Sensitization of the reinforcing value of food: a novel risk factor for overweight in adolescents

Jennifer L. Temple1,2,4, Amanda M. Ziegler1,2,4, Amanda K. Crandall2,4, Tegan Mansouri1,4, Leonard H. Epstein3,5

1Department of Exercise and Nutrition Sciences, University at Buffalo, Buffalo, NY 14214
2Department of Community Health and Health Behavior, University at Buffalo, Buffalo, NY 14214
3Department of Pediatrics, University at Buffalo, Buffalo, NY 14214
4Department of School of Public Health and Health Professions, University at Buffalo, Buffalo, NY 14214
5Department of Jacobs School of Medicine, University at Buffalo, Buffalo, NY 14214

Abstract

Background and Objectives—The relative reinforcing value (RRV) of food is associated with increased energy intake and obesity and increases in RRV of food after repeated intake (sensitization) are related cross-sectionally and prospectively to higher BMI in adults. We examined the factors, such as delay discounting (DD), associated with sensitization of RRV of high energy density (HED) and low energy density (LED) food and how sensitization relates to zBMI in adolescents. We hypothesized that sensitization to HED food would be positively associated with zBMI, that sensitization to LED food would be negatively associated with zBMI, that DD would be associated with HED sensitization, and that LED sensitization and DD would moderate the relationships between HED sensitization and zBMI.

Subjects and Methods—A population-based sample of 207 adolescents without obesity, aged 12 – 14 years was studied from June 2016 – March 2019. The RRV of LED and HED foods were measured before and after two weeks of daily consumption along with zBMI and other potential factors related to eating and weight, including dietary restraint, hunger, food liking, and delay discounting (DD). Hierarchical regression models were used to determine the associations between these factors and sensitization and zBMI. We also examined LED sensitization and DD as potential moderators of the relationship between sensitization and zBMI.

Results—As hypothesized, dietary restraint and sensitization to HED food were associated with greater zBMI. Contrary to our original hypotheses, DD was not associated with sensitization, there was no relationship between sensitization to LED food and zBMI and neither LED sensitization or DD moderated the relationship between HED sensitization and zBMI.
Conclusions—Sensitization to repeated intake of HED food was associated with higher zBMI in adolescents without obesity. Sensitization may be a novel behavioral phenotype that may relate to overweight in youth.

Keywords
reinforcing value; sensitization; obesity; delay discounting; reinforcement pathology; behavioral phenotypes; adolescents

Introduction
Understanding factors that impact energy balance across the lifespan is the first step toward developing evidence-based interventions to mitigate the obesity epidemic. One factor that has been reliably shown to relate to overweight and obesity across the lifespan is the relative reinforcing value (RRV), which is an empirical index of the motivation to get food (1–3). Greater RRV of food is associated with increased energy intake, and mediates the relationship between food intake and obesity (3–5).

One characteristic of reinforcers is that they can become more reinforcing after repeated exposure (6–9). This phenomenon is referred to as sensitization and has been well characterized in the substance use literature (10–13). Our earlier work was built on the framework of sensitization theory where we hypothesized that, like drugs of abuse, repeated exposure to food elicits sensitization, or increased motivation to eat, in a subset of people and that sensitization is associated with increased energy intake and body weight. We found that sensitization was observed in a subset of adults with overweight and obesity after two weeks high energy density (HED; > 4 kcals/g) food consumption compared with adults with healthy weight (8). We also showed that this sensitization phenotype was only elicited by repeated intake of HED food (compared with low energy density (LED) food) and when the portions used were larger (~300 kcal vs. 100 kcals) (6, 8). Finally, we found that greater sensitization both cross-sectionally and prospectively predicted higher BMI and more weight gain (6, 7, 14). When taken together, our work in adults shows that sensitization is a robust and repeatable phenotype that is associated with eating, weight, and weight change over time.

The expression of motivated behavior can be influenced by a number of other factors, including impulsivity. One aspect of impulsivity is an inability to delay gratification, which is conceptualized by delay discounting (DD), or the tendency to select smaller, more immediate rewards over larger, delayed rewards. Higher DD is associated with greater energy intake (15, 16), higher BMI (17–19), and poorer outcomes in weight loss studies (20). The relative reinforcing value of food and DD can impact obesity separately (21), but the combination of high DD and high RRV of food, a concept termed “reinforcement pathology”, may confer more risk than either one alone (22), as people will both respond more for rewards and have less of an inhibitory break on those responses. Individuals with high levels of reinforcement pathology consume more energy in the laboratory, have higher BMI, and gain more weight over time than individuals with either high RRV of food or high
Delay discounting and/or reinforcement pathology may be associated with the development of sensitization.

Previous work on sensitization and DD has been concentrated in adults, but adolescents may be particularly susceptible to the impact of sensitization as the adolescent brain is primed to respond to reward while areas involved in inhibitory control remain immature during this developmental period (23–25). Research is needed to determine factors associated with sensitization of RRV of HED food and to assess whether sensitization to HED food is associated with higher zBMI in this population in order to better understand risk factors for overweight. It is also important to understand the role of sensitization to LED food in zBMI. While most of the prior work on sensitization has focused on HED food (6, 8, 9, 14), it is possible that repeated intake of LED food can also elicit sensitization. Individuals who increase responding for LED food after repeated intake may be more likely to consume LED food, which could substitute for intake of some HED food and, perhaps, reduce energy intake and zBMI.

