

Sweetness and Food Preference^{1–3}

Adam Drewnowski,^{4*} Julie A. Mennella,⁵ Susan L. Johnson,⁶ and France Bellisle⁷

⁴The University of Washington, Nutritional Sciences Program, Seattle, WA; ⁵Monell Chemical Senses Center, Philadelphia, PA;

⁶University of Colorado, Anschutz Medical Campus, Denver, CO; and ⁷Unité d'Epidémiologie Nutritionnelle, Université Paris 13, Bobigny, France 90252012

Abstract

Human desire for sweet taste spans all ages, races, and cultures. Throughout evolution, sweetness has had a role in human nutrition, helping to orient feeding behavior toward foods providing both energy and essential nutrients. Infants and young children in particular base many of their food choices on familiarity and sweet taste. The low cost and ready availability of energy-containing sweeteners in the food supply has led to concerns that the rising consumption of added sugars is the driving force behind the obesity epidemic. Low-calorie sweeteners are one option for maintaining sweet taste while reducing the energy content of children's diets. However, their use has led to further concerns that dissociating sweetness from energy may disrupt the balance between taste response, appetite, and consumption patterns, especially during development. Further studies, preferably based on longitudinal cohorts, are needed to clarify the developmental trajectory of taste responses to low-calorie sweeteners and their potential impact on the diet quality of children and youth. *J. Nutr.* 142: 1142S–1148S, 2012.

Introduction

The consumption of energy-containing sweeteners in the form of added sugars has risen consistently among all age groups in the

United States (1,2). These consumption trends are paralleled by rising rates of obesity among children, adolescents, and adults (3). Given that sweetness has a powerful hedonic appeal, especially among children and young people, sweet foods and beverages have come under scrutiny as potential contributors to the obesity epidemic both in the United States and worldwide (4).

Current U.S. estimates have shown that the consumption of added sugars accounted for 15.9% (60 g/d) of energy in the diets of children aged 2–5 y and 18.6% (90 g/d) of energy in the diets of children aged 6–11 y. The bulk of this sugar was provided by energy-containing beverages, including sugar-sweetened sodas and flavored milk, which are a substantial source of added sugars (5) in the diets of children aged 2–11 y. Adolescent males consumed the most added sugars, primarily from sweetened grains, sweet beverages and sodas, table sugars, syrups, snacks and candies, and milk products. Added-sugar consumption decreased after adolescence and was much reduced in adult life.

The introduction of several low-calorie sweeteners (LCS) into the food supply, following approval by the U.S. FDA, has led to the creation of beverages and foods that taste sweet but provide less or no energy [see (5,6) for reviews]. There is currently considerable research on the biological mechanisms that influence sweet taste preferences and drive the consumption of sweet-tasting foods. In contrast, there is a paucity of pediatric research on the behavioral and physiological responses to LCS per se and the potential consequences of incorporating LCS into children's diets.

One key question is whether prolonged exposure to sweet, yet non- or low-energy foods in infancy and childhood can disrupt the delicate balance among taste responsiveness, appetite, and energy consumption in young children (7). Is it possible that repeated exposure to sweetness without energy can actually

¹ Published in a supplement to *The Journal of Nutrition*. Presented at the conference Low-Calorie Sweeteners, Appetite and Weight Control: What the Science Tells Us, held in Washington, DC, April 7–8, 2011. The conference was sponsored by the Committee on Low-calorie Sweeteners of the International Life Sciences Institute North America. The views expressed in these papers are not necessarily those of the supplement coordinator or guest editors. The supplement coordinator for this supplement was Adam Drewnowski, University of Washington. Supplement Coordinator disclosures: Adam Drewnowski received travel reimbursement for participation in the Low-Calorie Sweeteners Conference. The supplement is the responsibility of the Guest Editor to whom the Editor of *The Journal of Nutrition* has delegated supervision of both technical conformity to the published regulations of *The Journal of Nutrition* and general oversight of the scientific merit of each article. The Guest Editor for this supplement was Sibylle Kranz. Guest Editor disclosure: Sibylle Kranz has received funding from The Kellogg Company to conduct research projects unrelated to this supplement material. She has also been an invited speaker at a roundtable discussion funded by The Kellogg Company. Publication costs for this supplement were defrayed in part by the payment of page charges. This publication must therefore be hereby marked "advertisement" in accordance with 18 USC section 1734 solely to indicate this fact. The opinions expressed in this publication are those of the authors and are not attributable to the sponsors or the publisher, Editor, or Editorial Board of *The Journal of Nutrition*.

² Supported by the Committee on Low-Calorie Sweeteners of the North American Branch of the International Life Sciences Institute. A. Drewnowski, J. A. Mennella, S. Johnson, and F. Bellisle received a modest honorarium for their participation in the workshop and development of the manuscript. Travel was funded for all authors to attend the workshop.

³ Author disclosures: A. Drewnowski has received research grants from Ajinomoto on behalf of the University of Washington. F. Bellisle has received consulting fees and honoraria from food and beverage companies. J. A. Mennella is supported by grants from the National Institute of Deafness and Other Communication Disorders (grant DC011287) and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (grant HD37119). The content is solely the responsibility of the author and does not necessarily represent the official views of the Eunice Kennedy Shriver National Institute of Child Health and Human Development or the NIH. S. Johnson, no conflicts of interest.

