement by Richardson and Roberts [33] that “Which PR series is appropriate depends not only on the drug [reinforcer] under investigation, the type of subjects used and the length of the testing session, but on how the PR schedule is implemented.”

The above analysis has emphasized that the home cage history of shortening intake (intermittent v daily, and predictable v unpredictable presentation) is an important factor when assessing the reinforcing efficacy of shortening (number of reinforcers earned) in an operant context. In a related report [17] rats were first given a history of 1h access to shortening on either an intermittent or daily basis for several weeks. Then with no further access to shortening all rats were implanted with intravenous catheters and trained to lever press for infusions of cocaine. The rats with the intermittent history worked to higher breakpoints for cocaine compared to rats with the daily history. Although predictability was not assessed in that report, the results are consistent with the results obtained in the INT and D groups here, and suggest that the present findings with shortening may generalize to other reinforcers.

Bingeing in humans involves not only the consumption of a large amount of food in a brief period of time, but is also accompanied by what has been characterized as a sense of “loss of control” [25]. However, operational definitions of “loss of control” are difficult to establish in animal studies. In other studies, the willingness to expend effort to obtain an optional substance has been used as an indication of “loss of control”. For instance, alcohol-preferring rats work to higher breakpoints for ethanol and for sucrose during progressive ratio sessions compared to other strains [37] and “addiction-prone” rats work to higher breakpoints for cocaine than do rats that are “addiction-resistant” [30]. Using this criterion, “loss of control” would be attributed to the INT rats in the present study, since they earned more reinforcers during the PR1 sessions, than did the other groups. However, based upon the PR3 results, none of the groups would be considered to have “lost control”.

The inclusion of the SA/SNA components under the FR1 and FR3 schedules was an attempt to discern differences in either learning rates or “self-control” among the groups. The absence of a difference among any of the groups with respect to either the average number of responses emitted during the SNA components, or as a percentage of the total responses, also points to the challenge of modeling “loss of control” in animals. Logically, one might

assume that both the INT and ISO groups would have emitted more responses during the SNA components, however measured, than the D group, but this clearly was not the case. Furthermore, all of the groups learned the procedure within the same period of time.

In the present study, the distribution of reinforcers under all schedules of reinforcement was also analyzed. In some studies, the pattern of responding during fixed-ratio sessions has been used to define “loss of control”. For instance, alcohol-preferring rats emitted more responses for EtOH than for saccharin during the first 20 minutes of 2-hour fixed-ratio sessions (FR1, FR3, FR5) [38]. This was proposed as an indication of “bout” or “binge”-like loss of control. If the Nowak et al. [38] criterion is applied to the distribution of reinforcers reported in the present study (Fig. 2, top panel), “loss of control” would be attributed to the INT group, as this group earned more reinforcers than the D group during the first 18 minutes of the session, and more than ISO during the first 12 minutes. However, the D group also earned more than the ISO group during the first 6 minutes. Did the D rats also “lose control” relative to ISO, but the INT rats were even more “out of control”? If one tries to define “loss of control” using the percentage of reinforcers earned in each bin (Fig. 2, bottom panel), a different characterization emerges. The D group earned the same percentage of reinforcers during the first bin as the INT rats, but a greater percentage in the second bin (Fig. 2B), even though they earned fewer actual reinforcers than INT in both bins (Fig. 2, top panel). In this case, the D rats would be considered the most “out of control”.

One might also define “loss of control” as how long rats worked for reinforcers during the session. This would be analogous to the idea that once bingeing is initiated, it is difficult to stop [25]. In this case, “loss of control” would be attributed to the INT and ISO rats, as they responded throughout the entire session (Fig. 2, top and bottom panels) whereas responding for the D group nearly stopped completely after bin 8. Finally, if “loss of control” was defined by the amount of shortening that was consumed, then “loss of control” would be attributed to the ISO group in the home cage, but not in the operant chamber. These challenges point to the limit of animal models and the difficulty of attributing a human construct such as “loss of control” to animal behavior. In addition, the need for a battery of tests, rather than any single test, is emphasized. In the present case, INT rats worked to higher breakpoints during PR and earned more absolute reinforcers earlier in the session than did the ISO and D rats. Whether this represents “loss of control” is debatable. Regardless, results obtained in the ISO rats clearly demonstrate that predictability in the home cage affects operant responding in a manner that is distinct from that of home cage consumption.