The purpose of this study was to examine the relationship between sensitization and zBMI, to determine the extent to which DD and reinforcement pathology are related to sensitization, and to extend our prior work into an adolescent population. We achieved these aims by testing the following hypotheses 1) sensitization to repeated intake of HED food is associated with higher zBMI in adolescents 2) sensitization to repeated intake of low energy density (LED; < 1 kcal/gram) food is associated with lower zBMI 3) DD, and reinforcement pathology are associated with increased sensitization 4) sensitization to LED food and DD moderate the relationship between HED sensitization and zBMI.

METHODS

Study Participants

The data shown here are the baseline data from a 2-year longitudinal study assessing behavioral predictors of weight change in adolescents. Participants were 207 boys and girls aged 12 – 14 years without obesity recruited using flyers, e-mail and social media, personal referrals, and advertisements distributed in schools in the Buffalo, NY area (Figure 1). This narrow age range was selected to capture weight and height change in adolescents during pubertal growth. We focused our analysis on adolescents without obesity because, in the larger longitudinal study, we were interested in prospectively predicting the onset of obesity, as opposed to studying participants who already have obesity. Potential participants were included if they were 12 – 14 years old, rated the study foods as neutral to positive and reported a willingness to eat a serving of a study food every day for 13 days, were able to attend 5 visits within a 6 – 8 week period, and were willing to participate in a two-year study. Potential participants were excluded if they had a zBMI below −1.5 or above 2, had a metabolic or endocrine disorder, used medications that could affect appetite or weight gain (e.g. Adderall, Wellbutrin, Prednisone), were unable to complete light physical activity without assistance, were allergic to all study foods, had reading comprehension below the 4th grade level or were unable to read or speak English, or lacked an English speaking parent/guardian who could provide consent. We used a zBMI above 2 as our cutoff for obesity according to the WHO standards (26, 27).
Study Procedures

Participants came into the laboratory for five baseline visits lasting between 1 – 3 hours each (Figure 2). On the first visit, parents/guardians and participants read and signed consent and assent forms. Parents/guardians and participants then completed a series of assessments, including: demographic questionnaire (parent/guardian), ratings of food liking and wanting (participant), appetite (participant), and Dutch Eating Behavior Questionnaire (DEBQ; participant) (28, 29). Height and weight were measured for both parent/guardian and participant on the first visit and again at follow-up visits at 6, 15, and 24 months (data collection ongoing). Height and weight were not reassessed at visits 2 – 5, because substantial changes were unlikely in the 6 – 8 week timeframe and we wanted to minimize focus on body weight when completing RRV of food tasks. Participants also completed a delay discounting (DD) task.

Participants returned to the laboratory for visits 2 – 5 at least 2 hours post-prandial in order to test the RRV of their assigned foods. HED and LED foods were assigned using self-report of liking (>40 mm on a 100 mm visual analog scale anchored by “Not at all” and “The most possible”) and frequency of consumption (eaten < 4 times per week). We selected these criteria because we wanted the foods to be moderately liked (VAS > 40mm) to improve the likelihood that kids would work for them and would eat them every day for two weeks. We also wanted to make sure that kids were not already eating these foods every day (consumed < 4 times per week) in order to increase our chances of observing sensitization. Order of presentation of the assigned LED food (fruit cups, applesauce, and low-fat yogurt; energy density ≤1.0 kcal/g) and assigned HED food (chips, cookies, and chocolate candy; energy density ≥24 kcal/g) conditions were counterbalanced. Upon arrival, participants completed appetite sensation ratings (described below) and then consumed a 140-kcal preload (e.g. granola or cereal bar). Participants again rated appetite prior to completing the RRV task. At the end of visit 2, participants were given 14 portions of their assigned food. They were instructed to eat one portion per day beginning the following day and to complete an online survey each day to report that they had eaten their food. Compensation was partially based on compliance with these instructions. All participants whose data are included here reported consuming >80% of their assigned food portions for both LED and HED food. After consuming the same food every day for two weeks, participants returned to the laboratory to complete the RRV task again for the same food and a seated activity. Visits 4 and 5 were completed after a 1-week washout period and were identical to visits 2 and 3 except that the opposite food-type (HED/LED) was used. All study procedures were approved by the University at Buffalo Institutional Review Board. This study has been registered as a clinic trial on ClinicalTrials.gov (NCT04027608).

Reinforcing Value Task—Participants clicked a mouse button to earn portions of their assigned snack food (visits 2 – 5) on one computer and 2-minute allotments of time to engage in their preferred seated activity (e.g. art, electronic games, or puzzles; all visits) on the other computer. The preferred seated activity was selected from self-reported liking ratings and was offered in order to control for a non-specific desire to respond. Participants were instructed to click the mouse button on the computer that represented the reward that they wished to earn and that when they no longer wished to earn points for food or activity,
they could ring a bell or tell the researcher and their session would end, even if they had already begun a new session. Reinforcers were earned based on independent schedules of reinforcement presented on a progressive, variable ratio (± 5%) schedule ranging from 20 – 10240 clicks. Once the participant indicated they were done, they exchange their points for food and time for activity. All eating and activity was completed in the laboratory. This task has been validated for use in children, adolescents, and adults and has been shown to be reliable in repeated tests (5, 30–32).