* To whom correspondence should be addressed. E-mail: adamdrew@u.washington.edu.

rewire brain circuitry in the growing child (8)? What are the long-term consequences of children learning to associate sweetness with foods that are made to taste sweet by the addition of LCS? Should children be retrained to like a given food in its natural unsweetened form? Finally, given that children like more intensely sweet sensations than do adults, are they at greater risk of exposure to higher levels of LCS?

The role that LCS play in the development of preferences for and the physiological consequences of sweets consumption in children is an important area for research. A better understanding of the potential consequences of making low-energy foods and beverages available to overweight and obese children is needed to shape public health policy. The development of new tools for the prevention of childhood obesity and diabetes should be a research priority worldwide.

Responses to Sweet Taste during Development

In recent years, major scientific advances have helped identify the initial events underlying sweet taste recognition (9–11) and the brain mechanisms underlying the strong pleasure response to sweet taste (12). Sweet taste receptors are expressed not only in the mouth but also in other areas, particularly the gut and pancreas (13,14). These peripheral receptors do not distinguish between nutritive sweeteners and LCS when these compounds are equated for sweetness (15). When stimulated, the receptors result in a cascade of physiologic processes in the periphery and the brain (16).

The sensory pleasure derived from tasting sweet substances has an innate basis [see (17) for a review]. Tasting something sweet leads to the activation of pleasure-generating brain circuitry. According to clinical studies (18), this circuitry is the same or overlaps with that which mediates the addictive nature of drugs such as alcohol and opiates. The emotions or affects experienced upon tasting something sweet are complex processes that are phylogenetically remarkably well conserved (19). Thus, many drugs seem to be co-opting neural pathways originally designed for seeking sweet tastes, a human's natural reward. However, that is not to say that sweet taste preferences and food addictions are one and the same (20).

Research on the developmental trajectory of sweet taste preferences suggests that such preferences are innate and expressed even before birth (21). Many factors influence the development of food preferences in children, the first of which occur via in utero experience with flavors from the maternal diet and after birth from early experience with flavors occurring in human milk.

Before birth, the ability to detect sweet tastes is functioning and interacting with systems controlling affect (22). Newborns can differentiate varying degrees of sweetness and will consume a greater volume of a solution that tastes sweeter (23). Their faces relax when tasting something sweet, and this relaxation is often accompanied by a smile (24). The power of sweet tastes to control behaviors is evident early in life. For example, the confluence of tasting something sweet and making eye contact with an unfamiliar adult not only calmed 3- to 4-mo-old infants, but it also resulted in their preferential gazing at that adult (25). Additional research revealed that early exposure to sugar-sweetened items led to both an increased preference for sweetened items and a preference for higher levels of sugar in foods (26–28).

Taste preferences for sweetness, measured under laboratory conditions using a variety of sweeteners, have shown age-related differences. The most striking effect was that young children liked more intensely sweet solutions than did adults, with the more adult-like pattern emerging only during adolescence (29,30). Younger children preferred a more intense concentration of sucrose in solution than did adolescents, and adolescents likewise preferred sweeter solutions than did adults (31). For example, in a recent study of 930 participants, children most preferred a 0.54-mol/L sucrose concentration (32) that was equivalent to 11 tsp (~44 g) of sugar in an 8-oz (240 mL) glass of water, nearly twice the sugar concentration of a typical cola. Measuring the level of sweetness that is most preferred by children under laboratory conditions has real-world importance, because it can serve as a predictor of their preferred levels of sugar in beverages and cereals (32).

The fact that sugars have pain-reducing properties may also influence the liking for sweetness [see (33) for a Cochrane Database Systematic Review]. A sweet-tasting solution placed in an infant's mouth can reduce responses to painful stimuli; sweet taste perception mediates both endogenous opioid and non-opioid systems to block pain afferents (34). LCS, such as aspartame, mimic the time course and the magnitude of the increased calming (35,36) and mouthing and hand-to-mouth contact effects (35) of sucrose. Given that the administration of sucrose by direct stomach loading was ineffective (37), it may be that afferent signals from the mouth, rather than gastric or metabolic changes, are responsible for the analgesic properties of sweet tastes.

The ability of sweet taste to act as an analgesic continues throughout childhood (38–40). Tasting a concentrated sucrose (0.70 mol/L) solution, but not water, was shown to delay children's reporting of pain onset when undergoing a cold-induced pain stimulus test. The more that children liked this intensity of sweetness, the better that it worked for increasing pain tolerance. However, sucrose was not an effective analgesic for children exhibiting depressive symptoms (40) or for overweight children (39) despite the finding that children who were depressed reported a greater liking for sweet-tasting foods and candies (40).

Although sweet taste preferences are influenced by a variety of factors ranging from genetics and race/ethnicity to nutritional deficiencies, chronic disease, medication use, and addictions (27,41–47), the positive hedonic response to sweet taste is a universal trait. The finding that children liked higher intensities of sweet taste than did adults has been observed in many countries and cultures (47). Adolescents who preferred a higher concentration of sucrose exhibited greater rates of linear growth (48), suggesting that the reduction in sweet preferences may be associated with the cessation of growth. However, the mechanisms underlying the age-related decline in sweet preferences remain a mystery.

