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Sucrose-Induced Analgesia is related to Sweet Preferences in Children but not Adults

M. Yanina Pepino, PhD and **Julie A. Mennella, PhD**
Monell Chemical Senses Center Philadelphia, PA 19104-3308

Abstract

The present study tested the hypothesis that the efficacy of sucrose in reducing pain during the Cold Pressor Test (CPT) was related to its hedonic value. To this aim, we determined the most preferred level of sucrose and the analgesic properties of 24% w/v sucrose during the CPT in 242, 5- to 10-year-old children and their mothers. Outcome measures included pain thresholds (the time at which discomfort was first indicated) and pain tolerance (the length of time the hand was kept in the cold water bath). Although children, as a group, preferred significantly higher sucrose concentrations than adults, there were individual differences that allowed us to group them on the basis of those who preferred sucrose concentrations below that used in the CPT (24% w/v) and those who preferred levels ≥ 24% w/v sucrose. Regardless of such groupings, sucrose was not an effective analgesic in adult women. Unlike adults, the more children liked sucrose, the better its efficacy as an analgesic. That is, children who preferred ≥24%w/v sucrose exhibited an increased latency to report pain and tolerated pain for significantly longer periods of time when sucrose was held in their mouths relative to water. This effect was more pronounced among normal weight when compared to overweight/at risk for overweight children. The role that dietary habits and individual differences contribute to the preferences for sweet taste and its physiological consequences in children is an important area for future research.

Keywords

Taste analgesia; Sucrose; Children; Sweet Taste; Obesity

Introduction

Sweet-tasting solutions reduce pain in young infants (Blass and Hoffmeyer, 1991; Stevens et al., 1997). After painful procedures such as a heel stroke, infants who had sugar water, but not water alone, placed on their tongues spent less time crying and quickly attained a normal heart rate state (Blass and Watt, 1999; Fernandez et al., 2003). Tasting sucrose also attenuated a negative electroencephalographic response to the non-invasive, yet noxious, heelstroke procedure (Fernandez et al., 2003), thus suggesting that sucrose blocks pain afferents which, in turn, diminishes stress and cardiac changes. Because non-caloric sweet substances such as aspartame mimic the calming effects of sucrose (Barr et al., 1999; Bucher et al., 2000) and because the administration of sucrose by direct stomach loading is ineffective (Ramenghi et al., 1999), afferent signals from the mouth, rather than gastric or metabolic changes, appear to be responsible for the analgesic properties of sweet tastes.

Although the association between sweet taste and analgesia is evident during infancy, little is known about the pain-reducing properties of sugars during other stages of the lifespan. To our

Correspondence to be sent to: Julie A. Mennella, PhD, Monell Chemical Senses Center, 3500 Market Street, Philadelphia, PA 19104-3308, phone: 215.898.9230, fax: 215.898.2084, e-mail:mennella@monell.org.

knowledge, there is only one study that suggested a sucrose-induced analgesia during childhood (Miller et al., 1994). Here 8- to 11- year-old children underwent a cold-induced pain stimulus test, hereafter referred to as the Cold Pressor Test (CPT) on two successive days while holding either sucrose solution or water alone in their mouths. Intraoral sucrose, but not water, delayed children's reporting of pain onset (e.g., pain threshold), but did not affect the amount of time they kept their arms in the cold water bath (e.g., pain tolerance).

Studies on the sweet-taste-induced analgesia in adults are also limited. While some studies suggested no effects (see in Miller et al., 1994; Mercer and Holder, 1997) others reported increased tolerance to mechanical pain following consumption of palatable sweet food in women but not in men (Mercer and Holder, 1997). From these observations, it can be postulated that if the analgesic response to intraoral sucrose is present during adulthood, it is less robust than that during childhood. Sweet preferences also changed during ontogeny such that the heightened preference observed during childhood declines during late adolescence and early adulthood (Desor et al., 1975; Desor and Beauchamp,1987). Although the cause of and mechanism underlying this ontogenic change in sweet preference remain a mystery, it has been observed in other mammalian young (Wurtman and Wurtman, 1979; Marlin 1983). Therefore, one explanation for the age-related decline in sucrose's efficacy as an analgesic is that it mirrors the age-related decline in the hedonic value of sweet tastes (Miller et al., 1994). Because individual variations in sweet preferences exist at both ends of the age spectrum (Desor et al, 1977; Beauchamp and Moran, 1982; Enns et al., 1979; Pliner and Fleming, 1983), the present study tested the hypothesis that sucrose would be more effective in reducing pain in those who prefer sweet tastes.

2. Methods

2.1. Participants

Mothers were recruited from advertisements in local newspapers. They were provided with detailed descriptions of each procedure, but were unaware to the goals of the study and the hypotheses being tested. The mothers (n=198) were, on average, 35.4 ± 0.4 years of age and their children (143 girls, 99 boys) ranged in age from 5 to 10 years (Mean Age: 8.3±0.1 years). Included in this sample of 242 children were 36 sibling pairs and 4 sibling triads. The race/ ethnicity of the children, based on maternal reports of the racial background of both parents, was 49.0% Black, 32.4% White, 0.4% Hispanic, 0.8% Asian and 17.4% Other Ethnicity. All children were reported by their mothers to be healthy at the time of testing and all mothers reported that they were normotensive and not on any anti-hypertensive medications. Blood pressure was measured prior to testing (DINAMAP® PRO Series 100, GE Medical Systems, FL) in almost half of the mothers and normotensive status (systolic blood pressure < 140mmHg; diastolic blood pressure <90 mmHg) was verified in all but four women.