The specific cues that governed the predictability of shortening access were not determined. However, the effectiveness of contextual cues to predict shortening access in this study is exemplified if only by anecdotal evidence. The animal colony housing the ISO group was located at the end of a hallway devoid of normal traffic and sounds from other investigators and animal care staff, and the windowed door to this colony room was always locked to prevent inadvertent entry. By the third week of the protocol, simply jingling the keys to the locked door prior to unlocking it was enough to arouse all twelve rats who quickly paced back and forth in the cages until shortening was provided. In contrast, jingling the keys to the door of the colony room housing the INT and D rats, which was in the path of normal traffic and ambient noise and where investigators entered daily, did not have this effect. More often than not, the INT and D rats would continue to sleep in the back of their cages until their row of cages started to be pulled open and pushed shut when placing the bowls of shortening in them. Because of the arrangement of the vivarium (see methods), the INT group would be aroused when their associated D group would get shortening. The INT rats would watch us place the bowls of shortening in the D cages, but would only get their shortening 3 days per week.

One explanation for the present results could be that the behavior of the rats was governed by different cues. The ISO and D rats had a variety of contextual/environmental cues in the vivarium that reliably predicted when shortening would be available, but the INT rats did not. Only the actual presence of shortening predicted when intake could occur for the INT rats, thus they may have learned to pay attention to the shortening itself, rather than the contextual cues predicting its availability. After 5 weeks of home cage experience, the INT rats may have responded to shortening in the operant chamber in a manner similar to that of the home cage. That is, the shortening itself became the stimulus that stimulated intake in the home cage as well as responding in the operant chamber.

There is evidence from other studies supporting the idea that different types of cues may differentially modulate food-related behavior. For instance, contextual/environmental cues previously paired with a high-fat palatable food (Oreo cookies) have been reported to stimulate subsequent binge-type eating of chow in non-food-deprived rats. However, allowing the same rats to consume a small amount of the palatable food at the beginning of the measurement period promoted even greater intake [39]. In short, being able to eat a small amount of the palatable food itself provoked a behavioral response that was stronger than that induced simply by the associated cues. In the present study, eating the first bite of shortening in the home cage or the first reinforcer in the operant chamber may have contributed to the robust behavior of the INT rats in both environments. This is analogous to the difficulty stopping (loss of control) once a binge has been initiated that has been described for human binge eaters [25]. In a sense, the first bite of shortening may have served as a “priming dose” that promoted more reinforced behavior, in a manner similar to that of cocaine [33].

In contrast, the behavior of the ISO rats may have been in response to predictable environmental cues, rather than the shortening itself, which did not promote such a robust response. Although intermittency still promoted bingeing in the home cage environment in both the INT and ISO groups, the different behavior in the operant environment may have been due to the cues governing lever-pressing behavior. The comparable home cage intakes in the ISO and INT rats may have been due to ceiling effects imposed by the physiological capacity of the rat stomach. Thus, differences between the groups became clear only within the operant context where intakes were lower.

The mechanisms that account for the present results were not determined, but other research suggests the possible involvement of dopamine. As described above, the differential behavior of the INT and ISO rats may have been due to differential food-cue associations. Evidence from the reinstatement literature indicates that infusions of a D1-type antagonist into the dorsal medial prefrontal cortex decrease reinstatement that has been induced by food itself (a high-fat food pellet), but not reinstatement induced by a food-associated cue [40].

In addition to the possible differential food-cue associations, predictability itself can influence dopaminergic signaling. For instance, when contextual cues predicting cocaine delivery were certain or uncertain, cocaine-stimulated accumbens dopamine levels were greatest in the rats exposed to the uncertain conditions [41]. In addition, midbrain neuronal firing (presumably of dopamine cell bodies) in monkeys was differentially affected by the predictability of cues paired with a juice reward [42]. Thus, the predictable pairing of contextual cues with binge opportunities in the ISO rats may have attenuated operant performance due to alterations in dopamine signaling. Such a finding would be consistent with other research demonstrating the importance of dopamine to effort-based responding [43]. The possible involvement of dopamine in the present results would also be consistent with a report in which blockade of D1 and D2 receptors with flupenthixol reduced responding during PR tests, but had no effect on consumption during intake tests [44].

