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Individual Differences in Perceived Bitterness Predict Liking of Sweeteners

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Abstract

Although recent molecular studies suggest that only one receptor and one signaling pathway are involved in the perception of sweetness, this seems to contradict everyday experience that people not only have different likes and dislikes of certain sweeteners but also perceive the sweeteners differently. One possible explanation is that variation in liking of sweeteners is due, in part, to variation across individuals in sensitivity to nonsweet tastes, such as bitterness, which are transduced by a variety of receptors. Fifty individuals were asked to rate intensities of several taste attributes of 10 sweeteners and to give hedonic assessments of each sweetener. Additionally, their sensitivity to 6-*n*-propyl-3-thiouracil (PROP) was determined. Results indicated that when matched for sweetness, the perception of bitterness and the sweetener compound were the 2 largest factors contributing to overall liking of a sweetener. Sensitivity to PROP did not contribute significantly to the model.

Key words: bitterness, liking, PROP, sweeteners, sweetness

Introduction

Despite the wide variety of chemical structures that elicit sweetness, in 1972, McBurney demonstrated that when a subject was adapted to sucrose by prolonged exposure, she/he was also cross-adapted to a variety of sugars and other sweeteners. In contrast, when the same subject was adapted to saccharin, cross-adaptation was notably less complete. However, because saccharin did not self-adapt to the same extent as did sucrose, he concluded that sweetness was a unitary perception. Faurion et al. (1980) interpreted the findings of McBurney (1972) differently, taking it as evidence that "· · · all sweet compounds do not equally cross adapt." They examined individual difference in the perception of sweeteners and, based upon their multidimensional analyses, came to the conflicting conclusion that sweetness was not unitary and had at least 3 perceptual dimensions (Faurion et al. 1980). They further speculated that their findings were evidence for several receptor sites involved with the perception of sweet taste chemoreception. Based upon their own cross-adaptation research, Schiffman et al. (1981) concluded that more than one receptor mechanism may be responsible for the perception of the sweet quality, and Lawless and Stevens (1983) concluded that multiple peripheral mechanisms encode sweetness. Recent work by Breslin et al. (1996) indicated that, when matched for intensity, fructose, glucose, and sucrose are not distinguishable from one another. However, maltose often remained distinguishable from other sugars (even when nose clips were worn), suggesting that at least "· · · a second gustatory code" (Breslin et al. 1996) must exist.

Since McBurney's psychophysical study (1972), several biochemical and electrophysiological studies have been conducted on taste receptor cells. For example, in 1974, Frank classified chorda tympani nerve fibers by which of 4 taste compounds (sucrose, sodium chloride, hydrochloric acid, or quinine hydrochloride) elicited the largest response in both hamsters and squirrel monkeys. She discovered that some neurons (classified as "sucrose-best") responded more strongly to sucrose than fructose, whereas other neurons (classified as "NaCl-best") responded more strongly to fructose than sucrose. Until recently, cumulative research has suggested 2 models of sweet taste transduction (Herness and Gilbertson 1999). Several studies (Avenet et al. 1988a, 1988b; Tonosaki and Funakoshi 1988; Striem et al. 1989, 1991; Cummings et al. 1993, 1996; Bernhardt et al. 1996; Uchida and Sato 1997) indicate that sweeteners (often carbohydrate sweeteners) were transduced by a cAMP second messenger system in mice (Tonosaki and Funakoshi 1988), rats (Striem et al. 1989, 1991; Bernhardt et al. 1996), hamsters (Cummings et al. 1993, 1996), gerbils (Uchida and Sato 1997), and frogs (Avenet et al. 1988a, 1988b). Other findings (e.g., Bernhardt et al. 1996; Uchida and Sato 1997) indicated that taste perception of sweeteners (often artificial sweeteners and amino acids) was transduced by an inositol

trisphosphate second messenger system in rats (Bernhardt et al. 1996) and gerbils (Uchida and Sato 1997). Although these findings seem to correspond to the psychophysical findings, suggesting more than one sweet taste transduction mechanism, more recent research has suggested that there may well be only one receptor (Nelson et al. 2001; Li et al. 2002) and one signaling pathway (Zhang et al. 2003) involved in the perception of sweetness.