Eight mothers could not participate in the study because they were either pregnant or because of a prior medical condition. Fifty-nine additional children participated in the study but were excluded because they did not complete testing (n=56) or did not understand the task (n=3). All testing procedures were approved by the Office of Regulatory Affairs at the University of Pennsylvania and informed consent was obtained from each woman and assent was obtained from each child who was seven years of age or older.

2.2. Procedures

Following acclimation to the room and personnel and a 45- to 60-minute fast, children and mothers were individually tested at the Monell Center in a closed room specifically designed for sensory testing.

As described below, we determined sucrose preferences during one session and the analgesic properties of intraoral sucrose and water, via the CPT, during another test session (Miller et al., 1994). Sucrose preferences were assessed to determine whether the concentration of sucrose (24% weight/volume sucrose solution) used in the CPT was a better analgesic in individuals who preferred this or higher concentrations of sucrose when compared to those who preferred less sweet solutions. Both test sessions occurred on the same testing day. Children participated in the CPT during the first session and the sucrose preference test during the second; the order of testing was reversed for the mothers and a 40-minute interval separated the two sessions. To allow for comparisons, procedures were identical for children and mothers. To minimize the effects of the reverse order of testing between children and adults, participants did not swallow the sucrose during the sweet preference tracking procedures and the time since the subjects were last fed or experienced a flavor in their mouth before the CPT test was similar between the two groups.

The concentration of sucrose (24% w/v) used in the CPT was chosen because previous studies revealed that this concentration was an effective analgesic for day-old infants (Blass and Hoffmeyer, 1991) and 8- to 11-year-old children (Miller et al., 1994). Anthropometric measures and information on food preferences and habits were also obtained. At the end of the sessions, a subsample of subjects were cheek swabbed to determine associations between the genetic variation in the recently discovered TAS2R38 bitter taste receptor gene (Kim et al., 2003) and taste sensitivity and preference in children (data reported elsewhere; Mennella et al., 2005).

2.2.1. CPT—The CPT is a classical experimental model for the induction of pain in children and adults (Miller et al.,1994 ; Lewkowski et al., 2003). Modifying the previously published methods of Miller and colleagues (1994), subjects were told that they were going to play a game in which they will put their hand in a cold water bath. The following two directives were given to each subject: 1) When your hand starts to hurt or feel uncomfortable, raise your other hand to let me know; and 2) Keep your hand in the water for as long as you can. If you can't take it anymore, take your hand out of the water. At fixed intervals (every 10 seconds) throughout the testing, subjects were repeatedly encouraged and asked to keep their hand in the water bath as long as they possibly could.

In an attempt to standardize skin temperatures prior to the CPT test, each subject first placed their non-dominant hand in a 37°C water bath (Precision, Model 183; Chicago, IL) for 2 minutes. Thirty seconds before transferring their hand to the second water bath which contained 10°C water, subjects placed, without swallowing, 15–20 ml of a room-temperature sucrose solution (24% w/v) in their mouths during one trial and an equal volume of room temperature water during the other. Sixty percent of the children and 60% of the mothers held sucrose in their mouth during the first trial and water during the second one (S-W), the order was reversed (W-S) for the remaining subjects. A 10-minute interval separated the two trials. The volume of liquid placed in the oral cavity of the subjects bathed the taste receptors on the tongue without overfilling the mouth (see Miller et al.,1994). The cold water bath was connected to a Dip Cooler (Techne, RU-200, Cambridge, UK) and controlled by a thermoregulator (Techne, TE-10A; Cambridge, UK) to maintain, via continuous stirring, the water temperature at 10.00 ± 0.01C°.

The CPT was administered for a maximum of 4 minutes or until the subject withdrew their hand from the cold water bath, whichever came first. Pain threshold (the time in seconds at which discomfort was first indicated by raising the non-immersed hand) and pain tolerance (the number of seconds the hand was kept in the cold water) were recorded by the use of a stopwatch. Twenty five children and 21 mothers were excluded from the final analysis because they tolerated the cold water for the entire 4 minutes during both CPT. Of the 198 children and

164 mothers whose data were included in the analysis for pain tolerance, 48 of the children and 13 mothers did not raise their non-immerse hands to indicate when they first felt pain and therefore pain threshold data was not available for these subjects.

2.2.2 Sweet Preferences Tracking Procedures—Sucrose preferences were assessed by a forced-choice tracking technique that was embedded in the context of games and sensitive to the cognitive limitations of pediatric populations (Cowart and Beauchamp, 1990). Subjects were presented with pairs of solutions that differed in sucrose (Sigma–Aldrich, Inc. St Louis, MO) concentration (3%, 6%, 12%, 24%, 36% w/v) in opaque sip cups. They were first presented with a pair of samples chosen from the middle range (6% w/v vs. 24%w/v) and were asked to taste each without swallowing, and then to point to which of the pair they liked better. Each subsequent pair was then determined by the subject's preceding preference choice. The procedure continued until the subject had either chosen a given concentration of sucrose when it was paired with both a higher and lower concentration or had chosen the highest (36%w/v) or lowest (3%w/v) sucrose solution two consecutive times. The entire task was then repeated with stimulus pairs presented in reverse order (i.e. the weaker stimulus in the first pair was initially presented first and the stronger one was presented first in the second series). Subjects rinsed and expectorated with water before and after tasting each sample and a one-minute interval separated each pair of solutions.

