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Modulation of taste responsiveness and food preference by obesity and weight loss

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Abstract

Palatable foods lead to overeating, and it is almost a forgone conclusion that it is also an important contributor to the current obesity epidemic - there is even talk about food addiction. However, the cause-effect relationship between taste and obesity is far from clear. As discussed here, there is substantial evidence for altered taste sensitivity, taste-guided liking and wanting, and neural reward processing in the obese, but it is not clear whether such traits cause obesity or whether obesity secondarily alters these functions. Studies with calorie restriction-induced weight loss and bariatric surgery in humans and animal models suggest that at least some of the obesity-induced alterations are reversible and consequently represent secondary effects of the obese state. Thus, both genetic and non-genetic predisposition and acquired alterations in taste and reward functions appear to work in concert to aggravate palatability-induced hyperphagia. In addition, palatability is typically associated with high energy content, further challenging energy balance regulation. The mechanisms responsible for these alterations induced by the obese state, weight loss, and bariatric surgery, remain largely unexplored. Better understanding would be helpful in designing strategies to promote healthier eating and prevention of obesity and the accompanying chronic disease risks.

Keywords

Food reward; food addiction; palatability; calorie-restriction; ingestive behavior; neural control of food intake; sweet foods; fatty foods

1. Introduction

As the prevalence of obesity and diabetes continues to grow globally, particularly in children and adolescents, and there are no efficient drugs available, emphasis on prevention through nutrition and lifestyle has returned. However, to offer efficacious nutritional and behavioral recommendations, we need a better understanding of how the intake of different nutrients is controlled and how food choices are made. Specifically, what factors control consumption of palatable foods that are typically rich in calories? Here we provide a brief

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review of current knowledge about the relationship between body adiposity and pleasantness of sweet and fatty foods. We discuss the effects of calorie-restriction-induced weight loss and bariatric surgery on the perception and pleasantness of sweet and fatty taste stimuli in both preclinical and clinical studies.

It is thought that instinctual behaviors which are essential for survival have evolved over millions of years and that their neural control mechanisms are particularly powerful [1,2]. Food reward has been suggested to provide the necessary motivation to engage in ingestive behavior. Thus, food is a powerful natural reinforcer that out-competes most other behaviors, particularly when metabolically hungry. Ingestive behavior consists of procurement, consummatory, and post-consummatory phases [3] and each of these 3 phases contributes to reward, which then can guide future behaviors. During eating, immediate, direct pleasure is derived from mainly gustatory and olfactory sensations, driving consumption throughout the meal until satiation signals dominate [4]. Berridge and Robinson have parsed reward into separable psychological and neural components, liking, wanting, and learning [5]. The characteristic orofacial expressions displayed by decerebrate rats [6] and anencephalic infants [7] in response to sweet taste strongly suggests that the forebrain is not the only brain area involved in experiencing the hedonic impact or liking of pleasant stimuli. Berridge and Robinson [5] refer to these expressions as objective affective reactions or implicit affect and to the psychological process as implicit 'liking'. Besides neural circuits in the hindbrain, the nucleus accumbens and ventral pallidum in the limbic forebrain appear to be some of the other key components of the distributed neural network mediating 'liking' of palatable foods.

In humans, subjective liking can be assessed by questionnaires and visual-analog scales. In the "Power of Food Scale" (PFS), appetite for palatable food items is estimated by asking subjects how much they would like to eat certain foods when they were available, when they are present in front of their eyes, and when they are actually tasted, but not ingested [8]. These three levels of proximity clearly generate different neural response patterns, involving more or less visual, taste, and olfactory processing. To consciously experience and give subjective ratings of pleasure from palatable foods (liking), humans very likely use areas in the prefrontal and cingulate cortex [9].

Another component of reward is motivation or 'wanting'. Typically, motivation comes to fruition by "going for" something that has generated pleasure in the past through a learning process – wanting what we like. However, wanting can also be dissociated from liking as demonstrated by sodium-depleted rats 'wanting' hypertonic saline, a taste they had never 'liked' before and also by drug addicts that do no longer 'like' to inject themselves [10,11]. Dopamine signaling within the mesolimbic dopamine projection system appears to be a crucial component of this process. Phasic activity of dopamine neuron projections from the ventral tegmental area to the nucleus accumbens in the ventral striatum are specifically involved in the decision-making process during the preparatory (appetitive) phase of ingestive behavior [12,13]. In addition, when palatable foods such as sucrose are actually consumed, a sustained and sweetness-dependent increase occurs in nucleus accumbens dopamine levels and turnover [14–16]. Dopamine signaling in the nucleus accumbens thus appears to play a role in both the preparatory and consummatory phases of an ingestive bout. The nucleus accumbens shell is thereby part of a neural loop including the lateral hypothalamus and the ventral tegmental area, with orexin neurons playing a key role [2,17–24]. This loop is likely important for the attribution of incentive salience to goal objects by metabolic state and other need signals available to the lateral hypothalamus, as discussed below.

2. Obesity is associated with alterations in taste-related food reward behaviors and neural functions

It has long been suggested that, compared to normal weight subjects, obese subjects are more sensitive to external (e.g. availability, clock, social context) rather than internal (e.g. metabolites and hormones) signals related to the control of food intake [25,26], but the cause and effect was not clear. Some of these investigators demonstrated that weight loss did not change responses to visual and cognitive cue salience manipulation but that it did change responsiveness to taste stimuli [27], suggesting that the former might be caused by preexisting factors contributing to the development of obesity, while changes in taste responsiveness might be influenced by the obese state. Since then, the hypothesis was supported by some investigators [28–32], but not by others [33–35]. In one study, the use of visual signal detection theory methodology showed that while there was no difference in sensory sensitivity between obese and normal weight subjects, obese subjects had consistently lower response bias [36].

