The sweetness and bitterness of childhood: Insights from basic research on taste preferences

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Abstract

In this article, we review findings from basic, experimental research on children that suggests the liking of sweet and the dislike of bitter tastes reflects children's basic biology. Children are born preferring sweet tastes, which attract them to mother's milk and even act as an analgesic. They prefer higher levels of sweet than do adults, with preferences declining to adult levels during middle to late adolescence, which coincides with the cessation of physical growth. The level of sweetness most preferred by children has remained heightened relative to adults for nearly a decade, despite reductions in sugar, both consumed and in the food environment. In spite of these reductions, however, children's intake of sugar remains higher than that recommended by health organizations worldwide. In contrast to sweet taste, children dislike and reject bitter taste, which protects them from ingesting poisons. Although variation in bitter taste receptor genes such as *TAS2R38* accounts for people's marked differences in perceptions of the same bitter-tasting compounds, basic research revealed that these genotype-phenotype relationships are modified with age, with children of the same genotype being more bitter sensitive than adults and the changeover occurring during mid adolescence. This heightened bitter sensitivity is also evident in the taste of the foods (green vegetables) or medicines (liquid formulations of drugs) they dislike and reject. While bitter taste can be masked or blocked to varying degrees by sugars and salts, their efficacy in modulating bitterness is not only based on the type of bitter ligand but on the person's age. Children's heightened preference for sweet and dislike of bitter, though often detrimental in the modern food environment, reflects their basic biology. Increasing knowledge of individual variation in taste due to both age and genetics will shed light on potential strategies to promote healthier eating since chronic diseases derive in large part from poor food choice dictated by taste preferences as well as to contribute to a new era of drug formulations designed especially for the taste palate of children.

Keywords

children; taste; learning; genetic variation; diet

Introduction

Sweet tasting candies have been the first purchase children have made with their own money since the 19th century [1]. Removing the medicines from the colorful drops of flavored sugar typically found in druggists' stocks resulted in "penny candies"—the first confections to reach a mass audience in America, specifically targeted to working-class children who could afford the occasional penny's worth of bliss [2]. It's no surprise that easy access to cheap candy, manufactured on readily available machinery from inexpensive sugar, was a marketing success—children's proclivity for sweetness, not to mention its use to "make the medicine go down," is universal and evident among cultures around the world. In this article, we review findings from basic, experimental research in children that suggest the liking of sweet taste and the dislike of bitter taste are not solely a product of modern-day technology and advertising, but are reflective of children's basic biology.

The sense of taste, of which sweet and bitter are just two of the five modalities (which also include sour, salty, and umami), can be a source of pleasure or pain and serves as gatekeeper to ensure that animals correctly make one of the more important decisions they face: whether to accept or reject a food or liquid. The liking of sweet and rejection of bitter represent inborn responses, yet there is inherent plasticity in these senses—our biology is not necessarily our destiny. We acknowledge that, in the scientific research on the ontogeny of these diverse tastes, each psychophysical measure has its limitations. However, a convergence of findings suggests that the ability to detect tastes is present early in ontogeny [3], is remarkably well conserved phylogenetically [4], and that this ability can modulate complex behaviors, including dietary choices, throughout the life span [5].

Sweet: The Taste of Pleasure

The sensations experienced when tasting something sweet are mediated by taste receptors in the periphery and by multiple brain substrates [6, 7] which are associated with reward-related learning and behaviors [8]. Taste receptor cells produce proteins that participate in sweet taste transduction, and some of these proteins are inserted into the cell membrane to form taste receptors [9]. Two proteins, T1R2 and T1R3 (taste receptor family 1, proteins 2 and 3), combine to create a sweet receptor; their associated genes are *TAS1R2* and *TAS1R3*.

Several lines of evidence indicate that the liking for sweet taste is inborn. Before birth, the ability to detect sweet tastes is functioning and interacting with systems controlling affect and suckling [10]; thus, babies are born able to detect and prefer the predominant taste quality of the food they need to survive: mother's milk. Newborns respond to even dilute sweet tastes, differentiate varying degrees of sweetness, and, given the choice, will consume more of a sugar solution than water [11, 12]. When a sweet solution is placed in the oral cavity, the infant's face relaxes, resembling an expression of satisfaction that may be followed by a smile [4, 13, 14]. Two- to 3-day-old infants respond to sucrose administration

with asymmetrical brain electrical activity usually associated with hedonically positive emotional reactions or approach behavior [15]. Autonomic responses vary according to the behavioral state of the infant: when increasing concentrations of sucrose were placed in the mouths of calm infants, their heart rates increased proportionally [16], but when sweet tastes were introduced to agitated infants, their heart rates decreased, resulting in overall calmness [17].

Perhaps most investigated in the ontogeny of human sweet perception is the ability of sweet tastes to act as an analgesic in infants and children. Small amounts of a sweet solution placed on the tongue of a crying newborn exert a rapid, calming effect that persists for several minutes [18, 19]. Because non-caloric sweet substances such as aspartame mimic the calming effects of sucrose [19], and because the administration of sucrose by direct stomach loading is not effective [20], it appears that afferent signals from the mouth, rather than metabolic or gastric changes, are responsible for the analgesic properties of sweet tastes. Recent systematic reviews on this body of research concluded that administration of sweet tastes is safe and effective for reducing procedural pain in infants from single painful events such as heel lance, venipuncture, and circumcision in the short term [21].