These most recent findings seem to contradict everyday experience; anecdotal reports; and previous biochemical, electrophysiological, and psychophysical studies. When one sweetens their coffee or tea, the difference between these various sweeteners is often readily apparent. Zhao et al. (2003) suggest that "· · · many sweeteners are likely to activate receptors for other taste modalities, like T2R bitter sensing cells," which would account for the nonsweet tastes often reported for particular sweeteners. In contrast to findings with sweeteners, recent molecular studies suggest that bitter compounds are transduced via roughly 20–30 distinct receptor types (Adler et al. 2000; Chandrashekar et al. 2000; Matsunami et al. 2000; Caicecdo and Roper 2001). These results are in agreement with the psychophysical findings of Delwiche et al. (2001a), which demonstrated patterns of covariation across individuals based upon differences in bitter perception. However, it remains unclear if such differences exist for sweeteners. It is also unclear how these differences in individual perception of bitter and/or sweet compounds might relate to the liking of low-calorie sweeteners and products made from these sweeteners. Thus, this study examined the hypothesis that variation in liking of sweeteners is due, at least in part, to variation across individuals in sensitivity to the nonsweet tastes (bitter, sour, and metallic) stimulated by some sweeteners.

Materials and methods

Stimuli

Stimuli were aqueous solutions made from 11 sweeteners. Concentrations of sweeteners were selected to be equally sweet, as determined by Guinard et al. (1994) for most sweeteners (aspartame, cyclamate, D-tryptophan, sucrose, glucose, thaumatin, xylitol, glycine, and saccharin), and bench top testing for the remaining sweeteners (sucralose, fructose, and acesulfame potassium [ace-K]). Concentrations were as follows: 401 mM sucrose, 1120 mM glucose, 15 mM D-tryptophan, 0.0023 mM thaumatin, 930 mM xylitol, 5.21 mM sodium saccharin, 2.89 mM aspartame, 29.1 mM sodium cyclamate, 1.0 mM sucralose, 600 mM fructose, and 3.88 mM ace-K. All solutions were prepared with Millipore polished water (Millipore RiOs 16 and Milli-QR Gradient, Millipore Corporation, Bedford, MA) at least 24 h prior to testing and were remade every 5 days to ensure freshness.

In addition, before intensity assessments began, subject concepts of taste qualities were aligned via the presentation of reference standards. These references were 292 mM sucrose for "sweet," 5.2 mM citric acid for "sour," 125 mM sodium chloride for "salty," 0.032 mM quinine sulfate for "bitter," and two 250 mg ferrous sulfate tablets per liter for "metallic." A "sweet + bitter" reference containing 292 mM sucrose and 0.032 mM quinine sulfate was included with the references to familiarize subjects with rating a sample with more than one taste quality. In the final session, individuals' sensitivity to 6-*n*-propyl-3-thiouracil (PROP) was determined by panelists' ratings of PROP bitterness intensity at several concentrations: 0.055, 0.174, 0.55, 1.74, and 5.50 mM (PROP, Sigma Chemical, St Louis, MO).

Panelists

Fifty paid volunteers (35 females, 15 males; 18–35 years of age) were recruited from the Ohio State University campus. All subjects gave informed consent, in accordance with the approval of methods by The Ohio State University Office of Responsible Research Practices.

Procedure

Each panelist attended 3 sessions. All sessions were conducted in sensory testing booths equipped with computer monitors, keyboards, and a mouse at each of 10 stations. Data were collected using Compusense five version 4.6 software (Compusense Inc., Guelph, Ontario, Canada). In all sessions, samples were presented as 20-ml aliquots in 1-oz plastic cups (Solo Plastic Souffles, P100, Solo Cup Company, Baltimore, MD) labeled with random 3-digit codes. Samples were randomized and counterbalanced across panelists and blocked so that each panelist received all samples once before receiving a duplicate of any sample. In all sessions, panelists rinsed with water (Millipore polished) for 20 s between each sample. An on-screen 20-s countdown directed panelists during this interval. Panelists were instructed to expectorate all samples and rinse water.

In session 1, panelists rated overall liking of each of the 11 sweeteners in duplicate, for a total of 22 assessments. Overall liking was rated on the 9-point hedonic scale (Lawless and Heymann 1998), ranging from "1 = dislike extremely" to "9 = like extremely." This well-established scale (Lawless and Heymann 1998) was designed such that every point is labeled with a verbal descriptor, and the psychological distances between the verbal descriptors are approximately equal (Jones et al. 1955). In session 2, the panelists rated, in duplicate, perceived intensity of sweet, sour, salty, bitter, and metallic taste of the 11 sweeteners on the generalized labeled magnitude scale (LMS) (Bartoshuk et al. 2004) for a total of 22 assessments. Although this scale was developed relatively recently, it is believed to capture true differences in perceived intensities across individuals (Bartoshuk et al. 2004). Before assessing the sweeteners, panelists were familiarized with the taste qualities by sampling and rating labeled references (as described above).