The notion that responsiveness to taste stimuli is influenced by the obese state [27] coincided with the first descriptions of cafeteria diet-induced hyperphagia and obesity in rodents [37] and the idea that the palatability of a diet controls the body weight "set point' [38]. Although there are inconsistencies in the recent literature concerning the relationship between body weight, taste responsiveness, and sugar consumption [39–41], it is possible that obesity-induced or preexisting alterations in taste responsiveness and its associated changes in brain reward processing could contribute to increased food intake and obesity. Consistent with this idea are a number of observations in humans and rodents. For example, there were weak but significant positive correlations between the maximal hedonic response to taste stimuli at baseline and weight gain over the next 5 years in obesity-prone Pima Indians [42]. In animal studies, we have shown that high-fat diet-induced obese Sprague-Dawley rats shift sucrose and corn oil preference towards higher concentrations compared to chow-fed lean controls [43]. Similarly, obese OLETF rats show greater preference for high sucrose concentrations and less preference for low concentrations compared to lean control rats [44], and taste neurons in the parabrachial nucleus of obese rats also showed a rightward-shift of the sucrose concentration-response curve [45]. There is also a rapidly increasing number of neuroimaging studies in obese humans showing altered neural processing in brain areas associated with taste processing and reward functions (e.g. [46–52] (and see [53] for recent review).

In summary, existing evidence suggests that obesity is associated with alterations in taste responsiveness and reward functions. Specifically taste responsiveness and reward generation appear to be blunted in the obese compared with normal weight subjects [43–45,49,52]. But the cause and effect is not clear.

3. Effects of calorie-restriction-induced weight loss on taste responsiveness and food preferences

A simple initial approach to the question about cause or consequence is to test whether obesity-associated alterations (compared with normal weight) can be reversed by weight loss. Alterations that are reversed are more likely caused by secondary effects of the obese state, while alterations not reversed are more likely preexisting traits that may partly be causing obesity. It is clear that if non-reversible alterations are found, they need to be further examined to distinguish true causative traits from irreversible secondary effects of the obese state. Such additional preclinical and clinical approaches may include longitudinal studies, particularly studies starting at an early age before there are any signs of obesity, and

reassessment after development of obesity, as well as interventional studies testing specific candidate mechanisms. To identify the role of early-life nutritional programing via epigenetic and non-genetic mechanisms, studies in rodents have demonstrated that a maternal high-fat diet can dysregulate neural systems involved in food reward in the offspring [54–56]. Because of logistical problems with testing children at an early age and the high costs of longitudinal studies, only few reports can be found in the literature. For example, intensity ratings for sweetness in children of obese parents increased, with a similar trend for rating of fatness [57]. After 6 months of family-based behavioral weight loss treatment, obese but not normal weight children lost weight, reduced liking of foods high in fat and/or sugar, and showed increased rating for foods lower in fat and sugar [57]. The findings suggest that weight loss reversed the obesity-induced shift in preference towards highly sweet and fatty foods, and emphasize the importance of testing a range of concentrations. Similarly, after a 10 month weight reduction regimen, liking of fruits and vegetables, breakfast foods, and calorie-reduced foods increased significantly, whereas liking of animal products (presumably higher in fat and calories) decreased. Thus, liking and presumably intake of low fat foods was positively and liking of high-fat foods was negatively correlated with the decrease in body mass index [58]. Also, dieters, that could be considered in a weight reduced state, rated high concentrations of sucrose solutions less pleasant than non-dieters, both before and after an oral glucose load [59]. Finally, after 12 weeks of calorie-restriction-induced weight loss in Japanese women, sucrose sweet taste threshold decreased from 0.59% to 0.22% and was correlated to the decrease in serum leptin levels [60]. When using a relative scale for measuring sweet taste sensation, which takes into consideration individual differences in the strongest sensation of any kind, it was concluded that obese individuals report higher liking ratings for a given sweetness than normal weight subjects, in spite of decreased perceived sweetness [61]. Thus, liking as a function of sweetness increases more in obese subjects and more the higher the body mass index is. While in underweight individuals (BMI < 18.5) there was no increase in liking with increasing sweetness, but liking was particularly strong for high sweetness in the obese [61]. That obese subjects have reduced sweet taste perception has recently been confirmed [62], but instead of significantly increased liking of sweet taste stimuli, these authors found increased implicit attitude or ‘wanting’ towards sweet stimuli.

Studies in rodents yield similar observations. We have completed a series of studies in outbred and genetically selected lines of obesity-prone (OP) and obesity-resistant (OR) Sprague-Dawley rats [43]. We first compared chow-fed, lean with high-fat-fed, obese rats as verified by measurements of body composition and circulating leptin levels. We found that the obese rats shifted their sucrose and corn oil preference towards higher concentrations compared with the lean rats, as measured by the brief access (10 s) lick test in the Davis Rig. Specifically, obese rats licked significantly less for 0.01 and 0.03 M (0.34 and 1.02 %) sucrose and for 0.06 – 4% corn oil, but licked significantly more for 0.3 and 1 M (10 and 34%) sucrose and for 64% corn oil [43]. We then calorie-restricted another cohort of high-fat diet-induced obese rats by providing about 50% of the normal daily ration of high-fat diet before dark-onset for 3 weeks and kept them at a reduced body weight ~100 g below their obese level (and not significantly different from chow-fed rats) for another 2 weeks, by providing about 70% of their pre-restriction level. Reassessment of brief access lick performance during this weight-reduced plateau showed almost complete reversal of the obesity-induced right shift of the concentration-response curves for both sucrose and corn oil. In other words, weight-reduced rats behaved very similar to never obese, chow-fed rats, suggesting that the alterations in the obese rats were secondary to the obese state and fully reversible. The reversibility of the phenotype was further underscored by a renewed right-shift when the restricted animals were again allowed unlimited access to high-fat diet [43].

