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Short- and long-access palatable food self-administration results in different phenotypes of binge-type eating

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Abstract

Binge eating disorder (BED), the most common eating disorder in the United States, is characterized by binge-type eating and is associated with higher body mass index and greater motivation for food. This disorder tends to first appear in late adolescence or young adulthood and is more common in women than men. While some animal models of BED have recapitulated both the overeating and the excessive body weight / fat of BED, very few have examined the motivational aspects of this disorder or utilized young females as subjects. In the present study, female Long-Evans rats, starting in late adolescence, were trained in operant chambers to self-administer the highly palatable Milk Chocolate Ensure Plus®, in 30-minute (“short access”) or 6-hour (“long access”) sessions, 5 days per week, over 6.5 weeks. For comparison, other subjects were provided with Ensure *ad libitum* or maintained on chow and water only. Both short and long access to Ensure led rats to develop binge-type eating, measured as greater 30-minute caloric intake than rats with *ad libitum* or chow access and as increasing 30-minute intake across weeks. Compared to those with short access, rats with long access demonstrated moderately increased motivation for Ensure (measured by progressive ratio testing) and, compared to those with only chow access, they eventually showed significant hyperphagia on Ensure access days and hypophagia on non-access days. Rats with long access also showed greater body weight / fat than those maintained on chow. These findings suggest that, while both short and long operant access to Ensure causes young female rats to meet the definition of binge-type eating, they lead to different phenotypes of this behavior, with long access promoting the development of a greater number of features found in clinical BED. Ultimately, both models may be useful in future studies aimed at identifying the neurobiological basis of binge eating.

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Keywords

female; fixed ratio OR progressive ratio; food addiction; overweight OR obesity; operant; prone OR resistant

1. Introduction

Binge eating disorder (BED) is characterized by the consumption of an unusually large amount of food in a short time duration, despite the absence of hunger and without the use of extreme compensatory mechanisms [1]. In the United States, BED is the most common eating disorder, with an estimated lifetime prevalence of 1.26% in women and 0.42% in men [2]. Tending to first appear in late adolescence or young adulthood, BED is persistent, with average episodes lasting more than 4 years [3]. It is also associated with higher body mass index. Worldwide, 67% of those with BED are overweight or obese, compared to 50% of those without eating disorders [3].

Animal models of BED define binge-type eating by two major criteria: (1) the consumption of a larger amount of food in one group compared to another during the same period of time and / or (2) the escalation of intake within the same group across time [4]. These studies utilize restricted access to palatable food, high in sugar and / or fat, with the binge group generally receiving palatable food in the home cage for 30 minutes – 2 hours, but up to 24 hours, often only for 3 days per week [4–10]. Those animal studies that have investigated individual differences have found that relative level of binge-type eating is consistent across sessions. For example, Boggiano and colleagues reported that by 4 hours into palatable food access, rats that had eaten more or less than the median group score (binge-eating prone (BEP) and binge-eating resistant (BER)) were consistent in their relative intake across multiple tests and even with different palatable foods [11]. Similarly, Zorrilla and colleagues reported that rats showed stable individual differences in their 30-minute palatable food intake across 6 weeks of testing [8]. While body weight and body fat have been unaltered in a number of binge studies involving highly restricted access (eg. 30 minutes – 2 hours, 3 days per week) [6, 8, 12], both of these measures were significantly increased with longer or more frequent access [6, 8–10, 12, 13]. Many studies, but not all (see [8, 10, 12]) have used male rats, typically starting in adulthood. Thus, while some animal models of BED have recapitulated both the overeating and the body weight and fat gain often observed in humans with this disorder, and some animal studies have shown that relative level of binge-type eating is consistent across time, very few have utilized young female subjects, which represent the demographic of humans most affected by this disorder [3].

In addition to binge eating and weight gain, individuals with BED may display a number of features observed in drug addiction. Studies of humans with BED have reported that they have greater motivation for food, attentional bias for food, and impulsivity related to food [14, 15]. Animal studies, while limited in number, have examined the motivational aspect of binge-type eating by utilizing operant self-administration. In one study, rats given intermittent access to palatable food in the home cage, compared to those with *ad libitum* access or chow alone, were found when tested in operant chambers to show higher levels of active lever pressing on a fixed ratio 1 (FR1) schedule of reinforcement, where one active lever press results in the delivery of one palatable food reward [10]. They also showed a higher breakpoint in progressive-ratio (PR) testing, where the number of operant responses required to earn the palatable food reward increases in a multiplicative or exponential fashion, with the breakpoint being the ratio at which the subject ceases self-administration [10]. These findings indicate that intermittent access to palatable food leads to increased motivation for the palatable food [10]. In another study, in which rats were trained to binge eat in an operant chamber, those with high impulsive action were found to self-administer more palatable food under FR1, FR5 (five lever presses for one reward), and PR schedules [16]. To our knowledge, this latter model is the only one where palatable food is exclusively provided in the operant chambers, but while rats in this paradigm (involving daily one-hour FR1 sessions) consume significantly more food than rats self-administering chow, and they escalate their intake across sessions, they fail to gain excessive body weight [17]. Interestingly, studies with drugs of abuse have shown that, compared with shorter access sessions (1 hour per day), longer access sessions (6 hours per day) are more likely to induce behavioral features that correlate with addiction, as rats with longer access not only escalate their intake across sessions [18, 19], but also demonstrate resistance to reinforcer devaluation [20] and increased impulsive choice [21]. These findings suggest that more prolonged self-administration sessions with palatable food, by inducing greater body weight gain and greater food motivation, may potentially induce binge-type eating that recapitulates a greater number of features found in BED.

To establish a model of binge-type eating that utilizes palatable food self-administration and leads to the development of multiple features of BED, female rats, starting in adolescence, were trained in operant chambers to self-administer the highly palatable Milk Chocolate Ensure Plus®, in 30-minute (“short access”) or 6-hour (“long access”) sessions. For comparison, other rats were provided with Ensure *ad libitum* or maintained on chow and water only. Ensure and chow intake, body weight, and body fat were monitored. In addition, level of motivation was determined through measurement of lever-pressing under multiple operant requirements. The hypothesis was that, while both short and long access to palatable food in operant chambers would induce binge-type eating, long access would promote the development of a greater number of features found in BED.

2. Materials and methods

2.1. Animals

Forty-eight female Long-Evans rats, weighing 126 – 150 g (approximately 6 weeks) (Charles River Laboratories International, Inc., Malvern, PA) were housed in an AAALAC-accredited facility, on a 12-hour light/dark cycle (lights off at 0900 h). Throughout the experiment, they were individually housed in polycarbonate cages, with Beta Chip® bedding, and one Bed-r’Nest nestlet (The Andersons, Inc, Maumee, OH). They were given one week to acclimate to the facility and were handled daily prior to the start of experiments. In the home cage, all animals received *ad libitum* chow (Laboratory Rodent Diet 5001, Lab Diet, St. Louis, MO) via metal food hoppers and water via 16 oz Macrolon bottles (Ancare, Bellmore, NY) with non-drip sipper tubes. In the operant chambers, in addition to access to the palatable diet, animals had *ad libitum* access to water. All animals were weighed in the afternoon on Monday, Wednesday, and Friday throughout the experiment. Experiments were approved by the Institutional Animal Care and Use Committee of Drexel University College of Medicine and followed the NIH Guide for the Care and Use of Laboratory Animals.

2.2. Diets

The chow diet (Laboratory Rodent Diet 5001), which was provided *ad libitum* in the home cage, contained 3.36 kcal/g and was comprised of 58% carbohydrate (8% sucrose), 13% fat, and 29% protein. The Milk Chocolate Ensure Plus® (Abbott Nutrition, East Windsor, NJ), which was provided *ad libitum* in the home cage or made available in the operant chambers, contained 1.32 kcal/g and was comprised of 57% carbohydrate (23% sucrose), 28% fat, and 15% protein.

2.3. Self-administration apparatus

Operant testing with palatable food (Ensure) was performed in 29.5 × 23.5 × 27.3 cm chambers (Med Associates, Inc., St. Albans, VT) inside sound-attenuating, ventilated cubicles (Med Associates, Inc., St. Albans, VT). The chambers had a clear polycarbonate door and rear panel and stainless-steel side panels and top. The floor was a stainless-steel grid and below that was a stainless-steel waste pan. One wall contained two retractable levers, 6.5 cm above the floor, with a single cup liquid receptacle between them, connected to a contact lickometer. A white stimulus light and 2,900 Hz sonalert module were positioned above the receptacle. The start of each session was signaled by the extension of a single, active lever (for FR1 testing) or of both active and inactive levers (for FR5 and PR testing), which were kept extended for the duration of the testing session. All testing was conducted with the house lights off. Upon completion of a ratio requirement, 0.1 ml of Ensure was delivered into the receptacle over 3.6-seconds via an 18-gauge tube connected to a syringe pump and the white stimulus light and 2,900 Hz noise were activated during delivery. Active lever presses made during reward delivery were recorded but had no consequences. Consumption of the reinforcer was confirmed through comparison of the time-stamp of the ratio requirement completion and the lickometer beam break. Water was available *ad libitum* on the side of the chamber opposite the liquid receptacle, via a bottle with a sipper tube.