The geometric mean of the sucrose concentrations chosen during the two trial series provides the estimate of sucrose preferences. Subjects were classified into two groups: those who preferred sucrose concentrations below that used in the CPT (24% w/v) hereafter referred to as <24% w/v Sucrose Preference Group, and those who preferred solutions equal to or greater than 24% w/v, hereafter referred to as ≥24% w/v Sucrose Preference Group. Nineteen of the children and five of the mothers were excluded because their responses were inconsistent (e.g., they choose extreme opposing solutions during the two trials).

2.2.3. Food Preferences and Anthropometry—In order to relate the subject's sweet preferences, as assessed via the tracking procedure, with preferences for sweets in daily life, children were queried about their food and taste preferences. Because children often answer in the affirmative way, we modified a forced-choice procedure previously used to measure childhood depression (O'Connor and Kasari, 2000) to query children directly about their food likes/dislikes. In brief, children were presented with pictures of two side-by–side identical figures with neutral facial expressions (i.e., the figures corresponded to the sex and race of the child) and were told that the children in the picture look the same but that they like different things. Five pairs of food items were then recited and the child was told that one of the figures liked one of the foods whereas the other figure likes the other one. The child was then asked to point to the figure in the picture that was most like her/him. The pairs, recited in counterbalances order, included different food items. One of the pair was considered to have a sweet taste (ice cream, cookies, pancakes, candy, dessert), whereas the other in the pair was considered to be salty in nature (chips, pretzels, bacon, Doritos, salty snacks). The child was also told that one of the figures likes to add sugar to their cereal whereas the other one does not. Final sweet preference scores could range from 0 to 6 such that 6 indicate the child chose the sweeter food or habit every time.

Mothers also completed the Food Craving Inventory (FCI), a 28 food-item questionnaire designed to measure specific food cravings (White et al., 2002). Participants were asked to rate how often they experienced a craving for each of the foods over the past month using a 5-point Likert scale (1=never, 5=always/almost every day). This 28 items is comprised of four subscales: High Fats (8 items), Sweets (8 items), Carbohydrates/Starches (8 items) and Fast Food Fats (4 items); higher numbers for each of the subscales reflect greater cravings of that food type.

Mothers and children were also weighed and measured for height (Detecto Model 439, Physician Scale; Webb City, MO) and their body mass index (kg/m^2) was computed. Each child's BMI for age was then classified in one of four categories (i.e., underweight, normal, at risk of overweight or overweight) using the Center for Disease Control and Prevention pediatric grow charts (Kuczmarski et al., 2002).

2.3. Data Analyses

The primary measures were pain thresholds and tolerance data. These data were positively skewed and thus required logarithmic transformation to approximate a normal distribution (see Miller et al., 1994). Two-way mixed ANOVAs were conducted on the transformed data to determine whether there were significant differences in pain threshold and tolerance with Condition (sucrose, water) as the within-subjects factor and Sucrose Preference Group (<24% w/v or ≥24% w/v Sucrose Preference Group) and Order of testing (S-W, W-S) as the between-subjects factors. When significant, post hoc analyses (Fisher least significant difference tests) were conducted. Tolerance and threshold data are expressed as geometric means (GeoMeans) ± geometric standard errors (GeoSE). GeoSE were calculated as the difference between the geometric mean and the antilog of the arithmetic mean + standard error of the mean (SEM) of transformed data [$e^{(\text{Mean + SEM of the logged data})}$ – GeoMean] as well as the difference between the geometric mean and the antilog of.arithmetic mean – SEM of the transformed data; [GeoMean - $e^{(\text{Mean– SEM of the logged data})}$] (Bishop et al., 1975).

Differences in children pain threshold and pain tolerance while holding sucrose when compare to water in their mouths were also compared using the sign test, a non parametric test for related samples. One-way ANOVAs were conducted to analyze whether the children's sweet preference score and mothers' cravings for sweets with sucrose preference group (<24% w/v or ≥24% w/v Sucrose Preference Group) as the between-subject factor. Data obtained from mothers were analyzed separately from children. Preliminary analyses revealed no effect of the sex of the child on either pain threshold or tolerance. Consequently, sex was not factored into the final analyses.

3. Results

3.1 Individual Differences in Sucrose Preferences

As anticipated, children preferred significantly higher sucrose concentrations than did their mothers ($F(1,406)=16.37$; $P<0.0001$). As a group, children preferred 19.2± 0.7 % (w/v) and mothers preferred 14.7±0.8 % (w/v) sucrose solution. However, there were individual differences in both age groups in the degree of sweetness preferred. As shown in Table 1, approximately half (n=94) of the children and one quarter (n=47) of the mothers preferred sucrose concentrations that were at or above the level (≥24% w/v Sucrose Preference Group) used during the CPT.

3.2. CPT in Children

3.2.1 *Pain Thresholds and Tolerance*—There were significant interactions between Condition (Sucrose, Water) and Sucrose Preference Group (<24% w/v versus ≥24% w/v sucrose) in the length of time it took children to first indicate they felt discomfort by raising the non-immersed hand ($F(1,146)=4.24$, $P=0.041$). There was a significant increase in pain thresholds when sucrose as compared to water was in the oral cavity of children in the ≥24% w/v Sucrose Preference Group. In contrast, pain threshold was not affected by condition (holding sucrose or water in the mouth) in those children who preferred <24% w/v Sucrose (Figure 1, Table 2). Sixty seven percent (44/67) of children in the ≥24% w/v Sucrose Preference Group ($P= 0.015$), but only 53% (40/75) of children in the <24% w/v Sucrose Preference Group ($P=0.64$) took longer time to report pain when sucrose was in their mouths relative to water.