In separate experiments, we examined the effects of acute food deprivation and, although food deprivation generally increased lick performance, the significantly lesser licking for low concentrations of both tastants in obese rats was preserved [43]. These data suggest that the signal responsible for the reversal of lick performance after weight loss is different from signals generated by acute food deprivation. Because circulating leptin levels are proportional to adiposity, and leptin has been shown to directly affect taste receptor cells (see [63] for recent review), it is possible that a direct action of leptin on taste receptor function underlies these changes in taste responsiveness. We thus administered leptin (1 mg/kg, i.p.) or saline to our weight-reduced, formerly obese rats, 1-h before brief access testing. As mentioned above, after control saline administration, these weight-reduced rats licked the low sucrose and corn oil concentrations very eagerly, not much different from lean rats. After leptin administration, the concentration-response curve was shifted to the right, towards that seen in the obese state. Leptin significantly reduced responding to the lowest sucrose and corn oil concentrations, but did not affect licking of the higher concentrations [43]. Although consistent with a direct action of leptin on taste buds [64], these findings do not rule out leptin action in the brain. That leptin can act in the brain, possibly on the mesolimbic dopamine system to modulate food reward in general, and sweet reward specifically, is suggested by a number of studies [65–68]. Most recently, using optogenetic stimulation of dopamine neurons, it was demonstrated that leptin administration to the brain reverses the fasting-induced increase in the value of sucrose [68]. However, there are other potential signaling mechanisms besides leptin that could influence the rewarding effect of palatable foods under conditions of obesity and weight loss. For example, circulating levels of both insulin and the lower gut hormone GLP-1 are affected by obesity [69], and both have been shown to modulate reward functions [70,71]. It is also known that GLP-1 can directly modulate taste receptor cells, but it is not clear whether this is due circulating or locally produced GLP-1 [72].

Interestingly, and in stark contrast to self- or experimenter-imposed caloric restriction, patients with anorexia nervosa [73] or anorexia secondary to cancer [74,75] or cancer treatment therapies [76–78], have generally lower gustatory and olfactory sensitivities that improve with weight recovery and increasing body mass index. These observations suggest fundamentally different mechanisms for causing the taste alterations.

4. Effects of bariatric surgery on taste responsiveness and food reward functions

Given the difficulties in developing effective drugs, bariatric surgery has rapidly advanced to the most effective treatment of obesity, and the volume of surgeries has steadily increased [79]. Compared with available drugs and/or behavior and lifestyle changes, weight loss after bariatric surgeries is more profound and sustained. For example, in the Swedish Obese Subjects (SOS) study, average sustained weight loss, 15 years after Roux-en-Y gastric bypass surgery, was 25%, while the mean weight change in an unoperated control group was less than +/− 2% [80,81]. It also improved all traditional risk factors for diabetes and cardiovascular disease and decreased overall mortality.

It appears that weight loss induced by bariatric surgery does not trigger the same strong biological adaptive responses seen with dieting - decreased energy expenditure and increased hunger [82]. Current hypotheses propose increased secretion of the lower gut hormones GLP-1 and PYY as well as decreased levels of ghrelin and their actions on peripheral tissues and on the brain as major candidate mechanisms in the beneficial effects of at least Roux-en-Y gastric bypass surgery (e.g. [69,83,84]. It has been demonstrated that these hormones have powerful effects on neural circuits controlling food intake through homeostatic and non-homeostatic mechanisms (see [85] for recent review).

The first indication that bariatric surgery might reduce food intake by effects on taste responsiveness came from a study in severely obese subjects undergoing intestinal bypass surgery, leaving the gastric volume intact [86]. One year post-surgery, patients had lost about half of their body weight (~ 70kg) and reported daily calorie intake that was about half of the pre-surgical level. They rated the pleasantness of 40% sucrose solution lower than before surgery and lower compared to 10% sucrose, and this was not changed by a glucose load before the taste test [86]. More recent studies using Roux-en-Y gastric bypass showed that intake of sweets and high-calorie beverages, as well as milk and ice cream, was decreased at 6 and 24 months postsurgery, and to a lesser extent after gastroplasty [87]. In another study, the recognition threshold for sucrose fell from 0.047 mol/L (1.6%) to 0.024 mol/L (0.8%) at 6 weeks, and 0.019 (0.65%) at12 weeks postoperatively [88]. At 6 weeks postoperatively, all patients reported that foods tasted sweeter and they modified food selection accordingly [88]. There was also a trend for reduced taste acuity for sweet and salt as well as increased taste acuity of bitter and sour in a similar study [89]. A decreased preference for fatty foods was also noted after RYGB [90–92]. In a recent study, RYGB patients showed increased taste sensitivity to low sucrose concentrations compared to normal weight controls, but they both considered the same sucrose concentration as “just about right’ [93].

The observations in bariatric surgery patients prompted us to further examine taste responsiveness and other food reward behaviors in our RYGB rat model, eventually allowing more invasive analyses of the underlying mechanisms [94]. Using the brief access lick test described above, we found that 3–5 months after RYGB surgery, the concentration-response curves for sucrose and corn oil were not much different from chow-fed lean rats, except that after RYGB there was a tendency for reduced licking at the highest concentrations [95]. Similar RYGB-induced left-shifts in the concentration-response curves for sucrose and corn oil were also observed in genetically select obesity-prone rats [95]. Thus, RYGB and calorie-restriction (see section 2 above) had very similar effects on taste responsiveness as measured by the brief access test, suggesting that weight loss and its consequences, such as reduced leptin levels, may be the major common mechanism.

While in humans, the hedonic value or ‘liking’ of taste stimuli or foods can be assessed by explicit questioning, in non-humans, we can only measure implicit ‘liking’, e.g. by the taste reactivity test that quantitates the positive hedonic orofacial reactions to the taste of sucrose [96,97]. In this test, the sham-operated obese rats showed a right shift of the sucrose concentration-response curve, with obese rats liking the lowest sucrose concentration significantly less, but liking the highest sucrose concentration significantly more than chow-fed lean rats [95]. The results obtained with the brief access test and the taste reactivity test thus were similar. Three months after RYGB, the concentration-response curve shifted back to the left. RYGB rats liked the lowest sucrose concentration of 0.01 M significantly more than both sham-operated and chow-fed lean rats, but liked the highest concentration of 1 M significantly less than the sham-operated obese rats. In fact, they liked all three sucrose concentrations tested (0.01, 0.1, and 1.0 M) at an equally moderate level [95].