Stated otherwise, PR was sensitive to alterations in dopamine signaling, but intake was not. The fact that intake in the ISO and INT rats did not differ in the present report, but PR performance did, may have been due to dopaminergic differences in these two groups.

The contrasting results between consummatory and appetitive behavior in the INT and ISO rats may reflect differential activation of substrates mediating ‘wanting’, as defined by Berridge and colleagues. ‘Wanting’ is defined as the motivation for a reward, and is mediated by dopaminergic mechanisms. It has been suggested as a possible contributing factor to binge eating [45] and may also contribute to the craving that has been reported among those who binge (e.g. [46]). Appetitive behavior such as progressive ratio responding, and to a lesser extent fixed ratio responding, has been used to operationalize ‘wanting’ in animal studies. Thus, the differential operant responding in the INT and ISO rats reported here may model psychological aspects of human bingeing that are not reflected by intake alone.

CONCLUSIONS

Here we report that bingeing in rats depends upon the environmental context in which bingeing is assessed. In particular, the present results indicate that while intermittent consummatory behavior (as assessed by intake) is not affected by food-cue predictability, appetitive behavior (as assessed by operant responding) is.

The present results once more demonstrate the powerful effect that intermittency can have on consummatory behavior under non-food-deprived conditions. While it appears that uncertainty contributes to high intakes, intermittency also promotes high intakes, even when the available cues predicting consummatory opportunities are highly certain. This may be analogous to the large intakes in humans that typically occur on special holidays. These holidays are intermittent, but highly predictable, and intakes are typically more than would be consumed on a ‘normal’ day. However, such consumption is not usually accompanied by the psychological disturbances associated with binge eating. In short, large intakes can occur for a variety of reasons but do not always represent a ‘binge’. We are proposing that the stimulation of both consummatory and appetitive behavior in the INT rats may better represent human binge eating than simply the elevated intake that was seen in the ISO rats. In contrast, the behavior of the Daily rats may represent the idea that, within an environment of food abundance, perhaps a little bit of palatable food each day is not such a bad idea. Such an approach would introduce certainty and eliminate intermittency within the eating environment, which may be the most effective way to attenuate both the consummatory and appetitive aspects of binge-type behavior.

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RESEARCH HIGHLIGHTS

- Rats had intermittent or daily access to optional fat.
- Cues associated with fat access were predictable or unpredictable.
- Intermittent access to fat induced bingeing regardless of cue predictability.
- Predictable cues reduced operant responding regardless of fat access.

Figure 1.

Top Panel. Amount of shortening consumed in the home cage. Mean (+/- sem) amount of shortening (grams) consumed in the home cage at various points throughout the study. Different letters indicate significant differences among groups.

Bottom Panel. Reinforcers earned under each schedule of reinforcement. Mean (+/- sem) number of reinforcers earned under each schedule of reinforcement. Different letters indicate significant differences among groups. The schedules that appear on the graph were arranged for comparison purposes, not the order in which they were presented to the subjects.

Figure 2.

Top Panel. Average number of reinforcers earned in each 3-min bin for the combined sessions for the FR3-#1 and #2 schedules of reinforcement throughout 30-min sessions. Different letters indicate significant differences among groups.

Bottom Panel. Average percent of the total reinforcers earned in each 3-min bin for the combined sessions for the FR3-#1 and #2 schedules of reinforcement throughout 30-min sessions. Different letters indicate significant differences among groups.

