Homeostatic responses to palatable food consumption in satiated rats

Citation for published version:
Hume, C, Barbara, J & Menzies, J 2016, 'Homeostatic responses to palatable food consumption in satiated rats', Obesity. https://doi.org/10.1002/oby.21606

Digital Object Identifier (DOI):
10.1002/oby.21606

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Obesity

Publisher Rights Statement:
This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

General rights
Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.
Homeostatic Responses to Palatable Food Consumption in Satiated Rats

Catherine Hume, Barbara Jachs, and John Menzies

Objective: Energy intake is regulated by overlapping homeostatic and hedonic systems. Consumption of palatable foods has been implicated in weight gain, but this assumes that homeostatic control systems do not accurately detect this hedonically driven energy intake. This study tested this assumption, hypothesizing that satiated rats would reduce their voluntary food intake and maintain a stable body weight after consuming a palatable food.

Methods: Lean rats or rats previously exposed to an obesogenic diet were schedule-fed with fixed or varying amounts of palatable sweetened condensed milk (SCM) daily, and their voluntary energy intake and body weight were monitored.

Results: During scheduled feeding of SCM, rats voluntarily reduced bland food consumption and maintained a stable body weight. This behavior was also seen in rats with access to an obesogenic diet and was independent of the predictability of SCM access. However, lean rats offered large amounts of SCM showed an increase in total energy intake. To test whether a nutrient deficiency drove this under-compensatory behavior, SCM was enriched with protein. However, no effect was seen on voluntary energy intake.

Conclusions: In schedule-fed rats, compensatory reductions in voluntary energy intake were seen, but under-compensation was observed if large amounts of SCM were consumed.

Introduction

Most cases of obesity are multifactorial in onset, but it is commonly believed that overeating has a crucial role in its development (1). Appetite is generally considered to have two components: a homeostatic drive and a hedonic drive. It has been suggested that hedonic influences can overwhelm homeostatic control systems and lead to obesity (2,3). However, the discrete brain regions involved in homeostatic and hedonic control interact functionally and neuroanatomically (4), and eating behavior is not clearly separable into homeostatic and hedonic phases (5).

Nevertheless, overeating is often blamed on an inability to resist palatable foods, and it can be tempting to incriminate certain types of foods or drinks as having a disproportionate impact on energy balance. It is asserted that consuming small amounts of energy-dense foods represents a marginal increase in energy intake that, over time, could result in an increase in body weight (6). However, there is little evidence in humans for a relationship between obesity and eating outside of (arbitrarily set) meal times (7-14). One explanation is that short- or long-term compensatory responses mitigate against the effects of energy consumed outside meal times. However, caloric compensation is still not clearly understood (15).

To investigate behavioral responses to small amounts of palatable foods we developed a model of scheduled feeding using sweetened condensed milk (SCM) in satiated rats. We hypothesized that rats of either sex would maintain a stable body weight by reducing their voluntary intake of bland food after SCM access and that this homeostatic response would be maintained in rats exposed over a longer term to an ad lib palatable, high-energy diet. We also hypothesized that learning of the SCM access patterns would not be required.

However, we recognized that homeostatic responses were likely to be limited; rats offered larger amounts of SCM would likely consume more energy in total than rats receiving access to smaller amounts of SCM (“under-compensation”). This may be due to a relatively simple hedonic drive to consume the SCM; however, we...
tested an alternative explanation—that bland food intake is defended to homeostatically maintain nutrient intake. In other words, in addition to the energy and nutrients consumed as SCM, minimal requirements for other nutrients could drive additional eating of different foods, adding to total energy intake (16,17). To explore this, we hypothesized that we could prevent under-compensation by increasing the level of a specific macronutrient (protein) in SCM.

Methods

All procedures were carried out under UK Home Office regulations. Adult Sprague-Dawley rats were kept on a 12-h light cycle (on at 07.00) at 20 ± 1°C and given ad lib access to water and their normal bland food (RM1; Special Diet Services, UK; 13.73 kJ/g). In all experiments, SCM (Nestlé, UK; diluted 50% v/v in water; 9.52 kJ/g) was used; 1 g of SCM contained 0.04 g fat, 0.28 g sugar, 0.03 g protein, 0.001 g salt, and no fiber.