Our observations have recently been confirmed in other laboratories. Compared with sham-operated rats, RYGB in obese OLETF rats reduces brief access lick performance and 24-h two bottle sucrose preference for the highest sucrose concentrations [98]. Similarly, one month after RYGB in chow-fed Sprague-Dawley rats, there was significant decrease in lick performance for the highest, but not the lowest sucrose concentrations [99]. At the neuronal level, there was a rightward-shift of the concentration-response curve of recorded pontine parabrachial taste neurons after RYGB in OLETF rats [98]. Together, these findings confirm obesity-related alterations in taste functions and the ability of RYGB to reverse these impairments [98].

As discussed above, changes in taste sensitivity in bypass patients seem to translate into long-term changes in food preferences [88,90–92]. Can such changes in food selection also be demonstrated in rodent models of bypass surgery? We provided RYGB and sham-operated rats with a choice of two nutritionally complete diets, one low (10%) in fat and one high (30% of energy) in fat. When two solid diets were available throughout the postsurgical period starting one month after surgery, we observed a gradual decrease in fat preference after RYGB [94]. Preference for a solid high-fat (60% energy) diet before surgery and in sham-operated rats is generally between 95–100%, whereas after RYGB, preference decreased to about 85% at 2 months, and to between 50–60% at 5–8 months postoperatively [94,95]. Similarly, preference for a liquid high-fat diet as assessed in 12-h tests, was only 20% at 5 months after RYGB compared to 55% in sham-operated rats [94]. Together, these results demonstrate that like humans, rats with gastric bypass surgery change their eating habits by choosing less fatty and energy-dense foods, although the exact mechanisms involved remain to be identified.

5. Conclusions and Perspectives

Healthy eating is an important strategy in preventing and treating chronic diseases, yet we do not fully understand the physiological and psychological factors determining optimal food choice. Taste sensitivity, the hedonic response to taste (palatability), and the reinforcing value of taste are among these factors. The relationship between obesity and these factors is reciprocal, with high palatability assisting hyperphagia and possibly obesity, and the obese state secondarily altering taste sensitivity and hedonic processing. A review of the literature suggests that in general, obese humans and rodents are less resoponsive to sweet and fatty tastes and shift their preference to higher concentrations, thus further aggravating hyperphagia. Furthermore, reversibility of this right-shift in the concentration-response curve after weight loss suggests that it is due to secondary effects of the obese state and is not necessarily a preexisting trait.

Understanding the behavioral alterations associated with obesity, weight loss, and bariatric surgery is just the first step. An important second step is to understand the underlying mechanisms. Because of space limitations, the above discussion has offered little information regarding potential underlying mechanisms. Ultimately motivation and behavioral choices, including the selection of foods, are guided by a complex neural circuitry extending through most of the brain [100]. In particular, the midbrain dopamine system, with its projections to the ventral and dorsal striatum, prefrontal cortex, amygdala, hippocampus, and hypothalamus has been suggested to encode economic value of different actions and the best option in a given situation [101,102]. This system appears to be crucial for calculating the value of a particular food and making optimal decisions under given circumstances [1]. It also provides the strong motivation or implicit wanting to obtain a goal object such as palatable food. Operating at mostly subconscious levels, implicit wanting is difficult to suppress with “will power”, as demonstrated in alcohol and drug abuse.

However, whether implicit wanting of palatable food is neurologically equal to the self-destructive wanting of drugs remains to be determined. How this system interacts with metabolic signals and the homeostatic regulatory systems in the brainstem and medial hypothalamus has been recently reviewed [103,104]. Because leptin levels are closely correlated with these body weight-dependent changes and are known to modulate taste processing, leptin signaling is a potential mechanism. However, other changes in hormone signaling, as well as changes in central proinflammatory signaling associated with obesity and high-fat diets [105] are likely to play a role. An exciting prospect is that bariatric surgeries may impinge on mechanisms of taste sensitivity and hedonic processing to produce their powerful beneficial effects on body weight and chronic disease progression.

However, the weight loss-independent contributions of such surgeries on taste perception, hedonic processing, and reward generation remain to be demonstrated.