The ability of sweet tastes to reduce pain continues during childhood, as evidenced by the finding that the presence of sucrose, but not water, in the oral cavity delayed 8- to 11-year-old children's reporting of pain onset when undergoing a cold-induced pain stimulus test [22-24]. Sucrose's efficacy in reducing pain is related to the hedonic value of sweet taste for the child: the more children like sucrose, the better it works in increasing pain tolerance [24].

Children as young as 3 years of age are capable of participating in psychophysical tasks that measure the levels of taste most preferred. In 1990, a method for measuring an individual's most preferred level of salty taste was developed at the Monell Center [25], and later adapted for sweet taste and included in the NIH Toolbox [26]. In age-related comparisons, the same forced-choice, paired-comparison tracking method [27] is used for both pediatric and adult populations. This body of both longitudinal and cross-sectional research consistently reveals that the most preferred concentration of sweet taste remains heightened throughout childhood (~ 0.54-0.60M sucrose) and does not decline to adult levels until middle to late adolescence [27, 28]. To put this in perspective, a 0.60M sucrose concentration is equivalent to ~12 teaspoons (4 grams per teaspoon) of sugar in 230 ml of water (8 ounce glass), whereas a typical cola has a 0.34M sugar concentration (~ 7 teaspoons in 8 ounces of water, which is closer to adults' level of most preferred sweetness).

Data collected from two separate populations of children and adults, using the same methods but almost a decade apart, highlight the stability of the age-related bliss point in sweet tastes. These two study populations consisted of: (1) 244 children (5-10 years) and 235 adults (22-52 years) who participated in research studies at the Monell Center in 2002-2003 (33.4% white, 53.7% black, 12.9% other/more than one race), and (2) 109 children (5-12 years) and 83 adults (20-56 years) who participated in 2010 (31.4% white, 48.2% black, 20.4% other/more than one race). To measure the most preferred level of sweet taste, we used a 2-series, forced-choice tracking method (see [27] for more details). All procedures

were approved by the Office of Regulatory Affairs at the University of Pennsylvania and informed consent was obtained from each adult or parent of child and assent obtained from those children seven years and older.

The age-related differences in most preferred level of sweetness were remarkably consistent between 2002 and 2010, despite changes in overall sugar intake (i.e., both added sugar and dietary sugar inherent to fruit and dairy products) among both children and adults over this time period. As shown in Figure 1, children, on average, most preferred a 0.54-0.56 M whereas adults most preferred a 0.42-0.44 M sucrose solution. Although self-reported dietary recall data has its limitations [29], NHANES data collected over 2-year periods from 2001 to 2011 showed reductions in sugar consumption among both children (2-11 years) and adults (20-59 years) by more than 15 grams per day (2001-2002 [30], 2003-2004 [31], 2005-2006 [32], 2007-2008 [33], 2009-2010 [34], 2011-2012 [35]). Consistent with these data, food supply data from the Food and Agriculture Organization of the United Nations indicate a reduction of sugars available in the American food supply of approximately 7 kg per capita over the same period [36]. That the level of sweetness most preferred by children remained heightened relative to adults over nearly a decade despite reductions in sugar both consumed and in the food environment, provides further evidence that sweet preferences are largely driven by basic biology. It is important to note, however, that although the consumption of sugars declined over time, intakes continue to exceed recommended limits [37]. Moreover, how much sugar is in the child's diet may not be a good proxy for its overall level of "sweetness" given the increase use of non-nutritive sweeteners in the food supply, especially in foods geared for children.

What causes the age-related decline in sweet preference and consumption between childhood and adulthood remains a mystery, but it has been observed in other mammals [38]. One hypothesis is that heightened sweet preference early in life may be linked to the growing child's need for calories [39], which is supported by recent findings [40]. Coldwell and colleagues divided 11- to 15-year-olds into 'high' and 'low' sweet preference groups based on their sucrose preferences [40]. Although the groups did not differ in sucrose detection thresholds, age, body mass index, percent body fat, or pubertal development, they did differ in levels of N-telopeptides of type I collagen (NTx), a biomarker for bone resorption and growth [41] that is higher during growth spurts. NTx levels were significantly lower in the low sweet preference group than in the high sweet preference group, suggesting that the age-related decline in sucrose preferences may be related to the cessation of physical growth [40].

More recently, we confirmed this relationship between sweet taste preference and NTx in a younger cohort (5- to 10 years): children who were tall for their age preferred sweeter solutions than did those who were shorter. Further, sweet (as well as salty) taste preferences were related to real-world food preferences. That is, the level of sucrose most preferred by children, as measured in the laboratory, was significantly related to children's preferences for sweet-tasting foods, such as cereals [42, 43], puddings [44], and beverages [43]. Because genetic variation in the *TAS1R3* sweet receptor gene accounts for differences in sweet taste preference in adults but not in children [44, 45], we posit that children's desire for sweetness may relate to some aspect of development, such as the need for nutrients during periods of

maximal growth, which "trumps" the more subtle effects of genotype on sweet taste perception [44]. We emphasize here that there have been changes in our food supply, even in foods geared toward children, such that they often contain non-nutritive sweeteners (NNS) that provide sweetness with fewer calories [46]. With increasing use of NNS in the food supply, the sweetness of a food is no longer a reliable predictor of its sugar or energy content for the child.