Singly housed rats aged 7 to 10 weeks were used. SCM was presented for 15 min in the home cage in glass bowls. Rats were habituated to the empty bowl before access. Body weight, bland food intake, and water intake were measured daily between 09.00 and 10.00 each day. Any uneaten SCM was removed from the cage at the end of the access period and accounted for in energy intake calculations.

Experiment 1. Homeostatic compensation for regular SCM access in male and female rats

The purpose was to determine whether rats responded homeostatically to scheduled feeding of SCM. Energy intake and body weight were measured on days 1 to 8 in two groups of male rats and two groups of female rats (all n = 8) matched for initial body weight. From day 9, one male and one female group received SCM once daily at 10.00 (SCM access groups), 73 kJ for males and 52 kJ for females (~20% of mean daily voluntary energy intake). The control groups received no SCM access. On day 19, SCM access was stopped. Energy intake and body weight were measured in all groups until day 25.

Experiment 2. Effect of pre-exposure to a palatable, high-energy diet on compensation for regular SCM access in male rats

The purpose was to determine whether exposure to a palatable, energy-dense diet had an effect on homeostatic responses to scheduled feeding of SCM. Energy intake and body weight were measured in three groups of male rats matched for body weight: bland food-fed controls (“bland”), palatable food-fed controls (“palatable”), and palatable food-fed animals with SCM access (“palatable-SCM”). To mimic realistic eating choices, we offered the palatable and palatable-SCM groups a food choice (10% w/v sucrose solution (1.6 kJ/g), normal bland food (13.73 kJ/g), and a high-energy diet (45% fat/16% sucrose; Special Diet Services, UK; 19.1 kJ/g)).

In week 5, the palatable-SCM group was given once daily access to SCM (at 10.00 or 14.00, 45 kJ, ~10% of their daily voluntary energy intake while accessing the palatable diet). The palatable group was maintained on the palatable diet without access to SCM to act as a control. Rats in all groups had reached 10 weeks of age by the time SCM access was given.

On the final day of the experiment (day 41), all rats were decapitated under isoflurane anesthesia and trunk blood collected into heparinized tubes. Blood was centrifuged for 20 min at 14,000 rpm at 4°C and plasma collected. Plasma leptin levels were measured by ELISA (EIA-2395; DRG International). Intra-assay variability was <10%.

Experiment 3. Homeostatic compensation for irregular SCM access in male rats

There is strong evidence that rats can anticipate periods of scheduled feeding (18). The purpose of this experiment was to determine whether behavioral responses to SCM were dependent on anticipatory responses associated with a regular pattern of access. We hypothesized that rats would compensate accurately despite being unable to anticipate the timing or number of daily SCM access periods. To test this we varied the quantity and timing of SCM access each day. Energy intake and body weight were measured for 9 days in three groups of male rats (“control”, regular SCM access (“regular”) and irregular SCM access (“irregular”); all n = 8) matched for initial body weight. Both the regular and irregular groups received SCM twice daily on days 10 to 14 (at 10.00 and 16.00, each containing 45 kJ, ~12% of daily voluntary energy intake). On days 15 to 27, the regular group was maintained on this regular schedule, but the irregular group shifted to an unpredictable pattern of SCM access. The number of irregular access periods varied daily from zero to four and occurred at varying times between 08.00 and 18.00 (Supporting Information Table S1). The regular and irregular groups were given access to the same total amount of SCM across the entire protocol. The control group did not receive SCM access.

Experiment 4. Under-compensation in male rats and the effect of enriching SCM with protein

In experiment 3, we observed that rats under-compensated if they ate larger amounts of SCM daily. The purpose of this experiment was to test whether it was possible to induce under-compensation by scheduled feeding of larger amounts of SCM, and reverse under-compensation by increasing the levels of a specific macronutrient (protein) in SCM.

Energy intake and body weight were measured (days 1–7) in three groups of male rats (n = 8) matched for initial body weight. To provoke under-compensation, one group (“under-compensating”) received SCM three times daily at 10.00, 13.00, and 16.00. This contained a total of 286 kJ, representing ~63% of mean daily voluntary energy intake.

