Sweet taste preferences are partly genetically determined: identification of a trait locus on chromosome 16

Kaisu Keskitalo, Antti Knaapila, Mikko Kallela, Aarno Palottie, Maija Wessman, Sampo Sammalisto, Leena Peltonen, Hely Tuorila, and Markus Perola

ABSTRACT

Background: Humans have an innate preference for sweet taste, but the degree of liking for sweet foods varies individually.

Objective: The proportion of inherited sweet taste preference was studied. A genome-wide linkage analysis was performed to locate the underlying genetic elements in the genome.

Design: A total of 146 subjects (32% men, 68% women) aged 18–78 y from 26 Finnish families evaluated the intensity and pleasantness of 3 suprathreshold solutions of sucrose (3.0%, 7.5%, and 18.75%) and plain water and the intensity of filter paper impregnated with 6-n-propylthiouracil (PROP). The subjects also reported the pleasantness and the use frequency of 5 sweet foods (chocolate, candy, ice cream, sweet desserts, and sweet pastry) and completed a food-behavior questionnaire that measured their craving for sweet foods.

Results: Of the chemosensory functions, the pleasantness rating of the strongest (18.75%) sucrose solution and the intensity rating of PROP yielded the highest heritability estimates (41% and 66%, respectively). The pleasantness and the use frequency of sweet foods (both variables calculated as a mean of ratings for 5 food items) and the craving for sweet foods showed significant heritability (40%, 50%, and 31%, respectively). A logarithm of odds score of 3.5 ($P = 0.00003$) was detected for use frequency of sweet foods on chromosome 16p11.2 (marker D16S753).


KEY WORDS Family study, food preferences, genetic linkage, heritability, human genetics, sweet taste

INTRODUCTION

Humans are genetically predisposed to prefer sweet taste. Because sweet foods are naturally good and are safe sources of energy and nutrients, adaptive evolutionary development has resulted in a preference for them (1). However, this evolution happened long ago when food was scarce. Today, with a great variety of sweet foods readily available in Western countries, the preference for these foods may also have disadvantages. The perception of sweet taste is initiated by the interaction of a tandem with a TAS1R2/TAS1R3 heterodimer (taste receptor type 1, members 2 and 3)—a G protein–coupled receptor (GPCR) localized in the taste buds of the tongue and the palate (2, 3). The human sweet taste receptor genes, TAS1R2 and TAS1R3, which encode the receptors reacting with sweet tastants, are both located on chromosome 1p36 (4). These genes were first discovered in mice. Numerous groups have since investigated the effect of polymorphisms or knockout of the Tas1r3 gene (Sac locus) on sweet taste sensitivity and preferences in mice. Although several studies have shown that sequence variations in the Tas1r3 gene affect sweeterer preferences of inbred mice strains (5, 6), Sclafani (7) found no differences in motivation to obtain sugar between “low-sweetener-prefering” (129P3/J) and “high-sweetener-prefering” (C57BL/6J) strains. In addition, despite Tas1r3 knockout mice having diminished behavioral and neural responses to sugars (8, 9), no differences in sucrose detection thresholds between wild-type and knockout strains were observed by Delay et al (10). Thus, the effect of variations in Tas1r3 on the behavior of mice remains unclear.

Humans differ in their liking for sweet foods (11). Moreover, environmental factors play an important role in the development of preferences for sweet foods and other foods (for a review, see 12). Although newborns prefer sugar solutions to water (13, 14), dietary experiences modify the degree of the preference for sweet taste already at the age of 6 mo (15). To our knowledge, no studies of how quantitative trait loci (QTL) affect sweet taste preferences in humans have been published to date. Earlier genome-wide linkage studies have concentrated on identifying regions harboring genes affecting macronutrient intake. Collaku et al (16) found evidence of significant and suggestive linkage on chromosomes 1, 7, 10, and 11.