There was also a significant interaction between the Order of testing (S-W, W-S) and Sucrose Preference Groups for pain thresholds in children (F(1,146)=4.64, P=0.033). As shown in Table 2, children's latency to raise their hand to express pain onset was significantly increased when children in the ≥24% w/v Sucrose Preference Group held sucrose in their mouth during the first trial and water during the second one (S-W) when compared to those evaluated holding water first and sucrose during the second one (order W-S). The order of testing (S-W versus WS) did not affect children pain threshold in the <24% w/v Sucrose Preference Group.

Similar to that observed for pain thresholds, there were significant interactions between Condition and Sucrose Preference Group (F(1,194)=4.96; P=0.03) for pain tolerance. As shown in Figure 1, there were significant increases in pain tolerance when sucrose as compared to water was in the oral cavity of children who preferred ≥24% w/v sucrose solution. On average, sweet taste was associated with a 41% increase in pain tolerance. No such differences were observed in those children who preferred <24 % w/v sucrose solutions. Sixty two percent (56/90) of the children in the ≥24%w/v Preference Group (P=0.027), but only 47% of the <24% w/v Sucrose Preference Group (47/99; P=0.69) kept their hands in the cold water for longer periods of time when holding sucrose, as compared to water, in their mouths. That the children's hedonic value of the sucrose solution was related to the efficacy of sucrose as analgesic is also suggested by the significant correlation between the preferred level of sucrose (geometric mean) and the length of time children held their hand in the cold water when sucrose was held in the mouth relative to water (r=0.17; F(1,196)=6.18, P=0.014). That is, the higher the concentration of sucrose preferred, the longer children kept their hand in the cold water bath when sucrose was in their mouths relative to water.

There was also a significant interaction between Sucrose Preference Group and Order of testing for pain tolerance (F(1,194)=4.33, P=0.04). Children in the ≥24% w/v Sucrose Preference Group were more affected by the order of presentation such that those who were tested in the SW order had significantly higher pain tolerance during both conditions when compared to those who were tested in the WS order. Pain tolerance in the <24%w/v Sucrose Preference Group of children was the same under both conditions for both orders (SW, WS).

As shown in Table 2, the order of testing also interacted with Condition (F(1,194)=5.86, P=0.016) such that holding sucrose significantly increased pain tolerance when children were first tested in the sucrose condition (S-W) but not when sucrose was tested second (W-S). Furthermore, children who were tested during the W-S condition (N=110) were significantly more likely to stop their participation after the first CPT trial when water was held in their mouth (20%; 22/110) when compared to children who were tested in the S-W condition in which sucrose was experienced during the first CPT trial (8% (13/167); P<0.025).

3.2.2 Food Preferences and Anthropometry—As shown in Table 1, children in ≥24% w/v Sucrose Preference Group were significantly more likely to prefer sweet-tasting foods when compared to children in the <24% w/v Sucrose Preference Group (F(1,195)=7.17, P=0.008). There were no significant differences in BMI between those children who preferred <24%w/v sucrose when compared to those who preferred ≥24% w/v sucrose concentration (Table 1). We conducted further analyses to explore whether there was a relationship between BMI and the effectiveness of sucrose as an analgesic in those children who preferred ≥24% w/v or <24%w/v sucrose within those who were normal weight (N=90) and those who were overweight or at risk of overweight (N=54). Underweight children were excluded from this analysis because of the small sample size. There was a significant interaction between BMI category and sucrose preference group for pain thresholds (F (1,140)=7.40; P=0.007). Among those who preferred ≥24%w/v sucrose, sucrose significantly increased (P<0.05) pain thresholds for normal weight children (sucrose: 22.0 (19.1–25.3) vs. water: 15.6 (13.7–17.8) seconds; proportional response: 0.56±0.02) but not for overweight or at risk of overweight

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children (sucrose: 14.0 (11.7–16.7) vs. water: 13.9 (12.0–16.2); proportional response: 0.50 ±0.03). There were no significant differences in pain thresholds for normal weight when compared to overweight or at risk of overweight children among those who preferred <24% w/v sucrose. Figure 2 depicts the pain threshold values for sucrose relative to water for each of these groups of children.

3.3. CPT in Women

3.3.1 *Pain Thresholds and Tolerance*—As shown in Table 3, there were no significant main effects or interactions for pain threshold or pain tolerance in the mothers.

3.3.2 Food Preferences and Anthropometry in Women—Like children, there were no significant differences in BMI between those mothers who preferred <24% w/v sucrose when compared to those who preferred ≥24% w/v sucrose concentration (Table 1). Mothers who preferred sucrose concentrations ≥24% w/v had significantly higher craving scores for sweet foods when compared to the mothers in the <24% w/v Sucrose Preference Group ($F(1,158)=4.28$; $P=0.040$). This relationship between the sucrose preference measured in the laboratory and craving for different types of food was specific to sweet tasting food since there were no significant differences between the groups in their cravings for high fat, carbohydrates, or fats (all $P>0.20$).