In session 3, panelists rated the perceived loudness intensity of a series of tones (0, 20, 35, 50, 65, and 80 decibels) in

duplicate on the generalized LMS (Bartoshuk et al. 2004). The tones were played for 1 s at 4000 Hz. Tones were generated by an audiometer (AS208 audiometer, Interacoustics, Denmark) and presented to the right ear of each panelist via a headset. The intensity ratings of the tones were used to account for differences in scale usage, as described below. Also in session 3, panelist sensitivity to PROP was determined following the protocol of Delwiche et al. (2001a). Panelists rated the perceived bitterness of 5 concentrations of PROP in duplicate on the generalized LMS.

Statistical analysis

Differences across panelists in intensity ratings may be due to 2 things: differences in perceived intensity and differences in scale usage. As the focus of this investigation was upon differences in perceptual intensities, the desire was to minimize the discrepancies in scale usage by centralizing the means of the intensity ratings across participants. However, previous research (e.g., Gent and Bartoshuk 1983; Bartoshuk et al. 1994, 1996, 1999) suggests that even individuals with normal taste perception do differ in the perceived intensities of taste qualities, with large differences being found between PROP taste sensitivity groups, thus centralizing the mean using taste ratings would be ill-advised. Thus, it was necessary to centralize the means of a separate physical continuum, that is, loudness.

The loudness ratings of the tones were centralized as follows. First, the 2 replications of loudness ratings were first averaged for each subject. Then, the grand mean for loudness was calculated and subsequently divided by each panelist's average intensity rating for loudness across levels, creating a unique correction factor multiplier for each individual. Such a calculation effectively moves every panelist's loudness ratings to the same area on the scale, the assumption being that perceived loudness across these individuals (all with normal hearing) is similar and that differences in their ratings are due to more to differences in scale usage rather than differences in loudness perception. Each panelist's sweet, sour, salty, bitter, and metallic ratings from session 2, as well as PROP bitter intensity ratings from session 3, were then multiplied by each individual's unique correction factor (determined from the loudness ratings), thus accounting for differences in scale usage without masking true differences in taste sensitivity.

In contrast, the liking ratings were not centralized in the same manner. Although it is still desirable to minimize differences in scale usage, neither is there physical continuum underlying liking nor is there any universality to what constitutes a likeable stimulus. Although it is reasonable to assume that all participants (who reported having normal hearing) would rate the loudness of a series of tones in a similar fashion, there is no stimulus set for which it is reasonable to assume that all participants would rate liking of the items in a similar fashion, or even in the same rank order. This makes it impossible to present a separate stimulus set which could then be used to adjust for differences in scale usage. However, because the verbal labels of the 9-point hedonic scale are approximately equal psychological distances apart (Jones et al. 1955), a panelist's liking ratings should accurately reflect their opinions with minimal distortion. It is unknown how the use of a different scale, such as the labeled affective magnitude scale (Schutz and Cardello 2001), would impact the findings, but it is expected that they would be quite similar.

PROP taster status was determined from the bitter intensity ratings from session 3. Following the protocol developed by Delwiche et al. (2001a), panelists were separated into hypotasters (often called nontasters), tasters, and hypertasters (often called super-tasters; e.g., Bartoshuk et al. 1994, 1996; Prescott et al. 2004) based on natural breaks in the bitterness intensity ratings of 1.74 mM PROP. From these natural breaks, the subjects group was determined to contain 12 hypotasters, 23 tasters, and 15 hypertasters (see Table 1). It should be mentioned that panelists categorized as hypotasters can still taste PROP; they are simply less sensitive to it and may not taste it at lower concentrations. In contrast, hypertasters are very sensitive to PROP and find even low concentrations taste extremely bitter.

Repeated measures analysis of variance (ANOVA) was performed on the ratings for each of the taste qualities (sweet, sour, salty, bitter, metallic). Significant results were followed with Scheffé's post hoc analysis. Repeated measures ANOVAs were conducted with Statistica 7 (Statsoft Inc., Tulsa, OK).