1 From the Departments of Food Technology (KK, AK, and HT) and Medical Genetics (LP and MP), University of Helsinki, Helsinki, Finland; the Folkhalsan Research Institute, Helsinki, Finland (MW); the Department of Molecular Medicine, National Public Health Institute, Helsinki, Finland (KK, AK, and MP); the Department of Neurology, Helsinki University Central Hospital, Helsinki, Finland (MK); the Finnish Genome Center and the Department of Clinical Chemistry, University of Helsinki, Helsinki, Finland (AP and MW); and the Broad Institute of MIT and Harvard, Boston, MA (LP and AP).

2 Supported by the Academy of Finland (206327, 200923, and 00213), the GenomeEUtwin Project (QLG2-CT-2002-01254), EuroHead (LSHM-CT-2004-504837), the National Institutes of Health (RO1 NS37675), the Finnish Heart Association, the Oxnard Foundation, the Finnish Nutrition Foundation, the Helsinki University Central Hospital, and the Sigrid Juselius Foundation.

3 Address reprint requests to H Tuorila, Department of Food Technology, PO Box 66 (Agnes Sjobergin katu 2), University of Helsinki, FI-00014 Helsinki, Finland. E-mail: hely.tuorila@helsinki.fi.

Received December 5, 2006.

Accepted for publication February 8, 2007.
cm²). The PROP-containing filter paper pieces and plain filter square-shaped pieces so that each contained 0.6 mg PROP (1.2

The PROP filter papers were prepared by soaking filter paper disks (Whatman 1) in saturated PROP (6-propyl-2-thiouracil; Sigma-Aldrich Chemie GmBH 82460, Steinheim, Germany) disks (Whatman 1) in saturated PROP (6-propyl-2-thiouracil; Sigma-Aldrich Chemie GmBH 82460, Steinheim, Germany) water solution at boiling temperature for 30 s. The disks were left to dry overnight on aluminum foil at room temperature or in an oven at 121 °C for 1 h. The disks were weighed before and after the procedure, and the amount of absorbed PROP was calculated as the difference in weight. The filter paper disks were cut into square-shaped pieces so that each contained 0.6 mg PROP (1.2 cm²). The PROP-containing filter paper pieces and plain filter paper pieces were stored in sealed plastic sachets at room temperature for a maximum of 3 mo before use.

Three suprathreshold sucrose (Danisco Sugar, Kantvik, Finland) solutions (3.0%, 7.5%, and 18.75% wt:vol) were prepared in tap water. The samples were stored in the refrigerator (7 °C) temperature for a maximum of 3 mo before use.

The subjects were exposed to pure filter paper to later be able to distinguish the taste of the paper from that of PROP. The subjects placed filter paper containing PROP into the mouth, kept it on the tongue for 10 s, and after waiting a short while (the strongest sensation of PROP often comes with a delay) rated the intensity using a vertical 12.0-cm labeled magnitude scale (22).

The sweet and salty samples plus plain water as a control in both series (15 mL each) were labeled with 3-digit random codes. The order of sweet and salty series and the order of 4 samples within each series were randomized. The subjects were requested to rinse their mouths with tap water before starting the evaluations and between samples. The samples and the rinsing water were served at room temperature. The subjects were instructed to take the whole 15-mL sample into their mouth, twirl it around, expectorate, and provide a rating by placing a vertical line on each scale.

The instructions were given both orally and in written form, and the test administrator was present throughout the testing procedure. The intensity and pleasantness of the sweet or salty taste in the solutions were evaluated by using a 12.5-cm horizontal labeled magnitude scale (22) and labeled affective magnitude scale (23), respectively. The distance of the hash mark from the left end of the line made by the subject was measured manually. The verbal labels and their positions (cm from the left end) on the line were for the following intensity ratings: “no taste” (0.0), “barely detectable” (0.2), “weak” (0.7), “moderate” (2.1), “strong” (4.4), “very strong” (6.7), and “strongest imaginable sensation” (12.5). On the pleasantness scale, the labels were “greatest imaginable unpleasantness” (0.0), “extremely unpleasant” (1.3), “very unpleasant” (2.2), “moderately unpleasant” (4.0), “slightly unpleasant” (5.5), “neither pleasant nor unpleasant” (6.2), “slightly pleasant” (6.8), “moderately pleasant” (8.4), “very pleasant” (9.2), “extremely pleasant” (11.0), and “greatest imaginable pleasantness” (12.5). Because of the lack of the word dislike in the Finnish language, the translations refer to the pleasantness of the perception rather than to liking. In addition, the subjects evaluated how hungry they felt using a 9-point scale (1 = not hungry at all; 9 = very hungry).