The proper place of sweetness in the food supply is learned and modulated by experience. That is, the sensation of sweetness is context dependent and can acquire meaning through associative learning [see (49,50) for reviews]. Babies who were routinely fed sweetened water during the first months of life exhibited a greater preference for sweetened water when tested during infancy and several years later (26,46). Children who were repeatedly exposed to a sweetened orange-flavored drink for 8 consecutive days during their daily midmorning snack not only liked it better but also drank more of it at the end of the exposure period (28). However, there are no compelling data to suggest that such repeated exposure to a beverage leads to a

heightened hedonic response to sweetness in general. Rather, the matrix in which the sweet taste experience occurs is an important factor. Through familiarization, children develop a sense of what should, or what should not, taste sweet (26,27,49).

Evolution has shaped the child's response to sweet taste. Thus, the liking for sweet foods and beverages is not solely a product of modern-day technology and advertising but also reflects the basic biology of children. Our sensory systems evolved to detect and prefer the once-rare energy-rich foods that taste sweet. These responses are intensified during childhood, which may reflect the nutritional need for attracting children to energy-producing foods that are high in sugars, minerals, and vitamins (e.g., mother's milk, fruits) during periods of maximal growth (51). The liking for sweets may be promoted by the rewarding and pain-reducing properties of sugars and by repeated experience with highly processed, intensely sweet foods, which are now abundant and heavily marketed (4). Thus, attempts to limit the consumption of sweet foods and beverages may be more difficult for some children because of the individual differences in the inherent hedonic value of sweet taste and how sweets make them feel.

The Role of LCS in the Development of Children's Food Preferences

The majority of developmental studies on sweet taste responsiveness among children have been conducted with naturally occurring sugars: sucrose, lactose, or fructose. In general, infants and children selected sweet solutions over plain water and preferred the sweeter sugars to those that were less sweet. Similar studies of the developmental trajectory of sweet taste preferences based on LCS are still needed. As a result, the taste response to different LCS across this age range is less well defined.

Although our food supply now includes several LCS that provide sweetness with less energy (6), we know little of their impact on children's food acceptance, eating patterns, and growth. Repeated exposure to and experience with foods is perhaps the best predictor of liking and food acceptance (52). These findings are extended by recent research showing that repeated exposure to sweet- and sour-tasting drinks in children (aged 6–11 y; $n = 59$) and adults ($n = 46$) led to an increased preference for sweet-tasting drinks but no change in preference for the sour-tasting drinks. By contrast, the taste preferences of adults were not affected by exposure and did not change for either sweet or sour drinks (28).

One important factor that affects the development of children's food preferences is the energy density of the foods offered (53). In a series of human studies modeled on the animal study literature, Birch et al. (54,55) showed that, over time, children come to prefer flavors associated with higher energy density. In an early study ($n = 11$), children were offered novel flavored drinks that varied in energy density by virtue of their carbohydrate content (54). One novel flavor was paired with a low-energy, aspartame-sweetened drink, whereas the other flavor was paired with an energy-containing, sucrose-sweetened drink. After repeated consumption, children came to prefer the flavor that was associated with energy, suggesting that sweet taste alone was not sufficient to predict food preference. Rather, it was the pairing of sweet taste with dietary energy that was necessary to facilitate preference and liking.

The finding that energy, rather than sweet taste, may be the driver of food preferences may represent a potential confounding factor for previous studies that explored the impact of added sugars on liking and consumption of beverages and foods. In those studies, the effects of sweet taste had not been separated from those of increasing energy density (28). Further studies, preferably based on longitudinal cohorts, are needed to clarify the developmental trajectory of taste responses to LCS and their potential impact on the diet quality of children and youth.

The acceptance of LCS may vary across subgroups of children. For example, many LCS have a bitter taste component and can have an aversive metallic aftertaste, particularly at higher concentrations (56). Because children are more sensitive to bitter tastes than are adults (45,57), some children may be more sensitive to the unpleasant aftertastes of these LCS. These scientific findings lead to a number of questions about the potential role of LCS in the diets of children.

How do LCS impact children's dietary intake? There are little or no data from studies investigating the effects of LCS on the dietary quality of children (58). Most studies investigating the consumption of LCS by children focus more on the acceptable daily intakes or maximum intakes than on impacts on food preference. A few studies have probed how LCS can facilitate the acceptance of different foods. For example, aspartame, combined with chocolate flavor, was shown to increase preschoolers' milk consumption. Both sugar-sweetened and aspartame-sweetened milk were consumed to a larger extent by preschool-aged children than was plain milk (59). In the case of sugar-sweetened milk, the children consumed significantly more energy in response to the sucrose-containing beverage and did not compensate by reducing energy intake from the foods offered at meals (4 different meals). In contrast to preloading studies by Birch et al. (60), the milk drink was not administered as a preload but rather as part of a meal.

