Sweetness, Satiation, and Satiety[1–3]

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Abstract

Satiation and satiety are central concepts in the understanding of appetite control and both have to do with the inhibition of eating. Satiation occurs during an eating episode and brings it to an end. Satiety starts after the end of eating and prevents further eating before the return of hunger. Enhancing satiation and satiety derived from foodstuffs was perceived as a means to facilitate weight control. Many studies have examined the various sensory, cognitive, postingestive, and postabsorptive factors that can potentially contribute to the inhibition of eating. In such studies, careful attention to study design is crucial for correct interpretation of the results. Although sweetness is a potent sensory stimulus of intake, sweet-tasting products produce satiation and satiety as a result of their volume as well as their nutrient and energy content. The particular case of energy intake from fluids has generated much research and it is still debated whether energy from fluids is as satiating as energy ingested from solid foods. This review discusses the satiating power of foods and drinks containing nutritive and nonnutritive sweeteners. The brain mechanisms of food reward (in terms of "liking" and "wanting") are also addressed. Finally, we highlight the importance of reward homeostasis, which can help prevent eating in the absence of hunger, for the control of intake.   J. Nutr. 142: 1149S–1154S, 2012.

Introduction

This paper addresses the important notions of satiation and satiety, both of which relate to the inhibition of eating. Satiation occurs at the time of eating and represents the cumulative effect of inhibitory signals induced by the ingestion of food substances as the meal progresses. Such signals have many origins: sensory, cognitive, digestive, and hormonal. Satiation signals ultimately bring eating to an end. Following the end of an eating episode, a period of satiety begins and endures for some time before hunger returns. Again, the signals that contribute to the duration and intensity of satiety are of varied origin, as conceptualized in the notion of the "satiety cascade" (1). During satiety, sensory and cognitive processes interact with postingestive and postabsorptive peripheral and central mechanisms to inhibit further eating. Because satiation and satiety have to do with the inhibition of eating, they can potentially affect total intake and facilitate body weight control.

It is important to understand whether sweet-tasting foods and drinks exert a special influence on satiation and satiety. Their high palatability could trigger overeating, at least in some individuals under certain circumstances. In addition, the special case of energy obtained from fluids raises the crucial question of the potency of satiety signals following drinking rather than eating.

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This article presents the definitions of satiation and satiety, along with the experimental approaches that have been used to measure them in scientific studies of human appetite. Evidence is also reviewed on the satiating effects of nutritive compared with nonnutritive (or low-calorie) sweeteners (LCS)[9]. Brain mechanisms that influence satiation and satiety are also examined.

Measuring Satiety and Satiation: Study Designs and Outcomes

Obesity arises from energy intake chronically exceeding energy expenditure. This imbalance has been associated with physiologic factors, including sex, ethnic origin, age, pubertal stage, body fatness, and fitness, as well as a typical list of environmental and behavioral factors such as socioeconomic status, parenting, food composition, rapid eating, snacking, eating outside the home, quick-service restaurants, stress, television viewing, lack of exercise, peer group, and many more. Many public health actions have been undertaken or proposed to prevent obesity, yet the prevalence of obesity continues to increase.

What is missing in many discussions is an appreciation of the simple fact that food intake is driven by a powerful physiologic process aimed to ensure that energy intake meets energy requirements (2–4). Each of the above variables proposed to be causal factors of obesity may indeed contribute to energy intake exceeding requirements. However, it can be argued that the failure of food to provide satiety (the reduction of appetite or hunger after consuming a food or energy-containing beverage) and of meals to provide satiation (the termination of eating at a meal) are more important factors. Thus, food characteristics and environmental factors that diminish feelings of satiety and satiation may be plausible causes of energy imbalance. However, although satiety and satiation are easy to define (1,5), they are difficult to quantify (6). As a result, the factors leading to satiety and satiation and, ultimately, to body weight control are a matter of considerable debate. Different outcomes can be achieved depending on the question posed, the study design, and the age and sex of the participants (7–16), so the evidence required to make claims on foods is not always clear (17).