The subject rated the pleasantness and the use frequency of 30 foods using 7 categories. The response alternatives for pleasantness were 1 = very unpleasant, 2 = fairly unpleasant, 3 = slightly unpleasant, 4 = neither pleasant nor unpleasant, 5 = slightly pleasant, 6 = fairly pleasant, 7 = very pleasant. The response alternatives for use-frequency 1 = never, 2 = once a month or less often, 3 = 1–2 times a month, 4 = once a week, 5 = once a couple of times a week, 6 = almost every day, and 7 = at least once a day. For further analysis, foods were categorized by using principal component analysis and reliability analysis, and a group of sweet foods, including 5 food items with sweetness as the salient attribute (chocolate, sweets, ice cream, sweet pastry, and sweet desserts), was identified. Because the sweet foods formed a minor part of the questionnaire, the subjects were unaware of our particular interest in them. In addition to sweet foods, clusters of salty, fatty, and snack foods were identified. From here on we focus on the cluster of sweet foods only. The results for the pleasantness and use-frequency ratings of the other food groups were available from the authors on request. The phenotypes for pleasantness and use frequency of sweet foods were
calculated as a mean of ratings given to 5 food items. The reliability of the composite scales was tested by using Cronbach’s α; the values were 0.85 for pleasantness and 0.61 for use frequency of sweet foods.

The subjects also filled in a Craving for Sweet Foods scale that is a subscale of Health and Taste Attitude Scales (24, 25). This validated scale measures the tendency to crave sweet foods with 6 statements, each of which was evaluated by using a 7-point Likert scale: 1 = strongly disagree, 2 = moderately disagree, 3 = slightly disagree, 4 = neither agree nor disagree, 5 = slightly agree, 6 = moderately agree, and 7 = strongly agree. Cronbach’s α for the scale was 0.86. The questionnaire also included questions about food behavior and demographics. The questionnaires were mailed to subjects before their visit to the clinic. During the visit, the test administrator checked that subjects had replied to all questions.

Genotyping

The genome-wide linkage analysis was conducted by using microsatellite markers specific for 22 autosomes and the X chromosome (18). DNA was extracted from whole blood by using standard methods. Altogether, 108 subjects from 20 families were genotyped with 367 microsatellite markers [The Human MapPairs Genome-Wide Screening Set LI-COR, ninth version of Weber-lab set (26) with a few modifications] and 39 subjects from 6 families were genotyped with 383 microsatellite markers [The Human MapPairs Genome-Wide Screening Set LI-COR, ninth version of Weber-lab set (26) with a few modifications]. The order of the markers was determined by using sequence information from the UCSC database (http://genome.ucsc.edu/), and the genetic distance between markers was interpreted using DeCode map as a backbone to our in-house program Cartographer (27).

PedCheck (28) was used to check the genotype data for Mendelian inconsistencies. No level 0, 1, or 2 errors were detected by PedCheck. In addition, MERLIN (29) was used to screen for unlikely but Mendelian-consistent genotypes. The unlikely genotypes detected by the MERLIN error detection algorithm were erased from the pedigree file using the program Pedwipe provided by MERLIN (29).