2.4. Test procedures

Subjects were separated into the following groups: Short Access (N = 16), Long Access (N = 16), *Ad Libitum* (N = 7), and Chow Control (N = 8). The timeline for the test procedures is presented in Table 1. Those in the **Chow Control** group received only chow and water in the home cage, as described in Section 2.1, which was measured and changed daily at 1000 h. Those in the ***Ad Libitum*** group additionally received *ad libitum* access to Ensure via a 9 oz polycarbonate bottle (Ancare), which was fitted with a non-drip sipper tube of equal size to that of the water bottle. Ensure was measured and provided fresh at both 1000 h and 1700 h each day. These animals were maintained on these schedules for 6.5 weeks, in parallel with subjects in Short and Long Access groups (see below), until they were sacrificed for analysis of body fat. Animals in all other groups received access to Ensure only in operant chambers between Monday and Friday (starting one hour into the dark cycle, at 1000 h) and were otherwise handled identically to the Chow Control group. The duration of the experiment was selected based on prior studies showing that binge-type eating can take about 4 weeks to emerge and that differences in body weight and body fat can become apparent by 6 weeks [7, 9, 13, 22]. Initial training for the Short and Long Access groups consisted of 5 daily 1-hour sessions on an FR1 schedule of reinforcement, with Ensure as the reward. Following this, the **Short Access** group received daily 30-minute sessions on the FR1 schedule, between Monday and Friday, while the **Long Access** group received daily 6-hour sessions on the FR1 schedule, between Monday and Friday. During these sessions, Ensure continued to be provided as the reward and was the only source of calories. After testing in their respective schedules, for a total of 33 sessions (inclusive of the training period), a subset of the Short and Long Access groups (n = 8/group) was tested for 10 30-minute sessions on an FR5 schedule and then for 5 90-minute sessions on a PR schedule. Under the PR schedule, the following number of active lever presses was required to earn one reward: 1, 1, 2, 2, 3, 3, 4, 4, 5, 5, 7, 7, 9, 9, 11, 11, 13, 13, 15, 15, and then [5ê(n*0.20)] – 5 rounded to the nearest integer, where n = the number of rewards earned in the session, starting with n = 8. The remainder (n = 8/group) were instead sacrificed for analysis of body fat. Intake of chow, water, and Ensure was measured daily for all subjects. The first day of access to Ensure (or, for the Chow Control group, the equivalent day) was deemed “Experiment Day 1”.

2.5. Postmortem adipose tissue assessment

At the end of the 6.5-week experiment, rats in Short Access, Long Access, *Ad Libitum*, and Chow Control groups (N = 31, n = 7 – 8/group) were sacrificed on an access day via rapid decapitation. Epididymal, retroperitoneal, perirenal, and inguinal tissue was dissected from the fresh carcass and weighed to the nearest 0.1 g.

2.6. Statistical analysis

Caloric intake from chow was calculated by subtracting the weight of the food hopper plus any food found in the cage (in grams) from the weight of the food hopper when first placed into the cage, then multiplying this number by the calories of chow per gram. Caloric intake from Ensure in the home cage was calculated by subtracting the weight of the Ensure bottle (in grams) from the weight of the Ensure bottle when first placed into the cage, then multiplying this number by the calories of Ensure per gram. Caloric intake from Ensure during operant sessions was calculated by multiplying the number of rewards earned per session by the volume of the reward (0.1 ml), then multiplying this number by the calories of Ensure per ml. For subjects in the Short Access group, the rewards earned in 30 minutes was the total number of rewards earned per session. For subjects in the Long Access group, the rewards earned in 6 hours was the total number of rewards earned; their 30-minute rewards were calculated based on the number of rewards received in the first 30-minutes (by time stamp). Caloric intake normalized to body weight was calculated by dividing caloric intake of the food of interest by the subject‟s body weight in grams (either as measured the same day or as averaged from the two nearest days of measurement) scaled to the 2/3 power [23, 24].

To analyze various measures of Ensure intake, chow intake, total caloric intake, and body weight, a repeated measures analysis of variance (ANOVA) or mixed ANOVA was used, with group as the between-subject measure and day of measurement as the within-subject measure, where appropriate. To analyze postmortem adipose tissue, a repeated measures ANOVA was used, with group as the between-subject measure and fat depot as the within-subject measure. Significant main effects were followed up with one-way ANOVAs and Sidak pairwise comparisons as post-hoc tests when appropriate. Paired, two-tailed *t*-tests were used to compare intake on the first and last day of the measurement and to compare average intake on FR1 and FR5 schedules of reinforcement. Significance was determined at $p < 0.05$. Data are reported as mean ± standard error of the mean (SEM).

3. Results

3.1. Binge-type eating of palatable food

3.1.1. Binge-type intake during self-administration training sessions— Examining intake of Chocolate Ensure Plus® during the initial, training period of self-administration, which involved 5 days of 60-minute FR1 operant sessions, both Short Access and Long Access groups ($n = 16$/group) showed a significant increase in consumption across the sessions (from 1.3 ± 0.2 to 7.0 ± 0.8 kcal/60 min) ($F(4, 120) = 29.14$, $p < 0.001$) but no significant difference between groups ($F(1, 30) = 0.01$, *ns, not significant*) (data not shown). This confirms that the groups entered the testing phase with similar levels of self-administration of Ensure.

3.1.2. Binge-type intake compared across groups—Binge-type eating was significantly different between groups ($F(3, 43) = 20.60$, $p < 0.001$), when assessed as caloric intake in a 30-minute period, either during the first 30 minutes of Ensure access in FR1 operant sessions (for Short Access and Long Access groups, $n = 16$/group), or during the equivalent 30 minutes of Ensure and/or chow access in the home cage (for *Ad Libitum* and Chow Control groups, $n = 7$ and 8/group, respectively). Pairwise comparisons revealed that both Short and Long Access groups consumed significantly more calories during the 30-minute period than both the *Ad Libitum* and Chow Control groups ($p < 0.05$), but there was no difference in intake between Short Access and Long Access groups (*ns*) (Fig 1A). Examining the same 30-minute intake as a percentage of total daily caloric intake, there was once again a significant difference between groups ($F(3, 42) = 18.69$, $p < 0.001$), and pairwise comparisons again revealed that Short and Long Access groups consumed a significantly higher percentage of their daily calories during this period than the *Ad Libitum* and Chow Control groups ($p < 0.05$) (Fig 1B). Examining the 30-minute intake normalized to body weight, there was still a significant difference between groups ($F(3, 27) = 14.49$, $p < 0.001$), and pairwise comparisons still revealed that Short and Long Access groups consumed a significantly higher percentage of their daily calories than the *Ad Libitum* and Chow Control groups ($p < 0.05$) (Fig 1C). These results show that, through comparison of intake between groups, both Short and Long Access groups meet a major criterion for binge-type eating.

3.1.3. Binge-type intake compared across time—Examining Ensure intake in 30-minute FR1 operant sessions across time, both Short Access and Long Access groups (n = 16/group) showed an increase in consumption, as assessed by caloric intake (Short Access: $F(27, 405) = 9.63$, $p < 0.001$; Long Access: $F(27, 378) = 14.00$, $p < 0.001$), percentage of total daily caloric intake (Short Access: $F(27, 378) = 6.08$, $p < 0.001$; Long Access: $F(27, 351) = 8.03$, $p < 0.001$), and by caloric intake normalized to body weight (Short Access: $F(27, 405) = 4.82$, $p < 0.001$; Long Access: $F(27, 378) = 8.23$, $p < 0.001$) (Fig 2A, B, C). Indeed, 30-minute caloric intake was significantly greater on the last day of the experiment compared to the first, for both the Short Access group ($t(15) = -4.83$, $p < 0.001$) and the Long Access group ($t(15) = -7.26$, $p < 0.001$). Similarly, percentage of total daily caloric intake was significantly greater on the last day of the experiment compared to the first, for both the Short Access group ($t(15) = -4.09$, $p < 0.001$) and the Long Access group ($t(15) = -5.324$, $p < 0.001$). In addition, caloric intake normalized to body weight was significantly greater on the last day of the experiment compared to the first, for both the Short Access group ($t(15) = -3.52$, $p < 0.01$) and the Long Access group ($t(15) = -5.23$, $p < 0.001$). On the other hand, there was no difference in 30-minute intake between Short and Long Access groups, in terms of caloric intake ($F(1, 29) = 0.27$, *ns*), percentage of total daily caloric intake ($F(1,27) = 2.78$, *ns*), or caloric intake normalized to body weight ($F(1, 29) = 0.66$, *ns*). These results show that, through comparison of intake across time, both Short and Long Access groups meet another major criterion for binge-type eating.

