'Thermal Taste’ Predicts Higher Responsiveness to Chemical Taste and Flavor

Barry G. Green1,2 and Pravin George1

1The John B. Pierce Laboratory, New Haven, CT 06519, USA and 2Department of Surgery (Otolaryngology), Yale School of Medicine, New Haven, CT 06510, USA

Correspondence to be sent to: Barry G. Green, The John B. Pierce Laboratory, 290 Congress Avenue, New Haven, CT 06519, USA.
e-mail: green@jbpierce.org

Abstract

Individual differences in taste perception have been explained in part by variations in peripheral innervation associated with the genetic ability to taste the bitter substances PTC and PROP. In the present study we report evidence of another source of individual differences that is independent of taste stimulus, taste quality, or gustatory nerve. Individuals who perceived taste from thermal stimulation alone (thermal taste) gave significantly higher taste ratings to chemical stimuli—often by a factor of >2.1—than did individuals who perceived no taste from thermal stimulation. This was true for all taste stimuli tested (sucrose, saccharin, sodium chloride, citric acid, quinine sulfate, MSG and PROP), for all three gustatory areas of the mouth (anterior tongue, posterior tongue and soft palate) and for whole-mouth stimulation. Moreover, the same individuals reported stronger sensations from the olfactory stimulus vanillin, particularly when it was sensed retronasally. The generality of the thermal-taster advantage and its extension to an olfactory stimulus suggests that it arises from individual differences in CNS processes that are involved in perception of both taste and flavor.

Key words: human, individual differences, psychophysics, retronasal olfaction, taste

Introduction

Striking individual differences in taste perception were first demonstrated in experiments with the bitter-tasting chemicals phenylthiocarbamide (PTC) and 6-n-propylthiouracil (PROP) (Fox, 1931; Harris and Kalmus, 1949b; Fischer and Griffin, 1963; Hall et al., 1975) and subsequent studies uncovered associated differences in perception of other taste stimuli as well (Gent and Bartoshuk, 1983; Bartoshuk et al., 1988, 1994; Bartoshuk, 1993; Lucchina et al., 1998; Prescott et al., 2001). PROP sensitivity has been shown to be correlated with the number and density of taste buds and taste pores on the anterior tongue (Miller and Reedy, 1990) and sensitivity to PTC was recently linked to a gene that controls expression of a specific taste receptor protein (Kim et al., 2003). However, the failure in some studies to find a strong association between sensitivity to PROP/PTC and other tastes (e.g. Harris and Kalmus, 1949a; Schifferstein and Frijters, 1991; Yokomukai et al., 1993; Delwiche et al., 2001; Horne et al., 2002) has implied that additional, unknown factors contribute to individual differences in taste perception.

We recently uncovered evidence of a source of individual differences that appears unrelated to genetic expression of a specific taste receptor or to differences in innervation density of the chorda tympani nerve. The evidence came unexpectedly from a test of the hypothesis that the ability to perceive sweetness from thermal stimulation alone (thermal taste; Cruz and Green, 2000) might be associated with a high responsiveness to sweet-tasting carbohydrates, such as sucrose. Thermal sweetness is the most common of the thermally induced tastes experienced on the tongue tip and is perceived by ∼50% of individuals when the tongue is rapidly re-warmed after being briefly cooled to 15–20°C. The mechanism of thermal taste is unknown, though it has been hypothesized to result from a temperature-sensitive process related to chemical taste transduction (Cruz and Green, 2000). Prior to discovery of thermal taste, the principal effect of temperature on taste that had been observed was a modulation of perceived sweetness and bitterness: both tastes were reduced by cooling and enhanced by warming (Stone et al., 1969; Paulus and Reisch, 1980; Bartoshuk et al., 1982; Calvino, 1986; Green and Frankmann, 1987). However, a subsequent study showed that the enhancement occurred for the sweetness of sucrose, glucose or fructose, but not for the sweetness of saccharin (Green and Frankmann, 1988). The greater temperature dependence of carbohydrate sweetness raised the possibility that thermal sweetness is a byproduct of a heat-induced increase in the excitability of taste receptors or cells that are more sensitive to carbohydrates than to...
saccharin. Arguing against this possibility is the recent evidence that the sensitivity to carbohydrate and noncarbohydrate sweeteners depends upon the same two taste receptor proteins (Adler et al., 2000; Max et al., 2001; Zhao et al., 2003; Inoue et al., 2004). However, the greater thermal lability of sucrose sweetness, together with earlier psychophysical evidence of asymmetric cross-adaptation of sweetness between saccharin and sucrose (McBurney, 1972; Lawless and Stevens, 1983), suggested that differences may nevertheless exist in the way the two classes of sweeteners are transduced. We therefore hypothesized that perception of thermal sweetness caused by warming should be correlated with a higher responsiveness to sucrose compared to saccharin. The results of the first experiment, which indicated that individuals who perceived thermal sweetness were more responsive to both sweeteners as well as to a third taste stimulus, led to four additional experiments designed to discover more about the nature and extent of the association between thermal sweetness and perception of chemical taste and flavor. The results suggest that in addition to previously identified peripheral factors, variation in central neural processes may also contribute to individual differences in perception of both taste and flavor.