LCS have also been used to facilitate acceptance of lower-sugar products. Reports of dietary intakes of Navajo children suggest that sugar-sweetened foods are a significant part of their diet. In particular, 71% of children reported consuming sugar-sweetened beverages 3–5 times/wk (61). These populations are especially at risk for chronic diseases such as diabetes and obesity, which are associated with excess energy intake. In one study, participants were presented with conventional, high-sugar watermelon and low-sugar watermelon sweetened with the added LCS sucralose (62). Children (aged 6–18 y) and adult Choctaws (aged 20–90 y) accepted the product well and preferred the low-sugar watermelon with sucralose to the conventional, higher-sugar watermelon. Thus, sucralose facilitated acceptance of a low-sugar product over a higher-sugar, higher-energy product.

Although opportunities may exist to replace some conventional sugar intake with LCS, which could lead to improvements in overall diet quality and better weight outcomes, we caution that what remains unknown are the long-term consequences of children learning to associate sweet taste with certain foods that typically are not sweet but have been processed to taste sweet because of the addition of LCS. The role that dietary habits, including the use of LCS, play in the preferences and physiological consequences of sweets in children is an important area for future research.

What do we know about children's food preferences, intake patterns, and body weight? Children's food preferences directly affect the amounts of food consumed. It has been

stated that: “children eat what they like and leave the rest” (63). How these food preferences are developed relates to experience with foods, the taste and sensory characteristics of the foods, their energy density, and the social environments in which children live, learn, and play. Parents’ food preferences, intake patterns, and eating behaviors influence the foods available to young children. Parents also set the environments in which children eat by determining the characteristics of the setting (e.g., with or without distractions), the level of routine in eating, and whether they model healthy eating behaviors. In addition, parents set the emotional tone of the meal time. As stated by Anzman et al. (64): “Many of the parenting behaviors practiced today originate from times of food scarcity, or certainly less easily available food and energy.” The intersection of controlling or aggressive feeding strategies, a burgeoning food environment of highly palatable foods, and a built environment that favors inactivity is linked to increases in obesity rates for children. The evidence suggests that “obesogenic environments” may be created not only in the surrounding community but also in the home (64).

The effects of LCS on body weight have been studied in both animal and human models. Rats fed a yogurt-based diet mixed with saccharin gained more weight and had impaired energy compensation relative to rats given yogurt mixed with glucose. Increased body weight was also noted when animals consumed a yogurt diet sweetened with acesulfame potassium or saccharin-sweetened refried beans. Body weight differences persisted after LCS diets were discontinued and replaced with a glucose-sweetened diet (65). In humans, Fowler et al. reported that for individuals ($n = 5158$) who were normal weight or nonobese (BMI <30), consumption of >21 LCS beverages/wk was associated with twice the risk of obesity at follow-up 7–8 y later compared with nonusers (66,67).

No strong clinical evidence currently exists to suggest an association between children’s weight outcome and their consumption of LCS. A recent systematic review investigating the metabolic effects of artificial sweeteners in youth reviewed 18 studies and concluded that laboratory studies of immediate effects of LCS do not support that their ingestion results in increased energy intake. Observational studies tended to suggest a positive association between aspartame intake and weight gain, but intervention studies employing LCS to reduce weight showed no consistent effect on body weight (68).

There is a clear need for additional research to better understand the response to LCS across the lifespan. We need to know more about the impact of such sweeteners on children’s diets. Of particular interest is information related to: 1) children’s neuronal responses to LCS; 2) the impacts of LCS on diet quality, energy intake, and weight gain in children; and 3) the extent to which LCS can facilitate or hinder the acceptance of novel or less preferred foods.

Responses to Sweetness in Adults: from Perception to Intake

Responses to sweet tastes in adults show broad interpersonal differences. Such differences occur in terms of perception, liking, wanting, and intake.

Psychophysical studies on sweet taste perception have shown that the individual sensitivity to sweetness (detection and recognition of substances in solution as well as the intensity ratings given to a single concentration of one sweet solution) varies considerably (69). Sensitivity to a particular sweet

substance (e.g., glucose) does not predict sensitivity to other sweet substances (e.g., other sugars or nonnutritive sweeteners) (70). Genetic factors that determine the number and type of taste receptors in the mouth could influence such sensitivity. Sensitivity to bitterness, which is under the clear influence of genetic factors, co-varies with the perception of sweetness. There is little correlation between sensitivity to sweetness and liking or intake of sweet-tasting products (71). All sweet-tasting substances (sugars and nonnutritive sweeteners) have distinctive tastes that share the “sweet” dimension; for example, sucrose, fructose, and aspartame are recognized as sweet but can easily be discriminated by taste (70).

Studies of liking for sweetness have shown that although preferences for sweet taste are a universal trait, large variations exist in the preferred intensity and in the type of foods or drinks that are consumed sweet. Liking for sugars is reinforced by their nutritional effects, because they are a ready source of dietary energy. Many factors, such as age, race, and gender, modulate liking for sweetness. The preferred intensity of sweetness in foods and beverages is lower in adults than in children and adolescents (46,72); studies suggest that men prefer higher intensities than women (72,73). The phenotype “sweet tooth” has been addressed in scientific works (69). It is characterized by preferences for high sweetness intensity in a large number of foods and drinks and a preference for sweet-tasting, rather than savory, products (74). Body size or adiposity is not a predictor of liking sweet stimuli (75), but overweight and obese individuals often prefer high-fat, sweet, or nonsweet stimuli (76). Persons who frequently consume sweet-tasting products show a preference for sweeter beverages when tested in the laboratory; this effect is the same for frequent consumers of nonnutritive and nutritive sweeteners (77).