Examining Ensure intake in the entirety of the 6-hour FR1 operant sessions across time, the Long Access group (n = 16) also showed an increase in consumption, as assessed by caloric intake ($F(27, 351) = 11.96$, $p < 0.001$), percentage of total daily caloric intake ($F(27, 324) = 5.37$, $p < 0.001$), and caloric intake normalized to body weight ($F(27, 378) = 4.25$, $p < 0.001$) (Fig 2D, E, F). Once again, caloric intake, this time for the 6-hour sessions, was significantly greater on the last day of the experiment compared to the first ($t(15) = -5.32$, $p < 0.001$). Percentage of total daily caloric intake was also significantly greater on the last day of the experiment compared to the first ($t(15) = -3.11$, $p < 0.01$). Caloric intake normalized to body weight was also significantly greater on last day of the experiment compared to the first ($t(15) = -2.59$, $p < 0.05$). Thus, the pattern of overall palatable food intake with long access sessions paralleled the pattern demonstrated during the binge period.

3.2. Self-administration under different operant requirements

A subset of the Short and Long Access groups (N = 16) was also tested under paradigms with different operant requirements. Under an FR5 schedule of reinforcement, the difference between the Short Access group and Long Access group (n = 8/group) did not achieve statistical significance in caloric intake of Ensure in a 30-minute period ($F(1, 12) = 0.65$, *ns*) (Fig 3A). Notably, while caloric intake under the FR5 schedule was significantly lower than under the FR1 schedule (4.0 ± 0.7 vs. 7.4 ± 1.0 kcal in 30 min; ($t(15) = 4.59$, $p < 0.001$)), active lever pressing was significantly higher (50.1 ± 6.9 vs. 136.6 ± 22.3 presses in 30 min; ($t(15) = -4.77$, $p < 0.001$)). Under a PR schedule of reinforcement, there was a trend for a main effect of group on breakpoint ($F(1, 13) = 3.88$, $p = 0.07$), such that the Long Access subjects tended to show a higher breakpoint than the Short Access subjects (Fig 3B). This finding suggests that the Long Access group may be more motivated to obtain Ensure.

3.3. Total daily caloric intake compared across groups

Comparing weekday total daily caloric intake, the sum of calories consumed from Ensure plus chow in a 24-hour period, there was a significant main effect of group ($F(3, 26) = 41.59$, $p < 0.001$) and a significant interaction between group and time ($F(96, 832) = 2.56$, $p < 0.001$) (Fig 4A). Pairwise comparisons revealed that the *Ad Libitum* group consumed more total daily calories than all other groups ($p < 0.001$), while there was no overall difference in intake between Short Access, Long Access, and Chow Control groups (*ns*) (n = 8/group for Short Access, Long Access, and Chow; $n = 7$ for *Ad Libitum*). On the other hand, with a significant difference also detected between groups on Weeks 5 and 6 (Week 5: $F(3, 27) = 42.28$, $p < 0.001$); Week 6: $F(3, 27) = 31.01$, $p < 0.001$), pairwise comparisons revealed that the Long Access group consumed more calories than the Chow Control group during these later weeks of the experiment ($p < 0.05$). Examining caloric intake normalized to body weight, there was again a significant main effect of group ($F(3, 26) = 18.91$, $p < 0.001$) and a significant interaction between group and time ($F(96, 832) = 2,44$, $p < 0.001$) (Fig 4B). Pairwise comparisons again revealed that the *Ad Libitum* group consumed more total daily calories as a function of body weight than all other groups ($p < 0.05$), while there was no overall difference in intake between Short Access, Long Access, and Chow Control groups (*ns*). There was again a significant difference detected between groups on Week 5 ($F(3, 27) = 9.95$, $p < 0.001$), however, pairwise comparisons failed to reveal a significant difference between Short Access, Long Access, and Chow Control groups (*ns*). Thus, after 4 weeks, the Long Access group consumed more overall weekday calories than the control, Chow group, but this may have primarily been due to differences in body weight (see Section 3.5).

3.4. Chow intake compared across groups

Examining caloric intake from chow alone, there was a significant main effect of group ($F(3, 26) = 82.39$, $p < 0.001$) and a significant interaction between group and time on weekdays ($F(96, 832) = 5.39$, $p < 0.001$) (Fig 5A). Pairwise comparisons revealed that both the *Ad Libitum* and Long Access groups consumed significantly less chow than both the Short Access and Chow Control groups on weekdays ($p < 0.01$), while the Short Access group showed no significant difference in chow intake from the Chow controls (*ns*). Examining caloric intake normalized to body weight, there was again a significant main effect of group ($F(3, 26) = 116.95$, $p < 0.001$) and a significant interaction between group and time on weekdays ($F(96, 832) = 5.43$, $p < 0.001$) (Fig 5B). Pairwise comparisons in this case revealed that the *Ad Libitum*, Long Access, and Short Access groups all consumed significantly less chow than the Chow Control group on weekdays ($p < 0.05$). Examination of chow intake on weekends also revealed a significant main effect of group ($F(3, 27) = 61.27$, $p < 0.001$) and a significant interaction between group and time ($F(9, 81) = 2.01$, $p < 0.05$), with the Long Access group, after Week 4, consuming significantly less chow than the Short Access group ($p < 0.05$) and showing a strong trend for consuming less chow than the Chow Control group ($p = 0.05$), despite having no access to Ensure during this period (Fig 5A). In fact, in the Long Access group, chow intake during the last weekend of the experiment was significantly lower than intake during the first ($t(7) = 3.10$, $p < 0.05$). Similarly, examination of weekend chow intake normalized to body weight revealed a significant main effect of group ($F(3, 27) = 89.92$, $p < 0.001$) and a significant interaction between group and time (F(9, 81) = 2.66, $p < 0.001$), with the Long Access group, after Week 4, consuming significantly less chow than both the Short Access and the Chow Control groups ($p < 0.01$) (Fig 5B). These results suggest that the Long Access schedule leads to reduced chow intake not only in the hours following binge-type intake of Ensure, but also across several days following Ensure intake.

3.5. Body weight on weekdays

While the groups as a whole gained weight over the course of the experiment (F(20, 540) = 1137.47, $p < 0.001$) (n = 8/group for Short Access, Long Access, and Chow; $n = 7$ for *Ad Libitum*), there was also a significant main effect of group on weekday body weight across the 7 weeks of testing (F(3, 27) = 61.75, $p < 0.001$). Pairwise comparisons revealed that the *Ad Libitum* group weighed significantly more than all other groups (Short Access, Long Access, Chow) ($p < 0.001$) and the Long Access group weighed significantly more than the Chow Control group ($p < 0.05$), while the Short Access group did not have significantly different body weight than the Chow Control group (Fig 6A). While the body weight of the *Ad Libitum* group was greater than the other groups as early as the end of the first week, with pairwise comparisons showing a significant difference at every subsequent time-point ($p < 0.05$), the body weight of the Long Access group was greater than the Chow group by the end of the fourth week, with pairwise comparisons revealing a significant difference at every time-point until the completion of the experiment ($p < 0.05$). These results reveal that the Long Access group, while not gaining weight to the degree of the *Ad Libitum* group, still gained more weight than groups with more restricted or no access to Ensure.

3.6. Body weight on weekends

With measurements taken in the final two weekends of the experiment, there was a significant main effect of group on body weight (F(3, 27) = 68.09, $p < 0.001$) (n = 8/group for Short Access, Long Access, and Chow; $n = 7$ for *Ad Libitum*) (Fig 6B). Pairwise comparisons revealed that the *Ad Libitum* group weighed significantly more than all other groups on the weekends (Short Access, Long Access, Chow) ($p < 0.001$). In contrast to weekday measurements, body weight of the Long Access group was no longer significantly greater than the Chow Control group, although there was still a strong trend for a difference ($p = 0.06$). Thus, the greater body weight of the Long Access group that was evident on weekdays was not evident on weekends, when Ensure was not available for consumption.

3.7. Binge-eating prone and binge-eating resistant subjects

To determine the stability of individual differences across the experiment, subjects in the Short and Long Access groups (n = 16/group) were rank-ordered according to their average caloric intake during the five 60-minute FR1 operant training sessions and separated, using a median split, into BEP and BER groups. Throughout the remainder of the study, the BEP group compared to the BER group exhibited significantly greater 30-minute caloric intake (F(1,29) = 18.73, $p < 0.001$) (Fig 7A), a significantly greater percentage of total daily caloric intake in the first 30 minutes of their FR1 operant sessions (F(1,27) = 9.62, $p < 0.01$) (Fig 7B), and significantly greater 30-minute caloric intake normalized to body weight (F(1,29) = 17.78, $p < 0.001$) (Fig 7C). Under an FR5 schedule of reinforcement, the BEP group also exhibited significantly greater 30-minute caloric intake of Ensure (F(1,14) = 6.79, $p < 0.05$)

but, under a PR schedule of reinforcement, the difference in breakpoint between the BEP and BER group did not achieve statistical significance ($F(1,14) = 1.97$, *ns*) (Fig 7D, E). There was no significant difference between groups in their total daily caloric intake ($F(1,14) = 0.29$, *ns*) or body weight ($F(1,14) = 0.32$, *ns*). Thus, classification on the basis of initial self-administration of Ensure can identify relative level of operant responding over an additional 5.5 weeks of testing and under different operant requirements.