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References

1. Kelley AE, Berridge KC. The neuroscience of natural rewards: relevance to addictive drugs. J Neurosci. 2002; 22(9):3306–11. [PubMed: 11978804]
2. Liedtke WB, McKinley MJ, Walker LL, Zhang H, Pfenning AR, Drago J, Hochendoner SJ, Hilton DL, Lawrence AJ, Denton DA. Relation of addiction genes to hypothalamic gene changes subserving genesis and gratification of a classic instinct, sodium appetite. Proceedings of the National Academy of Sciences of the United States of America. 2011; 108(30):12509–14. [PubMed: 21746918]
3. Berthoud H-R. Multiple neural systems controlling food intake and body weight. Neuroscience & Biobehavioral Reviews. 2002; 26(4):393–428. [PubMed: 12204189]
4. Smith GP. The direct and indirect controls of meal size. Neurosci Biobehav Rev. 1996; 20(1):41–6. [PubMed: 8622828]
5. Berridge KC, Robinson TE. Parsing reward. Trends Neurosci. 2003; 26(9):507–13. [PubMed: 12948663]
6. Grill HJ, Norgren R. The taste reactivity test. II. Mimetic responses to gustatory stimuli in chronic thalamic and chronic decerebrate rats. Brain Res. 1978; 143(2):281–97. [PubMed: 630410]
7. Steiner, JE. The gustofacial response: observations on normal and anancephalic newborn infants. Bosma, JF., editor. Bethesda: U. S. Department of Health, Education, and Welfare; 1973. p. 125-167.
8. Lowe MR, Butryn ML, Didie ER, Annunziato RA, Thomas JG, Crerand CE, Ochner CN, Coletta MC, Bellace D, Wallaert M, et al. The Power of Food Scale. A new measure of the psychological influence of the food environment. Appetite. 2009; 53(1):114–8. [PubMed: 19500623]
9. Kringelbach ML. Food for thought: hedonic experience beyond homeostasis in the human brain. Neuroscience. 2004; 126(4):807–19. [PubMed: 15207316]
10. Wyvell CL, Berridge KC. Intra-accumbens amphetamine increases the conditioned incentive salience of sucrose reward: enhancement of reward "wanting" without enhanced "liking" or response reinforcement. J Neurosci. 2000; 20(21):8122–30. [PubMed: 11050134]
11. Tindell AJ, Smith KS, Berridge KC, Aldridge JW. Dynamic computation of incentive salience: "wanting" what was never "liked". J Neurosci. 2009; 29(39):12220–8. [PubMed: 19793980]
12. Schultz W, Dayan P, Montague PR. A neural substrate of prediction and reward. Science. 1997; 275(5306):1593–9. [PubMed: 9054347]
13. Carelli RM. The nucleus accumbens and reward: neurophysiological investigations in behaving animals. Behav Cogn Neurosci Rev. 2002; 1(4):281–96. [PubMed: 17712985]
14. Hernandez L, Hoebel BG. Feeding and hypothalamic stimulation increase dopamine turnover in the accumbens. Physiol Behav. 1988; 44(4–5):599–606. [PubMed: 3237847]
15. Hajnal A, Smith GP, Norgren R. Oral sucrose stimulation increases accumbens dopamine in the rat. Am J Physiol Regul Integr Comp Physiol. 2004; 286(1):R31–7. [PubMed: 12933362]
16. Smith GP. Accumbens dopamine mediates the rewarding effect of orosensory stimulation by sucrose. Appetite. 2004; 43(1):11–3. [PubMed: 15262012]
17. Stratford TR, Kelley AE. Evidence of a functional relationship between the nucleus accumbens shell and lateral hypothalamus subserving the control of feeding behavior. J Neurosci. 1999; 19(24):11040–8. [PubMed: 10594084]
18. Zheng H, Patterson LM, Berthoud HR. Orexin signaling in the ventral tegmental area is required for high-fat appetite induced by opioid stimulation of the nucleus accumbens. J Neurosci. 2007; 27(41):11075–82. [PubMed: 17928449]

19. Harris GC, Wimmer M, Aston-Jones G. A role for lateral hypothalamic orexin neurons in reward seeking. Nature. 2005; 437(7058):556–9. [PubMed: 16100511]
20. Peyron C, Tighe DK, van den Pol AN, de Lecea L, Heller HC, Sutcliffe JG, Kilduff TS. Neurons containing hypocretin (orexin) project to multiple neuronal systems. J Neurosci. 1998; 18(23): 9996–10015. [PubMed: 9822755]
21. Nakamura T, Uramura K, Nambu T, Yada T, Goto K, Yanagisawa M, Sakurai T. Orexin-induced hyperlocomotion and stereotypy are mediated by the dopaminergic system. Brain Res. 2000; 873(1):181–7. [PubMed: 10915829]
22. Balcita-Pedicino JJ, Sesack SR. Orexin axons in the rat ventral tegmental area synapse infrequently onto dopamine and gamma-aminobutyric acid neurons. J Comp Neurol. 2007; 503(5):668–684. [PubMed: 17559101]
23. Korotkova TM, Sergeeva OA, Eriksson KS, Haas HL, Brown RE. Excitation of ventral tegmental area dopaminergic and nondopaminergic neurons by orexins/hypocretins. J Neurosci. 2003; 23(1): 7–11. [PubMed: 12514194]
24. Borgland SL, Taha SA, Sarti F, Fields HL, Bonci A. Orexin A in the VTA is critical for the induction of synaptic plasticity and behavioral sensitization to cocaine. Neuron. 2006; 49(4):589–601. [PubMed: 16476667]
25. Schachter S. Obesity and eating. Internal and external cues differentially affect the eating behavior of obese and normal subjects. Science. 1968; 161(3843):751–6. [PubMed: 5663800]
26. Rodin J, Slochower J. Externality in the nonobese: effects of environmental responsiveness on weight. Journal of Personality and Social Psychology. 1976; 33(3):338–44. [PubMed: 1271215]
27. Rodin J, Slochower J, Fleming B. Effects of degree of obesity, age of onset, and weight loss on responsiveness to sensory and external stimuli. Journal of Comparative and Physiological Psychology. 1977; 91(3):586–97. [PubMed: 874124]
28. Costanzo PR, Woody EZ. Externality as a function of obesity in children: pervasive style or eating-specific attribute? Journal of Personality and Social Psychology. 1979; 37(12):2286–96. [PubMed: 529014]
29. Sobhany MS, Rogers CS. External responsiveness to food and non-food cues among obese and non-obese children. International Journal of Obesity. 1985; 9(2):99–106. [PubMed: 4030200]
30. Burton P, Smit HJ, Lightowler HJ. The influence of restrained and external eating patterns on overeating. Appetite. 2007; 49(1):191–7. [PubMed: 17349717]
31. Wansink B, Payne CR, Chandon P. Internal and external cues of meal cessation: the French paradox redux? Obesity (Silver Spring). 2007; 15(12):2920–4. [PubMed: 18198299]
32. Herman CP, Olmsted MP, Polivy J. Obesity, externality, and susceptibility to social influence: an integrated analysis. Journal of Personality and Social Psychology. 1983; 45(4):926–34. [PubMed: 6631668]
33. Isbitsky JR, White DR. Externality and locus of control in obese children. Journal of Psychology. 1981; 107(pt 2):163–72. [PubMed: 7230082]
34. Stager SF. Externality, environment, and obesity in children. Journal of General Psychology. 1981; 105(1st Half):141–7. [PubMed: 7264615]
35. Meyers AW, Stunkard AJ, Coll M. Food accessibility and food choice. A test of Schachter's externality hypothesis. Archives of General Psychiatry. 1980; 37(10):1133–5. [PubMed: 7425797]
36. Gardner RM, Brake SJ, Reyes B, Maestas D. Sensory and non-sensory factors and the concept of externality in obese subjects. Perceptual and Motor Skills. 1983; 57(1):247–54. [PubMed: 6622165]
37. Sclafani A, Springer D. Dietary obesity in adult rats: similarities to hypothalamic and human obesity syndromes. Physiol Behav. 1976; 17(3):461–71. [PubMed: 1013192]
38. Cabanac M, Rabe EF. Influence of a monotonous food on body weight regulation in humans. Physiology and Behavior. 1976; 17(4):675–8. [PubMed: 1013218]
39. Donaldson LF, Bennett L, Baic S, Melichar JK. Taste and weight: is there a link? American Journal of Clinical Nutrition. 2009; 90(3):800S–803S. [PubMed: 19571216]
40. Drewnowski A, Bellisle F. Liquid calories, sugar, and body weight. American Journal of Clinical Nutrition. 2007; 85(3):651–61. [PubMed: 17344485]