**General methods**

**Subjects**

A total of 95 subjects (63 females and 32 males) between the ages of 18 and 45 (average age = 22.8 years) participated in the study. Of this total, 51.8% of females and 34.6% of males were categorized as ‘thermal tasters’ (TTs). The subjects were recruited from public postings on the Yale University Medical School and Yale College campuses. All were self-reported healthy nonsmokers who had no known taste or smell disorders or deficiencies and who were not taking prescription pain or allergy medication. Each person gave informed consent and was paid for their participation. Approximately one-third of the subjects served in two or more of the experiments, though none were aware of the hypotheses under test.

**Thermal stimulation**

Temperature stimuli were delivered to the oral test sites using a 0.64 cm² Peltier thermoelectric module (referred to hereafter as the thermode), designed and built in the Pierce Laboratory Machine and Electronics shop. The thermode was epoxied to the top of a closed-loop, water-circulated heat sink that also served as a handle for positioning and holding the thermode against the tongue. Temperature was computer controlled and monitored via a 40 ga copper constantan thermocouple recessed in the stimulating face of the Peltier module. The base and target temperatures were set by the experimenter on each trial and the rate of temperature change was constant at ±1.5°C/s. The thermode was tightly wrapped in clean cellophane before each experimental session to provide hygienic protection without significantly altering thermal conduction. A second, larger Peltier thermode (4.84 cm²) powered from the same device and temperature-controlled in the same manner as the oral thermode, was used to measure thermal responsiveness of the hand in experiment 2.

**Chemical stimulation**

The chemical stimuli were prepared as aqueous solutions using deionized water. In experiment 1, 3 and 4 the stimuli were delivered using sanitary 6 in. cotton tipped swabs (McKesson) saturated with the test solution just prior to application. The swabs were rubbed gently onto the test site for ~5 s. In experiment 5, which used a sip-and-spit procedure, the stimuli were delivered in 10 ml samples that were sipped from medicine cups, gently swished in the mouth for ~5 s, then expectorated. In all cases subjects rinsed at least twice between trials with 37°C deionized water after each taste stimulus.

**Practice procedure and thermal taste screening**

Every experiment began with a practice session that acquainted subjects with the general Labeled Magnitude Scale (gLMS; Green et al., 1993, 1996; Bartoshuk et al., 2003) and gave them experience using it to rate the strength of taste sensations prior to actual data collection. Subjects were read instructions about how to use the computerized gLMS which emphasized that intensity ratings were to be made relative to the strongest imaginable stimulus of any kind. Ratings were made using a mouse to move a cursor along the scale to the desired location before clicking the mouse to register the response. After these initial instructions, subjects were asked to use the gLMS to rate a wide range of imagined oral sensations that are commonly experienced in daily life (e.g. the sweetness of cotton candy; the burn of cinnamon gum). This part of the practice session emphasized that intensity ratings should be made in the context of normal oral sensations and relative to the strongest imaginable sensation of any kind. Subjects were then given a practice series of actual taste stimuli (1.0 mM QSO₄, 0.056 M citric acid, 1.0 M sucrose, 0.56 M sodium chloride, 5.6 mM saccharin and dH₂O) which they rated on four separate gLMS scales (for sweetness, sourness, saltiness and bitterness) presented successively on a computer monitor. These warm-up stimuli provided practice with actual tastes before subjects were tested for possible perception of thermal taste.