Additionally, a linear model of the data was created, with overall liking ratings as the dependent variable. The independent variables were the intensity ratings of the sweet, sour, salty, bitter, and metallic taste qualities; the PROP sensitivity category (hypotaster, taster, or hypertaster); and the sweetener. The categorical variables (PROP category and sweetener) were included in the model by means of dummy coding (Aiken and West 1991). The linear model was created with SPSS 14.0 (SPSS Inc., Chicago, IL).

For the analyses, 2 extreme outliers were excluded from the data set. Two panelists gave "sourness" ratings for thaumatin that were 10 and 14 times the inner quartile range (IQR) greater than the 3rd quartile, respectively. The standard for an extreme outlier is a data point more than 3 times the IQR above the 3rd quartile. Although large individual variation in perception of these sweeteners was expected, these 2 data points were so extreme that they distorted the data set.

Table 1 PROP status of individual judges

PROP status	Panelists
Hypotaster	2, 5, 13, 19, 20, 28, 29, 33, 34, 41, 43, 45
Tasters	1, 3, 6, 9, 10, 11, 14, 15, 18, 24, 25, 26, 30, 31, 35, 36, 37, 38, 40, 44, 46, 48, 49
Hypertaster	4, 7, 8, 12, 16, 17, 21, 22, 23, 27, 32, 39, 42, 47, 50

Panelist numbers correspond to panelist ID numbers in Figures 1–3.

Results and discussion

Preliminary analysis of the sweetness ratings with 1-way repeated measures ANOVA indicated that ace-K was significantly lower in sweetness ($P < 0.05$) than the other 10 compounds (data not shown). Thus, ace-K was excluded from additional analysis. One-way repeated measures ANOVAs of the remaining 10 sweeteners showed that although the compounds did not differ significantly in sweetness or sourness ($P > 0.05$), there were significant differences ($P < 0.05$) between compounds for salty, bitter, and metallic (Table 2).

Although the average ratings of sweetness for 10 of the different compounds are not significantly different, Figures 1 and 2 (bottom) show individual differences in perceived sweetness for representative compounds and further demonstrate that the perceived sweet intensity is not obviously related to an individual's rating of liking. In contrast, with one notable exception (subject 32 for saccharin), if a panelist rated a given sweetener as more than "moderate" in bitterness, the liking rating was neutral or lower (Figures 1 and 2, top). The converse was not true for sweetness, that is, panelists who rated a compound high in sweetness were not always more likely to rate it high for liking. Sucrose (Figure 3), which was universally rated very low in bitterness, was also the most liked compound in the study (Table 2). In addition to individual differences, the average bitterness rating for a compound was also highly correlated ($P < 0.005$) with

Table 2 Results of 1-way repeated measures ANOVAs on attribute ratings

	Attribute mean ratings					
	Liking	Sweet	Sour	Salty	Bitter	Metallic
Aspartame	5.4^{def}	25.2	2.3	1.6^{ab}	2.2^{a}	1.8^{a}
Cyclamate	4.5^{bcd}	32.5	3.3	5.1^{b}	4.3^{a}	2.2^{a}
D-tryptophan	2.6^{a}	23.7	2.7	2.4^{ab}	20.2^{b}	4.0^{ab}
Fructose	5.5^{def}	29.6	4.6	1.9^{ab}	2.6^{a}	2.0^{a}
Glucose	5.0^{cde}	32.1	5.9	2.6^{ab}	4.2^{a}	1.9^{a}
Saccharin	3.8^{ab}	27.1	2.4	2.2^{ab}	14.2^{b}	3.5^{ab}
Sucralose	5.9^{ef}	31.5	2.0	1.0^{a}	2.9^{a}	2.3^{a}
Sucrose	6.4^{f}	33.2	2.4	0.7^{a}	1.9^{a}	2.0^{a}
Thaumatin	3.9^{bc}	24.4	2.4	3.8^{ab}	7.0^{a}	7.3^{b}
Xylitol	5.2^{def}	31.9	4.7	1.8^{ab}	3.4^{a}	2.1^{a}
P value	<0.001	0.080	0.110	<0.001	<0.001	<0.001

Within a column, means with the same superscript are not significantly different (Scheffé's $p > 0.05$).