Classification of the BEP group identified 8 subjects each from the Short Access group and Long Access group and classification of the BER group similarly identified 8 subjects from each access group. Examining 30-minute caloric intake under an FR1 schedule of reinforcement as a function of both Short / Long Access and BEP / BER classification revealed a significant difference between groups ($F(3,27) = 6.31$, $p < 0.01$). Pairwise comparisons revealed that the Short Access BEP but not Long Access BEP group exhibited significantly greater intake than both the Short Access and Long Access BER groups ($p < 0.05$), while the Short and Long Access BEP groups were not significantly different from each other (*ns*) and the Short and Long Access BER groups were not significantly different from each other (*ns*) (Fig 8A). Under an FR5 schedule of reinforcement, using this same group classification, there was a trend for a significant difference between groups ($F(3,12) = 3.07$, $p = 0.07$), and pairwise comparisons this time revealed a small albeit nonsignificant increase in caloric intake in the Long Access BEP group compared to both the Long Access and Short Access BER groups ($p = 0.11$) (Fig 8B). Under a PR schedule of reinforcement, the difference in breakpoint between groups did not achieve statistical significance ($F(3,12) = 1.87$, *ns*), although the Long Access BEP group exhibited a numerically higher breakpoint than all other groups (Fig 8C). These results suggest that the prone status of a subject modulates the effects of access schedule on measures of intake and motivation, with the Short Access BEP group showing the highest intake under an FR1 schedule of reinforcement and the Long Access BEP group showing the highest intake under higher operant requirements.

3.8. Postmortem adipose tissue assessment

Examining body composition at the completion of the experiment ($n = 8$/group for Short Access, Long Access, and Chow; $n = 7$ for *Ad Libitum*), there was a significant main effect of group on body fat ($F(3, 26) = 82.33$, $p < 0.001$) and a significant interaction effect between group and fat depot ($F(9, 78) = 21.43$, $p < 0.001$) (Fig 9A). For epididymal fat, the significant main effect of group ($F(1, 26) = 57.17$, $p < 0.001$) was due to a significant difference between the *Ad Libitum* group and all other groups ($p < 0.001$). For retroperitoneal fat, the significant main effect of group ($F(1, 26) = 74.48$, $p < 0.001$) was due to a significant difference between the *Ad Libitum* group and all other groups ($p < 0.001$) as well as to a significant difference between the Long Access and Chow Control groups ($p < 0.05$). For perirenal fat, the significant main effect of group ($F(1, 26) = 6.36$, $p < 0.001$) was once again due to a significant difference between the *Ad Libitum* group and all other groups ($p < 0.001$). Similarly, for inguinal fat, the significant main effect of group ($F(1, 26) = 39.42$, $p < 0.001$) was due to a significant difference between the *Ad Libitum* group and all other groups ($p < 0.001$).

Results were similar when body fat was examined as a percentage of body weight. As before, there was a significant main effect of group on body fat ($F(3, 26) = 56.29$, $p < 0.001$) and a significant interaction effect between group and fat depot ($F(9, 78) = 15.68$, $p < 0.001$) (Fig 9B). For epididymal fat, the significant main effect of group ($F(1, 26) = 25.19$, $p < 0.001$) was due to a significant difference between the *Ad Libitum* group and all other groups ($p < 0.001$). For retroperitoneal fat, the significant main effect of group ($F(1, 26) = 409.92$, $p < 0.001$) was due to a significant difference between the *Ad Libitum* group and all other groups ($p < 0.05$) as well as to a significant difference between the Long Access and Chow Control groups ($p < 0.05$). For inguinal fat, the significant main effect of group ($F(1, 26) = 34.60$, $p < 0.001$) was due to a significant difference between the *Ad Libitum* group and all other groups ($p < 0.001$). Only for perirenal fat was there no significant main effect of group ($F(1, 26) = 2.22$, *ns*). These results demonstrate that both the *Ad Libitum* and the Long Access groups had heavier fat pads than the Chow Control group after 7 weeks of access to Ensure.

4. Discussion

The present results (summarized in Table 2) show that, in an operant self-administration paradigm, young female rats with short access (30 minutes, 5 days-per-week) or long access (6 hours, 5 days-per-week) to Chocolate Ensure Plus® developed binge-type eating over the course of 6.5 weeks. Those with long access, particularly those designated as binge-eating prone, additionally demonstrated moderately increased motivation for this palatable food, ultimately overeating on palatable food access days, and undereating on non-access days. Moreover, they developed increased body weight and body fat. These findings suggest that, while both paradigms cause animals to meet the definition of binge-type eating, they lead to different phenotypes of this behavior.

4.1. Binge-type eating with short and long operant access to palatable food

Both the Short and Long Access groups met the traditional criteria for binge-type eating [4]. Animals in both groups consumed more in a 30-minute period than those with *ad libitum* access to the same palatable diet and those maintained only on chow. They also escalated their 30-minute intake of the palatable diet across time, measured as absolute calories, percentage of their total daily caloric intake, and as calories normalized to body weight. This is consistent with previous literature, which shows that rats with limited access to palatable food (30 minutes – 8 hours per session) consume more in a predefined period (30 minutes – 2 hours) than rats with *ad libitum* access to the same palatable food or only to chow [4, 6, 8, 9, 17] and that rats with limited access to palatable food can escalate their intake of this food across several weeks of testing [4]. To our knowledge, this is the first time that these effects have been demonstrated using female rats that were adolescent at the start of experimentation. In addition to young women being the population most vulnerable to developing BED [3], female rats as adults have been shown to engage in greater binge-type eating than adult male rats [10] and adolescent male rats have been shown to engage in this behavior with Ensure more than adult males [5]. Studies examining the timing of intake have found that rats consume the majority of the palatable food calories in the first 15 – 30 minutes of access [13, 25], suggesting that the 30-minute time-frame used in the present experiment was sufficient to assess binge-type behavior.

Not only did both short and long access paradigms lead animals to meet the criteria for binge-type eating, but the duration of the palatable food access overall did not affect the level of binge-type intake. Previous research has suggested that more time-limited access results in greater binge-type eating, showing that 30-minute intake is greater with 30-minute, 3-day-per-week home cage access to chocolate-flavored sucrose-rich pellets compared to 24-hour, 3-day-per-week access [8] and that 2-hour intake is greater with 2-hour access to the same diet compared to 4- or 8-hour access [9]. It is possible that, in the present experiment, the small operant requirement acted as a rate limiter for intake by the Short Access group, thus masking increased intake compared to the Long Access group. Indeed, the addition of an operant requirement has previously been found to reduce palatable food intake compared to comparable home cage access [26]. Alternatively, differences in macronutrient composition or diet state (solid vs. liquid) could contribute to the discrepancy between results in the present study and those of prior work.

4.2. Motivation for palatable food

The Long Access group tended to show greater motivation for palatable food than the Short Access group, as demonstrated by a strong trend for an increased breakpoint under a PR schedule. To our knowledge, only one other study has examined the effect of duration of palatable food access on operant PR performance, reporting that 3-day-per-week 24-hour home cage palatable food access leads to higher breakpoints than *ad libitum* palatable food access [10]. While it is possible that reducing palatable food access in the present study to 3 days per week would have augmented the difference between the Long and Short Access groups, it should be noted that 3-day-per-week compared to 5-day-per-week limited access has previously been shown not to lead to differences in intake of Ensure [5]. The present results, with time-limited operant access sessions, strongly parallel results from studies with drugs of abuse. Not only does long or extended access to drugs induce an escalation of intake across sessions [18, 19] but, compared to short access, it also leads to higher breakpoints in PR tests [27, 28]. Notably, individuals with BED are believed to have greater motivation for food [15] and recent application of the Yale Food Addiction Scale version 2.0 showed that nearly all individuals with BED meet the criteria for „food addiction‟ [29]. In the present study, the access paradigm for palatable food thus appears to induce a relationship that begins to parallel the relationship with drugs of abuse, with long access tending to induce greater motivation for the reinforcing substance.

In addition to increasing motivation for palatable food, the long access paradigm also reduced intake of the less palatable, standard laboratory chow. This occurred not only on weekdays, when rats may have experienced satiety following the prolonged access to Ensure, but also on weekends, when rats would presumably no longer have experienced satiety from the palatable food. It was not evident with the short access paradigm. This reduction of chow intake on non-access, chow days, which resembles the behavior of patients with bulimia nervosa, has similarly been observed in a number of other animal studies, involving shortening, sweet-fat pellets, and chocolate-flavored sucrose-rich pellets offered 3 days-per-week, compared chow alone [6, 8, 9, 30]. It may be due to negative contrast, whereby a previously neutral stimulus (in this case, chow) is subsequently evaluated as less palatable when presented following a more palatable stimulus (in this case, Ensure). Similar behavior is a hallmark of substance use disorder [31], as people with this disorder neglect previously pleasurable activities and relationships in favor of drug use. Indeed, there appears to be significant interaction between systems mediating the intake of drugs of abuse and those mediating intake of palatable food [32]. Thus, in the present study, the reduction in chow intake in the long access paradigm further parallels the development of addiction to drugs of abuse.