Following the practice stimuli, subjects were given a 5 min break during which they rinsed the mouth repeatedly to eliminate residual tastes. We then tested the subjects for perception of thermal taste on the tongue tip. Under the guidance of the experimenter, the subject used a mirror to place the stimulating surface of the thermode (set to 35°C) against the tongue tip. Once in place, the temperature of the thermode was decreased to 15°C and then immediately re-
warmed to 35°C (warming trial). Subjects were instructed to ‘attend now’ as soon as warming began and then to ‘rate’ the taste sensation (if one had been perceived) when the thermode reached 35°C. Ratings were made on the gLMS exactly as they had been with the chemical stimuli. If no taste sensations were perceived, subjects were instructed to rate ‘no sensation’ for all four taste qualities. After completion of the warming trial the thermode was reapplied to the tongue tip and cooled to 15°C, where it was held constant for 10 s and the taste ratings repeated. Finally, the thermode was applied a third time at 9°C and a final set of taste ratings were made. Because thermal taste is not always perceived to be strongest at the tongue tip, the stimuli were presented sequentially to three sites on the anterior edge of the tongue: the tongue tip followed by two sites ~1 cm to the left and right of the midline. Warming trials always preceded cooling trials to avoid possible contamination from adaptation due to the intense, sustained cold stimulation.

To avoid inducing a potential bias toward reporting thermal taste, subjects were told that not everyone perceives taste during thermal stimulation of the tongue and that we were interested in testing people who do not perceive tastes as well as those who do. Subjects were classified as TTs if they reported a taste that was at least ‘weak’ in intensity on the gLMS during either warming or cooling. When a taste was reported, the site was retested to confirm the reliability of the sensation. In experiments with multiple sessions, subjects were reclassified as ‘thermal non-tasters’ (TnTs) and their data analyzed accordingly if they failed to report thermal taste during testing sessions. This occurred for <10% of the subjects who were initially identified as TTs; no subjects who reported no thermal taste at the time of screening reported thermal taste in later sessions.

Statistical analyses

Perceived intensity ratings were averaged arithmetically across replicates (when they occurred). Because data from the gLMS is typically log-normally distributed across subjects, the within-subject means were converted to log10 before calculating across-subjects means and conducting parametric statistics. Prior to converting to logs, all zeros (ratings of ‘no sensation’) were replaced with 0.24, the lowest rating possible (one pixel) on the computerized gLMS. All data analyses were carried out using Statistica™ 6.1. Differences between groups and across stimuli and concentrations were assessed using repeated-measures MANOVA’s with multiple factors. The default significance level was \( P < 0.05 \). All statistical correlations were calculated using Pearson rs.

Experiment 1: perception of sucrose and saccharin

This experiment was designed to test the hypothesis that perception of thermal sweetness was associated with a higher responsiveness to sucrose compared to saccharin. Measurements were therefore made of the perceived intensity of taste for sucrose and saccharin, as well as for a third, non-sweet-tasting stimulus, NaCl, which was included as a control stimulus.

Procedure

Following the screening and practice session, 28 subjects (14 TTs and 14 TnTs) returned for two separate experimental sessions. At the beginning of each session subjects received three concentrations of three chemical taste stimuli: 1.0, 0.32 and 0.1 M sucrose (J.T. Baker); 0.56, 0.18 and 0.056 M NaCl (Sigma); and 5.6, 1.8 and 0.56 mM sodium saccharin (Janssen). The stimuli were applied in one of six pseudorandom sequences to the area of the tongue previously found to be most sensitive to thermal taste (TnTs were always tested on the tongue tip). Immediately following each stimulus application subjects rated the peak intensity of sweet, salty, sour and bitter sensations. Between trials subjects rinsed at least twice with de-ionized water to remove residual tastes. After rating the taste stimuli, subjects rinsed extensively to remove any residual stimulus and were given a 10 min break before being tested again in the thermal taste paradigm. After completing the thermal taste series, a 5 min break was given before a final thermal warming stimulus (15–35°C) was given to obtain an intensity rating for perceived warmth. This rating was used as an additional control stimulus to see if TTs rated warmth intensity higher than did TnTs. Warmth intensity was rated on a separate trial because we sought to make the temperature rating as independent as possible of thermal taste.

Results

Contrary to the hypothesis that TTs would perceive more intense sweetness compared to TnTs for sucrose but not saccharin, TTs rated the tastes of all three gustatory stimuli significantly higher than did TnTs [main effect of group, \( F(1,26) = 21.0, P < 0.001 \)]. Figure 1 shows that TTs rated the sweetness of sucrose and the saltiness of NaCl an average of 2.1 times stronger (an average difference in log-means of +0.32). The difference in ratings was even greater for saccharin [group \( \times \) stimulus interaction, \( F(2,52) = 8.6, P < 0.001 \)], which TTs rated an average of 3.7 times sweeter (+0.57 log units) than did TnTs (Figure 1b). TTs also rated warmth sensations significantly higher [\( t \)-test for independent groups, \( t(26) = 3.7, P < 0.005 \)] than did TnTs (Figure 1d), but the size of the difference between groups was much smaller than the differences for the three taste stimuli.