41. Frijters JE, Rasmussen-Conrad EL. Sensory discrimination, intensity perception, and affective judgment of sucrose-sweetness in the overweight. Journal of General Psychology. 1982; 107(2d Half):233–47. [PubMed: 7175511]
42. Salbe AD, DelParigi A, Pratley RE, Drewnowski A, Tataranni PA. Taste preferences and body weight changes in an obesity-prone population. American Journal of Clinical Nutrition. 2004; 79(3):372–8. [PubMed: 14985209]
43. Shin AC, Townsend RL, Patterson LM, Berthoud HR. "Liking" and "wanting" of sweet and oily food stimuli as affected by high-fat diet-induced obesity, weight loss, leptin, and genetic predisposition. Am J Physiol Regul Integr Comp Physiol. 2011; 301(5):R1267–80. [PubMed: 21849633]
44. De Jonghe BC, Hajnal A, Covasa M. Increased oral and decreased intestinal sensitivity to sucrose in obese, prediabetic CCK-A receptor-deficient OLETF rats. Am J Physiol Regul Integr Comp Physiol. 2005; 288(1):R292–300. [PubMed: 15358606]
45. Hajnal A, Norgren R, Kovacs P. Parabrachial coding of sapid sucrose: relevance to reward and obesity. Ann N Y Acad Sci. 2009; 1170:347–64. [PubMed: 19686159]
46. Del Parigi A, Gautier JF, Chen K, Salbe AD, Ravussin E, Reiman E, Tataranni PA. Neuroimaging and obesity: mapping the brain responses to hunger and satiation in humans using positron emission tomography. Ann N Y Acad Sci. 2002; 967:389–97. [PubMed: 12079866]
47. Rothemund Y, Preuschhof C, Bohner G, Bauknecht HC, Klingebiel R, Flor H, Klapp BF. Differential activation of the dorsal striatum by high-calorie visual food stimuli in obese individuals. Neuroimage. 2007; 37(2):410–21. [PubMed: 17566768]
48. Stoeckel LE, Weller RE, Cook EW 3rd, Twieg DB, Knowlton RC, Cox JE. Widespread reward-system activation in obese women in response to pictures of high-calorie foods. Neuroimage. 2008; 41(2):636–47. [PubMed: 18413289]
49. Stice E, Spoor S, Bohon C, Veldhuizen MG, Small DM. Relation of reward from food intake and anticipated food intake to obesity: a functional magnetic resonance imaging study. J Abnorm Psychol. 2008; 117(4):924–35. [PubMed: 19025237]
50. Cornier MA, Von Kaenel SS, Bessesen DH, Tregellas JR. Effects of overfeeding on the neuronal response to visual food cues. Am J Clin Nutr. 2007; 86(4):965–71. [PubMed: 17921372]
51. Castellanos EH, Charboneau E, Dietrich MS, Park S, Bradley BP, Mogg K, Cowan RL. Obese adults have visual attention bias for food cue images: evidence for altered reward system function. Int J Obes (Lond). 2009; 33(9):1063–73. [PubMed: 19621020]
52. Wang GJ, Volkow ND, Thanos PK, Fowler JS. Similarity between obesity and drug addiction as assessed by neurofunctional imaging: a concept review. J Addict Dis. 2004; 23(3):39–53. [PubMed: 15256343]
53. Carnell S, Gibson C, Benson L, Ochner CN, Geliebter A. Neuroimaging and obesity: current knowledge and future directions. Obes Rev. 2012; 13(1):43–56. [PubMed: 21902800]
54. Vucetic Z, Kimmel J, Reyes TM. Chronic high-fat diet drives postnatal epigenetic regulation of mu-opioid receptor in the brain. Neuropsychopharmacology. 2011; 36(6):1199–206. [PubMed: 21326195]
55. Vucetic Z, Kimmel J, Totoki K, Hollenbeck E, Reyes TM. Maternal high-fat diet alters methylation and gene expression of dopamine and opioid-related genes. Endocrinology. 2010; 151(10):4756–64. [PubMed: 20685869]
56. Vucetic Z, Carlin JL, Totoki K, Reyes TM. Epigenetic dysregulation of the dopamine system in diet-induced obesity. Journal of Neurochemistry. 2012; 120(6):891–8. [PubMed: 22220805]
57. Epstein LH, Valoski A, Wing RR, Perkins KA, Fernstrom M, Marks B, McCurley J. Perception of eating and exercise in children as a function of child and parent weight status. Appetite. 1989; 12(2):105–18. [PubMed: 2764552]
58. Monneuse MO, Rigal N, Frelut ML, Hladik CM, Simmen B, Pasquet P. Taste acuity of obese adolescents and changes in food neophobia and food preferences during a weight reduction session. Appetite. 2008; 50(2–3):302–7. [PubMed: 17904687]
59. Esses VM, Herman CP. Palatability of sucrose before and after glucose ingestion in dieters and nondieters. Physiology and Behavior. 1984; 32(5):711–5. [PubMed: 6494275]