Statistical analysis

Singlepoint and multipoint linkage analyses were performed by using a variance component method implemented in MERLIN (29) to locate genetic elements underlying traits analyzed across the genome. In the variance components framework, the expected allele sharing at a putative quantitative trait linkage between relatives is correlated with their phenotypic covariance, thus evaluating the linkage between a certain genetic trait and the trait of interest. Usually, a LOD score of 3 (P value of a single test = 0.0001) is regarded as significant for a monogenic trait and implies that the genetic marker is close to the trait locus, ie, the 2 loci are linked. For a complex trait, the concept of a significant LOD score is somewhat more ambiguous (30). In addition to linkage evidence, the variance component method also provides a heritability estimate for the trait analyzed. This estimate expresses the proportion of the variation that makes family members more similar with each other, including the effects of both their shared genetic parameters and their common environment.

The age, sex, and migraine status of each subject at the time of the clinic visit were used as covariates in the quantitative genetic model. In addition, the self-rated hunger was used as covariate for chemosensory measurements. In the linkage analysis, only the significant covariates were included [significances obtained from the heritability analysis of program SOLAR (31) assuming a polygenic model]. Except for quantitative genetic modeling, all statistical analyses were carried out by using the SPSS statistical package (32).

RESULTS

Characteristics and heritability estimates of the traits are shown in Table 1 and Table 2. Although differences in the mean perceived intensities of sucrose samples were observed, the mean pleasantness ratings of the samples did not differ. However, there was a trend for an increasing SD with increasing sweetness intensity in both the intensity and pleasantness evaluations. The 2 subjects who had given very low (<2 cm) intensity
We found a correlation with age for only the score on the Craving for Sweet Foods scale ($r = -0.37, P > 0.001$). The negative correlation means that younger subjects have a greater tendency than do older subjects to crave sweet foods. Self-rated hunger correlated significantly with the intensity ratings of 3.0% ($r = 0.17, P = 0.040$), 7.5% ($r = 0.24, P = 0.004$), and 18.75% ($r = 0.23, P = 0.005$) sucrose solutions. A negative correlation was found between the ratings of hunger and pleasantness for the 7.5% sucrose solution ($r = -0.23, P = 0.006$).

The heritability estimates for the intensity evaluations of sweet samples were all near zero. The heritability of the intensity evaluation of PROP filter paper was, however, high (66%). This implies that the labeled magnitude scale (LMS) was properly understood, and the scale was not the reason for the low heritability estimates in the sweetness intensity evaluations. The heritability estimates of the pleasantness ratings of the 2 strongest sucrose solutions of 7.5% and 18.75% (29.2% and 40.9%, respectively) and that of the plain water (27.3%) were all significant. The heritability estimates for the pleasantness evaluation and the user frequency of sweet foods were 40.3% and 50.2%, respectively. The heritability of the score on the Craving for Sweet Foods scale was lower, 31.0%. The heritability estimates of the intensity and pleasantness ratings of the salty solutions were all very low. The only significant heritability estimates were obtained for the pleasantness rating of the 0.2% NaCl solution and that of pure water (33.1% and 24.3%, respectively). The salty taste of the solution containing 0.2% NaCl is clearly detectable, albeit mild (33).

Pearson’s correlation coefficients between sweet taste perception and preference-related traits are provided in Table 3. Several significant correlations among the measured traits suggest that a common factor underlies them. The sweet taste preference-related phenotypes did not correlate significantly with PROP intensity ($r < 0.08$) or BMI ($r < 0.15$).

### Variance component quantitative trait linkage analysis

Quantitative trait linkage analysis for the use frequency of sweet foods produced a multipoint LOD score of 3.5 on chromosome 16p11.2 (Table 4), which peaked at the marker

---

**TABLE 2**

<table>
<thead>
<tr>
<th>Trait</th>
<th>Rating $^2$</th>
<th>Heritability estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensity of salty solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td>0.4 ± 0.5</td>
<td>4.6</td>
</tr>
<tr>
<td>0.2%</td>
<td>1.7 ± 1.5</td>
<td>4.4</td>
</tr>
<tr>
<td>0.5%</td>
<td>3.6 ± 2.1</td>
<td>0.0</td>
</tr>
<tr>
<td>1.25%</td>
<td>5.8 ± 2.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Pleasantness of salty solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td>6.8 ± 1.5</td>
<td>24.3</td>
</tr>
<tr>
<td>0.2%</td>
<td>5.8 ± 1.4</td>
<td>33.1</td>
</tr>
<tr>
<td>0.5%</td>
<td>5.3 ± 1.6</td>
<td>0.0</td>
</tr>
<tr>
<td>1.25%</td>
<td>4.2 ± 1.8</td>
<td>0.0</td>
</tr>
</tbody>
</table>

$^1$ Age, sex, migraine status, and self-rated hunger were used as covariates in the models.