Although psychophysical research indicates that age-related changes in the taste system relate to basic biology, there is also evidence that children learn through dietary experiences [47]. Children who were fed sugar water as infants preferred a more concentrated sugar solution at 2 years of age [48], and throughout later childhood (6–10 years), than did those without such experiences [49]. Whether there are sensitive periods during early infancy during which time experiences with sweets may shift overall sweet preference is unknown. In fact, no compelling data suggest that repeated exposure to sugar water results in a generalized heightened hedonic response to sweetness [48]. Instead, the practice of feeding sugar water may be an indicator of a mother's personal use of higher levels of added sugars, which may be related her child's preferences. In one study, 4- to 7-year-olds whose mothers reported adding sugar to their foods on a routine basis were significantly more likely to prefer apple juices with added sugar and cereals with higher sugar contents than similar-age children whose mothers reported never adding sugar to foods at home [42]. That children learn about the context of sweet is suggested by a study of 4- to 5-year-old children. Those who were repeatedly exposed to sweetened tofu (an unfamiliar food) preferred that version over salted and plain versions in a post-exposure taste test; that is, the sweetened preparation became familiar, appropriate, and therefore acceptable, ultimately affecting preference [47].

Taken together, the convergence of scientific evidence suggests that the ability to detect and prefer sweets is evident early in life and is largely a reflection of biology. Evolution has shaped the child's response to sweets and our sensory systems evolved to detect and prefer the once rare calorie-rich foods that taste sweet [50]. But the science also reveals that children learn the context in which the sweet taste experience occurs. That is, the sensation of sweetness is context dependent and can acquire meaning through associative learning [51, 52]. Through familiarization, children develop a sense of what should, or should not, taste sweet. During childhood, they learn the rules of cuisine: what to eat, how to eat, when to eat and how sweet a food is supposed to taste [47, 53-57].

Bitter: The Taste of Poison

Bitter is often considered the opposite of sweet—many consider its taste to be bad and undesirable. However, bitter perception actually shares several features with sweet perception [58]. Both bitter and sweet compounds bind to similar types of taste receptors (G-protein coupled receptors). However, whereas the family of sweet receptor proteins is small, with only three known genes, there are about 25 different bitter receptors (T2Rs), with genes clustered primarily on chromosomes 7 and 12 [59, 60]. Of the five basic tastes, bitter taste is the most diverse at both psychophysical (e.g., sensitivity to a particular ligand) and genetic levels of analyses (e.g., variation in haplotypes and numerous receptors, and molecular receptive ranges of bitter taste receptors) [61].

People of all ages differ markedly in their perceptions of the same compound. For example, polymorphisms in *TAS2R38*, the most studied of all taste receptor variants, relate to differences in the perception of 6-*n*-propylthiouracil (PROP), recognized primarily by the T2R38 bitter receptor, as well as bitter-tasting compounds (e.g., glucosinolates [62]) commonly found in cruciferous vegetables [63-65]. Certain polymorphisms result in changes to a section of the *TAS2R38* receptor's amino acid sequence from alanine-valine-isoleucine (AVI) in nontasters to proline-alanine-valine (PAV) in tasters [66-68]. These polymorphisms allow people who are homozygous AVI/AVI to enjoy broccoli or turnips without perceiving the bitterness that heterozygous AVI/PAV and especially homozygous PAV/PAV people taste [65].

We recently investigated whether person-to-person differences in bitter perception were related to the expression of this receptor's mRNA [69], in addition to genotype. Variation in mRNA abundance in taste cells may reflect the number of receptors present in the taste papillae, which in turn may explain some of the wide variation evident in bitter taste perception among those sharing the same genotype [68]. Although one may expect individuals with the heterozygous *TAS2R38* genotype (PAV/AVI) to have a sensitivity to PROP intermediate to that of both homozygous genotypes (PAV/PAV and AVI/AVI), as a group these individuals show a wide range of sensitivities [66, 68]. In order to explore the hypothesis that this range is related to expression of PAV-*TAS2R38* messenger RNA, heterozygous adult subjects evaluated bitterness of a variety of ligands and provided fungiform papillae samples that were used to quantify amounts of PAV "taster" allele mRNA, as those with more mRNA for a given gene make more of the encoded receptor. PAV-*TAS2R38* mRNA expression varied widely among adults, but those with more mRNA expression of the taster allele reported more bitterness from the ligands of PROP and broccoli juice, highlighting the value of combining psychophysics with genetic measures to clarify the relationship among taste, diet, and gene expression.

The ontogeny of bitter taste perception has been less studied than that reviewed above for sweet [3]. Neonates will gape, wrinkle their noses, shake their heads, flail their arms, and frown when a bitter-tasting solution is placed in the oral cavity [4, 13, 14]. Beginning around 2 weeks of age, an infant will consume less and suck less while tasting a bitter-tasting (urea) solution [70]. And as the child develops, rejection of bitter is evident in their rejection of liquid formulations of medicine and of certain foods (e.g., dark green vegetables). However, we have evidence that children differ from adults in their sensitivity to some bitters. Using identical psychophysical methodologies for adults, adolescents and children, we found a phenotype-genotype relationship for PROP sensitivity that varies with age: children with bitter-sensitive *TAS2R38* genotypes were more sensitive to the bitter taste of PROP than were adults with the same genotype [43], with the changeover occurring during adolescence [68]. These results imply that, within the same genotype, taste can change from more to less sensitive over the life span (see also [71]).