Discussion

Sucrose's efficacy in reducing pain in children was related to its hedonic value. When a 24% w/v sucrose solution was in the oral cavity, children who preferred this or higher levels of sucrose exhibited an increased latency to report pain and tolerated pain for significantly longer periods of time when compared to when water was held in their mouths. This concentration of sucrose did not affect pain responses in children who preferred lower levels of sweetness, however. Whether lower concentrations of sucrose would be effective analgesics for such children remains to be determined. Those children who preferred higher levels of sucrose were more likely to prefer sweet-tasting foods suggesting that some children eat sweet-tasting foods for reasons other than its tastes. It is unknown whether sweet-tasting foods are also analgesic in these children.

There were significant effects on the order in which children were tested such that sucrose was more effective in the high preferring sucrose group when experienced during the first pain test. That children were significantly more likely to discontinue the CPT if they experienced the water condition during the first trial further highlights the saliency of pain for children. As suggested by Miller and colleagues (1994), experience with pain modifies children's performances as well as their expectations during subsequent experiences.

Because sucrose was not an effective analgesic in adult women who preferred ≥24% w/v concentrations of sucrose, sweet taste liking may not be a sufficient factor in inducing analgesia. Thus, the absence of an analgesic response to sucrose in adults is apparently not due to the lowered sucrose preference observed in adults overall (Miller et al., 1994) and is consistent with animal model studies that revealed that sweet-induced analgesia progressively declines during development and is absent by the third week of life in the rat (Anseloni et al., 2002). Nevertheless, more research is warranted before one can conclude that sucrose is an ineffective analgesic during adulthood. For example, the efficacy of sweet taste in reducing pain appears to be moderated by resting blood pressure in normotensive young adults (Lewkowski, et al., 2003). That the increased pain tolerance induced by sweet tastes during the CPT was attenuated in individuals with high-normal blood pressure suggests that they may not be as sensitive to opioid-mediated sweet-taste analgesia, perhaps because of opioid dysregulation (Lewkowski et al., 2003; see Bruehl and Chung, 2004 for review). Whether the large proportion of overweight/obese individuals in the adult sample contributed to the lack of the analgesic effect is an important area for future research.

Although the mechanisms underlying sucrose-induced analgesia in human infants and children is not fully established (Taddio et al., 2003; Gradin and Schollin, 2005), animal model studies suggest the involvement of the endogenous opioid system (Segato et al., 1997). For example, the effects of sucrose are abolished by the administration of the opiate receptor antagonists naloxone or naltrexone in rat pups (Blass et al., 1987). Moreover, the ingestion of sweeteners increases beta-endorphin levels in plasma and cerebrospinal fluid (Yamamoto, 2003). Of interest is the finding that sucrose does not release endorphins in rats that had acquired a condition taste aversion to sucrose (Yamamoto et al., 2000). That opiate antagonists decrease the hedonic value of sucrose solutions in humans (Bertino et al., 1991; Fantino et al., 1986) further support the hypothesis that the positive hedonic value of the sweet stimulus, and not sweetness itself, contributes to beta-endorphin release.

Although the present study was not designed to examine the effect of obesity on the efficacy of sweets to elicit analgesia, we found that among those children who preferred the higher levels of sucrose, sucrose was an effective analgesic for those who were normal weight but not for those who were overweight or at risk of overweight. Whether this attenuation in the analgesic properties of sucrose was due to an impairment of the hypothalamo-pituitary control and higher than normal beta endorphin plasma levels which have been observed in obese children (Bernasconi et al., 1988) is not yet known. Nor do we know whether these children consumed higher amounts of carbohydrates and sweet tasting foods which could, in turn, modify opioid as well as dopamine receptor binding (see Colantuoni et al., 2001; Levine et al., 2003) and sucrose's analgesic properties (Kanarek et al., 1997; D'Anci et al., 1996). The role that dietary habits and individual differences contribute to the preferences for sweet taste and its physiological consequences in children is an important area for future research.

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References

Anseloni VC, Weng HR, Terayama R, Letizia D, Davis BJ, Ren K, Dubner R, Ennis M. Age-dependency of analgesia elicited by intraoral sucrose in acute and persistent pain models. Pain 2002;97:93–103. [PubMed: 12031783]

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]

Beauchamp GK, Moran M. Dietary experience and sweet taste preference in human infants. Appetite 1982;3:139–52. [PubMed: 7137993]

Bernasconi S, Petraglia F, Iughetti L, Marcellini C, Lamborghini A, Facchinetti F, Genazzani. Impaired beta-endorphin response to human corticotropin-releasing hormone in obese children. Acta Endocrinol (Copenh) 1988;119:7–10. [PubMed: 2842994]

Bertino M, Beauchamp GK, Engelman K. Naltrexone, an opioid blocker, alters taste perception and nutrient intake in humans. Am J Physiol 1991;261:R59–63. [PubMed: 1858956]

Bishop YMM, Fienberg SE, Holland PW. Discrete Multivariate analysis: Theory and practice, Cambridge, MA: MIT press, 1975. pp 486–501.

Blass E, Fitzgerald E, Kehoe P. Interactions between sucrose, pain and isolation distress. Pharmacol Biochem Behav 1987;26:483–9. [PubMed: 3575365]

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

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

Bruehl S, Chung OY. Interactions between the cardiovascular and pain regulatory systems: an updated review of mechanisms and possible alterations in chronic pain. Neurosci Biobehav Rev 2004;28:395–414. [PubMed: 15341037]

Bucher HU, Baumgartner R, Bucher N, Seiler M, Fauchere JC. Artificial sweetener reduces nociceptive reaction in term newborn infants. Early Hum Dev 2000;59:51–60. [PubMed: 10962167]

Colantuoni C, Schwenker J, McCarthy J, Rada P, Ladenheim B, Cadet JL, Schwartz GJ, Moran TH, Hoebel BG. Excessive sugar intake alters binding to dopamine and mu-opioid receptors in the brain. Neuroreport 2001;12:3549–52. [PubMed: 11733709]

Cowart BJ, Beauchamp GK. Early development of taste perception. In: McBride R and MacFie H, editors. Psychological Basis of Sensory Evaluation. London: Elsevier, 1990. pp. 1–17.