**Delay Discounting Task**—Delay discounting assesses one’s preference for a small immediate reward over a larger, delayed reward. Participants made choices between two cards. One card displayed a fixed reward ($50) available after a time delay (e.g. 1 week) and an immediate reward (e.g. $40) whose magnitude was adjusted in specific dollar increments, in both ascending and descending order (33). The trials were presented across a series of time delays (e.g., 1 day, 2 days, 1 week, 2 weeks, 1 month, and 6 months). Participants who showed nonsystematic patterns of responses were excluded from all DD analyses based on the recommendations from Johnson and Bickel (n = 8; (34)). The indifference point was determined by taking the average of the immediate reward values just prior to and following a switch in choice to the delayed reward, in each direction. The average indifference points across the six delays were then plotted on a line and the rate of discounting was calculated using Mazur’s hyperbolic discounting equation (33). This task has been validated for use in children and adolescents and shown to have strong test-retest reliability in adolescents (35, 36).

**Measures and Questionnaires**

**Anthropometrics**—Anthropometric measurements were taken in parents/guardians and participants without shoes while wearing light clothing with everything removed from pockets. Body weight was assessed using a SECA digital scale (Hanover, MD). Height was assessed using a wall-mounted, SECA stadiometer (Hanover, MD). z-BMI values are developed for each sex and age based on population values (37).

**Appetite and Hedonic Ratings**—Participants were asked to rate their degree of hunger, thirst, liking, and wanting of the study foods by drawing a vertical line along a 100-mm visual analog scale anchored at 0mm by “not at all” and 100mm by “the most possible”(38).

**Dutch Eating Behavior Questionnaire (DEBQ)**—Participants completed DEBQ, revised and validated for use in children ages 8–12, to measure dietary restraint (28, 29). There are 9 items on this questionnaire where the participant was asked to “circle answers that are true for you” from the choices of “never”, “sometimes” and “very often”, which were scored as 0, 1, and 2 respectively. We used the total score in our statistical models.

**Sample Size Determination and Analytic Plan**—This study was powered to examine the relationship between sensitization to HED and LED foods and weight change over time. Sample size was determined using data collected on the relationship between sensitization and weight change in adults (3, 7) which had an effect size of 0.19. With an alpha of 0.05,
and a power of 0.80, statistical significance could be achieved with a total of 180 participants.

Relative reinforcing value (RRV) was conceptualized as the area under the curve for responses across the schedules of reinforcement. Sensitization score was calculated by subtracting the participant’s baseline RRV of HED/LED food from the RRV of HED/LED food after two weeks of daily intake of that food. Participant characteristics and differences in dependent measures were analyzed using ANOVA and Chi-squared analyses using HED sensitization category (sensitization score > 1 as “sensitizers” and those with ≤1 as “satiators”), as a between subjects’ factor. For all other analyses, sensitization score was used as a continuous variable. Skew of all variables were assessed by visual examination of the histograms and transformations were applied where appropriate. Due to skew, log transformations were applied to RRV, DDT, and reinforcement pathology scores.

Pearson product moment correlations were then used to examine relationships among factors associated with zBMI and baseline RRV and sensitization to HED and LED foods (Table 1). zBMI was calculated using height and weight measures taken on the first laboratory visit. Associations between HED and LED sensitization scores and zBMI were analyzed using hierarchical regression models in order to assess the change in the variance explained by the addition of new variables. For all regression models, normality of the residuals was assessed by visual examination of the histogram, multicollinearity was assessed using the variance inflation factor (all < 2), and heteroskedasticity was assessed using the Breusch-Pagan test. In the case of a violation, heteroskedastic-robust errors were calculated using the PROCESS macro version 3.3 for SPSS (39) (IBM SPSS Statistics for Windows, Version 26; Armonk, NY). We first examined factors associated with HED and LED sensitization. For these models, we included DD in step 1, RRV in step 2, and reinforcement pathology in step 3. To examine associations with zBMI: DEBQ scores were included in step 1 and sensitization was added in step 2. In order to test the hypothesis that LED sensitization and DD, separately, moderate the relationship between HED sensitization and zBMI, we used the PROCESS macro version 3.3 for SPSS (39) (IBM SPSS Statistics for Windows, Version 26; Armonk, NY), and created an interaction term from the two variables. Relationships were considered significant if p<0.05. These analyses were conducted using SPSS 26 (IBM SPSS Statistics for Windows, Version 26; Armonk, NY).

RESULTS

Participant Characteristics and Correlations

Participant characteristics and descriptive statistics are shown in Table 2 grouped by HED sensitization category. There were no differences in any participant characteristics by HED sensitization category.

Predictors of Sensitization of HED and LED Food

The hierarchical regression showed that including DD in the first step did not account for a significant amount of variance in sensitization. Adding RRV of HED food in Step 2 increased the variance accounted for to 16%, (F_{inc}(1, 196) = 34.9; p < 0.0001). Adding
reinforcement pathology in Step 3 did not significantly increase the variance accounted for ($F_{inc}(1, 195) = 3.6; p = 0.061; \text{Table 3}$).