$^2$ All values are $\bar{x} \pm SD$.

ratings for the 18.75% sucrose solution had rated the intensities of the sweet solutions in an ascending order and had given higher intensity ratings for the salty solutions. Thus, we concluded that these subjects were not ageusic; therefore, they were not excluded from the analyses. The hunger estimates varied from 1 to 9; the mean (±SD) was 4.9 ± 2.2.

Our study design allowed evaluation of the effects of age, sex, self-rated hunger, and migraine status on the traits. The pleasantness rating of the solution containing 18.75% sucrose was the only trait affected by sex; on average, females rated the solution as less pleasant (mean: 6.0 cm) than did males (mean: 6.7, $t_{143} = 2.14, P = 0.034$). To investigate the effect of migraine on the traits, the subjects were divided by their migraine status into 2 groups: 1) patients with a diagnosis of migraine with aura and 2) healthy family members. The $t$ test showed a difference between these 2 groups for only one trait, namely the intensity rating of the 3.0% sucrose solution. On average, the healthy family members rated this mildly sweet solution as more intensive (mean: 2.3 cm) than did the migraine patients (mean: 1.6 cm, $t_{143} = 2.7, P = 0.007$).

### TABLE 3

<table>
<thead>
<tr>
<th></th>
<th>Intensity of sucrose solution</th>
<th>Pleasantness of sucrose solution</th>
<th>Sweet foods</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0% 3.0% 7.5% 18.75%</td>
<td>0% 3.0% 7.5% 18.75%</td>
<td>Pleasants</td>
</tr>
<tr>
<td>Intensity of sucrose solution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>3.0%</td>
<td>0.09</td>
<td>0.09</td>
<td>0.09</td>
</tr>
<tr>
<td>7.5%</td>
<td>0.12</td>
<td>$0.29^1$</td>
<td>0.29</td>
</tr>
<tr>
<td>18.75%</td>
<td>$-0.03^2$</td>
<td>0.46</td>
<td>0.46</td>
</tr>
<tr>
<td>Pleasants of sucrose solution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td>$-0.09^1$</td>
<td>0.09</td>
<td>0.13</td>
</tr>
<tr>
<td>3.0%</td>
<td>$-0.03^1$</td>
<td>$-0.07^1$</td>
<td>$-0.03^1$</td>
</tr>
<tr>
<td>7.5%</td>
<td>$-0.07^1$</td>
<td>$-0.11^1$</td>
<td>$-0.38^2$</td>
</tr>
<tr>
<td>18.75%</td>
<td>$-0.03^1$</td>
<td>$-0.24^2$</td>
<td>$-0.23^2$</td>
</tr>
<tr>
<td>Sweet foods</td>
<td>Pleasants</td>
<td>Use</td>
<td>Craving</td>
</tr>
<tr>
<td>Pleasants</td>
<td>$-0.05^1$</td>
<td>0.10</td>
<td>0.05</td>
</tr>
<tr>
<td>Use</td>
<td>$-0.04^1$</td>
<td>0.08</td>
<td>0.04</td>
</tr>
<tr>
<td>Craving</td>
<td>$-0.01^1$</td>
<td>0.05</td>
<td>$-0.07^2$</td>
</tr>
</tbody>
</table>

$^1$ P $< 0.05$.