The liking for sweetness may change during the course of a meal. Sweetness preferences are reported to be higher before a meal than after a meal, reflecting perhaps the organism’s need for energy (78). Ingestion of sweet-tasting products induces “sensory-specific satiety,” a general decrease in the attractiveness of all sweet products (79). In addition, intake of a sugar-containing food or drink induces negative “alliesthesia,” a decrease in pleasantness due to the metabolic effects of sugars (80). Longer term changes in the nutritional and hormonal status of the body, such as what happens in weight loss, may also influence the palatability of sweet products.

There is a major theoretical distinction between liking and wanting. Wanting has to do with actual foods and drinks, rather than the simple stimuli (solutions) often used in tests of liking and preferences. Wanting of sweet-tasting products is strongly influenced by liking of sweetness, but it is also dependent on other factors such as the current nutritional status (before vs. after meals), social norms, or behavior of others who share the meal (81). The appetite for sweet-tasting foods and drinks can take place in the context of a healthy motivation of intake, and control mechanisms (alliesthesia, sensory-specific satiety, post-ingestive hormonal changes, etc.) can effectively suppress appetite (wanting) for sweet-tasting products (80,82). However, easily accessible, highly palatable foods (among which many are sweet) are wanted by adults as well as children and can trigger intake even in satiated persons. This strong stimulation of inappropriate intake by palatable products is one critical characteristic of the “obesogenic” environment (81).

What impact do sweet taste preferences have on consumption? Sweet-tasting foods and drinks are consumed as a part of the habitual diet of most adults. Again, there are large individual differences in intake. Evidence exists that genetic factors could

account for a modest portion of individual differences in the consumption of sweet products (83). In many countries, dietary surveys have reported that the diets of overweight or obese persons are not particularly rich in sugar or sweet products (but they are rather high in fat) (84). Consumers (children, adolescents, and adults) of large amounts of sugar and sweet products are often lean (3,85). Evidence obtained from biomarkers, rather than self-reports of intake, suggests a higher intake of sweet products by obese persons compared with their normal-weight peers, particularly those with psychological vulnerability (86).

In addition to their nutritional value, sweet-tasting foods can be ingested for their soothing properties and have been reported to alleviate depression (87), premenstrual symptoms, or responses to stress (88). In such situations, the selected "comfort" foods are highly palatable items that are rich in both fat and sugar. Individual preference for very high concentrations of sucrose is associated with elevated sensitivity to the mood-altering effects of sweetness and impaired control over eating sweets (89).

Disordered and/or excessive eating are undisputed etiological factors in the development of overweight and obesity (90). There is no evidence that they can be triggered by sugar itself in human adults. However, palatable, sweet, fatty, high-energy density foods can easily induce hyperphagia with deleterious consequences on body weight control (91).

Summary and Conclusions

The liking for sweet taste is both innate and universal. Although infants and young children typically select the most intensely sweet tastes, the pleasure response to sweet taste is observed across individuals of all ages, races, and cultures. It is basic biology that dictates a liking for sweetness across the lifespan.

By contrast, preferences for sweetness in specific foods are context dependent and can be influenced by prior exposure to those foods. Dissociating sweetness from energy may affect expectations for sweetness in foods and, potentially, food-seeking behavior. The ability to compensate for variability in energy intake seems to decrease with age; thus, the impact of LCS use in the weight management of children may not parallel that of adults. However, the biologic response to sweetness is only one aspect of food preference and food selection. Important areas for future research include determining the role that dietary habits, including the use of LCS, play in the preferences and physiological consequences of sweets in children as well as elucidating the impact of culture and economics on the choice and purchases of sweet-tasting foods across the lifespan. More knowledge about the consequences of feeding such foods and beverages to children, who today struggle with obesity and diabetes more than any previous generation, should be a research priority.

Acknowledgments

The authors thank Drs. Karen L. Teff and Danielle R. Reed for comments on earlier content on a portion of this manuscript. A. Drewnowski, J. A. Mennella, S. L. Johnson, and F. Bellisle contributed to portions of manuscript writing. All authors read and approved the final manuscript.

Literature Cited

- Guthrie JF, Morton JF. Food sources of added sweeteners in the diets of Americans. *J Am Diet Assoc.* 2000;100:43–51.