None of our models accounted for a significant amount of the variance in sensitization of LED food ($F_{inc}(1, 195) = 0.95; p = 0.33$), with the final model accounting for 1% of the variance.

**Sensitization of Responses to HED and LED Food and zBMI**

The hierarchical regression model (Table 4) found that DEBQ score in step 1 accounted for 18% of the variance in zBMI. Adding sensitization to HED food in step 2 increased the variance accounted for to 19%; ($F_{inc}(1, 202) = 4.11; p = 0.044$). LED sensitization was not related to zBMI ($F_{inc}(1, 202) = 0.10; p = 0.748$).

**Sensitization to LED Food and DD as Moderators of HED Sensitization and zBMI**

When LED sensitization was included as a moderator of the relationship between HED sensitization and zBMI, the interaction term was not significant ($b = 0.000; p = 0.212$) and the relationship between sensitization and zBMI remained significant ($b = 0.001; p = 0.039$). Likewise, DD did not significantly interact with HED sensitization in terms of zBMI ($b = 0.000; p = 0.882$) and the relationship between sensitization and zBMI remained significant ($b = 0.001; p = 0.016$).

**DISCUSSION**

This study is the first to show that sensitization to repeated intake of HED food is associated with zBMI in adolescents without obesity, as we hypothesized. This relationship is similar to what we have previously shown in adults (6–8) and suggests that sensitization might be a risk factor for overweight in youth. Contrary to our initial hypotheses, we did not find that LED sensitization was associated with lower zBMI nor did LED sensitization moderate the relationship between HED sensitization and zBMI. Also contrary to our original hypotheses, DD and reinforcement pathology were not associated with sensitization to HED food and DD did not moderate the relationship between sensitization and zBMI. These data, in a large cohort of adolescents, suggest that sensitization to repeated HED food intake is a unique behavioral phenotype that is associated with zBMI in adolescents. This may be a useful behavioral target for future interventions.

The data presented here are consistent with our previous studies in adults showing a positive relationship between sensitization to repeated HED food administration and weight (6, 8, 14). It is important to note that, when we create categorical variables for “sensitizers” and “satiators”, there is no difference between the two groups in zBMI. However, consistent with our findings in adults (6, 8) and given the significant relationship revealed by the regression model, we conclude that greater magnitude of sensitization is related to greater zBMI. There were some differences between what we found here and what has been reported in adults. First, the current study had a smaller proportion of individuals who were classified as sensitizers compared with adults (7). This may be because the adult studies contained participants with obesity and the current study did not (6, 8, 14). Second, we did not find that baseline RRV of HED food was associated with zBMI (6, 8, 14). The reason for this
discrepancy is unclear, but suggests that RRV of HED food is not consistently associated with body weight across different studies, different groups of participants, or across development.

We hypothesized that sensitization to repeated intake of LED food would be associated with lower zBMI, but instead found no relationship (6). We also hypothesized that sensitization to LED food would moderate the relationship between HED sensitization and zBMI, which we also did not find. The LED foods used in this study were low-fat foods that consisted primarily of fruit and yogurt. It is possible that these foods do not elicit the same response as high fat and/or high sugar foods. In fact, sensitization is more likely to occur after repeated intake of HED foods, with both animal and human data showing that foods with higher amounts of sugar and fat are more reinforcing (40–42). It is also possible that a certain threshold of energy is required to elicit sensitization and the LED food did not meet that threshold. In a previous study in adults, we showed that repeated intake of 100 kcal portions of HED food did not result in sensitization of RRV of food, whereas 300 kcal portions did produce sensitization (8). When designing this study, we aimed to provide a portion of LED food that would be equivalent in size to the HED foods, and not be so large that it would be aversive. We used portions that were around 165 kcals, as 300 kcal portions were very large and we felt they would be too difficult for participants to consume every day.

Ability to delay gratification may impact the development of sensitization and also may mitigate the impact of sensitization on zBMI (14,22). We, therefore, hypothesized that higher DD would be associated with greater HED sensitization and that DD would moderate the relationship between sensitization and zBMI. However, when we examined factors associated with HED sensitization, we found that neither DD nor reinforcement pathology were significantly associated with sensitization. Baseline RRV of HED food was negatively associated with sensitization. This is consistent with our previous findings in adults without obesity (14). This may be because when participants have higher baseline RRV of HED food, there is less room to increase responding after two weeks of daily intake than in those who begin with lower RRV of food. It is also possible that participants with higher baseline RRV of HED food had already partially sensitized to the food that we provided, so ability to further sensitize was limited. Finally, we did not find that DD moderated the relationship between sensitization and zBMI. It is possible that DD and reinforcement pathology moderate the relationship between sensitization and zBMI change over time.