SCM is a poor source of protein. To determine whether increasing the levels of protein could reverse under-compensation, we enriched SCM with protein (“protein-enriched SCM”; 43% SCM v/v in water containing 6.6 mg/mL whey protein; Holland & Barratt, UK). We calculated the amount of energy contained in the SCM offered to the under-compensating group, calculated to what degree protein intake would decrease if the rats reduced their intake of bland food by that amount, and provided the predicted protein deficiency in excess of the enriched isocaloric SCM.
The control group received no access to SCM. On day 19, SCM access was stopped. Energy intake and body weight were measured in all groups until day 23.

### Statistical analyses
Data are expressed as mean ± SEM. Significance was set at $P < 0.05$. Details of the statistical tests used are given in Supporting Information.

### Results
There were no changes in *ad lib* water intake (experiment 1, $P = 0.9$ in males, $P = 0.4$ in females; experiment 2, $P = 0.9$; experiment 3, $P = 0.7$; experiment 4, $P = 0.7$).

#### Experiment 1. Homeostatic compensation for regular SCM access in male and female rats
Control male rats maintained a stable bland food intake for the entire experiment ($P = 0.06$, $P = 0.2$, respectively). Before SCM access, both control and SCM access groups consumed the same amount of bland food (control, 388 ± 11 kJ; SCM, 380 ± 11 kJ; $P = 0.6$; Figure 1A). During daily SCM access, rats reduced their bland food intake (control, 397 ± 11 kJ; SCM, 327 ± 11 kJ; $P = 0.002$, Figure 1B), but total energy intake in the SCM access group (kJ from bland food and SCM) was no different to controls (control, 397 ± 11 kJ; SCM, 398 ± 11 kJ; $P > 0.99$, Figure 1C). The body weight of SCM access and control rats did not diverge ($P = 0.8$; Figure 1D). Qualitatively similar results were obtained using female rats (Supporting Information Figures S1 and S2).

#### Experiment 2. Effect of pre-exposure to a palatable, high-energy diet on compensation for regular SCM access in male rats
Here we determined the effect of *ad lib* access to a high-energy diet on homeostatic responses to scheduled feeding of SCM. After 4 weeks’ diet choice, the palatable and palatable-SCM groups had a higher daily energy intake compared with the bland-fed group (bland: $n = 8$, 369 ± 9 kJ; palatable and palatable-SCM pooled: $n = 16$, 494 ± 16 kJ; $P < 0.0001$), which was accompanied by a nonsignificant divergence in body weight ($P = 0.08$). Plasma leptin levels measured at the end of the study were significantly higher in the pooled palatable groups compared with bland controls (bland: $n = 7$, 6.8 ± 1.0 ng/mL and pooled palatable and palatable-SCM: $n = 15$, 12.4 ± 0.8 ng/mL; $P = 0.005$). Plasma leptin levels in all groups correlated positively with body weight (slope = 0.05 ± 0.02, $r^2 = 0.2$, $P = 0.006$).

There was no difference in total energy intake between the palatable group and the palatable-SCM group before SCM access (palatable, 412 ± 10 kJ; palatable-SCM, 409 ± 15 kJ; $P = 0.9$). During SCM access, the palatable-SCM group reduced voluntary food intake (palatable, 416 ± 10 kJ; palatable-SCM, 375 ± 11 kJ; $P = 0.01$, Figure 2A). There was no difference in daily total energy intake during SCM access between the palatable group and palatable-SCM access group (palatable, 416 ± 10 kJ; palatable-SCM, 406 ± 12 kJ; $P = 0.1$, Figure 2B). Rats selectively reduced sucrose solution intake (before SCM access, 184 ± 8 kJ; during SCM access, 132 ± 13 kJ; $P = 0.03$) but did not alter bland food intake or palatable solid food intake (Figure 2C). There was no divergence in body weights.
between the palatable and palatable-SCM groups across the entire experiment (Figure 2D; \( P = 0.24 \)).