Variation in the *TAS2R38* gene is not only related to vegetable intake by college-aged students [72], but recent work in children has shown it is related to acceptance of certain formulation of medicines [73]. Because the active pharmaceutical ingredients (API) in drugs by their very nature often taste unpleasant, with bitter taste a primary culprit, a central

challenge of administering medicine to children is a "matter of taste" [17]. In fact, the more potent a medication's pharmacologic activity, the more bitter its taste [74]. Unlike the adult who often takes medication in solid oral dosage forms (pills, tablets) that have the advantage of encapsulating the bitter taste of API (and consequently tasting less bitter), many children have difficulty swallowing pills, and so liquid formulations are often used. We wondered whether children who are most sensitive to bitterness due to their taste genotypes may be more likely to try solid formulations (pills). Indeed, children with at least one bitter-sensitive allele were more likely to have taken medication in a solid formulation than were children with the bitter-insensitive genotype [73], perhaps because their bitter sensitivity makes them more motivated to take pills or tablets.

Although dislike of bitter is inborn, bitterness can be masked or blocked. Psychophysical studies in adults suggest that the mode of action for bitterness suppression differs between salts and sugars. Sodium salts appear to suppress bitter taste in the periphery (receptor level), and this suppression is compound specific [75-78]. Sugars, on the other hand, act along the central gustatory pathway (cognitive level) and have been shown to suppress the bitterness of a range of bitter agents in adults [45, 76, 79]. Of particular interest is the use of sucrose in commonly consumed caffeinated and alcoholic beverages. Though both produce mild psycho-stimulant effects [80, 81] that are thought to underlie their widespread use, both often contain added sweeteners, which in addition to providing well-liked sweetness, serve to mask unwanted bitterness.

In recent years, we have developed methods to conduct basic research on bitter taste in children to determine whether the same methods that work in the blocking or suppression of bitter taste in adults also work for children [45, 77, 78]. To examine age-related efficacy of bitter blockers (both sodium salts and sucrose), we conducted basic research studies using PROP and the generally recognized as safe (GRAS) bitter agents urea, caffeine, quinine, denatonium benzoate (a compound typically added to detergents to deter ingestion by children), and tetralone (i.e., iso-alpha acids commonly found in beer) as test stimuli. The ability of two sodium salts (sodium gluconate and monosodium glutamate) to block bitter taste was both compound specific, consistent with adult studies [75, 78], and age specific [77, 78]. In general, if the sodium salt worked in blocking (or enhancing) bitterness for a given bitter ligand in children, it also worked for adults, but not *vice versa* (Table 1). Sucrose, in contrast, was much more effective overall in suppressing bitterness than were sodium salts for both age groups [45, 82]. Sweetened, caffeinated energy drinks, which are heavily marketed toward children and adolescents [83] and which have grown in popularity in recent years [84], may be particularly attractive to children because of the added sugars not only impart a sweet taste but mask the bitterness of caffeine as well.

Concluding Remarks

The research findings reviewed in this article suggest that the innate preference for sweets and rejection of bitters in humans are consequences of evolutionary selection, favoring consumption of high-energy, vitamin-rich mother milk and fruits [50] and avoidance of bitter, poisonous plants [85]. Thus, when we examine children's dietary patterns or medication compliance from the perspective of the development of taste, we should not be

surprised at what children naturally prefer (e.g., sweet snacks) and what they dislike (e.g., bitter-tasting green vegetables, liquid formulations of medicines), which reflect their basic biology.

In a food environment replete with sugars and sweetened foods, including commercially prepared foods for toddlers [86], children's heightened preference for sweet may make them vulnerable to overconsumption as early exposure to sweetened foods teaches them the context in which sweet taste should be experienced [51, 87]. Basic research from the biological, psychological and social aspects of food intake, taste, and feeding in both human and non-human animals, has provided important insights [17, 88] that will continue to help improve ingestive behavior of pediatric populations. Increasing knowledge of individual variation in taste due to both age and genetics may help realize a new era in development of personalized medicines specially designed for children who are particularly sensitive to bitter taste [89, 90]. Because of the differences in bitter taste perception between children and adults, we suggest that research aimed at reducing the bitterness of medicine, such as evaluating the effectiveness of bitter blockers, should directly involve children rather than extrapolating from data collected from adults. Further, greater knowledge on the ontogeny of taste and flavor learning will continue to contribute to the development of strategies to promote healthier eating that account for children's taste preferences [91]. Despite the knowledge that children prefer heightened levels of sweet (and salty) tastes, there is no research to date that addresses whether their preferences can be shifted to prefer as well as consume lower levels, which could have an important impact on health outcomes in the long term. Understanding the unique vulnerability of children to the modern food system is a critical first step, one that sets the stage for developing informed, evidence-based strategies to address what has become an issue of great public health importance since many chronic diseases that plague modern society derive in large part from poor food choice, dictated by our flavor preferences and the types of foods that are available and deemed appropriate for children.

ACKNOWLEDGMENTS

References

[1]. Woloson, WA. Refined Tastes: Sugar, Confectionery, and Consumers in Nineteenth - Century America. The Johns Hopkins University Press; Baltimore, Maryland: 2002.

[2]. Smith, AF., editor. Oxford Encyclopedia of Food and Drink in America. Oxford University Press; New York, NY: 2004.