60. Umabiki M, Tsuzaki K, Kotani K, Nagai N, Sano Y, Matsuoka Y, Kitaoka K, Okami Y, Sakane N, Higashi A. The improvement of sweet taste sensitivity with decrease in serum leptin levels during weight loss in obese females. Tohoku Journal of Experimental Medicine. 2010; 220(4):267–71. [PubMed: 20383037]
61. Bartoshuk LM, Duffy VB, Hayes JE, Moskowitz HR, Snyder DJ. Psychophysics of sweet and fat perception in obesity: problems, solutions and new perspectives. Philos Trans R Soc Lond B Biol Sci. 2006; 361(1471):1137–48. [PubMed: 16815797]
62. Sartor F, Donaldson LF, Markland DA, Loveday H, Jackson MJ, Kubis HP. Taste perception and implicit attitude toward sweet related to body mass index and soft drink supplementation. Appetite. 2011; 57(1):237–46. [PubMed: 21600942]
63. Niki M, Jyotaki M, Yoshida R, Ninomiya Y. Reciprocal modulation of sweet taste by leptin and endocannabinoids. Results and Problems in Cell Differentiation. 2010; 52:101–14. [PubMed: 20865375]
64. Shigemura N, Ohta R, Kusakabe Y, Miura H, Hino A, Koyano K, Nakashima K, Ninomiya Y. Leptin modulates behavioral responses to sweet substances by influencing peripheral taste structures. Endocrinology. 2004; 145(2):839–47. [PubMed: 14592964]
65. Figlewicz DP. Adiposity signals and food reward: expanding the CNS roles of insulin and leptin. Am J Physiol Regul Integr Comp Physiol. 2003; 284(4):R882–92. [PubMed: 12626355]
66. Hommel JD, Trinko R, Sears RM, Georgescu D, Liu ZW, Gao XB, Thurmon JJ, Marinelli M, DiLeone RJ. Leptin receptor signaling in midbrain dopamine neurons regulates feeding. Neuron. 2006; 51(6):801–10. [PubMed: 16982424]
67. Fulton S, Pissios P, Manchon RP, Stiles L, Frank L, Pothos EN, Maratos-Flier E, Flier JS. Leptin regulation of the mesoaccumbens dopamine pathway. Neuron. 2006; 51(6):811–22. [PubMed: 16982425]
68. Domingos AI, Vaynshteyn J, Voss HU, Ren X, Gradinaru V, Zang F, Deisseroth K, de Araujo IE, Friedman J. Leptin regulates the reward value of nutrient. Nature Neuroscience. 2011; 14(12): 1562–8.
69. le Roux CW, Welbourn R, Werling M, Osborne A, Kokkinos A, Laurenius A, Lonroth H, Fandriks L, Ghatei MA, Bloom SR, et al. Gut hormones as mediators of appetite and weight loss after Roux-en-Y gastric bypass. Ann Surg. 2007; 246(5):780–5. [PubMed: 17968169]
70. Dossat AM, Lilly N, Kay K, Williams DL. Glucagon-like peptide 1 receptors in nucleus accumbens affect food intake. Journal of Neuroscience. 2011; 31(41):14453–7. [PubMed: 21994361]
71. Konner AC, Hess S, Tovar S, Mesaros A, Sanchez-Lasheras C, Evers N, Verhagen LA, Bronneke HS, Kleinridders A, Hampel B, et al. Role for insulin signaling in catecholaminergic neurons in control of energy homeostasis. Cell Metab. 2011; 13(6):720–8. [PubMed: 21641553]
72. Shin YK, Martin B, Golden E, Dotson CD, Maudsley S, Kim W, Jang HJ, Mattson MP, Drucker DJ, Egan JM, et al. Modulation of taste sensitivity by GLP-1 signaling. J Neurochem. 2008
73. Aschenbrenner K, Scholze N, Joraschky P, Hummel T. Gustatory and olfactory sensitivity in patients with anorexia and bulimia in the course of treatment. Journal of Psychiatric Research. 2008; 43(2):129–37. [PubMed: 18423668]
74. DeWys WD, Walters K. Abnormalities of taste sensation in cancer patients. Cancer. 1975; 36(5): 1888–96. [PubMed: 1192373]
75. Hutton JL, Baracos VE, Wismer WV. Chemosensory dysfunction is a primary factor in the evolution of declining nutritional status and quality of life in patients with advanced cancer. Journal of Pain and Symptom Management. 2007; 33(2):156–65. [PubMed: 17280921]
76. Ruo Redda MG, Allis S. Radiotherapy-induced taste impairment. Cancer Treatment Reviews. 2006; 32(7):541–7. [PubMed: 16887272]
77. Steinbach S, Hummel T, Bohner C, Berktold S, Hundt W, Kriner M, Heinrich P, Sommer H, Hanusch C, Prechtl A, et al. Qualitative and quantitative assessment of taste and smell changes in patients undergoing chemotherapy for breast cancer or gynecologic malignancies. Journal of Clinical Oncology. 2009; 27(11):1899–905. [PubMed: 19289621]

78. Sanchez-Lara K, Sosa-Sanchez R, Green-Renner D, Rodriguez C, Laviano A, Motola-Kuba D, Arrieta O. Influence of taste disorders on dietary behaviors in cancer patients under chemotherapy. Nutr J. 2010; 9:15. [PubMed: 20334666]

79. Eldar S, Heneghan HM, Brethauer SA, Schauer PR. Bariatric surgery for treatment of obesity. Int J Obes (Lond). 2011; 35 (Suppl 3):S16–21. [PubMed: 21912381]

80. Sjostrom L. Bariatric surgery and reduction in morbidity and mortality: experiences from the SOS study. Int J Obes (Lond). 2008; 32 (Suppl 7):S93–7. [PubMed: 19136998]

81. Sjostrom L, Peltonen M, Jacobson P, Sjostrom CD, Karason K, Wedel H, Ahlin S, Anveden A, Bengtsson C, Bergmark G, et al. Bariatric surgery and long-term cardiovascular events. JAMA. 2012; 307(1):56–65. [PubMed: 22215166]

82. Redman LM, Heilbronn LK, Martin CK, de Jonge L, Williamson DA, Delany JP, Ravussin E. Metabolic and behavioral compensations in response to caloric restriction: implications for the maintenance of weight loss. PLoS ONE. 2009; 4(2):e4377. [PubMed: 19198647]