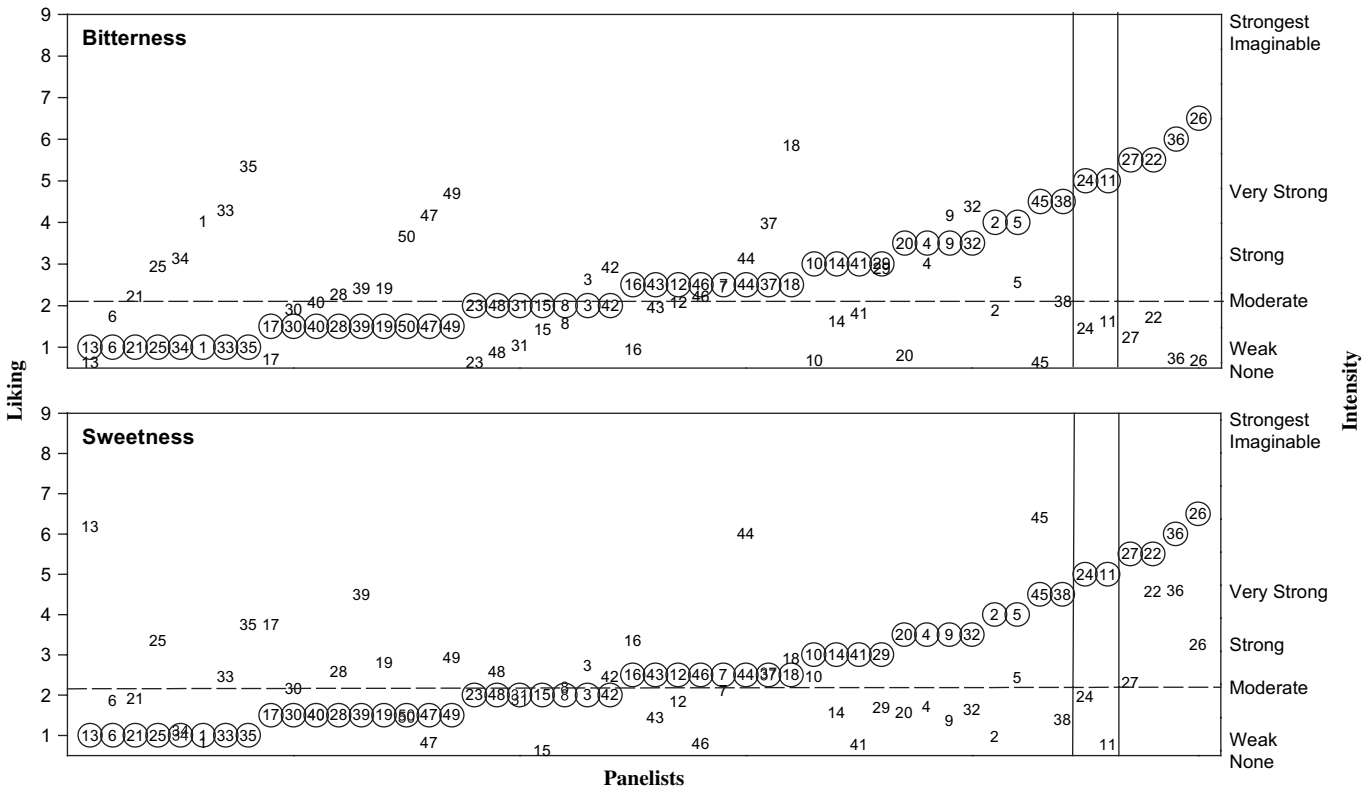

Figure 1 Individual assessments of D-tryptophan. Each individual's average ratings are indicated by subject ID. Liking ratings are circled, whereas intensity ratings are not. Moderate intensity is marked by a dashed horizontal line. Neutral liking ratings fall between 2 vertical bars. Top: bitter intensity, sorted first by liking, then by bitter intensity. Liking and intensity ratings overlap for panelists 29 and 46. Bottom: sweet intensity, with panelists' ratings vertically corresponding to their placement in the bitter figure. Liking and intensity ratings overlap for panelist 31, 34, 37, and 50.