**Experiment 3. Homeostatic compensation for irregular SCM access in male rats**

There was no difference in the total energy intake consumed by the control, regular, and irregular groups across the entire experiment (8,890 \( \pm \) 262 kJ, 9,313 \( \pm \) 225 kJ, 8,879 \( \pm \) 187 kJ, respectively; \( P = 0.4 \)), nor was there a difference in total SCM consumed between groups (regular, 1,299 \( \pm \) 84 kJ; irregular, 1,305 \( \pm \) 214 kJ; \( P = 0.9 \)).

The control group maintained a stable bland food intake for the entire experiment (\( P = 0.1 \)). After the onset of SCM access both the regular and irregular groups (both receiving regular twice daily access to SCM in this phase) reduced their bland food intake (control, 328 \( \pm \) 10 kJ; regular, 267 \( \pm \) 7 kJ; irregular, 255 \( \pm \) 7 kJ). During the irregular SCM access phase of the experiment, the irregular group varied its bland food intake in response to the amount of SCM presented in the previous 24 h (Figure 3A). There was no divergence in body weights across the entire experiment (\( P = 0.8 \); Figure 3B).

To examine the extent and time scale of compensation, we studied the relationship between energy consumed from SCM and energy consumed from bland food. For each animal on each day we set the onset of SCM access as \( t = 0 \) then measured the amount of bland food eaten in the 0 to 24 h period, the 24 to 48 h period, and the 48 to 72 h period after \( t = 0 \). Rats compensated in the 0 to 24 h period after SCM access, reducing their bland food intake to account for the different amounts of energy consumed as SCM at \( t = 0 \). In the 0 to 24 h period there was a negative correlation between energy intake from SCM and bland food (\( -0.52 \pm 0.05 \), \( r^2 = 0.98 \), \( P = 0.002 \); Figure 3C). There was no correlation in the 24 to 48 h or 48 to 72 h periods after \( t = 0 \) (24–48 h: +0.18 \( \pm \) 0.09, \( r^2 = 0.6 \), \( P = 0.1 \); 48–72 h: +0.15 \( \pm \) 0.19, \( r^2 = 0.2 \), \( P = 0.5 \)).

**Experiment 4. Under-compensation in male rats and the effect of enriching SCM with protein**

Control rats maintained a stable bland food intake for the entire experiment (\( P = 0.15 \)). Before SCM access, all groups consumed the same amount of bland food (control, 443 \( \pm \) 7 kJ; undercompensating, 468 \( \pm \) 11 kJ; protein-enriched SCM, 460 \( \pm \) 18 kJ; \( P = 0.37 \)). During SCM access, the under-compensating group reduced their bland food intake (control, 425 \( \pm \) 13 kJ; under-compensating, 253 \( \pm \) 11 kJ; \( P < 0.0001 \), Figure 4A), but total daily energy intake in this group was higher than controls (control, 425 \( \pm \) 13 kJ; under-compensating, 549 \( \pm \) 14 kJ; \( P < 0.0001 \), Figure 4B). The protein-enriched SCM group reduced their bland food intake (control, 425 \( \pm \) 13 kJ; protein-enriched SCM, 249 \( \pm \) 12 kJ; \( P < 0.0001 \), Figure 4A) but total energy intake was identical to the under-compensating group (protein-enriched SCM group, 549 \( \pm \) 14 kJ; under-compensating, 549 \( \pm \) 14 kJ; \( P > 0.99 \), Figure 4B).

Throughout SCM access, there was no difference in energy consumed from the unenriched and protein-enriched SCM (under-compensating, 3,067 \( \pm \) 59 kJ; protein-enriched SCM, 2,961 \( \pm \) 94 kJ; \( P = 0.36 \)). During SCM access, protein consumption was significantly lower in the under-compensating group and higher in the protein-enriched SCM group in comparison with the control group (control,
Discussion

We investigated eating behavior in satiated rats after access to a palatable food. We observed a robust and reproducible compensatory effect; rats could adapt to the onset and offset of SCM access and to dynamic changes in access. The specific physiological mechanisms underlying this are unknown. The two major variables that contribute to body weight are energy intake and energy expenditure. We did not measure energy expenditure in this study, but it seems likely that observed alterations in voluntary bland food consumption underlie the observed stability of body weight.