Experiment 2: thermal perception at nongustatory sites

The purpose of this experiment was to test whether TTs also rated nongustatory sensations (i.e. thermal) higher than TnTs. The across the board higher ratings of taste and temperature by TTs led us to consider the possibility that the
The difference between groups resulted from a response bias rather than from a true difference in sensory perception (Ekman et al., 1968). In particular, it was possible that TTs rated all sensations higher on the response scale (the gLMS; Green et al., 1993, 1996; Bartoshuk et al., 2003), regardless of sensory modality.

**Procedure**

To test this hypothesis we invited back 22 of the 28 subjects of experiment 1 (11 TTs and 11 TnTs) to rate the perceived intensity of five heating (36–44°C) and five cooling (25–5°C) stimuli on two non-lingual sites: the vermilion border of the lip and the palm of the hand. The lip was chosen because it is a nongustatory site which, like the tongue, is innervated by the trigeminal nerve; the hand was chosen because it is remote from the oral cavity and served by different cutaneous nerves. The subjects’ task was to rate the intensity of thermal sensations using the gLMS with the same instructions as experiment 1, except that no taste ratings were made. To standardize the initial hand temperature before testing began, subjects wore a waterproof glove (Flexigloves; Recombinant Technologies LLC) on the left hand and submerged the hand up to the wrist for 5 min in a 30°C water bath. Subjects then removed the hand from the bath, took off the glove and placed the hand in a cotton-lined (oven) mitten to help keep hand temperature stable throughout testing. Because warmth sensitivity is spatially heterogeneous (Green and Cruz, 1998), it was important to reduce spatial differences in sensitivity as a source of inter-individual variability by locating and testing only the most sensitive sites on the hand. Sensitivity was surveyed by obtaining heat intensity ratings for the four quadrants of the palm (the thenar eminence, hypothenar eminence and the pads at the base of the first and fourth digits) in response to 5 s applications of the 4.84 cm² thermode set to 40°C. Stimuli were separated by a 1 min inter-stimulus interval (ISI) during which the hand was placed back inside the mitten. The two sites that yielded the highest average intensity ratings were used as test sites in the experiment proper. The 40°C stimulus was then delivered to two sites on the lip (the left and right sides adjacent to the midline) in successive trials using the 0.64 cm² oral thermode, followed by 15°C delivered to the same sites in the same manner. Finally, the cold stimulus was applied to the four quadrants of the hand using the 4.84 cm² thermode. In addition to identifying the most sensitive
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palmar sites, this testing provided practice in rating cutaneous thermal stimuli on both the hand and lip.

In the main part of the experiment five warm temperatures (36, 38, 40, 42 and 44°C) and five cold temperatures (25, 20, 15, 10 and 5°C) were applied to the palm of the hand and the lip. Stimuli were delivered in blocks by temperature, with the warm stimuli presented first. Within each block the temperatures were presented in one of three pseudorandom orders with a 1 min ISI. Testing was alternated between the palm and lip across trials such that stimulation occurred on the same site no more often than once every 2 min. The procedure for adjusting and stabilizing hand skin temperature was the same as in the practice session. All temperature ratings were made on the gLMS using the same instructions as for the taste measurements.

Results

There was no significant difference in thermal responsiveness between groups (Figure 2). The perceived intensity of warmth and cold did not differ between TTs and TnTs \(F(1,20) = 0.07, P = 0.80\) at either anatomical site (Figure 2a,b). Log-mean ratings for TnTs were actually slightly higher for both warmth and cold on the palm and for warmth on the lip, though not significantly so \(\text{group} \times \text{temperature} \times \text{site}, F(1,180) = 1.61, P = 0.11\). Accordingly, the results rule out the possibility that the group differences in taste perception of experiment 1 were the result of a difference in scale use between the two groups.

Experiment 3: taste responsiveness of the back of the tongue

After response bias was eliminated as a significant factor, we investigated whether differences in taste perception between TTs and TnTs might be limited to the tongue tip, where the criterion for thermal tasting was determined. It was possible that the heightened ability to taste both thermal and chemical taste at that site resulted primarily from more abundant taste innervation by the chorda tympani nerve, which has been implicated before as a source of individual differences in taste perception (Miller and Reedy, 1990; Bartoshuk et al., 1994; Doty et al., 2001). If so, no difference should be found between TTs and TnTs on the back of the tongue, where taste is mediated by a different cranial nerve (glossopharyngeal; Zotterman, 1935; Bradley et al., 1986).