83. Berthoud HR, Shin AC, Zheng H. Obesity surgery and gut-brain communication. Physiology and Behavior. 2011

84. Morinigo R, Moize V, Musri M, Lacy AM, Navarro S, Marin JL, Delgado S, Casamitjana R, Vidal J. Glucagon-like peptide-1, peptide YY, hunger, and satiety after gastric bypass surgery in morbidly obese subjects. J Clin Endocrinol Metab. 2006; 91(5):1735–40. [PubMed: 16478824]

85. Moran TH. Gut peptides in the control of food intake. Int J Obes (Lond). 2009; 33 (Suppl 1):S7–10. [PubMed: 19363513]

86. Bray GA, Barry RE, Benfield JR, Castelnuovo-Tedesco P, Rodin J. Intestinal bypass surgery for obesity decreases food intake and taste preferences. Am J Clin Nutr. 1976; 29(7):779–83. [PubMed: 937232]

87. Kenler HA, Brolin RE, Cody RP. Changes in eating behavior after horizontal gastroplasty and Roux-en-Y gastric bypass. Am J Clin Nutr. 1990; 52(1):87–92. [PubMed: 2360554]

88. Burge JC, Schaumburg JZ, Choban PS, DiSilvestro RA, Flancbaum L. Changes in patients' taste acuity after Roux-en-Y gastric bypass for clinically severe obesity. J Am Diet Assoc. 1995; 95(6): 666–70. [PubMed: 7759742]

89. Scruggs DM, Buffington C, Cowan GS Jr. Taste Acuity of the Morbidly Obese before and after Gastric Bypass Surgery. Obes Surg. 1994; 4(1):24–28. [PubMed: 10742759]

90. Thirlby RC, Bahiraei F, Randall J, Drewnoski A. Effect of Roux-en-Y gastric bypass on satiety and food likes: the role of genetics. J Gastrointest Surg. 2006; 10(2):270–7. [PubMed: 16455461]

91. Thomas JR, Marcus E. High and low fat food selection with reported frequency intolerance following Roux-en-Y gastric bypass. Obes Surg. 2008; 18(3):282–7. [PubMed: 18214629]

92. Olbers T, Bjorkman S, Lindroos A, Maleckas A, Lonn L, Sjostrom L, Lonroth H. Body composition, dietary intake, and energy expenditure after laparoscopic Roux-en-Y gastric bypass and laparoscopic vertical banded gastroplasty: a randomized clinical trial. Ann Surg. 2006; 244(5): 715–22. [PubMed: 17060764]

93. Bueter M, Miras AD, Chichger H, Fenske W, Ghatei MA, Bloom SR, Unwin RJ, Lutz TA, Spector AC, le Roux CW. Alterations of sucrose preference after Roux-en-Y gastric bypass. Physiology and Behavior. 2011; 104(5):709–21. [PubMed: 21827777]

94. Zheng H, Shin AC, Lenard NR, Townsend RL, Patterson LM, Sigalet DL, Berthoud HR. Meal patterns, satiety, and food choice in a rat model of Rouxen-Y gastric bypass surgery. Am J Physiol Regul Integr Comp Physiol. 2009; 297(5):R1273–82. [PubMed: 19726714]

95. Shin AC, Zheng H, Pistell PJ, Berthoud HR. Roux-en-Y gastric bypass surgery changes food reward in rats. Int J Obes (Lond). 2011; 35:642–651. [PubMed: 20805826]

96. Grill HJ, Norgren R. The taste reactivity test. I. Mimetic responses to gustatory stimuli in neurologically normal rats. Brain Res. 1978; 143(2):263–79. [PubMed: 630409]

97. Berridge KC, Robinson TE, Aldridge JW. Dissecting components of reward: 'liking', 'wanting', and learning. Curr Opin Pharmacol. 2009; 9(1):65–73. [PubMed: 19162544]

98. Hajnal A, Kovacs P, Ahmed TA, Meirelles K, Lynch CJ, Cooney RN. Gastric bypass surgery alters behavioral and neural taste functions for sweet taste in obese rats. Am J Physiol Gastrointest Liver Physiol. 2010; 299:G967–G979. [PubMed: 20634436]

99. Tichansky DS, Glatt AR, Madan AK, Harper J, Tokita K, Boughter JD. Decrease in sweet taste in rats after gastric bypass surgery. Surgical Endoscopy. 2011; 25(4):1176–81. [PubMed: 20844896]

100. Berthoud HR, Morrison C. The brain, appetite, and obesity. Annu Rev Psychol. 2008; 59:55–92. [PubMed: 18154499]

101. Glimcher PW, Rustichini A. Neuroeconomics: the consilience of brain and decision. Science. 2004; 306(5695):447–52. [PubMed: 15486291]

102. Roesch MR, Calu DJ, Schoenbaum G. Dopamine neurons encode the better option in rats deciding between differently delayed or sized rewards. Nature Neuroscience. 2007; 10(12):1615–24.

103. Berthoud HR. Metabolic and hedonic drives in the neural control of appetite: who is the boss? Current Opinion in Neurobiology. 2011; 21(6):888–96. [PubMed: 21981809]

104. Berthoud HR, Munzberg H. The lateral hypothalamus as integrator of metabolic and environmental needs: From electrical self-stimulation to opto-genetics. Physiology and Behavior. 2011; 104(1):29–39. [PubMed: 21549732]

105. Thaler JP, Yi CX, Schur EA, Guyenet SJ, Hwang BH, Dietrich MO, Zhao X, Sarruf DA, Izgur V, Maravilla KR, et al. Obesity is associated with hypothalamic injury in rodents and humans. Journal of Clinical Investigation. 2012; 122(1):153–62. [PubMed: 22201683]

Highlights

- Examines existing literature on taste sensitivity and food reward as affected by obesity and weight loss
- Describes recent studies in rats with calorie-restriction-induced and gastric bypass-induced weight loss
- Concludes that taste sensitivity and reward functions are influenced by both preexisting traits and secondary effects of obesity