D'Anci KE, Kanarek RB, Marks-Kaufman R. Duration of sucrose availability differentially alters morphine-induced analgesia in rats. Pharmacol Biochem Behav 1996;54:693–7. [PubMed: 8853191]

Desor JA, Greene LS, Maller O. Preferences for sweet and salty in 9- to 15-year-old and adult humans. Science 1975;190:686–7. [PubMed: 1188365]

Desor JA, Maller O, Greene LS. Preference for sweet in humans: Infants, children, and adults. In: Weiffenbach JM, editor. Taste and Development: the genesis of sweet preference. Washington, D.C.: U.S. Government Printing Office, 1977. pp. 161–72.

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

Enns MP, Van Itallie TB, Grinker JA. Contributions of age, sex and degree of fatness on preferences and magnitude estimations for sucrose in humans. Physiol Behav 1979;22:999–1003. [PubMed: 504405]

Fantino M, Hosotte J, Apfelbaum M. An opioid antagonist, naltrexone, reduces preference for sucrose in humans. Am J Physiol 1986;251:R91–6. [PubMed: 3728712]

Fernandez M, Blass EM, Hernandez-Reif M, Field T, Diego M, Sanders C. Sucrose attenuates a negative electroencephalographic response to an aversive stimulus for newborns. J Dev Behav Pediatr 2003;24:261–6. [PubMed: 12915798]

Gradin M, Schollin J. The role of endogenous opioids in mediating pain reduction by orally administered glucose among newborns. Pediatrics 2005;115:1004–7. [PubMed: 15805377]

Kanarek RB, Mathes WF, Heisler LK, Lima RP, Monfared LS. Prior exposure to palatable solutions enhances the effects of naltrexone on food intake in rats. Pharmacol Biochem Behav 1997;57:377–81. [PubMed: 9164597]

Kim UK, 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]

Kuczmarski RJ, Ogden CL, Guo SS, Grummer-Strawn LM, Flegal KM, Mei Z, Wei R, Curtin LR, Roche AF, Johnson CL. 2000 CDC Growth Charts for the United States: methods and development. Vital Health Stat 2002;11:1–190.

Levine AS, Kotz CM, Gosnell BA. Sugars and fats: the neurobiology of preference. J Nutr 2003;133:831S–834S. [PubMed: 12612162]

Lewkowski MD, Ditto B, Roussos M, Young SN. Sweet taste and blood pressure-related analgesia. Pain 2003;106:181–6. [PubMed: 14581126]

Marlin NA. Early exposure to sugars influences the sugar preference of the adult rat. Physiol Behav 1983;31:619–23. [PubMed: 6665052]

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

Mercer ME, Holder MD. Antinociceptive effects of palatable sweet ingesta on human responsivity to pressure pain. Physiol Behav 1997;61:311–8. [PubMed: 9035263]

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]

O'Connor MJ, Kasari C. Prenatal alcohol exposure and depressive features in children. Alcohol Clin Exp Res 2000;24:1084–92. [PubMed: 10924014]

Pliner P, Fleming AS. Food intake, body weight, and sweetness preferences over the menstrual cycle in humans. Physiol Behav 1983;30:663–6. [PubMed: 6878471]

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]

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. [PubMed: 9361728]

Stevens B, Yamada J, Ohlsson A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database Syst Rev 2004; CD001069.

Taddio A, Shah V, Shah P, Katz J. Beta-endorphin concentration after administration of sucrose in preterm infants. Arch Pediatr Adolesc Med 2003;157:1071–4. [PubMed: 14609895]

White MA, Whisenhunt BL, Williamson DA, Greenway FL, Netemeyer RG. Development and validation of the food-craving inventory. Obes Res 2002;10:107–14. [PubMed: 11836456]

Wurtman JJ, Wurtman RJ. Sucrose consumption early in life fails to modify the appetite of adult rats for sweet foods. Science 1979;205:321–2. [PubMed: 451607]

Yamamoto T, Sako N, Maeda S. Effects of taste stimulation on beta-endorphin levels in rat cerebrospinal fluid and plasma. Physiol Behav 2000;69:345–50. [PubMed: 10869601]

Yamamoto T. Brain mechanisms of sweetness and palatability of sugars. Nutr Rev 2003;61:S5–9. [PubMed: 12828186]