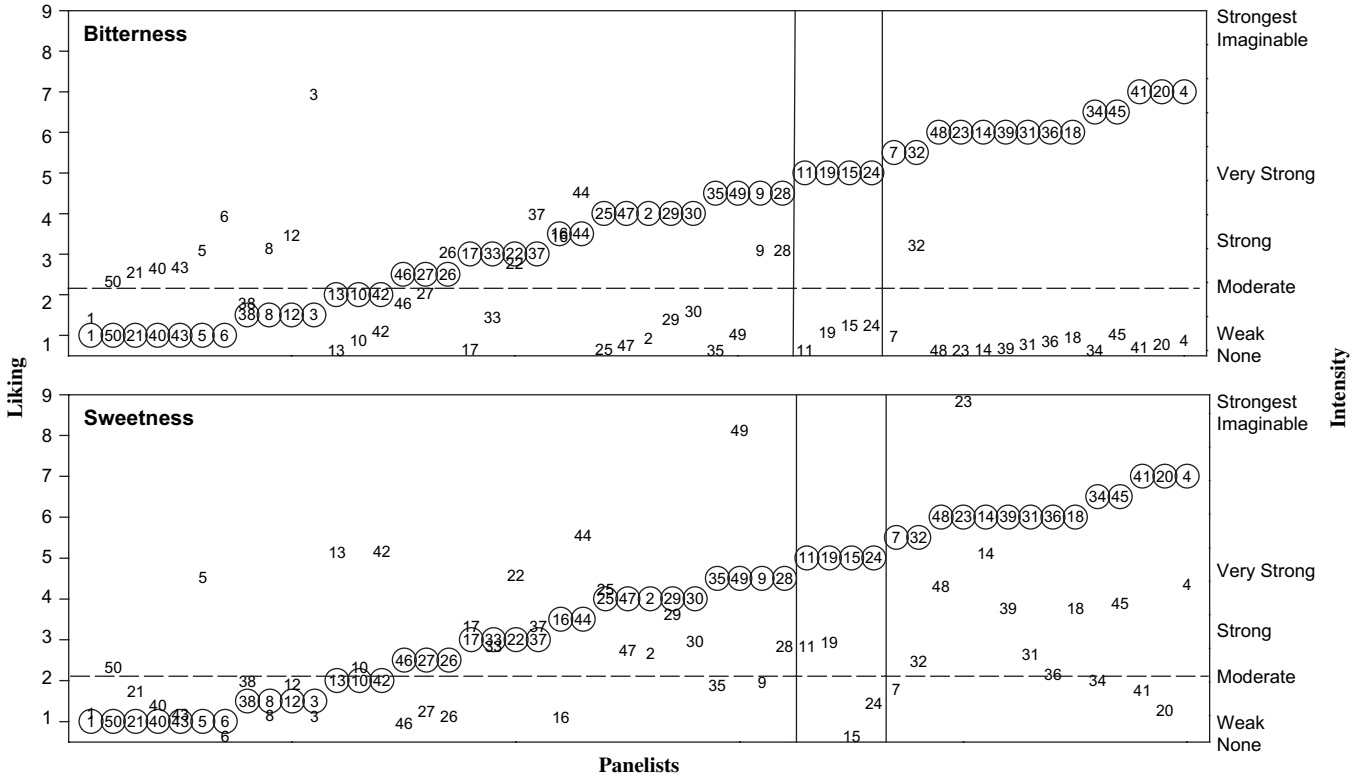

Figure 2 Individual assessments of sodium saccharin. Each individual's average ratings are indicated by subject ID. Liking ratings are circled, whereas intensity ratings are not. Moderate intensity is marked by a dashed horizontal line. Neutral liking ratings fall between 2 vertical bars. Top: bitter intensity, sorted first by liking, then by bitter intensity. Liking and intensity ratings overlap for panelists 16, 22, and 38. Bottom: sweet intensity, with panelists' ratings vertically corresponding to their placement in the bitter figure. Liking and intensity ratings overlap for panelists 1, 10, 17, 25, 33, 37, and 43.

liking (Figure 4), whereas the average sweetness rating for a compound was not ($P > 0.05$, figure not shown).

General linear modeling of liking for the 10 iso-sweet compounds indicates that 2 variables were significant (Table 3): sweetener compound ($P < 0.001$) and bitter intensity ($P < 0.001$). Perceived sweetness did not contribute significantly to overall liking ($P = 0.848$). PROP sensitivity category did not significantly impact overall liking ($P = 0.381$), nor was it a significant predictor of panelists' ratings of perceived bitterness of the sweeteners ($P = 0.211$—results not shown). Very similar results were found when ace-K was included in the general linear model (i.e., compound, $P < 0.001$; bitter intensity, $P < 0.001$; sweet intensity, $P = 0.765$; PROP category, $P = 0.536$).