$^2$ P $< 0.01$.
D16S753. The singlepoint LOD score at this marker was 2.9. The information content on the peak area was fairly high (78%), and a decrease of one LOD (34) on this locus covers a region of ≈10 cM harboring >30 genes. However, no obvious candidate genes for this trait were identified. A significant LOD for this novel phenotype and low \( r = 0.06 \) spousal correlation suggest that the heritability estimate here indicates a true effect of genes rather than a mere familial correlation. In addition, some evidence for linkage for the use frequency of sweet foods was found on chromosomes 9q32.1 (LOD = 2.1 marker D9S286), 20q13.2 (LOD = 1.9 marker D20S480), and 3p26.3 (LOD = 1.9 marker D3S2387). A graph of the genome-wide multipoint linkage scan with the information contents of the markers for the use frequency of sweet foods is presented in Figure 1. The corresponding multipoint and singlepoint linkage scans of chromosome 16 are shown in Figure 2.

The multipoint linkage analysis also produced a LOD score of 1.9 on chromosome 1q41 for the pleasantness rating of 18.75% sucrose solution (singlepoint LOD score at the marker = 0.68). The genome-wide multipoint scan results are shown in Figure 3, and the multipoint and singlepoint scans of chromosome 1 are shown in Figure 4.

**Genome-wide \( P \) values**

To determine the empirical significance of our linkage findings, we simulated 100 genome-wide scans of comparable structure using MERLIN and analyzed each simulated scan identically to the original data analysis. MERLIN performs gene-dropping simulation while retaining the genetic map, phenotype data, pedigree structure, and missing genotype data patterns, creating comparable data with random marker genotypes. Because the data are simulated under the hypothesis of no linkage, any linkage seen is due to chance alone, which therefore allows the evaluation of the false-positive rate of the data set analyzed. The empirical \( P \) value for a LOD score was defined as the proportion of simulated genomes where the LOD score in question was reached or exceeded. Subsequently, the corresponding 95% Wilson CIs were calculated for the empirical \( P \) value (35).

<table>
<thead>
<tr>
<th>Trait and covariate</th>
<th>LOD</th>
<th>Marker</th>
<th>Location</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use frequency of sweet foods</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Migraine, age</td>
<td>3.5</td>
<td>D16S753</td>
<td>16p11.2</td>
<td>0.00003</td>
</tr>
<tr>
<td>Migraine, age</td>
<td>2.0</td>
<td>D9S286</td>
<td>9q32.1</td>
<td>0.0010</td>
</tr>
<tr>
<td>Migraine, age</td>
<td>1.9</td>
<td>D3S2387</td>
<td>3p26.3</td>
<td>0.0014</td>
</tr>
<tr>
<td>Migraine, age</td>
<td>1.9</td>
<td>D20S480</td>
<td>20q13.2</td>
<td>0.0015</td>
</tr>
<tr>
<td>Pleasantness of 18.75% sucrose solution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hunger, migraine, age</td>
<td>1.9</td>
<td>D1S549</td>
<td>1q41</td>
<td>0.0014</td>
</tr>
</tbody>
</table>

\( ' \) LOD, logarithm of odds.

**TABLE 4**

Results of a genome-wide scan showing some evidence of linkage

---

**FIGURE 1.** Genome-wide multipoint linkage analysis results (thick line) and the information content curves (thin line) for the use frequency of sweet foods. LOD, logarithm of odds.
best LOD score (3.5 on chromosome 16p11.3) produced an empirical $P$ value of 0.07 (95% Wilson CI: 0.03, 0.14) in the permutation analyses. The other suggestive loci did not survive the permutation tests, the second lowest empirical $P$ value being 0.25 (95% Wilson CI: 0.18, 0.34) for the LOD score of 1.9 for pleasantness rating of 18.75% sucrose solution.