[3]. Forestell, CA.; Mennella, JA. The ontogeny of taste perception and preference throughout childhood. In: Doty, RL., editor. Handbook of Olfaction and Gustation. 3rd edition. Marcel Dekker; New York: 2015.

[4]. 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. [PubMed: 11166078]

[5]. Glanz K, Basil M, Maibach E, Goldberg J, Snyder D. Why Americans eat what they do: Taste, nutrition, cost, convenience, and weight control concerns as influences on food consumption. J Am Diet Assoc. 1998; 98:1118–26. [PubMed: 9787717]

[6]. Berridge KC. Pleasures of the brain. Brain Cogn. 2003; 52:106–28. [PubMed: 12812810]

[7]. Small DM. Flavor is in the brain. Physiol Behav. 2012; 107:540–52. [PubMed: 22542991]

[8]. Small DM. Individual differences in the neurophysiology of reward and the obesity epidemic. Int J Obes (Lond). 2009; 33(Suppl 2):S44–8. [PubMed: 19528979]

[9]. Nelson G, Hoon MA, Chandrashekar J, Zhang Y, Ryba NJ, Zuker CS. Mammalian sweet taste receptors. Cell. 2001; 106:381–90. [PubMed: 11509186]

[10]. 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; 13:179–91. [PubMed: 2365138]

[11]. Nowlis GH, Kessen W. Human newborns differentiate differing concentrations of sucrose and glucose. Science. 1976; 191:865–6. [PubMed: 1251200]

[12]. Desor, JA.; Maller, O.; Turner, RE. Preference for sweet in humans: Infants, children and adults. In: Weiffenbach, JM., editor. Taste and Development: The Genesis of Sweet Preference. US Government Printing Office; Washington, DC: 1977.

[13]. Rosenstein D, Oster H. Differential facial responses to four basic tastes in newborns. Child Dev. 1988; 59:1555–68. [PubMed: 3208567]

[14]. Steiner, JE. Facial expressions of the neonate infant indicating the hedonics of food-related chemical stimuli. In: Weiffenbach, JM., editor. Taste and Development: The Genesis of Sweet Preference. U.S. Government Printing Office; Washington, DC: 1977.

[15]. Fox NA, Davidson RJ. Taste-elicited changes in facial signs of emotion and the asymmetry of brain electrical activity in human newborns. Neuropsychologia. 1986; 24:417–22. [PubMed: 3736825]

[16]. Ashmead DH, Reilly BM, Lipsitt LP. Neonates' heart rate, sucking rhythm, and sucking amplitude as a function of the sweet taste. J Exp Child Psychol. 1980; 29:264–81. [PubMed: 7365425]

[17]. Blass EM, Watt LB. Suckling- and sucrose-induced analgesia in human newborns. Pain. 1999; 83:611–23. [PubMed: 10568870]

[18]. Blass EM, Hoffmeyer LB. Sucrose as an analgesic for newborn infants. Pediatrics. 1991; 87:215–8. [PubMed: 1987534]

[19]. 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. [PubMed: 10357429]

[20]. Ramenghi LA, Evans DJ, Levene MI. "Sucrose analgesia": Absorptive mechanism or taste perception? Arch Dis Child Fetal Neonatal Ed. 1999; 80:F146–7. [PubMed: 10325795]

[21]. Stevens B, Yamada J, Ohlsson A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database Syst Rev. 2010 CD001069.

[22]. 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. [PubMed: 8008408]

[23]. 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. [PubMed: 20148789]

[24]. Pepino MY, Mennella JA. Sucrose-induced analgesia is related to sweet preferences in children but not adults. Pain. 2005; 119:210–8. [PubMed: 16298489]

[25]. Cowart, BJ.; Beauchamp, GK. Early development of taste perception. In: McBride, R.; MacFie, H., editors. Psychological Basis of Sensory Evaluation. London, England: 1990. p. 1-7.

[26]. Coldwell SE, Mennella JA, Duffy VB, Pelchat ML, Griffith JW, Smutzer G, et al. Gustation assessment using the NIH Toolbox. Neurology. 2013; 80:S20–4. [PubMed: 23479539]

[27]. 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

[28]. Desor JA, Beauchamp GK. Longitudinal changes in sweet preferences in humans. Physiol Behav. 1987; 39:639–41. [PubMed: 3588712]

[29]. Dhurandhar NV, Schoeller D, Brown AW, Heymsfield SB, Thomas D, Sorensen TI, et al. Energy balance measurement: when something is not better than nothing. Int J Obes (Lond). 2014 [Epub ahead of print] doi: 10.1038/ijo.2014.199.

[30]. U.S. Department of Agriculture ARS. Beltsville Human Nutrition Research Center. Food Surveys Research Group (Beltsville, MD). U.S. Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Health Statistics (Hyattsville, MD). [Accessed on: January 7, 2015] What we eat in America, NHANES 2001-2002, Dietary Interview - Total Nutrients Intakes. [http://www.ars.usda.gov/SP2UserFiles/Place/80400530/pdf/0102/Table_1_BIA.pdf]

[31]. U.S. Department of Agriculture ARS. Beltsville Human Nutrition Research Center. Food Surveys Research Group (Beltsville, MD). U.S. Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Health Statistics (Hyattsville, MD). [Accessed on: January 7, 2015] What we eat in America, NHANES 2003-2004, Dietary Interview - Total Nutrients Intakes. [http://www.ars.usda.gov/SP2UserFiles/Place/80400530/pdf/0304/Table_1_NIF.pdf]

[32]. U.S. Department of Agriculture ARS. Beltsville Human Nutrition Research Center. Food Surveys Research Group (Beltsville, MD). U.S. Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Health Statistics (Hyattsville, MD). What we eat in America, NHANES 2005-2006, Dietary Interview - Total Nutrients Intakes.