The goal of research on satiety and satiation has been to identify characteristics of foods and beverages that contribute to reduced energy intake (17,18). Short-term indicators include subjective measures of sensations associated with appetite, the amount of food eaten, and a variety of biomarkers (6). Satiety in response to the ingestion of foods and beverages is often evaluated by subjective measures of the sensations attributed to appetite, which may or may not be driven by hunger (the physiologic drive to replace an energy deficit) (2,3). For example, study participants are typically asked to rate their sensations of hunger, fullness, prospective food consumption, and desire to eat following the consumption of a snack, meal, or diet (19). The response may be measured over a few minutes, hours, or throughout the day. Although it is clear that the ingestion of a food or beverage containing energy decreases appetite (increases satiety), the effects are transient. They may or may not be predictive of later food intake, depending on the amount ingested, the macronutrient composition, and the time at which food is ingested (20,21). The magnitude and time course of satiety effects on later intake critically depend on the experimental design. In some cases, short-term studies using a "preload

paradigm" show that the forced intake of energy in foods or beverages consumed between meals, when compared with not eating or consuming a very low-energy or energy-free item, has little impact on the amount consumed at a later eating occasion. Hence, some short-term preload studies suggest that the cumulative effect of between-meal eating combined with a later meal is an increase in energy intake.

The effect of food and beverage characteristics on satiation can be quantitatively assessed in experimental studies by measuring the amount of food eaten ad libitum from a meal. In these studies, the individual is often isolated from environmental stimuli. Even so, many factors other than physiologic signals arising during the meal influence how much is eaten. For example, habitual behavior, socioeconomic status, and perceptions of the appropriate amounts to eat can be major factors, depending on the age group selected.

Considerable research has focused on the metabolic correlates of satiation and satiety. Many gastrointestinal peptides, other hormones, and metabolic products of digestion provide signals to the regions of the brain responsible for food intake control (2,3,22). However, their individual or collective association with satiety or satiation remains unclear (6). Lemmens et al. (22) compared the dynamics of hunger and fullness ratings on visual analogue scale (VAS) with the dynamics of glucagon-like peptide-1, peptide YY, ghrelin, glucose, and insulin concentrations throughout different meal patterns, and thus different timings of nutrient delivery to the gut, by using a statistical approach that focused on within-subject variables. The question was whether appetite ratings were synchronized with, or lagged behind or in front of changes in hormone and glucose concentrations. The results indicated that VAS scores and hormone or glucose concentrations seemed to change synchronously. Changes in ghrelin concentrations lagged 10–30 min behind changes in hunger scores and insulin concentrations, suggesting a role for insulin as a possible negative regulator of ghrelin. This method may be useful for understanding possible differences in the relationship between VAS scores and hormone and glucose concentrations between participants or conditions. Yet the reported explained variation of 40–70% seems too small to use hormone and glucose concentrations as appropriate biomarkers for appetite, at least at the individual level and likely at the group level (6,22).

Despite the caveats in study designs for measuring satiety and satiation, the majority of outcomes indicate that in the absence of energy, neither one occurs. It is difficult to fool physiologic systems of intake control in the face of an energy deficit (23). In contrast, short-term studies of satiety and satiation suggest that the physiologic control system is relatively vulnerable to overconsumption in response to situations of energy excess (23).

The Impact of Sweetened Beverages on Satiety and Satiation

Human desire for sweet taste spans all ages, races, and cultures. Human newborns exposed to different taste stimuli accept sweetness but reject bitter taste. Young children prefer those foods that are both familiar and sweet. Throughout evolution, sweetness has had a role in human nutrition, helping to orient feeding behavior toward nourishing foods. Beginning with mother's milk, liquids have been important sources of both energy and nutrients.

Excessive consumption of sugar-sweetened beverages has been linked to rising rates of obesity in the United States and

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[9] Abbreviations used: HFCS, high-fructose corn syrup; LCS, low-calorie sweetener; RCT, randomized controlled trial; VAS, visual analogue scale.

worldwide (24,25). Sugar-containing beverages that taste sweet include still and carbonated soft drinks, juice-based beverages, 100% juices, and flavored milk. Beverages sweetened with high-fructose corn syrup (HFCS) rather than sucrose have come under particular scrutiny. The association between sweetened beverages and obesity rates rests largely on temporal trends and cross-sectional studies (26). The similarity in time trends between added-sugars consumption and rising obesity rates in the United States is striking. However, such temporal associations can be modified by secular trends, shifts in diet composition, and more sedentary lifestyles. Cross-sectional studies, based on a single point in time, cannot establish a causal relation between beverage consumption and weight change (26).