This study had several significant strengths. This was a large sample of adolescents that completed a series of well-controlled laboratory measures, with very high rates of compliance with our study procedures and we used objective measures of RRV and DD rather than relying on subjective data. This study was not without limitations. First, the sample is largely white and upper middle class, thus we are unable to generalize these findings to lower income and minority communities. Second, our LED food selections were restricted to fruit and yogurt. It is possible that if other types of LED foods, such as vegetables, had been included we may have seen a stronger negative relationship with zBMI. Third, our age range began at 12 years, which is a time when puberty in females is largely underway and puberty in males is just beginning. These differences in pubertal stage are associated with differences in height velocity and energy needs that may account for some of
the variance in our outcomes. Fourth, we excluded adolescents with obesity from this sample. While this was important for the aims of the larger, longitudinal study, it may have limited our ability to see relationships between baseline zBMI and sensitization and suggests that the magnitude of the relationships that we observed may be conservative compared to what we would find in a sample that included children with obesity.

Conclusions and Future Directions

When taken together, the results of this study suggest that sensitization to repeated intake of HED foods is associated with greater zBMI in adolescents. Sensitization to HED food may be a novel risk factor for excessive weight accumulation and obesity in adolescents, which is the focus of our ongoing longitudinal study. Now that we have characterized this phenotype, we can work towards developing novel interventions strategies to prevent or reduce sensitization. Since sensitization is based on increasing response to repeated presentations of the same food, the most obvious approach is to change eating patterns so that the same food, at the same dose, is not presented repeatedly over days. A second approach to preventing sensitization might be to provide alternative reinforcers to food (4, 43). The value of any commodity depends on what else is available at the time of the choice, and it may be that providing strong alternatives could reduce the choice of the food, and prevent sensitization. It is also worthwhile to consider how to increase the reinforcing value of LED foods, which would be a goal for any program designed to prevent or treat obesity. It may be that the dose or type of food is important, and should not be limited to the foods used in this study. Understanding ways to increase the reinforcing value of healthy foods could have a major impact on promoting healthy eating behavior change.

Acknowledgements

This study was funded by R01 DK106265 (JLT). We thank Lori Hazinger, Aaron Anderson, Meredith Edelman, and Alessia Galante for their years of help in collecting these data.