[33]. U.S. Department of Agriculture ARS. Beltsville Human Nutrition Research Center. Food Surveys Research Group (Beltsville, MD). U.S. Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Health Statistics (Hyattsville, MD). [Accessed on: January 7, 2015] What we eat in America, NHANES 2007-2008, Dietary Interview - Total Nutrients Intakes. [http://www.ars.usda.gov/SP2UserFiles/Place/80400530/pdf/0708/Table_1_NIN_GEN_07.pdf]

[34]. U.S. Department of Agriculture ARS. Beltsville Human Nutrition Research Center. Food Surveys Research Group (Beltsville, MD). U.S. Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Health Statistics (Hyattsville, MD). [Accessed on: January 7, 2015] What we eat in America, NHANES 2009-2010, Dietary Interview - Total Nutrients Intakes. [http://www.ars.usda.gov/SP2UserFiles/Place/80400530/pdf/0910/Table_1_NIN_GEN_09.pdf]

[35]. U.S. Department of Agriculture ARS. Beltsville Human Nutrition Research Center. Food Surveys Research Group (Beltsville, MD). U.S. Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Health Statistics (Hyattsville, MD). [Accessed on: January 7, 2015] What we eat in America, NHANES 2011-2012, Dietary Interview - Total Nutrients Intakes. [http://www.ars.usda.gov/SP2UserFiles/Place/80400530/pdf/1112/Table_1_NIN_GEN_11.pdf]

[36]. Food and Agriculture Organization of the United Nations. [Accessed on: January 7, 2015] Food balance sheets. [http://faostat3.fao.org/download/FB/*/E]

[37]. Slining MM, Popkin BM. Trends in intakes and sources of solid fats and added sugars among U.S. children and adolescents: 1994-2010. Pediatr Obes. 2013; 8:307–24. [PubMed: 23554397]

[38]. Bertino M, Wehmer F. Dietary influences on the development of sucrose acceptability in rats. Dev Psychobiol. 1981; 14:19–28. [PubMed: 7274574]

[39]. Drewnowski A. Sensory control of energy density at different life stages. Proc Nutr Soc. 2000; 59:239–44. [PubMed: 10946792]

[40]. 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. [PubMed: 19150454]

[41]. Yang L, Grey V. Pediatric reference intervals for bone markers. Clin Biochem. 2006; 39:561–8. [PubMed: 16423337]

[42]. Liem DG, Mennella JA. Sweet and sour preferences during childhood: Role of early experiences. Dev Psychobiol. 2002; 41:388–95. [PubMed: 12430162]

[43]. Mennella JA, Pepino MY, Reed DR. Genetic and environmental determinants of bitter perception and sweet preferences. Pediatrics. 2005; 115:e216–22. [PubMed: 15687429]

[44]. Mennella JA, Finkbeiner S, Reed DR. The proof is in the pudding: Children prefer lower fat but higher sugar than do mothers. Int J Obes (Lond). 2012; 36:1285–91. [PubMed: 22546773]

[45]. Mennella JA, Reed DR, Mathew PS, Roberts KM, Mansfield CJ. "A spoonful of sugar helps the medicine go down": Bitter masking by sucrose among children and adults. Chem Senses. 2014; 40:17–25. [PubMed: 25381313]

[46]. 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. [PubMed: 19056571]

[47]. Sullivan SA, Birch LL. Pass the sugar, pass, the salt: Experience dictates preference. Dev Psychol. 1990; 26:546–51.

[48]. Beauchamp GK, Moran M. Acceptance of sweet and salty tastes in 2-year-old children. Appetite. 1984; 5:291–305. [PubMed: 6529258]

[49]. Pepino MY, Mennella JA. Factors contributing to individual differences in sucrose preference. Chem Senses. 2005; 30(Suppl 1):i319–i20. [PubMed: 15738179]

[50]. Simmen B, Hladik CM. Sweet and bitter taste discrimination in primates: Scaling effects across species. Folia Primatol (Basel). 1998; 69:129–38. [PubMed: 9595682]

[51]. Beauchamp GK, Cowart BJ. Congenital and experiential factors in the development of human flavor preferences. Appetite. 1985; 6:357–72. [PubMed: 3911888]

[52]. Sclafani A. Oral and postoral determinants of food reward. Physiol Behav. 2004; 81:773–9. [PubMed: 15234183]

[53]. Mennella JA, Nicklaus S, Jagolino AL, Yourshaw LM. Variety is the spice of life: Strategies for promoting fruit and vegetable acceptance during infancy. Physiol Behav. 2008; 94:29–38. [PubMed: 18222499]

[54]. Gerrish CJ, Mennella JA. Flavor variety enhances food acceptance in formula-fed infants. Am J Clin Nutr. 2001; 73:1080–5. [PubMed: 11382663]

[55]. Forestell CA, Mennella JA. Early determinants of fruit and vegetable acceptance. Pediatrics. 2007; 120:1247–54. [PubMed: 18055673]

[56]. Rozin, P. The acquisition of food habits and preferences. In: Mattarazzo, HD.; Weiss, SM.; Herd, JA.; Miller, NE.; Weiss, SM., editors. Behavioral Health: A Handbook of Health Enhancement and Disease Prevention. John Wiley and Sons; New York, New York: 1984. p. 590-607.