- Wang YC, Bleich SN, Gortmaker SL. Increasing caloric contribution from sugar-sweetened beverages and 100% fruit juices among US children and adolescents, 1988–2004. *Pediatrics.* 2008;121:e1604–14.
- Drewnowski A. The real contribution of added sugars and fats to obesity. *Epidemiol Rev.* 2007;29:160–71.
- Popkin BM, Nielsen SJ. The sweetening of the world's diet. *Obes Res.* 2003;11:1325–32.
- Bellisle F, Drewnowski A. Intense sweeteners, energy intake and the control of body weight. *Eur J Clin Nutr.* 2007;61:691–700.
- Mattes RD, Popkin BM. Nonnutritive sweetener consumption in humans: effects on appetite and food intake and their putative mechanisms. *Am J Clin Nutr.* 2009;89:1–14.
- Egan JM, Margolskee RF. Taste cells of the gut and gastrointestinal chemosensation. *Mol Interv.* 2008;8:78–81.
- Ren X, Ferreira JG, Zhou L, Shammah-Lagnado SJ, Yeckel CW, de Araujo IE. Nutrient selection in the absence of taste receptor signaling. *J Neurosci.* 2010;30:8012–23.
- Yarmolinsky DA, Zuker CS, Ryba NJ. Common sense about taste: from mammals to insects. *Cell.* 2009;139:234–44.
- Reed DR, Knaapila A. Genetics of taste and smell: poisons and pleasures. *Prog Mol Biol Transl Sci.* 2010;94:213–40.
- Vigues S, Dotson CD, Munger SD. The receptor basis of sweet taste in mammals. *Results Probl Cell Differ.* 2009;47:187–202.
- Fernstrom JD, Munger SD, Sclafani A, De Arujo I, Roberts A, Molinary S. Mechanisms for sweetness - low-calorie sweeteners, appetite and weight control: what the science tells us - mechanisms for sweetness." *J Nutr.* 2012;142:1134S.
- Margolskee RF, Dyer J, Kokrashvili Z, Salmon KS, Illegems E, Daly K, Maillat EL, Ninomiya Y, Mosinger B, Shirazi-Beechey SP. T1R3 and gustducin in gut sense sugars to regulate expression of Na⁺glucose cotransporter 1. *Proc Natl Acad Sci USA.* 2007;104:15075–80.
- Sclafani A. Sweet taste signaling in the gut. *Proc Natl Acad Sci USA.* 2007;104:14887–8.
- Jang HJ, Kokrashvili Z, Theodorakis MJ, Carlson OD, Kim BJ, Zhou J, Kim HH, Xu X, Chan SL, Juhaszova M, et al. Gut-expressed gustducin and taste receptors regulate secretion of glucagon-like peptide-1. *Proc Natl Acad Sci USA.* 2007;104:15069–74.
- Kokrashvili Z, Mosinger B, Margolskee RF. Taste signaling elements expressed in gut enteroendocrine cells regulate nutrient-responsive secretion of gut hormones. *Am J Clin Nutr.* 2009;90:S822–5.
- Mennella J. The sweet taste of childhood. In: *The senses: a comprehensive reference.* Basbaum AI, Kaneko A, Shephers CM, Westheimer G, editors. San Diego: Academic Press; 2008. p. 183–8.
- Drewnowski A, Krahn DD, Demitrack MA, Nairn K, Gosnell BA. Naloxone, an opiate blocker, reduces the consumption of sweet high-fat foods in obese and lean female binge eaters. *Am J Clin Nutr.* 1995;61:1206–12.
- Berridge KC, Ho CY, Richard JM, DiFeliceantonio AG. The tempted brain eats: pleasure and desire circuits in obesity and eating disorders. *Brain Res.* 2010;1350:43–64.
- Drewnowski A, Bellisle F. Is sweetness addictive? *Nutr Bull.* 2007;32 Suppl 1:52–60.
- Mennella JA, Beauchamp GK. Early flavor experiences: research update. *Nutr Rev.* 1998;56:205–11.
- Maone TR, Mattes RD, Bernbaum JC, Beauchamp GK. A new method for delivering a taste without fluids to preterm and term infants. *Dev Psychobiol.* 1990;23:179–91.
- Maller O, Desor JA. Effect of taste on ingestion by human newborns. *Symp Oral Sens Percept.* 1973;279–91.
- Steiner JE, Glaser D, Hawilo ME, Berridge KC. Comparative expression of hedonic impact: affective reactions to taste by human infants and other primates. *Neurosci Biobehav Rev.* 2001;25:53–74.
- Blass EM, Camp CA. The ontogeny of face recognition: eye contact and sweet taste induce face preference in 9- and 12-week-old human infants. *Dev Psychol.* 2001;37:762–74.
- Beauchamp GK, Moran M. Dietary experience and sweet taste preference in human infants. *Appetite.* 1982;3:139–52.
- Beauchamp GK, Moran M. Acceptance of sweet and salty tastes in 2-year-old children. *Appetite.* 1984;5:291–305.
- Liem DG, de Graaf C. Sweet and sour preferences in young children and adults: role of repeated exposure. *Physiol Behav.* 2004;83:421–9.
- Desor JA, Beauchamp GK. Longitudinal changes in sweet preferences in humans. *Physiol Behav.* 1987;39:639–41.