Rats had ad lib access to normal bland food throughout so were never in negative energy balance. Thus, voluntary SCM consumption was presumably driven by mechanisms distinct to those involved in homeostatic control (19), including mechanisms linked to the hedonic value of SCM. In all experiments, rats given access to moderate amounts of SCM swiftly and remarkably accurately reduced their bland food intake and maintained total energy intake and body weight equivalent to controls. Male rats in the schedule-fed group consumed 99 ± 1% of the energy consumed by the control group, and females consumed 100 ± 1% compared with controls.

Many rodent studies using scheduled feeding of bland or palatable foods impose food restriction outside the scheduled feeding periods. However, several rodent studies are comparable to ours in that they feature regular scheduled feeding of a palatable food for 2 h or less per day alongside ad lib access to standard bland food. The majority show a decrease in voluntary bland food consumption after scheduled feeding (20-29) although some, using scheduled feeding paradigms where larger amounts of palatable food are consumed, show moderate increases in total energy intake (23,30,31). Reports of changes in body weight and/or body composition reflect the reported degree of compensation—no changes in animals that compensate well (19,20,27-29), but increases in animals that do not (30,31). Broadly, our data are in line with these findings. It would be of interest to determine whether this behavior is driven purely by the absolute amount of SCM consumed in 24 h or whether the number and relative timing of SCM access periods are influential, particularly timing with respect to the dark phase when rats consume the bulk of their daily energy intake (32).

We showed that compensatory behavior is evident in rats consuming a palatable, high-energy diet. The body weight of these rats was not significantly different from bland-fed controls during the SCM access period but palatable-fed rats had higher plasma levels of leptin indicating greater adiposity. Broadly, leptin has an inhibitory effect on food intake and has an emerging role in reward-related eating behavior (33). In our study, however, increased plasma levels of leptin had no apparent effect on compensatory behaviors.

We sought to determine whether the food anticipation potentially associated with a regular pattern of access was required for a reduction in voluntary food intake. We showed that compensation occurs when SCM is presented randomly and in differing quantities, suggesting that learning of temporal access patterns is not required for compensation. In this experiment, there was a negative correlation between bland food intake and SCM intake, but only in the 24 h immediately following a bout of SCM consumption (there was no correlation in the two subsequent 24-h periods). The slope of the response was fit well by linear regression but did not equal −1.

Figure 3 Effects of irregular consumption of SCM on bland food intake and body weight in male rats. All data presented as mean ± SEM. Two rats in the regular group did not eat the SCM and were excluded. (A) Bland food intake (kJ) for control and irregular SCM access groups across the experiment. The number of daily rewards presented to the irregular group is shown in parentheses (*P < 0.05, repeated measures one-way ANOVA (P = 0.002) with Bonferroni for irregular SCM access group across the experiment). (B) Body weight for control and irregular SCM access groups across the experiment. Inset: % body weight change between the first and last day of SCM access (day 1 to day 27) for control and irregular SCM access groups (unpaired t-test (P = 0.33)). (C) The relationship between bland food intake (kJ) and SCM intake (kJ) within the 0 to 24 h post-SCM access period (slope = −0.032 ± 0.05, r² = 0.98, P = 0.0015). SCM, sweetened condensed milk.
indicating that rats do not compensate entirely for the energy in SCM. We studied this under-compensation in experiment 4 and showed that giving access to larger amounts of SCM resulted in an increase in total daily energy intake. In other words, rats did not reduce sufficiently their voluntary bland food intake to account for the energy consumed in SCM.

Next we investigated what may drive under-compensation. It is unlikely to be an energy deficit, but an optimal amount of energy is not the only characteristic of an optimal diet, it must also contain a variety of nutrients. It is possible that certain nutrients present in low levels in SCM are found in bland food, and bland food intake is defended to maintain nutrient intake. Simultaneously, hedonic mechanisms stimulate SCM intake. The net result is a surplus total daily energy intake.

Indirect support for this idea comes from experiment 2. The sucrose solution was the energy source with the least nutritional diversity (but is also the least energy-dense) and rats selectively reduced their voluntary intake of sucrose solution after SCM access. We tested this idea more directly by enriching SCM with protein. However, enrichment with protein had no effect on under-compensation. It is unlikely that this lack of effect was due to insufficient protein in the Protein-enriched-SCM group’s diet, instead it is possible that other nutritional, hedonic, or habitual factors drive under-compensation.