[57]. Rozin P, Vollmecke TA. Food likes and dislikes. Annu Rev Nutr. 1986; 6:433–56. [PubMed: 3524623]

[58]. Reed DR, Tanaka T, McDaniel AH. Diverse tastes: Genetics of sweet and bitter perception. Physiol Behav. 2006; 88:215–26. [PubMed: 16782140]

[59]. Adler E, Hoon MA, Mueller KL, Chandrashekar J, Ryba NJ, Zuker CS. A novel family of mammalian taste receptors. Cell. 2000; 100:693–702. [PubMed: 10761934]

[60]. Chandrashekar J, Mueller KL, Hoon MA, Adler E, Feng L, Guo W, et al. T2Rs function as bitter taste receptors. Cell. 2000; 100:703–11. [PubMed: 10761935]

[61]. Meyerhof W, Batram C, Kuhn C, Brockhoff A, Chudoba E, Bufe B, et al. The molecular receptive ranges of human TAS2R bitter taste receptors. Chem Senses. 2010; 35:157–70. [PubMed: 20022913]

[62]. Lund E. Non-nutritive bioactive constituents of plants: Dietary sources and health benefits of glucosinolates. Int J Vitam Nutr Res. 2003; 73:135–43. [PubMed: 12747221]

[63]. Bartoshuk LM, Duffy VB, Reed D, Williams A. Supertasting, earaches and head injury: Genetics and pathology alter our taste worlds. Neurosci Biobehav R. 1996; 20:79–87.

[64]. Duffy VB. Variation in oral sensation: Implications for diet and health. Curr Opin Gastroenterol. 2007; 23:171–7. [PubMed: 17268246]

[65]. Sandell MA, Breslin PA. Variability in a taste-receptor gene determines whether we taste toxins in food. Curr Biol. 2006; 16:R792–4. [PubMed: 16979544]

[66]. Bufe B, Breslin PA, Kuhn C, Reed DR, Tharp CD, Slack JP, et al. The molecular basis of individual differences in phenylthiocarbamide and propylthiouracil bitterness perception. Curr Biol. 2005; 15:322–7. [PubMed: 15723792]

[67]. Kim U, Jorgenson E, Coon H, Leppert M, Risch N, Drayna D. Positional cloning of the human quantitative trait locus underlying taste sensitivity to phenylthiocarbamide. Science. 2003; 299:1221–5. [PubMed: 12595690]

[68]. Mennella JA, Pepino MY, Duke FF, Reed DR. Age modifies the genotype-phenotype relationship for the bitter receptor TAS2R38. BMC Genet. 2010; 11:60. [PubMed: 20594349]

[69]. Lipchock SV, Mennella JA, Spielman AI, Reed DR. Human bitter perception correlates with bitter receptor messenger RNA expression in taste cells. Am J Clin Nutr. 2013; 98:1136–43. [PubMed: 24025627]

[70]. Kajuira H, Cowart BJ, Beauchamp GK. Early developmental change in bitter taste responses in human infants. Dev Psychobiol. 1992; 25:375–86. [PubMed: 1526325]

[71]. Cowart BJ, Yokomukai Y, Beauchamp GK. Bitter taste in aging: compound-specific decline in sensitivity. Physiology and Behavior. 1994; 56:1237–41. [PubMed: 7878096]

[72]. Duffy VB, Hayes JE, Davidson AC, Kidd JR, Kidd KK, Bartoshuk LM. Vegetable intake in college-aged adults is explained by oral sensory phenotypes and TAS2R38 genotype. Chemosens Percept. 2010; 3:137–48. [PubMed: 21157576]

[73]. Lipchock SV, Reed DR, Mennella JA. Relationship between bitter-taste receptor genotype and solid medication formulation usage among young children: A retrospective analysis. Clin Ther. 2012; 34:728–33. [PubMed: 22440514]

[74]. Fischer R, Griffin F. Pharmacogenetic aspects of gustation. Arzneimittelforschung. 1964; 14:673–86. [PubMed: 14249066]

[75]. Breslin PA, Beauchamp GK. Suppression of bitterness by sodium: variation among bitter taste stimuli. Chem Senses. 1995; 20:609–23. [PubMed: 8788095]

[76]. Keast RS, Canty TM, Breslin PA. The influence of sodium salts on binary mixtures of bitter-tasting compounds. Chem Senses. 2004; 29:431–9. [PubMed: 15201210]

[77]. Mennella JA, Reed DR, Roberts KM, Mathew PS, Mansfield CJ. Age-related differences in bitter taste and efficacy of bitter blockers. PLoS One. 2014; 9:e103107. [PubMed: 25050705]

[78]. Mennella JA, Pepino MY, Beauchamp GK. Modification of bitter taste in children. Dev Psychobiol. 2003; 43:120–7. [PubMed: 12918091]

[79]. Kroeze JH, Bartoshuk LM. Bitterness suppression as revealed by split-tongue taste stimulation in humans. Physiol Behav. 1985; 35:779–83. [PubMed: 4080842]