Table 1

Length and sequence of conditions

Sequence of Conditions	Exposure
Home cage protocol	5 weeks
Chamber adaptation	1 session
Reinforcer delivery training	1 session
Autoshaping	9 sessions
Home cage protocol	2 weeks
FR3 #1	12 sessions
Home cage protocol	1 week
PR1	6 sessions
FR1 SA/SNA (Alternating)	12 sessions
Home cage protocol	1 week
FR3 SA/SNA (Alternating)	12 sessions
FR3 #2	12 sessions
PR3	4 sessions
Home cage protocol	1 week

Table 2A

F and p-values for home cage protocol periods

Home Cage Protocol Period	F values	Group Differences
Initial (Wk 4–5)	$F(2,35) = 9.95$ p 0.0004	INT = ISO>D
Post Autoshaping	$F(2,35) = 6.89$ p 0.0032	INT = ISO>D
Post FR3 #1	$F(2,35) = 6.41$ p 0.0045	INT = ISO>D
Post FR1 SA/SNA	$F(2,35) = 9.95$ p 0.0006	INT = ISO>D
Post PR3	$F(2,35) = 10.09$ p 0.0004	INT = ISO>D

Table 2B

F and p-values for average number of reinforcers earned during the last 4 sessions of each condition.

Schedule of Reinforcement	F values	Group Differences
FR1 SA	$F(2,35) = 4.16$ p 0.0244	INT > ISO = D
FR3 SA	$F(2,35) = 3.39$ p 0.0457	INT > ISO = D
FR3#1	$F(2,35) = 5.67$ p 0.0076	INT > ISO = D
FR3#2	$F(2,35) = 10.73$ p 0.0003	INT > ISO = D
PR1	$F(2,35) = 4.32$ p 0.0216	INT > ISO = D
PR3 ^I	$F(2,35) = 2.36$ p NS	NS

^I All three non-deprived sessions were used for PR3

Table 3AReinforcer Distribution Across Ten 3-Minute Bins¹

F and p-values for bin analysis				
Schedule	Group Main Effect	Bin Main Effect	Bin x Group Interaction	Bins with group differences ²
FR3#1	F(2,33) = 5.62 p 0.0079	F(9,297) = 68.30 p 0.0001	F(18,297) = 5.61 p 0.0001	1,2,3,4,6
FR3#2	F(2,33) = 10.75 p 0.0003	F(9,297) = 99.28 p 0.0001	F(18,297) = 8.51 p 0.0001	1,2,3,4,5,6,10
FR3 # 1 & 2 Combined	F(2,33) = 8.99 p 0.0008	F(9,297) = 132.82 p 0.0001	F(18,297) = 10.34 p 0.0001	1,2,3,4,5,6
FR1 SA/SNA	F(2,33) = 4.10 p 0.0258	F(9,297) = 122.90 p 0.0001	F(18,297) = 3.14 p 0.0001	1,2,8
FR3 SA/SNA	NS	F(9,288) = 65.33 p 0.0001	F(18,288) = 2.75 p 0.0002	1,3
PR1	F(2,33) = 4.70 p 0.0160	F(9,297) = 105.16 p 0.0001	F(18,297) = 6.62 p 0.0010	1,5,6
PR3	NS	F(9,297) = 62.06 p 0.0001	F(18,297) = 5.53 p 0.0001	1

¹Sessions were 30-min in length²See text for details

Table 3BPercent Reinforcer Distribution Across Ten 3-Minute Bins¹

F and p-values for bin analysis				
Schedule	Group Main Effect ²	Bin (3 min) Main Effect	Bin x Group Interaction	Bins with group differences ³
FR3#1	NA	F(9,297) = 43.46 p 0.0001	F(18,297) = 4.93 p 0.0001	1,2,6,9
FR3#2	NA	F(9,297) = 42.29 p 0.0001	F(18,297) = 5.12 p 0.0001	1,2,5,6
FR3 # 1 & 2 Combined	NA	F(9,297) = 102.28 p 0.0001	F(18,297) = 8.27 p 0.0001	1,2,4,5,6,9,10
FR1 SA/SNA	NA	F(9,297) = 85.81 p 0.0001	F(18,297) = 2.92 p 0.0001	1,3,8
FR3 SA/SNA	NA	F(9,288) = 34.51 p 0.0001	F(18,288) = 2.14 p 0.0051	1,10
PR1	NA	F(9,297) = 66.66 p 0.0001	F(18,297) = 2.00 p 0.0097	1,5,6
PR3	NA	F(9,297) = 32.95 p 0.0001	F(18,297) = 2.01 p 0.0095	1

¹ Sessions were 30-min in length² Because all groups always earned 100% of their reinforcers, significant main effects of group were not statistically possible.³ See text for details