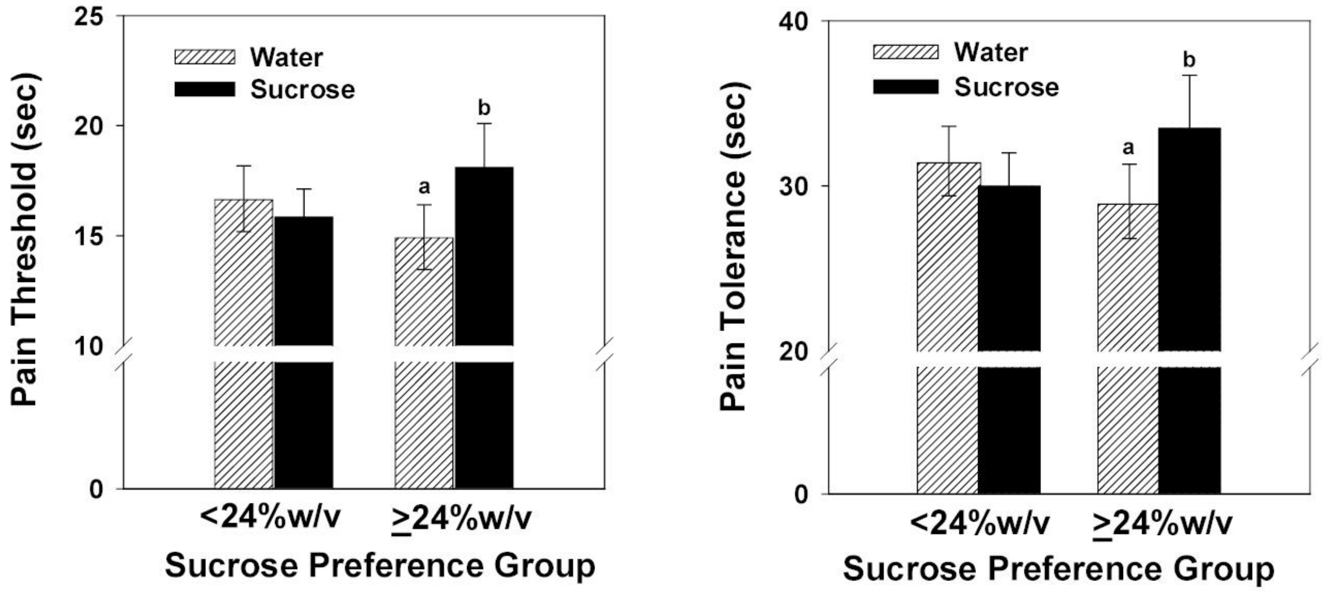

Figure 1.

Pain threshold (left panel) and pain tolerance (right panel) in seconds when 24% w/v sucrose (solid bars) or water (hatched bars) was held in the children's mouths during the CPT. Children were divided into two groups based on their most preferred level of sucrose: those who preferred sucrose concentrations below that used in the CPT and those who preferred levels equal to or greater than 24% w/v sucrose. Data are presented as geometric means ± geometric standard errors (GeoSEs). Notice that the upward-deflecting GeoSEs are greater than the downward-deflecting GeoSEs (see Data Analysis for explanation). a values are significantly different from b at the P<0.05 level.

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Figure 2.
Mean (±SEM) proportional pain threshold responses during sucrose relative to water condition (pain threshold with sucrose/(pain threshold with sucrose+ pain threshold with water)) in children who were normal weight and those who were overweight or at risk of overweight. Children were divided into two groups based on their most preferred level of sucrose: those who preferred sucrose concentrations below that used in the CPT (hatched bars) and those who preferred levels equal to or greater than 24% w/v sucrose (solid bars).

Table 1

Characteristics and demographics of the two groups of subjects based on their sucrose preferences. Values represent Means ±SEM unless otherwise indicated.

	<24% w/v Sucrose Preference Group	≥24% w/vSucrose Preference Group
Children		
Age in years	8.3±0.2	8.3±0.1
Sex		
Number of Girls	58	58
Number of Boys	46	36
BMI	17.8±0.3	18.2±0.4
BMI Category (number, % in parenthesis)		
Underweight	3 (2.9%)	4 (4.3%)
Normal weight	69 (66.3%)	57 (60.6%)
At risk of overweight	18 (17.3%)	11 (11.7%)
Overweight	14 (13.5%)	22 (23.4%)
Most Preferred Sucrose Concentration (w/v).	9.7±0.6	29.7±0.4*
Sweet Preference Score (Range: 0–6).	3.6±0.1	4.1±0.1*
Number of Children	104	94
Mothers		
Age (years)	35.2±0.5	36.2±0.8
Weight (kg)	79.6±2.0	77.9±3.1
Height (m)	1.65±0.01	1.66±0.01
BMI (kg/m^2).	29.1±0.7	28.1±1.0
BMI Category (Number, percent in parenthesis)		
Underweight	1(0.9%)	3(6.4%)
Normal weight	42(35.9%)	15(31.9%)
Overweight	28(23.9%)	16(34.0%)
Obese	46(39.3%)	13(27.7%)
Most Preferred Sucrose Concentration (w/v).	8.5±0.5	28.6±0.7*
Food Craving Inventory (FCI) (1=never, 5=always/almost every day)		
Craving for Sweets	2.8±0.1	3.1±0.1†
Craving for High Fat	2.4±0.1	2.6±0.1
Craving for Carbohydrates	2.7±0.1	2.8±0.1
Craving for Fat	3.0±0.1	3.2±0.1
Number of Mothers	117	47

* indicates P<0.01 when compared to <24%w/v Sucrose Preference Group

† indicates P<0.04 when compared to <24%w/v Sucrose Preference Group

Table 2

Children's pain threshold and pain tolerance in seconds based on sucrose preference group, the order of testing (S-W, W-S) and condition (sucrose, water). Data are presented as Geometric Means. Values in parentheses are the Geometric Mean - GeoSE followed by the Geometric Mean + GeoSE.