4.3. Obesity with long operant access to palatable food

In the last weeks of the experiment, rats in the Long Access group demonstrated greater body weight and ultimately had more retroperitoneal body fat than rats consuming only chow. While neither of these measures was as great as in the *Ad Libitum* group, they were nonetheless significant, not demonstrated by rats in the Short Access group, and together form a larger picture that indicates the development of obesity. Elevated body weight has been observed in rats binge-eating sweet-fat pellets, high-fat pellets, and chocolate-flavored sucrose-rich pellets (provided the access sessions are longer than 30 minutes) [6, 8, 9, 13], but not in rats binge-eating vegetable shortening [7, 12] or self-administering chocolate-flavored sucrose-rich pellets [17]. In the present experiment, the palatable food, Ensure, contained high levels of sucrose and moderate levels of fat, a combination that is known to promote body weight gain [33, 34]. Notably, while previous experiments have detected excessive body weight as early as the second week of palatable food access (eg. [6, 7, 30]), the present results indicate that these did not occur until the end of the fourth week of access. With rats in this study receiving all of their palatable food access in operant self-administration chambers, it is possible that this delay reflects a learning period not required with home cage access. Alternatively, the operant requirement may have acted as a rate limiter for intake and delayed the onset of overeating and body weight gain. It is also possible that the young age of the rats at the start of the experiment allowed them to metabolize their ingested calories more quickly [35], so that they only began to gain excessive weight from the palatable food intake as they reached adulthood. Regardless of the explanation, the long-lasting nature of BED makes the eventual development of these differences notable in this long access paradigm.

At the end of the experiment, rats in the Long Access group had more retroperitoneal body fat than rats consuming only chow, as measured both by absolute fat pad weight and fat pad weight as a percentage of body weight. That is, even accounting for the elevated body weight, the long access paradigm resulted in greater visceral body fat. Results with other binge-type paradigms have been inconsistent, with some studies showing greater body fat and others reporting no difference [8–10, 12]. In humans, the area of retroperitoneal fat has been found to correlate with metabolic syndrome, plasma glycemic indices, lipid profile, and leptin [36] and it is considered to be a major contributor to obesity. Thus, the prolonged, excessive intake of sugar and fat in the long access paradigm, in addition to leading to indicators of addiction, also lead to indicators of obesity.

4.4. Stability of individual differences in operant self-administration of and motivation for palatable food

Classification of animals as BEP or BER, based on their first week of operant self-administration, identified groups that showed stable individual differences in binge-type eating throughout the entirety of the experiment and that showed higher motivation for the palatable food, as assessed under an FR5 schedule of reinforcement. Similar classifications of female rats using an array of different palatable foods, including Ensure, have successfully identified subjects prone and resistant to home cage binge-type eating, not only of those same foods but also of different palatable foods [8, 11, 37]. They have also identified subjects with greater motivation for palatable food, demonstrating that, compared to BER rats, BEP rats will tolerate higher levels of footshock to consume palatable food [38] and they will continue to consume more palatable food even after they have been conditioned to associate it with delayed abdominal discomfort [37]. To our knowledge, this is the first time that the effects of BEP classification on motivation for palatable food have been demonstrated using operant self-administration. Interestingly, the other studies as well as the present one have found that BEP and BER rats show no difference in intake of standard laboratory chow or in body weight [11], suggesting that this distinction is specific for binge-type intake of and motivation for palatable food and that it is dissociable from body weight gain in a binge paradigm.

When further classified according to their short or long access to palatable food, it was the Short Access BEP subjects that demonstrated higher levels of bingeing throughout the experiment but the Long Access BEP subjects that demonstrated higher motivation for the palatable food. These findings are consistent with published results showing that shorter access to palatable food results in greater binge-type eating [8, 9] and they suggest that the lack of difference in the overall Short and Long Access groups on the binge eating measure may have been masked by other factors. In contrast to the measure of intake, it was the Long Access BEP subjects under an FR5 schedule of reinforcement that showed higher motivation. This result is broadly consistent with our finding that the Long Access group showed greater motivation for palatable food than the Short Access group and reinforces the idea that the long access paradigm induces a relationship with palatable food that parallels the development of addiction to drugs of abuse. Interestingly, BEP subjects with restricted access to palatable food have been found to go on to exhibit greater craving for cocaine [39]. This further supports the idea that the systems mediating intake of palatable food may not only parallel those mediating the intake of drugs of abuse, but they may in fact interact with them.

5. Conclusions

In conclusion, we have developed two paradigms that induce binge-type eating in young female rats. With short operant access to Chocolate Ensure Plus®, rats meet the criteria for binge-type eating, and otherwise resemble rats maintained on chow, in their total daily caloric intake, body weight, and body composition. In contrast, with long operant access, rats not only meet the criteria for binge-type eating, but they also develop greater motivation for Ensure, greater body weight, and greater body fat than rats maintained on chow. These two access paradigms therefore appear to lead to two distinct phenotypes of binge-type eating, with long access promoting the development of a greater number of features found in clinical BED. Both models may be useful in future studies aimed at identifying the neurobiological basis of binge eating.

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Highlights

- Long and short operant sessions for Ensure induce binge eating in female rats.
- Rats given long access show greater motivation for Ensure.
- Rats with long access show hyperphagia on Ensure days and hypophagia on other days.
- Long access to Ensure for 6.5 weeks results in greater weight gain and body fat.
- Rats maintained on chow or with *ad libitum* access to Ensure do not binge eat.

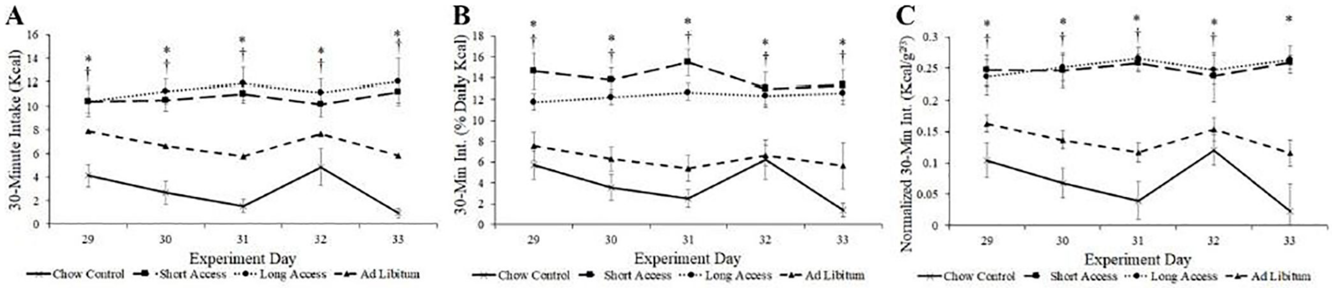

Fig. 1.

Both short (30-minute sessions) and long access (6-hour sessions) to Milk Chocolate Ensure Plus® in operant chambers on a fixed ratio 1 (FR1) schedule of reinforcement (Monday – Friday) results in binge-type eating, when assessed compared to *ad libitum* Ensure access in the home cage or access to chow and water only. **A.** Subjects in the Short Access and Long Access groups (n = 16/group) consumed significantly more total calories during a 30-minute period than those in the *Ad Libitum* (n = 7) and Chow Control groups (n = 8). **B.** Subjects in the Short Access and Long Access groups also consumed a higher percentage of their total daily calories in this 30-minute period than those in the *Ad Libitum* and Chow Control groups. **C.** Subjects in the Short Access and Long Access groups also consumed more total daily calories normalized to body weight in the 30-minute period than those in the *Ad Libitum* and Chow Control groups. Values are mean ± S.E.M.; $^*p < 0.05$ Short Access vs. *Ad Libitum* and Chow Control, $^\dagger p < 0.05$ Long Access vs. *Ad Libitum* and Chow Control.