30. Schwartz C, Issanchou S, Nicklaus S. Developmental changes in the acceptance of the five basic tastes in the first year of life. *Br J Nutr*. 2009;102:1375–85.
31. De Graaf C, Zandstra EH. Sweetness intensity and pleasantness in children, adolescents, and adults. *Physiol Behav*. 1999;67:513–20.
32. Mennella JA, Lukasewycz LD, Griffith JW, Beauchamp GK. Evaluation of the Monell forced-choice, paired-comparison tracking procedure for determining sweet taste preferences across the lifespan. *Chem Senses*. 2011;36:345–55.
33. Stevens B, Yamada J, Ohlsson A. Sucrose for analgesia in newborn infants undergoing painful procedures. *Cochrane Database Syst Rev*. 2004;CD001069.
34. Segato FN, Castro-Souza C, Segato EN, Morato S, Coimbra NC. Sucrose ingestion causes opioid analgesia. *Braz J Med Biol Res*. 1997;30:981–4.
35. Barr RG, Pantel MS, Young SN, Wright JH, Hendricks LA, Gravel R. The response of crying newborns to sucrose: is it a "sweetness" effect? *Physiol Behav*. 1999;66:409–17.
36. Mucignat V, Ducrocq S, Lebas F, Mochel F, Baudon JJ, Gold F. Analgesic effects of Emla cream and saccharose solution for subcutaneous injections in preterm newborns: a prospective study of 265 injections. *Arch Pediatr*. 2004;11:921–5.
37. Ramenghi LA, Evans DJ, Levene MI. "Sucrose analgesia": absorptive mechanism or taste perception? *Arch Dis Child Fetal Neonatal Ed*. 1999;80:F146–7.
38. Miller A, Barr RG, Young SN. The cold pressor test in children: methodological aspects and the analgesic effect of intraoral sucrose. *Pain*. 1994;56:175–83.
39. Pepino MY, Mennella JA. Sucrose-induced analgesia is related to sweet preferences in children but not adults. *Pain*. 2005;119:210–8.
40. Mennella JA, Pepino MY, Lehmann-Castor SM, Yourshaw LM. Sweet preferences and analgesia during childhood: effects of family history of alcoholism and depression. *Addiction*. 2010;105:666–75.
41. Bartoshuk LMDV, 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;361:1137–48.
42. Bacon AW, Miles JS, Schiffman SS. Effect of race on perception of fat alone and in combination with sugar. *Physiol Behav*. 1994;55:603–6.
43. Drewnowski A, Levine AS. Sugar and fat: from genes to culture. *J Nutr*. 2003;133:S829–30.
44. Levine MD, Marcus MD, Perkins KA. A history of depression and smoking cessation outcomes among women concerned about post-cessation weight gain. *Nicotine Tob Res*. 2003;5:69–76.
45. Mennella JA, Pepino MY, Reed DR. Genetic and environmental determinants of bitter perception and sweet preferences. *Pediatrics*. 2005;115:e216–22.
46. Pepino MY, Mennella JA. Factors contributing to individual differences in sucrose preference. *Chem Senses*. 2005;30 Suppl 1:i319–20.
47. Liem DG, Mennella JA. Sweet and sour preferences during childhood: role of early experiences. *Dev Psychobiol*. 2002;41:388–95.
48. Coldwell SE, Oswald TK, Reed DR. A marker of growth differs between adolescents with high vs. low sugar preference. *Physiol Behav*. 2009;96:574–80.
49. Beauchamp GK, Cowart BJ. Congenital and experiential factors in the development of human flavor preferences. *Appetite*. 1985;6:357–72.
50. Sclafani A. Oral and postoral determinants of food reward. *Physiol Behav*. 2004;81:773–9.
51. Drewnowski A. Sensory control of energy density at different life stages. *Proc Nutr Soc*. 2000;59:239–44.
52. Sullivan SA, Birch LL. Pass the sugar, pass the salt: experience dictates preference. *Dev Psychol*. 1990;26:546–51.
53. Gibson EL, Wardle J. Energy density predicts preferences for fruit and vegetables in 4-year-old children. *Appetite*. 2003;41:97–8.
54. Birch LL, McPhee L, Steinberg L, Sullivan S. Conditioned flavor preferences in young children. *Physiol Behav*. 1990;47:501–5.
55. Johnson SL, McPhee L, Birch LL. Conditioned preferences: young children prefer flavors associated with high dietary fat. *Physiol Behav*. 1991;50:1245–51.
56. Riera CE, Vogel H, Simon SA, le Coutre J. Artificial sweeteners and salts producing a metallic taste sensation activate TRPV1 receptors. *Am J Physiol Regul Integr Comp Physiol*. 2007;293:R626–34.
57. Mennella JA, Pepino MY, Duke FF, Reed DR. Age modifies the genotype-phenotype relationship for the bitter receptor TAS2R38. *BMC Genet*. 2010;11:60.
58. American Dietetic Association. Position of the American Dietetic Association. Use of nutritive and nonnutritive sweeteners. *J Am Diet Assoc*. 2004;104:255–75.
59. Wilson JF. Does type of milk beverage affect lunchtime eating patterns and food choice by preschool children? *Appetite*. 1994;23:90–2.
60. Birch LL, McPhee L, Sullivan S. Children's food intake following drinks sweetened with sucrose or aspartame: time course effects. *Physiol Behav*. 1989;45:387–95.
61. Wharton CM, Hampl JS. Beverage consumption and risk of obesity among Native Americans in Arizona. *Nutr Rev*. 2004;62:153–9.
62. Collins JK, Davis AR, Adams A, Manness N, Perkins-Veazie PM. Consumer acceptability of low-sugar watermelon sweetened with non-calorie sweetener by a Native American community. *Int J Food Sci Nutr*. 2006;57:363–8.
63. Birch LL, Fisher JO. Development of eating behaviors among children and adolescents. *Pediatrics*. 1998;101:539–49.
64. Anzman SL, Rollins BY, Birch LL. Parental influence on children's early eating environments and obesity risk: implications for prevention. *Int J Obes (Lond)*. 2010;34:1116–24.
65. Swithers SE, Baker CR, Davidson TL. General and persistent effects of high-intensity sweeteners on body weight gain and caloric compensation in rats. *Behav Neurosci*. 2009;123:772–80.
66. Fowler SP, Williams K, Resendez RG, Hunt KJ, Hazuda HP, Stern MP. Fueling the obesity epidemic? Artificially sweetened beverage use and long-term weight gain. *Obesity (Silver Spring)*. 2008;16:1894–900.
67. Swithers SE, Martin AA, Davidson TL. High-intensity sweeteners and energy balance. *Physiol Behav*. 2010;100:55–62.
68. Brown RJ, de Banate MA, Rother KI. Artificial sweeteners: a systematic review of metabolic effects in youth. *Int J Pediatr Obes*. 2010;5:305–12.
69. Reed DR, McDaniel AH. The human sweet tooth. *BMC Oral Health*. 2006;6 Suppl 1:S17.
70. Faure A. Physiology of the sweet taste. In: *Progress in sensory physiology*. Autrum H, Ottoson D, Perl E, Schmidt R, Shimazu H, Willis W, editors. Berlin: Springer-Verlag; 1987.
71. Mattes RD. Gustation as a determinant of ingestion: methodological issues. *Am J Clin Nutr*. 1985;41:672–83.
72. Monneuse MO, Bellisle F, Louis-Sylvestre J. Impact of sex and age on sensory evaluation of sugar and fat in dairy products. *Physiol Behav*. 1991;50:1111–7.
73. Hayes JE, Duffy VB. Oral sensory phenotype identifies level of sugar and fat required for maximal liking. *Physiol Behav*. 2008;95:77–87.
74. Conner MT, Haddon AV, Pickering ES, Booth DA. Sweet tooth demonstrated: individual differences in preference for both sweet foods and foods highly sweetened. *J Appl Psychol*. 1988;73:275–80.
75. Salbe AD, DelParigi A, Pratley RE, Drewnowski A, Tataranni PA. Taste preferences and body weight changes in an obesity-prone population. *Am J Clin Nutr*. 2004;79:372–8.
76. Drewnowski A, Brunzell JD, Sande K, Iverius PH, Greenwood MR. Sweet tooth reconsidered: taste responsiveness in human obesity. *Physiol Behav*. 1985;35:617–22.
77. Mahar A, Duizer LM. The effect of frequency of consumption of artificial sweeteners on the sweetness liking by women. *J Food Sci*. 2007;72: S714–8.
78. Laeng B, Berridge KC, Butter CM. Pleasantness of a sweet taste during hunger and satiety: effects of gender and "sweet tooth". *Appetite*. 1993;21:247–54.
79. Hetherington M, Rolls BJ, Burley VJ. The time course of sensory-specific satiety. *Appetite*. 1989;12:57–68.
80. Frankham P, Gosselin C, Cabanac M. Diet induced weight loss accelerates onset of negative alliesthesia in obese women. *BMC Public Health*. 2005;5:112.
81. Berridge KC. Wanting and liking: observations from the Neuroscience and Psychology Laboratory. *Inquiry*. 2009;52:378.
82. Brondel L, Cabanac M. Alliesthesia in visual and auditory sensations from environmental signals. *Physiol Behav*. 2007;91:196–201.
83. Collaku A, Rankinen T, Rice T, Leon AS, Rao DC, Skinner JS, Wilmore JH, Bouchard C. A genome-wide linkage scan for dietary energy and nutrient intakes: the Health, Risk Factors, Exercise Training, and Genetics (HERITAGE) Family Study. *Am J Clin Nutr*. 2004;79:881–6.