Equally, the physical form of SCM may be relevant. In humans, the balance of evidence suggests that energy consumed as liquids is less satiating compared with energy consumed as solids (15). In rodents, taking accurate compensation as an indicator of satiety, it has been shown that animals can compensate accurately for solid and liquid foods (19-29). We hypothesise that consumption of solid or semi-solid foods of similar amounts and energy densities would lead to accurate compensation in our model. Indeed, we have preliminary
data indicating that this is the case using a semisolid jelly made with SCM.

In summary, we show that lean, satiated rats behaviorally regulate energy intake after consumption of small amounts of a palatable food and that this response is dynamic and relatively resilient to change. It is unclear which mechanisms underlie this, but they do not seem to be tuned to prevent under-compensation when larger amounts of palatable food are available. It is difficult to speculate how these findings may relate to complex human behaviors, but we believe this model represents a useful basis to investigate brain and hormonal mechanisms involved in physiological responses to palatable food in satiated rats.

Acknowledgments

The authors thank Julie Sutherland, Jill Williamson, and Yukuong Ko for their help with experiments.

© 2016 The Authors Obesity published by Wiley Periodicals, Inc. on behalf of The Obesity Society (TOS)

References

1. Ludwig DS, Friedman MI. Increasing adiposity: consequence or cause of overeating? JAMA 2014;311:2167-2168.
2. Yu YH, Vasseli JR, Zhang Y, Mechanick JI, Korner J, Peterli R. Metabolic vs. hedonic obesity: a conceptual distinction and its clinical implications. Obes Rev 2015;16:234-247.
3. Zheng H, Lenard NR, Shin AC, Berthoud HR. Appetite control and energy balance regulation in the modern world: reward-driven brain overrides repletion signals. Int J Obes (Lond) 2009;33:S8-S13.
4. Blundell J, Finlayson G, Halford J, King N. The regulation of food intake in humans. In: De Groot LJ, Beck-Peccoz P, Chrousos G, et al., eds. www.Endotext. Int J Obes (Lond) 2010;34:319-326.
5. Bake T, Duncan JS, Morgan DG, Mercer JG. Arcuate nucleus homeostatic systems are not altered immediately before the scheduled consumption of large, binge-type meals of palatable solid or liquid diet in rats and mice. J Neuroendocrinol 2013;25:357-371.
6. Casazza K, Fontaine KR, Astrup A, et al. Myths, presumptions, and facts about obesity. N Engl J Med 2013;368:446-454.
7. Field AE, Austin SB, Gillman MW, Rosner B, Rocket HR, Colditz GA. Snack food intake does not predict weight change among children and adolescents. Int J Obes (Lond) 2004;28:1210-1216.
8. Keast DR, Nicklas TA, O’Neil CE. Snacking is associated with reduced risk of overweight and reduced abdominal obesity in adolescents: National Health and Nutrition Examination Survey (NHANES) 1999-2004. Am J Clin Nutr 2010;92:428-435.
9. Viskal-van Dongen M, Kok FJ, de Graaf C. Effects of snack consumption for 8 weeks on energy intake and body weight. Int J Obes (Lond) 2010;34:319-326.
10. Larson N, Story M. A review of snacking patterns among children and adolescents: what are the implications of snacking for weight status? Child Obes 2013;9:104-105.
11. O’Neil CE, Nicklas TA, Liu Y, Berenson GS. Candy consumption in childhood is not predictive of weight, adiposity measures or cardiovascular risk factors in young adults: the Bogalusa Heart Study. J Hum Nutr Diet 2015;28:59-69.
12. Chapelot D. The role of snacking in energy balance: a biobehavioral approach. J Nutr 2011;141:158-162.
13. Trier C, Fonvig CE, Bujeste C, et al. No influence of sugar, snacks and fast food intake on the degree of obesity or treatment effect in childhood obesity. Pediatr Obes 2016. doi: 10.1111/jpo.12094.