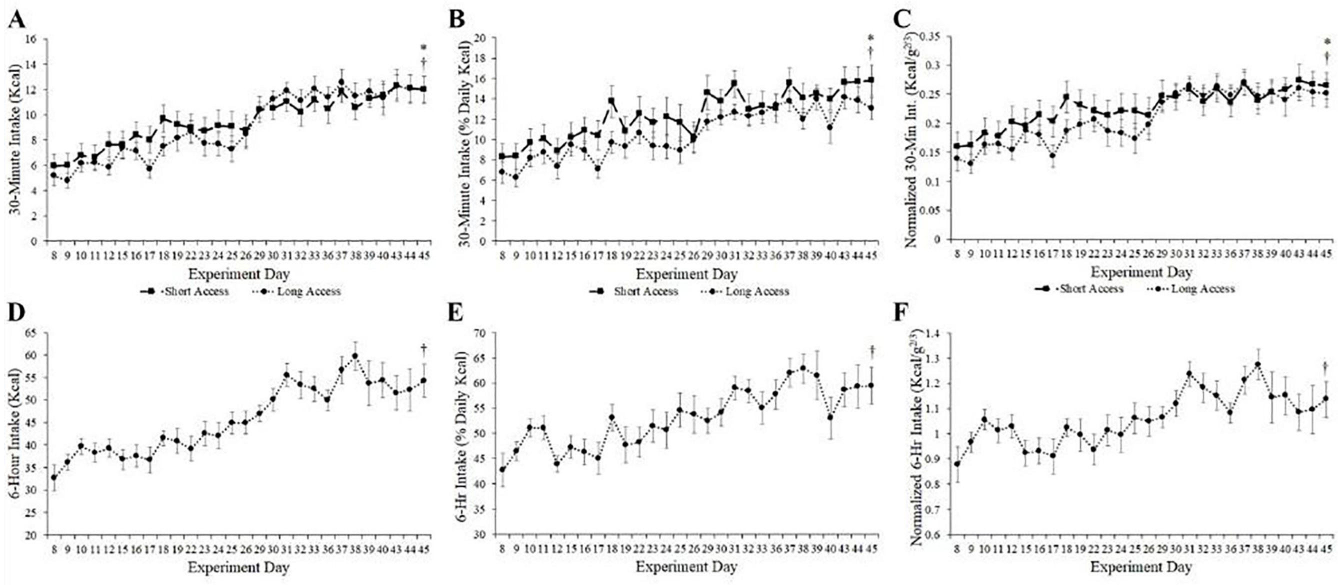

Fig. 2.

Both short (30-minute sessions) and long access (6-hour sessions) to Milk Chocolate Ensure Plus® in operant chambers on a fixed ratio 1 schedule of reinforcement (Monday – Friday) result in binge-type eating, when assessed across time. **A.** Subjects in the Short Access and Long Access groups (n = 16/group) consumed significantly greater calories during the 30-minute binge period across 28 sessions, such that intake on the final session was greater than intake on the first. **B.** Subjects in the Short Access and Long Access groups consumed a significantly higher percentage of their total daily calories in this 30-minute period across 28 sessions, such that intake on the final session was greater than intake on the first. **C.** Subjects in the Short Access and Long Access groups consumed significantly greater calories normalized to body weight during the 30-minute binge period across 28 sessions, such that intake on the final session was greater than intake on the first. **D.** Subjects in the Long Access group also consumed significantly greater calories during their 6-hour sessions across the 28 sessions, such that intake on the final session was greater than intake on the first. **E.** Subjects in the Long Access group also consumed a significantly higher percentage of their total daily calories during their 6-hour sessions across the 28 sessions. **F.** Subjects in the Long Access group also consumed significantly greater calories normalized to body weight during their 6-hour sessions across the 28 sessions. Values are mean ± S.E.M.; $^*p < 0.05$ Short Access last day vs. first, $^\dagger p < 0.05$ Long Access last day vs. first.

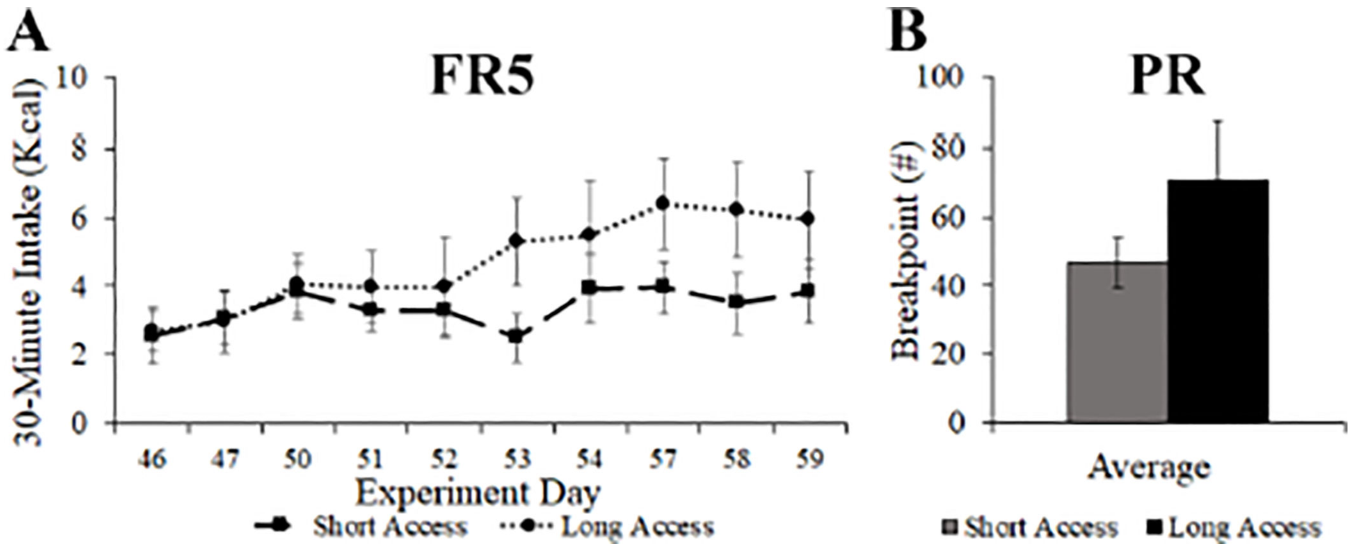

Fig. 3.

The Long Access group showed a trend for greater motivation for Milk Chocolate Ensure Plus® in operant chambers than the Short Access group. **A.** Under a fixed ratio 5 (FR5) schedule of reinforcement, the difference between the Short Access group and Long Access group ($n = 8$/group) did not achieve statistical significance in caloric intake of Ensure in a 30-minute period. **B.** Under a progressive ratio (PR) schedule of reinforcement, the Long Access group tended to show a higher breakpoint than the Short Access group. Values are mean ± S.E.M.

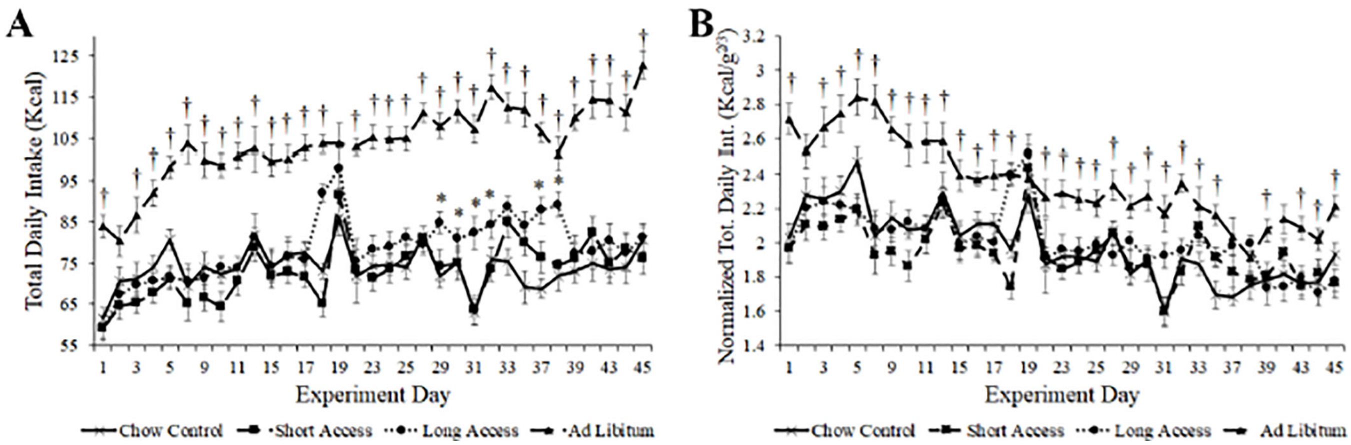

Fig. 4.

Total daily caloric intake on weekdays (the sum of calories consumed from Ensure plus chow in a 24-hour period) was higher in the *Ad Libitum* group compared to all other groups. **A.** While total daily caloric intake on weekdays was consistently higher in the *Ad Libitum* group ($n = 7$) compared to all other groups ($n = 8$/group), it was also greater in the Long Access group during the later weeks of the experiment. **B.** When normalized to body weight, total daily caloric intake on weekdays was also higher in the *Ad Libitum* group compared to all other groups. Values are mean ± S.E.M.; *$p < 0.05$ Long Access vs. Chow Control, $^{\dagger}p < 0.05$ *Ad Libitum* vs. all other groups.