Children	<24%w/v Sucrose Preference Group	≥24%w/v Sucrose Preference Group	Both Sucrose Preference Groups Combined
Pain Threshold (sec) *†*			
Order S-W			
Sucrose Condition	15.0 (13.5–16.8)	20.6 (17.8–24.1)	17.6 (16.1–19.2)
Water Condition	16.0 (14.3–17.8)	17.9 (15.8–20.1)	16.9 (15.6–18.3)
Both Conditions	15.5 (14.0–17.1)	19.3 (17.3–21.5)[c]	17.3 (16.0–18.6)
Order W-S			
Sucrose Condition	18.0 (16.0–20.3)	14.9 (12.7–17.5)	16.3 (14.5–18.3)
Water Condition	18.1(15.5–20.9)	11.3 (9.8–13.2)	14.3 (12.8–15.9)
Both Conditions	18.0 (15.5–20.9)	12.9 (11.3–14.9)[d]	15.3 (13.8–16.9)
Both Orders (S-W , W-S)			
Sucrose Condition	15.9 (14.6–17.1)	18.1 (16.1–20.1)[a]	17.0 (15.8–18.2)
Water Condition	16.6 (15.2–18.2)	14.9 (13.5–16.4)[b]	15.6 (14.5–16.6)
Number of Subjects	78	72	150
Pain Tolerance (sec) *†‡*			
Order S-W			
Sucrose Condition	29.7 (27.5–32.2)	40.3 (35.5–45.8)	34.5 (32.1–37.0)[i]
Water Condition	29.9 (27.7–32.4)	31.1 (28.3–34.3)	30.6 (28.8–32.5)[j]
Both conditions	30.0 (27.7–32.5)	35.5 (32.5–38.9)[g]	32.5 (30.6–34.5)
Order W-S			
Sucrose Condition	30.6 (27.4–34.1)	25.3 (22.7–28.1)	27.7 (25.3–30.3)
Water Condition	35.0 (30.8–39.7)	25.8 (22.8–29.4)	30.0 (27.4–32.8)
Both Conditions	32.8 (29.1–37.0)	25.5 (22.9–28.5)[h]	28.9(26.7–31.3)
Both Orders (S-W , W-S)			
Sucrose Condition	30.0 (28.2–32.0)	33.5 (30.7–36.7)[e]	31.0 (29.2–32.9)
Water Condition	31.4 (29.4–33.6)	28.9 (26.8–31.3)[f]	30.3 (28.8–31.9)
Number of Subjects	104	94	198

* represent a significant Condition X Sucrose Preference Group interaction;

† represent a significant Order X Sucrose Preference Group interaction,

‡ represent a significant Order X Condition interaction.

[a] is significantly different from [b]; [c] is significantly different from [d], [e] is significantly different from [f], [g] is significantly different from [h] and [i] is significantly different from [j].

Table 3

Mother's pain threshold and pain tolerance in seconds based on sucrose preference group, the order of testing (S-W, W-S) and condition (sucrose, water). Data are presented as Geometric Means. Values in parentheses are the Geometric Mean - GeoSE followed by the Geometric Mean + GeoSE.

Mothers	<24%w/v Sucrose Preference Group	≥24% w/v Sucrose Preference Group	Both Sucrose Preference Groups Combined
Pain Threshold (sec)			
Order S-W			
Sucrose Condition	16.6 (15.5–17.8)	16.7 (15.0–18.7)	16.4 (15.2–17.7)
Water Condition	17.9 (16.4–19.3)	15.2 (13.5–17.1)	16.1 (14.9–17.4)
Both Conditions	16.6 (15.4–18.0)	16.0 (14.1–18.1)	16.3 (15.1–17.5)
Order W-S			
Sucrose Condition	21.1 (18.5–24.1)	17.1 (14.0–20.9)	18.9 (17.1–21.0)
Water Condition	19.3 (17.3–21.5)	18.0 (14.9–21.8)	18.5 (16.7–20.6)
Both Conditions	20.1 (18.1–22.3)	17.5 (14.8–20.7)	18.7 (17.0–20.7)
Both Orders (S-W , W-S)			
Sucrose Condition	18.1 (17.1–19.3)	16.9 (15.2–18.5)	17.6 (16.6–18.7)
Water Condition	18.4 (17.3–19.5)	16.1 (14.6–17.8)	17.3 (16.2–18.5)
Number of Subjects	108	43	151
Pain Tolerance (sec)			
Order S-W			
Sucrose Condition	30.4 (28.7–32.3)	31.3 (28.2–34.8)	30.0 (28.0–32.1)
Water Condition	33.6 (31.4–36.0)	32.2 (29.6–35.1)	32.5 (30.2–34.9)
Both Conditions	31.8 (29.7–34.1)	30.6 (27.4–34.1)	30.0 (29.2–33.4)
Order W-S			
Sucrose Condition	34.0 (30.8–37.5)	27.7 (23.7–32.4)	31.2 (28.4–34.3)
Water Condition	33.9 (31.0–37.0)	27.3 (23.2–32.1)	31.2 (28.3–34.4)
Both Conditions	33.7 (30.5–37.2)	28.8 (24.6–33.7)	30.0 (28.5–34.2)
Both Orders (S-W , W-S)			
Sucrose Condition	31.6 (30.0–33.2)	30.0 (27.5–32.7)	30.6 (28.9–32.4)
Water Condition	33.7 (31.9–35.6)	30.3 (28.0–32.9)	31.8 (30.0–33.8)
Number of Subjects	117	47	164