REFERENCES

1. Epstein LH, Lin H, Carr KA, Fletcher KD. Food reinforcement and obesity. Psychological moderators. Appetite. 2012;58(1):157–62. [PubMed: 22005184]
2. Epstein LH, Yokum S, Feda DM, Stice E. Food reinforcement and parental obesity predict future weight gain in non-obese adolescents. Appetite. 2014;82:138–42. [PubMed: 25045864]
3. Temple JL. Factors that influence the reinforcing value of foods and beverages. Physiol Behav. 2014;136:97–103. [PubMed: 24793218]
4. Epstein LH, Leddy JJ, Temple JL, Faith MS. Food reinforcement and eating: a multilevel analysis. Psychol Bull. 2007;133(5):884–906. [PubMed: 17723034]
5. Temple JL, Legierski CM, Giacomelli AM, Salvy SJ, Epstein LH. Overweight children find food more reinforcing and consume more energy than do nonoverweight children. Am J Clin Nutr. 2008;87(5):1121–7. [PubMed: 18469229]
6. Clark EN, Dewey AM, Temple JL. Effects of daily snack food intake on food reinforcement depend on body mass index and energy density. Am J Clin Nutr. 2010;91(2):300–8. [PubMed: 20016012]
7. Temple JL. Behavioral sensitization of the reinforcing value of food: What food and drugs have in common. Prev Med. 2016;92:90–9. [PubMed: 27346758]
8. Temple JL, Bulkley AM, Badawy RL, Krause N, McCann S, Epstein LH. Differential effects of daily snack food intake on the reinforcing value of food in obese and nonobese women. Am J Clin Nutr. 2009;90(2):304–13. [PubMed: 19458018]
9. Temple JL, Chappel A, Shalik J, Volcy S, Epstein LH. Daily consumption of individual snack foods decreases their reinforcing value. Eating behaviors. 2008;9(3):267–76. [PubMed: 18549985]
10. Berridge KC, Robinson TE. Liking, wanting, and the incentive-sensitization theory of addiction. Am Psychol. 2016;71(8):670–9. [PubMed: 27977239]
11. Robinson TE, Berridge KC. The neural basis of drug craving: an incentive-sensitization theory of addiction. Brain Res Brain Res Rev. 1993;18(3):247–91. [PubMed: 8401595]
12. Robinson TE, Berridge KC. The psychology and neurobiology of addiction: an incentive-sensitization view. Addiction. 2000;95 Suppl 2:S91–117. [PubMed: 11002906]
13. Robinson TE, Berridge KC. Review. The incentive sensitization theory of addiction: some current issues. Philos Trans R Soc Lond B Biol Sci. 2008;363(1507):3137–46. [PubMed: 18640920]
14. Temple JL, Epstein LH. Sensitization of food reinforcement is related to weight status and baseline food reinforcement. Int J Obes (Lond). 2012;36(8):1102–7. [PubMed: 22041984]
15. Appelhans BM, Waring ME, Schneider KL, Pagoto SL, DeBiasse MA, Whited MC, et al. Delay discounting and intake of ready-to-eat and away-from-home foods in overweight and obese women. Appetite. 2012;59(2):576–84. [PubMed: 22819735]
16. Appelhans BM, Woolf K, Pagoto SL, Schneider KL, Whited MC, Liebman R. Inhibiting food reward: delay discounting, food reward sensitivity, and palatable food intake in overweight and obese women. Appetite. 2011;59(2):568–70. [PubMed: 21108217]
17. Fields SA, Sabet M, Peal A, Reynolds B. Relationship between weight status and delay discounting in a sample of adolescent cigarette smokers. Behav Pharmacol. 2011;22(3):266–8. [PubMed: 21430520]
18. Rasmussen EB, Lawyer SR, Reilly W. Percent body fat is related to delay and probability discounting for food in humans. Behavioural processes. 2010;83(1):23–30. [PubMed: 19744547]
19. Weller RE, Cook EW 3rd, Avsar KB, Cox JE. Obese women show greater delay discounting than healthy-weight women. Appetite. 2008;51(3):563–9. [PubMed: 18513828]
20. Best JR, Theim KR, Gredysa DM, Stein RI, Welch RR, Saelens BE, et al. Behavioral economic predictors of overweight children’s weight loss. J Consult Clin Psychol. 2012;80(6):1086–96. [PubMed: 22924332]
21. Stojek MMK, MacKillop J. Relative reinforcing value of food and delayed reward discounting in obesity and disordered eating: A systematic review. Clin Psychol Rev. 2017;55:1–11. [PubMed: 28478269]
22. Carr KA, Daniel TO, Lin H, Epstein LH. Reinforcement pathology and obesity. Current drug abuse reviews. 2011;4(3):190–6. [PubMed: 21999693]
23. Konrad K, Firk C, Uhlhaas PJ. Brain development during adolescence: neuroscientific insights into this developmental period. Dtsch Arztebl Int. 2013;110(25):425–31. [PubMed: 23840287]
24. Moreno-Lopez L, Soriano-Mas C, Delgado-Rico E, Rio-Valle JS, Verdejo-Garcia A. Brain structural correlates of reward sensitivity and impulsivity in adolescents with normal and excess weight. PLoS One. 2012;7(11):e49185. [PubMed: 23185306]
25. Vara AS, Pang EW, Vidal J, Anagnostou E, Taylor MJ. Neural mechanisms of inhibitory control continue to mature in adolescence. Dev Cogn Neurosci. 2014;10C:129–39.
26. Koebnick C, Coleman KJ, Black MH, Smith N, Der-Sarkissian JK, Jacobsen SJ, et al. Cohort profile: the KPSC Children’s Health Study, a population-based study of 920 000 children and adolescents in southern California. Int J Epidemiol. 2012;41(3):627–33. [PubMed: 21257603]
27. Shields M, Tremblay MS. Canadian childhood obesity estimates based on WHO, IOTF and CDC cut-points. Int J Pediatr Obes. 2010;5(5):265–73. [PubMed: 20210678]
28. Hill AJ, Pallin V. Dieting awareness and low self-worth: related issues in 8-year-old girls. Int J Eat Disord. 1998;24(4):405–13. [PubMed: 9813765]
29. van Strien T, Herman CP, Verheijden MW. Dietary restraint and body mass change. A 3-year follow up study in a representative Dutch sample. Appetite. 2014;76:44–9. [PubMed: 24480668]
30. Epstein LH, Kilanowski CK, Consalvi AR, Paluch RA. Reinforcing value of physical activity as a determinant of child activity level. Health Psychol. 1999;18(6):599–603. [PubMed: 10619533]
31. Epstein LH, Temple JL, Neaderhiser BJ, Salis RJ, Erbe RW, Leddy JJ. Food reinforcement, the dopamine D2 receptor genotype, and energy intake in obese and nonobese humans. Behav Neurosci. 2007;121(5):877–86. [PubMed: 17907820]

32. Temple JL, Bulkley AM, Briatico L, Dewey AM. Sex differences in reinforcing value of caffeinated beverages in adolescents. Behav Pharmacol. 2009;20(8):731–41. [PubMed: 19890207]

33. Rollins BY, Dearing KK, Epstein LH. Delay discounting moderates the effect of food reinforcement on energy intake among non-obese women. Appetite. 2010;55(3):420–5. [PubMed: 20678532]

34. Johnson MW, Bickel WK. An algorithm for identifying nonsystematic delay-discounting data. Exp Clin Psychopharmacol. 2008;16(3):264–74. [PubMed: 18540786]

35. Anokhin AP, Golosheykin S, Mulligan RC. Long-term test-retest reliability of delayed reward discounting in adolescents. Behavioural processes. 2015;111:55–9. [PubMed: 25447508]

36. Isen JD, Sparks JC, Iacono WG. Predictive validity of delay discounting behavior in adolescence: a longitudinal twin study. Exp Clin Psychopharmacol. 2014;22(5):434–43. [PubMed: 24999868]

37. Himes JH, Dietz WH. Guidelines for overweight in adolescent preventive services: recommendations from an expert committee. The Expert Committee on Clinical Guidelines for Overweight in Adolescent Preventive Services. Am J Clin Nutr. 1994;59(2):307–16. [PubMed: 8310979]

38. Stubbs RJ, Hughes DA, Johnstone AM, Rowley E, Reid C, Elia M, et al. The use of visual analogue scales to assess motivation to eat in human subjects: a review of their reliability and validity with an evaluation of new hand-held computerized systems for temporal tracking of appetite ratings. Br J Nutr. 2000;84(4):405–15. [PubMed: 11103211]