Although it may initially seem somewhat counter-intuitive that bitterness and the sweetener compound were the 2 largest factors contributing to overall liking, it actually makes sense that in these circumstances perceived sweetness would not play a major role in determining overall liking of sweeteners. After all, concentration levels of the sweeteners were selected to be similar, and greater variation in nonsweet tastes was expected. However, it was interesting that metallic taste, a common complaint associated with certain sweeteners (e.g., Lindner et al. 1977; Schiffman et al. 1985; Portmann and Kilcast 1996), was not a significant factor. Clearly, the factors indicated here do not account for all the variance across individuals in the liking of sweeteners (as indicated by the adjusted R^2 value of 0.43). It is quite likely that the onset and off-times of these sweeteners, although not measured, also greatly contribute to individuals' hedonic responses. Previous research has not only shown that these sweeteners differ in their time–intensity profiles (Ayya and Lawless 1992; Portmann et al. 1992; Calvino, Garrido, Garcia 2000; Calvino, Iglesias, Tamasi 2000; Cardello et al. 2003) but also that these differences impact liking of sweeteners (DuBois 1993).

PROP sensitivity did not contribute to overall liking of the sweeteners. As mentioned above, it seems reasonable to assume that those less sensitive to bitterness, presumable nontasters, would like sweeteners with some bitterness more than would those more sensitive to bitterness, presumably hypertasters. However, research has shown that hypertasters are more sensitive to all tastes, including sweetness (e.g., Gent and Bartoshuk 1983; Pelchat and Danowski 1992; Bartoshuk et al. 1994, 1996, 1999; Tepper and Nurse 1997). Perhaps no consistent difference between groups was found because hypertasters not only perceive more bitterness than do the nontasters but also more sweetness which in turn suppressed the additional bitterness. Furthermore, individual differences in the perception of bitter compounds are