**DISCUSSION**

We found evidence of significant linkage between the use frequency of sweet foods and a marker located on chromosome 16. Our results show that pleasantness of an extremely sweet solution and pleasantness and use frequency of sweet foods are

![FIGURE 2. Results of singlepoint and multipoint linkage analyses on chromosome 16 for the use frequency of sweet foods. LOD, logarithm of odds.](image)

![FIGURE 3. Genome-wide multipoint linkage analysis results for the pleasantness rating of the 18.75% sucrose solution. LOD, logarithm of odds.](image)
partly heritable; 40–50% of the variation in these traits is explained by inherited mechanisms. The intensity and pleasantness ratings of the salty solutions were, in turn, mostly not inherited. The latter observation agrees with earlier results. A comparison of our results with variance components obtained from twin studies suggests that the significant heritability estimates may be due to common family environment rather than to genetic effects (36).

To our knowledge, no other QTL affecting sweet taste preference in humans have been identified to date. Collaku et al (16) and Cai et al (17) have both performed genome-wide linkage analysis on macronutrient intakes, calculated from food-frequency-questionnaire data. Neither of the studies showed suggestive or significant linkages for sucrose intake, maybe because of the fairly general level of measurement of food intake. Studies evaluating the proportion of heritable effects on sweet taste preferences, with actual psychophysical testing of the subjects, are also very rare. Using data from 13 monozygotic and 10 dizygotic twin pairs, Krondl et al (37) found no significant heritability for the recognition threshold of sucrose or for preferences for and use frequency of 4 sweet foods (honey, jam, ice cream, and doughnuts) using the Holzinger index of heritability:

\[
\text{Holzinger index of heritability} = \frac{(\text{Var}_{MZ} - \text{Var}_{DZ})}{\text{Var}_{DZ}},
\]

where Var is the within-pair variance of the mean difference. The negative result may have resulted because of the small sample size or because the statistical method used was not sufficiently sophisticated to reveal heritable effects.

The linkage peak for use frequency of sweet foods with a multipoint LOD score of 3.5 (empirical \( P = 0.07 \)) was located on chromosome 16p11.2. This area does not harbor genes known to affect the trait. However, Chr16p11.2 does contain 3 locations of hypothetical proteins, ie, locations harboring a gene whose function remains unknown. The p arm of chromosome 16 was previously linked to taste-related traits. Drayna et al (38) identified a QTL on Chr16p on 2-locus whole-genome scan conditional on Chr7 QTL for PTC (phenylthiocarbamide) tasting ability. The QTL on Chr16p provided a 2-locus LOD score of 3.33 at 14 cM. However, though located in the same chromosomal arm as our peak for the use frequency of sweet foods (marker located at 56.8 cM), these peaks are rather far away from each others. Another interesting linkage was obtained for the pleasantness of the 18.75% sucrose solution. Although the phenotype may better reflect the biological mechanism underlying the sweetness preference than a variable obtained from the use-frequency questionnaire, the result on chromosome 1q41 needs to be replicated in another sample because it did not reach genome-wide significance. Our linkage analysis of PROP intensity did not show any significant or suggestive QTLs. This discrepancy with earlier studies (20, 38) finding linkage on Chr7 (gene TAS2R38) may be due to methodologic differences in PROP sensitivity measurement.

The fact that a significant linkage result was found for use frequency, and not for the pleasantness ratings, does not disprove the hypothesis that the same genes affect these heritable traits. Many of the variables were correlated, which implies that a common factor underlies these traits. Evaluating the use frequency of a food is perhaps more exact than is evaluating pleasantness, because rating the pleasantness of foods without tasting or seeing them may target to different products (eg, a different type of candy) (39). Also, subjects may avoid using the ends of a hedonic scale (40). In the use-frequency evaluation, the central tendency is less likely, because both ends of the scale are explicit frequency estimations. Thus, the use-frequency evaluation may represent sweetness preference and thereby reveal the underlying genetic tendency to like (or dislike) sweetness. Measuring the
sweet taste preference in humans is complicated: intensity and pleasantness ratings of aqueous solutions may poorly generalize to behavior. On the other hand, sweet foods always possess sensory attributes other than sweetness, and the preferred level of sweetness is often food-specific (41). However, we decided to include many measures of sweet preferences because the predictive value of separate measures on actual dietary intake of sweet foods may be limited (42).