39. Hayes AF, Cai L. Using heteroskedasticity-consistent standard error estimators in OLS regression: an introduction and software implementation. Behav Res Methods. 2007;39(4):709–22. [PubMed: 18183883]

40. Epstein LH, Carr KA, Lin H, Fletcher KD. Food reinforcement, energy intake, and macronutrient choice. Am J Clin Nutr. 2011;94(1):12–8. [PubMed: 21543545]

41. Steele CC, Pirkle JRA, Davis IR, Kirkpatrick K. Dietary effects on the determinants of food choice: Impulsive choice, discrimination, incentive motivation, preference, and liking in male rats. Appetite. 2019;136:160–72. [PubMed: 30721744]

42. Westwater ML, Fletcher PC, Ziaudddeen H. Sugar addiction: the state of the science. Eur J Nutr. 2016;55(Suppl 2):55–69.

43. Carr KA, Epstein LH. Influence of sedentary, social, and physical alternatives on food reinforcement. Health Psychol. 2018;37(2):125–31. [PubMed: 29154609]
**Figure 1:**
Consort diagram showing the number of participants screened, consented, retained for five baseline visits, and included in the analysis. Text boxes to the right explain the reasons for the decrease in numbers of participants at each step.
**Figure 2:**
Outline of the flow of participant visits. Participants completed 5 baseline visits, separated by 1 – 2 weeks. The visits are shown with open circles with the data collected at each visit shown with bullets. The smaller closed circles represent a 1-week period of time. There was, on average, one week in between visits 1 and 2, two weeks in between visits 2 and 3 and 4 and 5. There was one week in between visits 3 and 4. Visits where participants completed a task for HED food and consumed HED food daily for two weeks are shown in red and visits/daily consumption of LED food are shown in green. Finally, the large, bidirectional arrow at the bottom indicates that the type of food presented first (and second) was counterbalanced across participants.
Table 1:

Pearson Product Correlations among Study Variables

|       | 1      | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 10  | 11  | 12  | 13  | 14  | 15  |
|-------|--------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 1     | 1.00   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 2     |        | .418** | 1.00 |     |     |     |     |     |     |     |     |     |     |     |     |
| 3     | −.026  | −.066 | 1.00 |     |     |     |     |     |     |     |     |     |     |     |     |
| 4     | −.194**| −.064 | .024 | 1.00 |     |     |     |     |     |     |     |     |     |     |     |
| 5     | −.033  | .042 | .013 | .316**| 1.00 |     |     |     |     |     |     |     |     |     |     |
| 6     | −.111  | −.048 | .308**| .213**| .151 | 1.00 |     |     |     |     |     |     |     |     |     |
| 7     | .013   | −.023 | .103 | −.034 | −.023 | .225**| 1.00 |     |     |     |     |     |     |     |     |
| 8     | −.147  | −.15* | −.010 | .332**| .056 | .104 | −.088 | 1.00 |     |     |     |     |     |     |     |
| 9     | −.098  | −.15* | −.003 | .101 | .217**| .078 | .057 | .206**| 1.00 |     |     |     |     |     |     |
| 10    | −.120  | −.117 | .322**| .040 | −.018 | .550**| .286**| .236**| .321**| 1.00 |     |     |     |     |     |
| 11    | −.001  | .136 | .201**| .043 | −.025 | .158**| .578**| .060 | −.101 | .182**| 1.00 |     |     |     |     |
| 12    | .041   | .006 | .006 | .002 | .090 | .027 | .035 | .033 | .039 | .091 | .089 | 1.00 |     |     |     |
| 13    | .019   | −.044 | .258**| .075 | .077 | .248**| .118 | .153 | .200**| .540**| .125 | .795**| 1.00 |     |     |
| 14    | .006   | .060 | −.033 | .017 | .055 | −.059 | .042 | −.061 | .143* | .075 | −.14* | .032 | .057 | 1.00 |     |
| 15    | .16*   | .034 | .077 | .063 | −.021 | −.068 | −.039 | −.152*| −.127 | −.389**| .031 | −.095 | −.21**| .13 | 1.00 |

The table shows the correlation coefficients for the relationships between variables. Statistically significant correlations are highlighted with * (p < 0.05) or ** (p < 0.01). Bold font denotes R^2 values < −0.4 or > 0.4.
### Table 2:
Participant Characteristics and Descriptive Statistics as a function of HED Sensitization Group