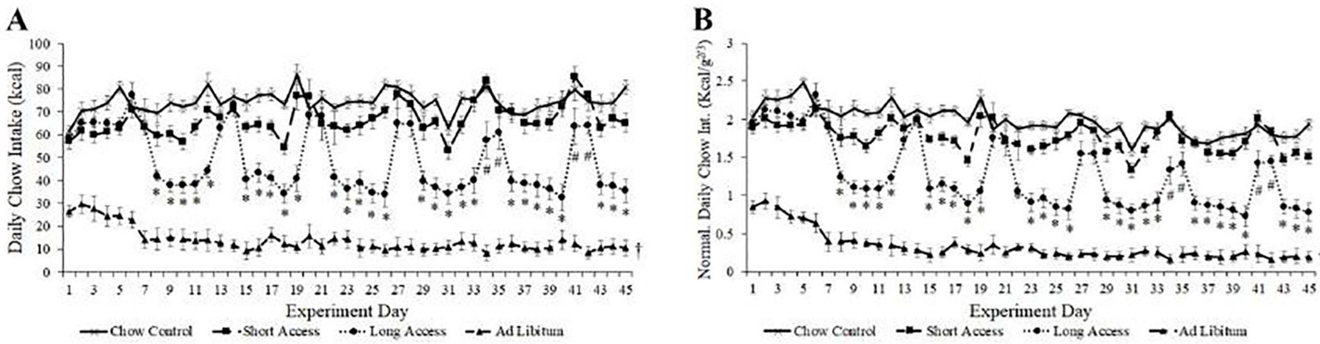

Fig. 5.

Chow intake was significantly lower in the *Ad Libitum* group and the Long Access group compared to both the Short Access and Chow Control groups. **A.** While the difference between the *Ad Libitum* ($n = 7$) and Long Access groups ($n = 8$) compared to both the Short Access and Chow Control groups ($n = 8$/group) was most notable on weekdays, the Long Access group, after Week 4, also consumed less chow than the Chow Control group on weekends. **B.** This difference was also evident when chow intake was normalized to body weight. Values are mean ± S.E.M.; $^*p < 0.05$ Long Access vs. Chow Control, $^{\#}p = 0.05$ Long Access vs. Chow Control (weekends), $^{\dagger}p < 0.05$ *Ad Libitum* vs. all other groups on all experiment days.

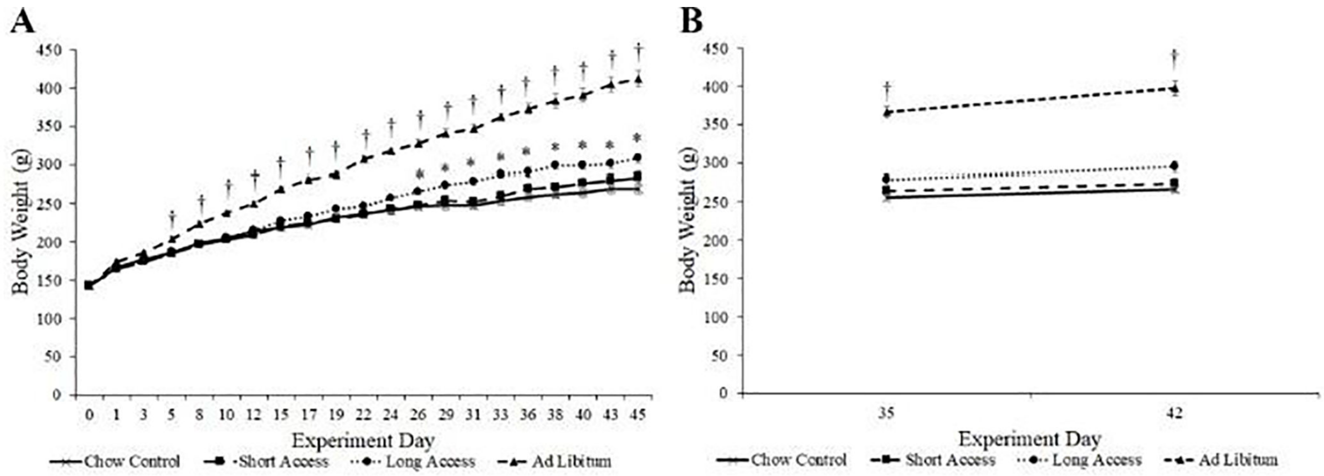

Fig. 6.

Over the course of the experiment, both the *Ad Libitum* and the Long Access groups gained excessive body weight. **A.** On weekdays, the *Ad Libitum* group ($n = 7$) weighed significantly more than all other groups ($n = 8$/group) as early as the end of the first week of the experiment, while the Long Access group weighed significantly more than the Chow Control group by the end of the fourth week. **B.** On weekends, the *Ad Libitum* group continued to weigh significantly more than all other groups, while the Long Access group no longer weighed significantly more than the Chow Control group. Values are mean ± S.E.M.; $^{*}p < 0.05$ Long Access vs. Chow Control, $^{\dagger}p < 0.05$ *Ad Libitum* vs. all other groups.

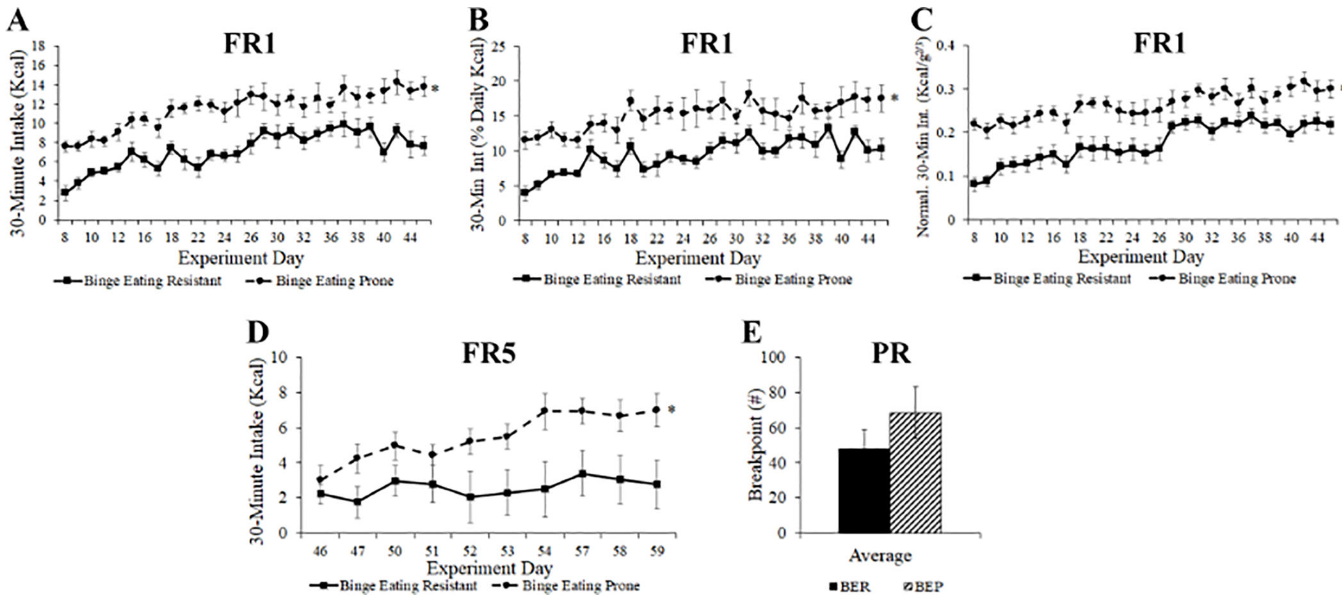

Fig. 7.

Binge-eating prone (BEP) subjects, classified by average caloric intake during the five 60-minute fixed-ratio 1 (FR1) operant training sessions, showed consistently greater binge-type eating than binge-eating resistant (BER) subjects across the remaining 28 FR1 sessions of the experiment and greater motivation for Milk Chocolate Ensure Plus® in operant chambers. **A.** The BEP group consumed significantly more calories during the 30-minute FR1 binge period than the BER group ($n = 16$/group). **B.** The BEP group consumed a significantly greater percentage of total daily caloric intake during the 30-minute binge period than the BER group. **C.** The BEP group consumed significantly more calories normalized to body weight during the 30-minute binge period than the BER group. **D.** Under a fixed ratio 5 (FR5) schedule of reinforcement, the BEP group consumed significantly more calories of Ensure in a 30-minute period. **E.** Under a progressive ratio (PR) schedule of reinforcement, the difference in breakpoint between the BEP and BER group did not achieve statistical significance. Values are mean ± S.E.M.; $*p < 0.05$ BEP vs. BER on all experiment days.