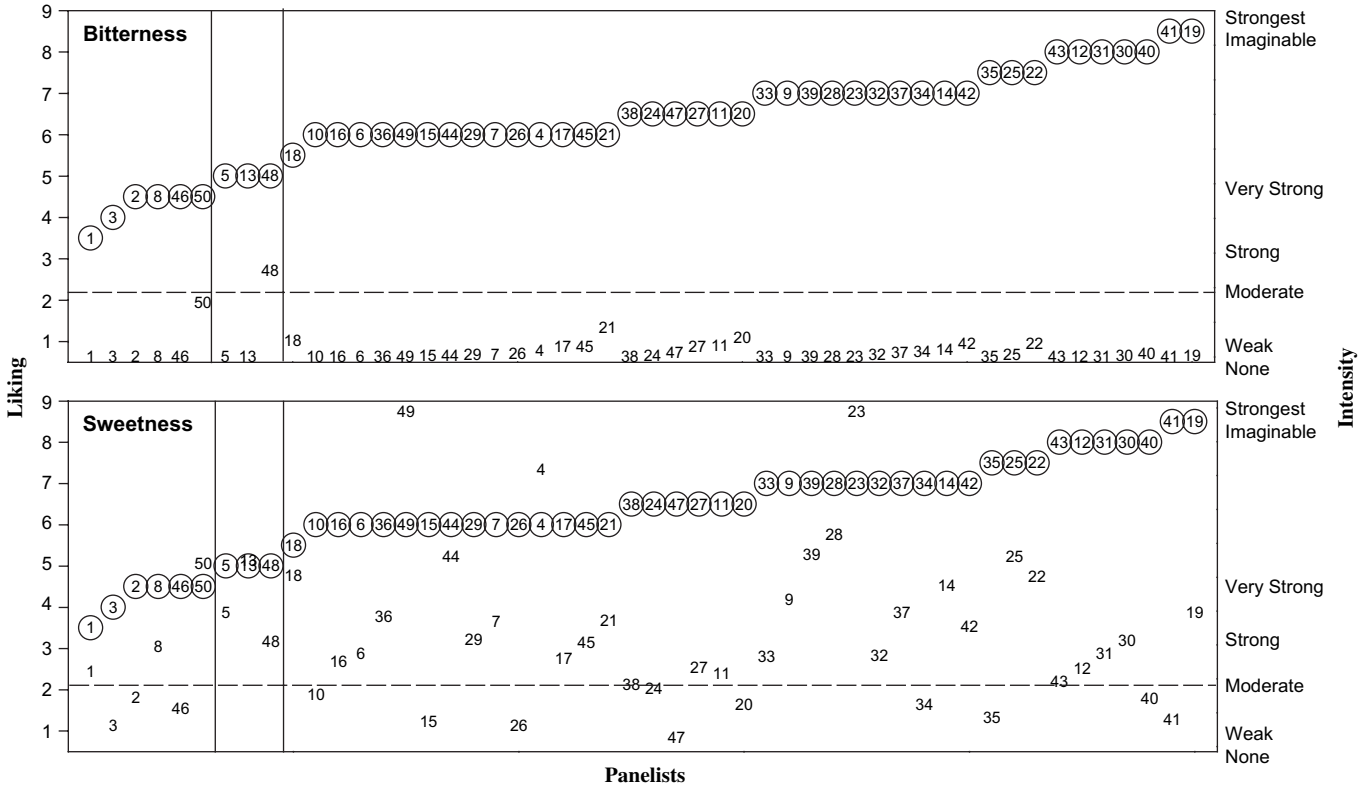

Figure 3 Individual assessments of sucrose. Each individual's average ratings are indicated by subject ID. Liking ratings are circled, whereas intensity ratings are not. Moderate intensity is marked by a dashed horizontal line. Neutral liking ratings fall between 2 vertical bars. Top: bitter intensity, sorted first by liking, then by bitter intensity. Bottom: sweet intensity, with panelists' ratings vertically corresponding to their placement in the bitter figure. Liking and intensity ratings overlap for panelist 13.

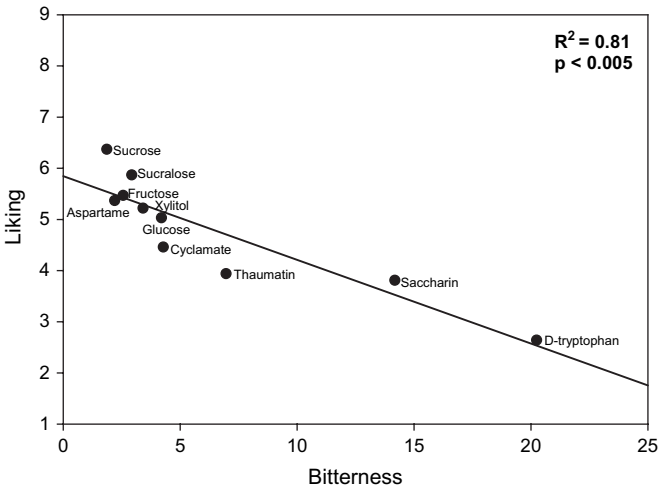

Figure 4 Mean bitterness versus mean liking for 10 sweetener compounds.

Table 3 *P* values and adjusted R^2 values for linear model

Variable	Contribution significance
Sweet	0.848
Sour	0.182
Salty	0.481
Bitter	**<0.001**
Metallic	0.917
Compound	**<0.001**
PROP status	0.381
Adjusted R^2	**0.431**

Values in bold were significant ($P < 0.05$).

profound—a PROP hypotaster can rate a given amount of quinine as more intense than a PROP hypertaster (Delwiche et al. 2001b). It appears that individual differences in the perception of bitterness in sweeteners, so important to liking, do not map onto differences in PROP sensitivity.

These findings do suggest a way in which the latest understanding of taste transduction, which suggests a single receptor (Nelson et al. 2001; Li et al. 2002) and signaling pathway (Zhang et al. 2003) are involved in the perception of sweetness, with everyday experience and previous psychophysical studies, which suggest that more than one receptor and/or pathway, can be reconciled. These results indicate that individuals vary in their perception of sweetness and bitterness of a set concentration of a particular sweetener. One can speculate that the difference in perceived sweetness intensity has to do with differences in either the number of receptor cells

and/or the precise allele an individual has. In contrast, the differences in the perceived bitterness can arise not only from these 2 sources but also from differences in the proportions of the different bitter receptors. It is the combination of the sweet tastes and the nonsweet tastes, including bitterness, that give rise to the final perception of the sweeteners. Thus, whereas taste transduction is focused upon a single cell's response and leads to one conclusion, the psychophysical studies are focused upon the response of the entire organism and thus lead to a different conclusion. Furthermore, because bitterness is an important contributor to an individual's liking of a sweetener and the factors that contribute to individual differences in the perception of bitter compounds are even greater, this could help explain why some sweeteners are liked by some and yet disliked by others.

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