|                      | Entire Sample | Satiators | Sensitizers |
|----------------------|---------------|-----------|-------------|
|                      | n = 207       | n = 156   | n = 51      |
| **n**                | **%**         | **%**     | **%**       |
| **p**                |               |           |             |
| **Ethnicity**        |               |           |             |
| Hispanic or Latino   | 16            | 11        | 7           | 10          |
| Non-Hispanic or Latino | 190         | 92        | 144         | 93          | 46          | 90          | 0.36        |
| **Race**             |               |           |             |
| American Indian/Alaska Native | 3 | 1 | 3 | 2 | 0 | 0 | 0.43 |
| Asian                | 6             | 2         | 5           | 3           | 1           | 2           | 0.55        |
| Black/African American | 23        | 11        | 18          | 7           | 5           | 10          | 0.50        |
| White or Caucasian   | 173           | 80        | 131         | 80          | 42          | 81          | 0.60        |
| Other                | 11            | 5         | 7           | 8           | 4           | 7           | 0.20        |
| **Household Income** |               |           |             |
| < $9,999             | 1             | 0.5       | 1            | 1           | 0           | 0           |
| $10,000 - $49,999    | 33            | 16        | 24           | 15          | 9           | 18          |
| $50,000 - $69,999    | 33            | 16        | 20           | 13          | 13          | 24          | 0.20        |
| $70,000 - $89,999    | 31            | 15        | 24           | 15          | 7           | 14          |
| $90,000 - $109,999   | 31            | 15        | 29           | 19          | 2           | 4           |
| $110,000 - $139,999  | 37            | 18        | 29           | 19          | 8           | 16          |
| > $140,000           | 40            | 19        | 28           | 18          | 12          | 24          |
| **Parental Education** |           |           |             |
| Completed high school | 9           | 4         | 6            | 4           | 3           | 6           |
| Some college/completed vocational training | 31       | 15        | 24           | 16          | 7           | 14          | 0.75        |
| Complete college/university | 86    | 42        | 64           | 42          | 22          | 43          |
| Completed graduate degree | 80  | 39        | 61           | 38          | 19          | 37          |
| **Mean**             | **SEM**       | **Mean**  | **SEM**      |
| Age (years)          | 13.3          | 0.06      | 13.3         | 0.07        | 13.2        | 0.12        | 0.86        |
| zBMI                 | 0.40          | 0.07      | 0.36         | 0.08        | 0.56        | 0.13        | 0.18        |
| Pubertal Development Score | 12.9 | 0.24 | 2.6 | 0.06 | 2.5 | 0.1 | 0.47 |
| Delay Discounting    | 0.12          | 0.03      | 0.13         | 0.04        | 0.09        | 0.06        | 0.47        |
| DEBQ Score           | 4.1           | 0.20      | 4.1          | 0.24        | 4.4         | 0.42        | 0.46        |
| **HED Food Measures** |             |           |             |
| Hunger on HED Visit  | 55.2          | 1.7       | 55.4         | 2.0         | 52.6        | 3.5         | 0.47        |
|                  | Entire Sample | Satiators | Sensitizers |
|------------------|---------------|-----------|-------------|
| **n**            | *207*         | *156*     | *51*        |
| **HED Food Liking** | 78.1          | 1.2       | 78.7        | 1.5       | 75.5 | 2.5 | 0.29 |
| **RRV of HED Food** | 152.7         | 17.9      | 158.2       | 20.8      | 115.6 | 36.2 | 0.34 |
| **RRV of Seated Activity** | 151.9         | 19.9      | 125.1       | 23.4      | 184.8 | 40.6 | 0.18 |
| **HED Sensitization** | −53.6        | 13.4      | −94.4       | 13.8      | 82.6 | 24.2 | <0.0001 |
| **LED Food Measures** |              |           |             |           |      |     |     |
| Hunger on LED Visit | 54.3          | 1.7       | 52.7        | 1.9       | 60.8 | 3.5 | 0.04 |
| **LED Food Liking** | 67.9          | 1.4       | 69.5        | 1.6       | 64.7 | 2.8 | 0.14 |
| **RRV of LED Food** | 83.9          | 10.8      | 75.9        | 12.6      | 98.0 | 22.1 | 0.39 |
| **RRV of Seated Activity** | 151.9        | 19.9      | 148.1       | 24.1      | 159.5 | 42.3 | 0.81 |
| **LED Sensitization** | −4.8          | 14.0      | −4.0        | 15.7      | −8.9 | 13.9 | 0.89 |
Table 3:

Hierarchical model of associations with sensitization to HED Food

|            | Step 1 |          | Step 2 |          | Step 3 |          |
|------------|--------|----------|--------|----------|--------|----------|
|            | ΔR²    | B        | β      | t        | ΔR²    | B        | β      | t        |
| Delay Discounting | 0.009  | -3.52    | -0.095 | -1.35    | 0.15   | -2.22    | -0.06  | -0.91    | 0.02   | -10.8   | -293    | -2.09   |
| RRV HED Food   |        |          |        |          | -42.69 | -0.39    | -5.91  | ***      | -58.4  | -0.53   | -5.32   | ***     |
| Reinforcement Pathology |        |          |        |          | 8.89   | 0.31     | 1.89   |          |        |         |         |         |

* = p < 0.05.
** = p < 0.01
*** = p < 0.001
Table 4:
Hierarchical model of associations with zBMI

|          | Step 1 |          |          |          | Step 2 |          |          |
|----------|--------|----------|----------|----------|--------|----------|----------|
|          | ΔR²    | B        | β        | t        | ΔR²    | B        | β        | t        |
| DEBQ     | .18*** | .135     | .418***  | 6.55***  | .016   | .134     | .413     | 6.69***  |
| Sensitization to HED Food |          |          |          |          | .001   | .128     | 2.03*    |

* = p < 0.05
** = p < 0.01
*** = p < 0.001.

Asterisks in the top row indicate statistical significance for the entire model at each step. Significant improvements to the model are demonstrated with asterisks in the rows below next to the individual factors in each step.