84. van Baak MA, Astrup A. Consumption of sugars and body weight. *Obes Rev.* 2009;10 Suppl 1:9–23.
85. Macdiarmid JI, Vail A, Cade JE, Blundell JE. The sugar-fat relationship revisited: differences in consumption between men and women of varying BMI. *Int J Obes Relat Metab Disord.* 1998;22:1053–61.
86. Barkeling B, Andersson I, Lindroos AK, Birkhed D, Rossner S. Intake of sweet foods and counts of cariogenic microorganisms in obese and normal-weight women. *Eur J Clin Nutr.* 2001;55:850–5.
87. Oliver G, Wardle J, Gibson EL. Stress and food choice: a laboratory study. *Psychosom Med.* 2000;62:853–65.
88. Gibson EL. Emotional influences on food choice: sensory, physiological and psychological pathways. *Physiol Behav.* 2006;89:53–61.
89. Kampov-Polevoy AB, Alterman A, Khalitov E, Garbutt JC. Sweet preference predicts mood altering effect of and impaired control over eating sweet foods. *Eat Behav.* 2006;7:181–7.
90. Striegel-Moore RH, Bulik CM. Risk factors for eating disorders. *Am Psychol.* 2007;62:181–98.
91. Simon Y, Bellisle F, Monneuse MO, Samuel-Lajeunesse B, Drewnowski A. Taste responsiveness in anorexia nervosa. *Br J Psychiatry.* 1993;162:244–6.