14. León-Muñoz LM, García-Esquinas E, Soler-Vila H, Guillar-Castillón P, Banegas JR, Rodríguez-Artalejo F. Unhealthy eating behaviors and weight gain: a prospective study in young and middle-age adults. Obesity (Silver Spring) 2016;24:1178-1184.
15. Almiren-Roig E, Palla L, Guest K, Ricchiuti C, Vint N, Jebb SA, Drewnowski A. Factors that determine energy compensation: a systematic review of preload studies. Nutr Rev 2013;71:458-473.
16. Wiater MF, Hudson BD, Virgin Y, Ritter S. Protein appetite is increased after central leptin-induced fat depletion. Am J Physiol Regul Integr Comp Physiol 2007;293:R1468-R1473.
17. Simpson SJ, Raubenheimer D. Perspective: tricks of the trade. Nature 2014;508:566.
18. Patton DF, Mislimberger RE. Circadian adaptations to meal timing: neuroendocrine mechanisms. Front Neurosci 2013;7:185.
19. Bake T, Duncan JS, Morgan DG, Mercer JG. Arcuate nucleus homeostatic systems are not altered immediately before the scheduled consumption of large, binge-type meals of palatable solid or liquid diet in rats and mice. J Neuroendocrinol 2013;25:357-371.
20. Corwin RL, Wojnicki FH, Fisher JO, Dimitriou SG, Rice HB, Young MA. Limited access to a dietary fat option affects ingestive behavior but not body composition in male rats. Physiol Behav 1998;65:545-553.
21. Dimitriou SG, Rice HB, Corwin RL. Effects of limited access to a fat option on food intake and body composition in female rats. Int J Eat Disord 2000;28:436-445.
22. Sahr AE, Sindelar DK, Alexander-Chucko JT, Eastwood BJ, Mitch CH, Statnick MA. Activation of mesolimbic dopamine neurons during novel and daily limited access to palatable food is blocked by the opioid antagonist LY255582. Am J Physiol Regul Integr Comp Physiol 2008;295:R463-R471.
23. Berner LA, Avena NM, Hoebel BG. Bingeing, self-restriction, and increased body weight in rats with limited access to a sweet-fat diet. Obesity (Silver Spring) 2008;16:1998-2002.
24. Hsu CT, Patton DF, Mislimberger RE, Steele AD. Palatable meal anticipation in mice. PLoS One 2010;5:e12003.
25. Gallardo CM, Gunapala KM, King OD, Steele AD. Daily scheduled high fat meals moderately entrain behavioral anticipatory activity, body temperature, and hypothalamic c-Fos activation. PLoS One 2012;7:e41161.
26. Merkestøen M, Brans MA, Luinjendijk MC, et al. Ghrelin mediates anticipation to a palatable meal in rats. Obesity (Silver Spring) 2012;20:963-971.
27. Dailey MJ, Stingl KC, Moran TH. Disassociation between preprandial gut peptide release and food-anticipatory activity. Endocrinology 2012;153:132-142.
28. Soto M, Chaumontet C, Even PC, et al. Intermittent access to liquid sucrose differentially modulates energy intake and related central pathways in control or high-fat fed mice. Physiol Behav 2015;140:44-53.
29. Soto M, Chaumontet C, Mauduit CD, et al. Intermittent access to a sucrose solution impairs metabolism in obesity-prone but not obesity-resistant mice. Physiol Behav 2016;154:175-183.
30. Bake T, Murphy M, Morgan DG, Mercer JG. Large, binge-type meals of high fat diet change feeding behavior and entrain food anticipatory activity in mice. Appetite 2014;77:60-71.
31. Bake T, Morgan DG, Mercer JG. Feeding and metabolic consequences of scheduled consumption of large, binge-type meals of high fat diet in the Sprague-Dawley rat. Physiol Behav 2014;128:70-79.
32. Borbély AA, Neuhaus HV. Daily patterns of sleep, motor activity, and feeding in the rat: effects of regular and gradually extended photoperiods. J Comp Physiol 1978;124:1-14.
33. van der Plass G, van Zessen R, Luinjendijk MC, et al. Modulation of cue-induced firing of ventral tegmental area dopamine neurons by leptin and ghrelin. Int J Obes (Lond) 2015;39:1742-1749.