[80]. Childs E, de Wit H. Subjective, behavioral, and physiological effects of acute caffeine in light, nondependent caffeine users. Psychopharmacology (Berl). 2006; 185:514–23. [PubMed: 16541243]

[81]. Holdstock L, King AC, de Wit H. Subjective and objective responses to ethanol in moderate/heavy and light social drinkers. Alcohol Clin Exp Res. 2000; 24:789–94. [PubMed: 10888066]

[82]. Stevens JC. Detection of tastes in mixture with other tastes: issues of masking and aging. Chem Senses. 1996; 21:211–21. [PubMed: 8670700]

[83]. Temple JL. Caffeine use in children: what we know, what we have left to learn, and why we should worry. Neurosci Biobehav R. 2009; 33:793–806.

[84]. Branum AM, Rossen LM, Schoendorf KC. Trends in caffeine intake among U. S. children and adolescents. Pediatrics. 2014; 133:386–93. [PubMed: 24515508]

[85]. Glendinning JI. Is the bitter rejection response always adaptive? Physiol Behav. 1994; 56:1217–27. [PubMed: 7878094]

[86]. Cogswell ME, Gunn JP, Yuan K, Park S, Merritt R. Sodium and sugar in complementary infant and toddler foods sold in the United States. Pediatrics. 2015; 135

[87]. Baker SS, Baker RD. Early exposure to dietary sugar and salt. Pediatrics. 2015; 135

[88]. Kissileff HR, Ladenheim E. The evolution of the Society for the Study of Ingestive Behavior (SSIB). Physiol Behav. 2013; 121:3–9. [PubMed: 23416174]

[89]. Mennella JA, Spector AC, Reed DR, Coldwell SE. The bad taste of medicines: Overview of basic research on bitter taste. Clin Ther. 2013; 35:1225–46. [PubMed: 23886820]

[90]. Giacoia GP, Taylor-Zapata P, Zajicek A. Eunice Kennedy Shriver National Institute of Child Health and Human Development Pediatrics Formulation Initiative: Proceedings from the Second Workshop on Pediatric Formulations. Clin Ther. 2012; 34:S1–10. [PubMed: 23149008]

[91]. Mennella JA. Ontogeny of taste preferences: basic biology and implications for health. Am J Clin Nutr. 2014; 99:704S–11S. [PubMed: 24452237]

Bullet Points

- Children's preference for sweet and dislike of bitter reflect in part their basic biology.

- Children prefer higher levels of sweet and are more sensitive to bitter tastes until adolescence.

- Children's elevated preferences for sweet have remained stable during the past decade.

- Sodium salts are more likely to block bitter tastes in adults than children.

- For children, sugars are a better blocker of some bitter tastes than are sodium salts.
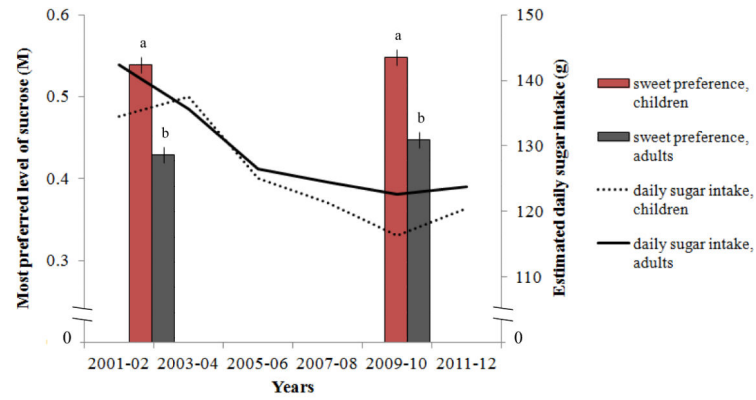
Figure 1.
Most preferred level of sucrose was collected at two time points (2002-3, 2010) in two separate populations of children (red bars) and adults (gray bars) living in Philadelphia, PA. Estimated daily sugar intake for children (2-11 years, dotted line) and adults (20-59 years, solid line) was derived from NHANES dietary recall data collected during two-year intervals from 2001-2012 (*see text for references*). There was a main effect of age group ($F_{(1,650)}=18.97$, $p<0.001$) but no main effect of time period ($F_{(1,650)}=0.65$, $p=0.42$) on level of sweet most preferred. Different letters indicate significant differences between groups.

Table 1

Efficacy of sucrose versus sodium salts (sodium gluconate, monosodium glutamate) in reducing bitterness of bitter agents in aqueous solutions among adults and children.[a]

| Bitter agent | Blocking/masking agent | | | | | |
| | Sodium gluconate | | Monosodium Glutamate | | Sucrose | |
	Children	Adults	Children	Adults	Children	Adults
Urea	↓	↓	↓	↓	↓	↓
Caffeine	↔	↓	↔	↔	↓	↓
Quinine	↓	↓	↔	↓	↓	↓
Denatonium	↔	↓	↔	↓	↓	↓
PROP	↔	↔	↔	↔	↓	↓
Tetralone	↑	↑	NA	NA	NA	NA

PROP, 6-*n*-propylthiouracil; ↓, decreased bitterness; ↑, increased bitterness; ↔, no effect; NA, not assessed.

[a]Adapted from Mennella et al. [45, 77, 78].