The use frequency may also be affected by many factors other than liking for foods. If people always ate foods that they like the best, we would expect the use frequency of sweet foods to be higher. Some factors affecting use frequency, apart from liking the food, may also be heritable. For example, 44% and 59% of the variation in cognitive restraint of eating was shown to be heritable in twin studies by de Castro (43) and Tholin et al (44), respectively.

Our results imply that the intensity perception of the suprathreshold sweet taste is not heritable. The affective processing of the sensation seems, however, to be partly genetically steered. Thus, it is not surprising that the LOD peak for use frequency of sweet foods was not located near the sweet taste receptors. Experiments with mice have shown that polymorphisms in sweet taste receptor genes do influence the preference for sweet solutions (5, 6). Whereas mice eat any acceptable and available food, the food choices in humans are more complex. For example, the brand knowledge has been suggested to alter the behavioral preferences and neural responses to a sweet, culturally familiar drink (45). No evidence of polymorphisms in taste receptor genes mediating the sweet taste preference in humans has been published. Different brain regions are responsive to sweetness intensity and pleasantness perceptions in humans (46), and one might therefore expect that different mechanisms underlie these phenotypes.

The men evaluated the 18.75% sucrose solution as more pleasant than did the women. This observation is consistent with the results of Conner and Booth (47). In their study of the most preferred concentration of sugar in a lime drink, the men showed a greater sweetness preference than did the females on average. A difference between migraine patients and healthy family members was found in the intensity evaluation of the weakly sweet 3.0% sucrose solution. Taste abnormality during an acute migraine attack has been reported by some migraine patients (48), but the degree of these patients’ taste abnormality when not having an attack has not been investigated. Significant, albeit not very high, correlations were found between self-rated hunger and intensity evaluations of all 3 sucrose solutions. This finding is in line with the literature. Caloric deprivation and hunger have been shown to increase taste sensitivity to sweet taste (49, 50). Age did not correlate with any of the psychophysical measurements. Although taste sensitivity decreases with age, the sensitivity to sweet taste does not decline as much as does the sensitivity to other tastes (51).

The strong correlations among heritable phenotypes, the limited sample size, and the inability to distinguish between effects of common family environment and genetic effects in our study call for further evaluation of the phenotypes and the genetic effects using larger populations of monozygous and dizygous twins or family members reared apart. Despite the limited sample size, the nature of variance component linkage analysis in which the possible phenotypic data errors also masked unrelated familial clustering, thus increasing noise and hindering signal detection, and the finding of both a significant LOD score (LOD = 3.5) and heritability estimate (P = 0.007) for a trait, do not support a false-positive result.

In conclusion, individual differences in sweet taste preferences appear to be partly heritable. A locus on chromosome 16 was found to affect the use frequency of sweet foods. This result can be considered to be very significant, because a sweet taste preference has not been previously shown to be heritable in humans. This observation broadens our understanding of human food choice.

We thank the families for participating in the study and Kaisa Taskila, Eija Hämäläinen, and Tanja Moinilan for excellent technical assistance.

The authors’ responsibilities were as follows—KK: drafted the manuscript; KK and AK: analyzed the data; MP and SS: assisted in the quantitative genetic analysis; MK, KK, AK, AP, and MW: collected the data; HT, LP, and MP: planned the study; MW: analyzed the genotypes. All authors contributed to the interpretation of the results and to the writing of the manuscript and accepted the final version. None of the authors had a conflict of interest.

REFERENCES


7. Sclafani A. Sucrose motivation in sweet “sensitive” (C57BL/6J) and “sub-sensitive” (129P3/J) mice measured by progressive ratio licking. Phys Behav 2006;87:734–44.


10. Delay ER, Hernandez NP, Bromley K, Margolskee RF. Sucrose and monosodium glutamate taste thresholds and discrimination ability of T1r3 knockout mice. Chem Senses 2006;31:351–7.


19. Zhao L, Kirkmeyer SV, Tepper BJ. A paper screening test to assess
SWEET TASTE PREFERENCES ARE PARTLY INHERITED