In evidence-based medicine, one criterion for establishing causality is a biologically plausible mechanism. The biological mechanism that is often invoked in support of a causal linkage is the notion that the body does not perceive liquid energy (27,28). The standard explanation for the obesity epidemic is that energy-containing liquids are less satiating than are solid foods. Despite the fact that short-term satiety signals may have little to do with the long-term homeostatic mechanisms determining body weight, deficits in physiologic satiety are routinely cited in epidemiologic studies. Much attention has been paid to satiation and satiety as well as to the nature of energy-containing and energy-free sweeteners (27–29). Less attention has been paid to taste, cost, and convenience and the manner in which beverages are incorporated into the everyday diet (28). When it comes to the consumption of liquids and body weight change, studies have tended to implicate satiety mechanisms rather than to explore human dietary behavior or the economics of food choice.

Satiety-driven mechanisms, however, do not fully account for the proposed links between liquid sugar energy and body weight. Research comparing the short-term satiating power of different types of liquids and solids remains inconclusive (30,31). For one, numerous clinical studies have shown that sugar-containing liquids, when consumed in place of usual meals, can lead to a significant and sustained weight loss. The principal ingredient of liquid meal-replacement shakes is sugar, often HFCS, which is present in amounts comparable to those in soft drinks. Indeed, one such liquid shake is marketed on the grounds that it helps control hunger and prevents hunger longer when consumed for the purpose of weight loss (28). The diverging results of studies addressing the satiating power of liquids suggest that the impact of sweetened beverages on energy intake can also depend on the behavioral intent, context, and mode of use as well as the availability and cost of sweetened liquids.

LCS have also been implicated in the obesity epidemic (29). Studies have claimed that LCS, providing sweetness without energy, confuse the body's regulatory mechanisms (32). However, early suggestions that LCS lead to increased appetite and intake (33) have not been confirmed. LCS in beverages and yogurts do not promote either hunger or overeating compared with unsweetened stimuli (34,35). Whereas both energy-containing and energy-free soft drinks exert their initial effect on satiety through sheer volume, the impact of energy on satiety becomes apparent later. There is no satiety-driven mechanism that might cause consumers of low-energy beverages to gain weight compared with consumers of plain or flavored water (35).

In observational studies, the use of low-energy beverages was associated with higher body weight (29). However, Nettleton et al. (36) observed that those consumers were also better educated and had healthier lifestyles and higher quality diets. It has been suggested that weight problems of health-conscious consumers drive the use of LCS (35). In such studies, the

existence and direction of a causal link between LCS and weight status are impossible to ascertain. It is difficult to link health outcomes such as obesity with specific foods and beverages.

Sugars, LCS, and Satiety

Artificial sweeteners (e.g., aspartame and sucralose) provide a no- or low-energy alternative to sweetening foods and beverages with sugar. Unlike consumption of sugar-sweetened beverages, consumption of artificially sweetened beverages has been found to be inversely associated with blood pressure (37) and not associated with risk of type 2 diabetes after controlling for health status, weight change, dieting, and other factors (38). Nonetheless, many of these conclusions were derived from association studies and there are limited data from randomized controlled trials (RCT). Such trials allow investigators to determine causality with greater certainty, yet conducting RCT can be costly and time consuming, particularly when effect sizes are modest or manifest over prolonged periods of time.

Most of the RCT that have been conducted are short-term studies that manipulated dietary intake at a meal or preload and examined acute effects on energy intake, appetite ratings, and glucose and insulin levels. Such studies were conducted to determine if artificial sweeteners might paradoxically stimulate appetite (33,39,40) and ultimately increase body weight. Analysis of these data suggests that the effect of consuming sucrose or artificially sweetened beverages differs between children and adults. For example, in 2 studies, small samples of boys ($n = 14$) consumed sucralose or sucrose-sweetened liquid preloads 30 min before lunch and were found to ingest less energy after consuming the sucrose-sweetened preload (14,15). Hence, the boys compensated for the energy in the sucrose preload by eating less energy at lunch; however, these studies had a few notable limitations, including enrollment of small samples of only boys and the use of liquid preloads. Another study showed similar results in young children but not in adults (41). One hypothesis to explain the discrepant finding between children and adults is that infants and children have an innate ability to internally self-regulate food intake that is lost as people age (41). This loss is due to factors such as socialization around food as well as the development of expectancies regarding the satiating value of foods that develop through repeated exposure to foods.