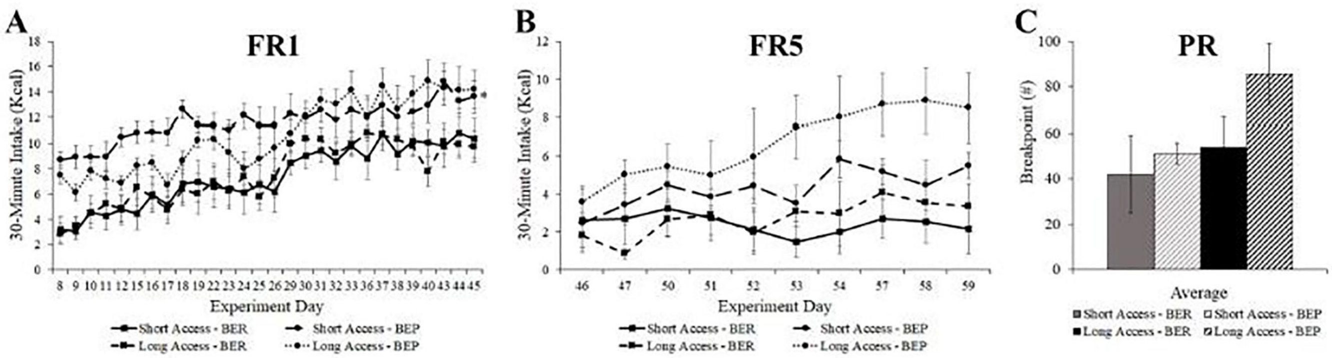

Fig. 8.

Binge-eating prone (BEP) subjects in the Short and Long Access groups differentially exhibited greater binge-type eating and greater motivation for Milk Chocolate Ensure Plus® in operant chambers than binge-eating resistant (BER) subjects. **A.** The Short Access BEP group consumed significantly more calories during the 30-minute FR1 binge period than both the Short Access and Long Access BER groups ($n = 8$/group). **B.** Under a fixed ratio 5 (FR5) schedule of reinforcement, the Long Access BEP group tended to consume more calories of Ensure in a 30-minute period than both the Long Access and Short Access BER groups. **C.** Under a progressive ratio (PR) schedule of reinforcement, the difference in breakpoint between the groups did not achieve statistical significance. Values are mean ± S.E.M.; $*p < 0.05$ Short Access BEP vs. BER groups on all experiment days.

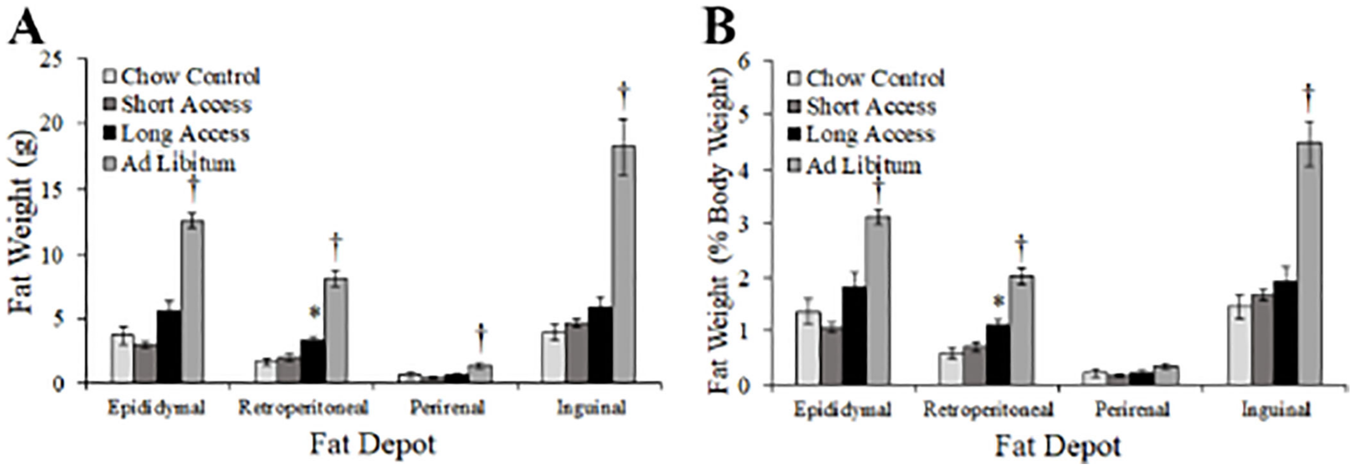

Fig. 9.

At the end of the experiment, both the *Ad Libitum* and the Long Access groups showed elevated levels of body fat. **A.** Measuring absolute weight of the fat depots, the *Ad Libitum* group ($n = 7$) showed significantly elevated weight of all measured fat depots compared to all other groups ($n = 8$/group), while the Long Access group showed significantly greater retroperitoneal body fat than the Chow Control group. **B.** Measuring fat depot as a percentage of total body weight, the *Ad Libitum* group showed significantly greater epididymal, retroperitoneal, and inguinal fat compared to all other groups, while the Long Access group showed significantly greater retroperitoneal body fat than the Chow Control group. Values are mean ± S.E.M.; *$p < 0.05$ Long Access vs. Chow Control, $^{\dagger}p < 0.05$ *Ad Libitum* vs. all other groups.

Table 1.

Timeline of experimental procedures.

Group	*n*	Paradigm			
Short Access	8	1 week, 1-hour training FR1	5.5 weeks, 30-minute FR1		
	8	1 week, 1-hour training FR1	5.5 weeks, 30-minute FR1	2 weeks, 30-minute FR5	1 week PR
Long Access	8	1 week, 1-hour training FR1	5.5 weeks, 6-hour FR1		
	8	1 week, 1-hour training FR1	5.5 weeks, 6-hour FR1	2 weeks, 6-hour FR5	1 week PR
Ad Libitum	7	6.5 weeks, unlimited home-cage access to Ensure			
Chow Control	8	6.5 weeks, no access to Ensure			

Subjects in the Long Access and Short Access groups all underwent 5 days of 1-hour training on fixed ratio 1 (FR1) schedule of reinforcement, followed by 5.5 weeks of either 30-minute or 6-hour access to Ensure on an FR1 schedule of reinforcement. A subset of each of these groups subsequently received 2 weeks of 30-minute access on a fixed ratio 5 (FR5) schedule of reinforcement and then 1 week of 90-minute access under a progressive ratio (PR) schedule. Subjects in the *Ad Libitum* group received 6.5 weeks of unlimited access to Ensure in their home cage. Subjects in the Chow Control group received 6.5 weeks of only chow and water in the home cage.

Table 2.

Summary of experimental analyses and main results.

Analysis (Section)	Groups	Main Results
Binge-type intake during FR1 training (3.1.1)	Short Access (*n*=16) Long Access (*n*=16)	• No difference
Binge-type intake compared across groups (3.1.2)	Short Access (*n*=16) Long Access (*n*=16) *Ad Libitum* (*n*=7) Chow Control (*n*=8)	• Short Access and Long Access > *Ad Libitum* and Chow Control
Binge-type intake compared across time (3.1.3)	Short Access (*n*=16) Long Access (*n*=16)	• Increased caloric intake across time in both groups • Increased caloric intake across time in 6-hour sessions in Long Access
FR5 and PR operant requirements (3.2)	Short Access (*n*=8) Long Access (*n*=8)	• FR5: increased lever pressing in both groups • PR breakpoint: Long Access > Short Access
Total daily caloric intake (3.3)	Short Access (*n*=8) Long Access (*n*=8) *Ad Libitum* (*n*=7) Chow Control (*n*=8)	• Ad Libitum > all other groups • Weeks 5 and 6: Long Access > Chow Control and Short Access (but not when normalized to body weight)
Chow intake (3.4)	Short Access (*n*=8) Long Access (*n*=8) *Ad Libitum* (*n*=7) Chow Control (*n*=8)	• Overall: *Ad Libitum* and Long Access < Chow Control • Weekends: *Ad Libitum* and Long Access < Chow Control and Short Access
Body weight on weekdays (3.5)	Short Access (*n*=8) Long Access (*n*=8) *Ad Libitum* (*n*=7) Chow Control (*n*=8)	• All groups gained weight over time • *Ad Libitum* > all other groups • After week 4: Long Access > Chow Control
Body weight on weekends (3.6)	Short Access (*n*=8) Long Access (*n*= 8) *Ad Libitum* (*n*=7) Chow Control (*n*=8)	• *Ad Libitum* > all other groups
Binge-eating prone and binge-eating resistant (3.7)	BEP (*n*=16 or 8) BER (*n*=16 or 8)	• FR1 30-minute: BEP > BER • FR5: BEP > BER • PR breakpoint: no difference
Binge-eating prone and resistant as a function of short and long access (3.7)	SA/BEP (*n*=8 or 4) SA/BER (*n*=8 or 4) LA/BEP (*n*=8 or 4) LA/BER (*n*=8 or 4)	• FR1 30-minute: SA/BEP > SA/BER and LA/BER • FR5: LA/BEP > LA/BER and SA/BER (trend) • PR breakpoint: no difference
Adipose tissue (3.8)	Short Access (*n*=8) Long Access (*n*=8) *Ad Libitum* (*n*=7) Chow Control (*n*=8)	• Epididymal: *Ad Libitum* > all groups • Retroperitoneal: *Ad Libitum* > all groups, Long Access > Chow Control • Perirenal: *Ad Libitum* > all groups (no effect for body fat as percent of total body weight) • Inguinal: *Ad Libitum* > all groups