A recent study in adults found that the consumption of stevia, a natural energy-free sweetener, and aspartame in a preload resulted in less energy intake over the course of the day compared to a higher-energy preload that contained sucrose (42). Similar to aspartame, stevia can be used as a sugar substitute. The observed differences in daily energy intake were due to the higher energy content of the sucrose-sweetened preload; that is, the adults in this study did not eat significantly less after a preload containing sucrose. Although participants consumed ~300 kcal/d less in the stevia and aspartame conditions compared to the sucrose condition, ratings of appetite did not differ. These studies suggest that children compensate for the energy contained in preloads and adults do not; however, these conclusions are tempered by the limited number of studies.

A handful of RCT were longer in duration and these studies manipulated dietary intake for 3–10 wk to determine if experimentally imposed consumption of sucrose or artificially sweetened foods and beverages affected end points such as body weight or blood pressure. These studies indicate that consumption of artificially sweetened foods and beverages does not promote weight gain and might lead to modest weight loss. In contrast,

consumption of sugar-sweetened foods and beverages produced deleterious effects, such as increased body weight and blood pressure. For example, eating artificially sweetened foods and beverages for >10 wk resulted in weight loss among overweight men and women. Conversely, in the same study, eating sucrose-sweetened foods and beverages for >10 wk resulted in weight and fat gain as well as increased energy intake and blood pressure (43). Similar results were obtained in another study that manipulated the dietary intake of healthy-weight participants for 3 wk, in which participants were asked to consume a 1150-g soda, sweetened with either aspartame or HFCS, daily for 3 wk (44). Consumption of the HFCS-sweetened soda for 3 wk resulted in increased body weight and energy intake, whereas consumption of the aspartame-sweetened soda resulted in lower levels of energy intake and, among males, decreased body weight (44). These studies suggest that consumption of artificial and low-energy sweeteners might provide an effective strategy to manage energy intake and body weight, a conclusion that has been supported by other authors (45). The beneficial effect of artificially sweetened beverages compared with HFCS-sweetened beverages on body weight is secondary to the failure to compensate for the energy content of HFCS-sweetened beverages. Hence, when consuming diets containing HFCS-sweetened beverages, the total daily energy intake is higher than when artificially sweetened beverages are consumed (44).

The effect of artificial sweeteners on postprandial glucose and insulin levels has received less research attention, although the natural sweetener stevia has been found to beneficially affect blood glucose and insulin levels of humans (42). Another study showed that, compared with consuming a preload containing sucrose, consuming a preload containing stevia resulted in lower postprandial glucose levels (46). In addition, the stevia preload was associated with lower postprandial insulin levels compared to both an aspartame and sucrose preload. Post-prandial glucose effects are expected for preloads that have different amounts of energy and carbohydrate; in the study by Anton et al. (42), both the stevia and aspartame preloads had less energy and carbohydrate than the preload containing sucrose. The observed difference on insulin levels between the stevia and aspartame conditions suggests that stevia might beneficially influence insulin levels.

Sweetness, Reward-Related Brain Signaling, Food Choice, and Energy Intake

Food intake meets homeostatic needs in terms of energy and also reward. For instance, the association of sweet taste with the intake of carbohydrates elicits rapid satiety signals (47,48) in conjunction with a potent sensory reward (48). Food reward is analyzed in terms of "liking" and "wanting," which are represented in the brain in distinct but overlapping areas (47). In the fasted state, wanting is signaled in the hypothalamus and striatum and coincides with hunger signaling in the hypothalamus, whereas liking is signaled in the nucleus accumbens in anticipation of food intake (47). Postprandially, in the absence of hunger, wanting signaling in the pallidum and liking signaling in the striatum, anterior insula, and cingulate cortex predict food intake (47). Postprandial food choice and food intake in the absence of hunger seem to be reward related and are exaggerated under stress, especially in overweight individuals with visceral adiposity (48,49). In this situation, reward-related brain signaling in the putamen and reward sensitivity are significantly

decreased, suggesting the existence of reward deficiency, and coincide with increased energy intake (48). Overweight individuals with visceral adiposity have augmented food wanting and energy intake in the absence of hunger (49). Vulnerability to carbohydrate intake under stress is reflected in the cortisol response, which decreases after protein and fat intake but not after carbohydrate intake (50). Stress-induced eating is not only related to enhanced postprandial wanting but also to reduced postprandial liking. Characterization of food perception is less pronounced and liking scores are consistently lower in overweight than in normal-weight individuals under stress (51). Therefore, postprandial stress-induced eating in overweight individuals seems to be due to relatively decreased liking and increased wanting, again suggesting the presence of reward deficiency in these individuals (47). Reward deficiency is most apparent in the absence of hunger, in agreement with the notion that reward deficiency leads to reward seeking that may result in overeating (47).

A recent hypothesis proposes that, in order to avoid reward deficiency, it might be beneficial for an individual to eat what he or she likes as long as this happens in the appropriate physiologic condition (i.e., when hungry) (52). As long as meal-time food intake meets energy as well as reward homeostasis, this could prevent overeating between meals. For instance, a study showed that when the third course (i.e., the dessert) of a lunch meal consisted of a highly liked chocolate mousse, wanting for the complete "dessert category" was significantly decreased, whereas it was still present when dessert consisted of an iso-energetic cottage cheese of the same weight and energy density but differing in taste and perception (i.e., sweetness vs. sourness, color, perception of healthiness, or characterization as a "forbidden" food) (52,53). Then, even dietary-restrained individuals run the risk of overeating "healthy" foods by avoiding the forbidden but attractive, dessert-type, really wanted foods (53).

Thus far, foods that were cited in the examples were solids or semi-solids eaten with a spoon from a bowl. The mode of conveyance plays an important role in easing hunger and thirst, because hunger is alleviated mainly by eating, whereas thirst is quenched mainly by drinking. In a recent study, the majority of participants required further consumption after drinking a meal or an energy-containing soft drink. Further consumption is motivated by a mixture of hunger and thirst, suggesting that the intake of energy from drinks causes confusion that may imply a risk of overconsumption (54).

Taken together, in the fasted state and in the presence of hunger, hunger-, wanting-, and liking-related brain signaling coincides and facilitates food intake in agreement with energy and reward homeostasis. Postprandially, consumption in the absence of hunger may be caused by previously failing to achieve reward homeostasis. This is most pronounced under stress and in overweight individuals.

Summary and Conclusions

Appetite control is a physiologically complex mechanism. In addition to stimulatory influences, among which sweetness is a potent reward, inhibitory influences of various origins contribute to limit intake within and between eating episodes. Satiation, which brings eating to an end, and satiety, which inhibits eating between meals, are well-documented mechanisms. When studying the satiating power of a food substance, it is important to pay close attention to experimental design, because the magnitude and duration of effects are critically dependent on the experimental context.

Many of the controversies that remain in this field could be reconciled (at least partially) if the sociotemporal context of satiety and satiation effects is kept in mind. The issue of whether energy from fluids is as satiating as energy from solids is still controversial. In the literature addressing this question, it seems that temporal aspects are of particular importance. Volume can be expected to exert satiety effects in the very short term, whereas nutrient and energy contents play a decisive role in the longer term.

Beyond the immediate effects observed in short-term studies, enhancing satiation and/or satiety must beneficially affect energy balance over a reasonable time to affect body weight. This caveat is especially important when satiety and satiation claims are made for commercially available foods. In a recent note, the European Food Safety Authority (55) stated that: "Changes in appetite ratings after consumption of a 'test' food should also be observed after chronic consumption of the food (e.g., after one month), and therefore tests performed on a single occasion would not be considered sufficient for substantiation." The medium-term and longer term effects on satiation and satiety should be ascertained before substances are recommended in the context of a weight control program.

Early hypotheses that LCS might stimulate excessive intake and overweight have not been confirmed by later works. Studies of free-living users of LCS indicate that these sweeteners can be used in the context of a healthy diet for the purpose of limiting energy intake.

One very interesting new area of research is the investigation of the cerebral mechanisms underpinning food reward. New methods of brain imaging have allowed researchers to identify brain sites where activity corresponds to food liking and food wanting. Activity in these brain sites is different according to physiologic state (hungry vs. sated) and also between overweight and normal-weight individuals, particularly under stress. The concept of "reward homeostasis" suggests that food-derived pleasure must be satisfied in order to facilitate body weight control and particularly to avoid eating in the absence of hunger. More research is clearly needed in this emerging field, but its early results open promising new avenues for the study of food motivation and reward.

Acknowledgments

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