Procedure

A total of 19 TTs and 27 TnTs served in the experiment. Each experimental session began with a brief practice sequence in which subjects rated the taste intensity of five of the six stimuli to be used in the experiment [0.18 M sucrose, 0.10 M NaCl, 0.18 mM QSO4 (J.T. Baker), 0.018 M citric acid, 0.056 mM PROP (Aldrich) and 29 mM DL-monosodium glutamate (MSG; Accent™)]. PROP was not given as practice because of concerns about inducing context effects in subjects who might be exceptionally sensitive to it (Bartoshuk et al., 1998). MSG was added in this experiment because it is known to be an effective taste stimulus in the back of the mouth. To accommodate the unusual taste quality (for non-Asian subjects) of MSG, we included the response category ‘other’ in addition to the taste qualities of sweet, sour, salty and bitter. Instructions directed subjects to use the ‘other’ category to rate any sensations that could not be described in terms of the four qualities. The five stimuli were applied once each via cotton-tipped swabs to the tongue-tip and to the posterior-lateral region of the tongue (on separate trials) to stimulate the circumvallate papillae. Stimulation of some foliate papilla on the rear edge of the tongue may also have occurred. Following the practice block and extensive rinsing, subjects were tested for thermal taste in the manner of preceding experiments. Categoriza-
tion as TTs and TnTs were based on the results of this screening test.

In the experimental session, subjects again received the chemical taste stimuli on both the front and back of the tongue via cotton swabs. To minimize taste adaptation, stimuli were applied to the front and back of the tongue and to the left and right sides, in alternating fashion. Thus each lingual site was stimulated on every fourth trial. This procedure was repeated until all of the chemicals were applied once to the front of the tongue and once to the back of the tongue. The stimuli were themselves presented in a pseudorandom sequence, with PROP again given last to avoid a potential context effect and complications from lingering bitterness in highly sensitive individuals.

Results
Taste responsiveness to sucrose, NaCl, citric acid, QSO₄, PROP and MSG was again significantly higher for TTs (effect of group, $F(1,44) = 12.4, P < 0.001$), with the magnitude of the difference between groups at least as large on the back of the tongue as on the front (Figure 3). A trend toward an even larger difference on the back of the tongue fell just short of statistical significance (group $\times$ site interaction, $F(1,44) = 3.7, P = 0.061$). This trend was strongest for PROP, where TTs rated its bitterness on the back of the tongue to be an average of 5.1 times stronger than did TnTs, compared to two times stronger on the tongue tip. MSG was not reliably perceived on the tongue tip in the concentration we tested (29 mM) and was only marginally perceived on the back of the tongue. Nevertheless, TTs also showed a slight tendency to rate the very weak taste of MSG higher on the back of the tongue than did TnTs (Figure 3f).

Experiment 4: taste responsiveness of the palate
After replicating the group difference on the back of the tongue we decided to compare taste perception of TTs and TnTs on the soft palate, where a third taste nerve, the superficial petrosal nerve, mediates taste perception (Rollin, 1977; Harada et al., 1997).

Procedure
A total of 12 TTs and 12 TnTs were screened and tested in the main part of the experiment. As in experiment 3, subjects were again familiarized with five of the six taste stimuli (all but PROP) during the practice session. Following practice,
thermal taste was measured on the tongue tip as before to enable subjects to be grouped according to thermal tasting. The chemical stimuli (0.18 M sucrose, 0.18 M NaCl, 0.18 mM citric acid, 0.18 mM QSO₄, 180 mM MSG and 0.1 mM PROP) were swabbed onto alternate sides of the soft palate across trials in pseudorandom sequence with the exception of PROP, which was always delivered last. Subjects again rated the intensity of sweetness, sourness, saltiness, bitterness and ‘other’ on the gLMS, then rinsed at least twice before the next trial. The site of stimulation was just anterior to the uvula on the roof of the mouth; exact localization of the taste-sensitive region of the palate is not otherwise possible. However, swabbing an area a few square centimeters in area proved adequate to produce reliable taste sensations in all subjects. To avoid spreading the stimulus to the tongue, subjects were asked to keep the tongue resting on the bottom of the mouth until they had completed their intensity ratings. Stimuli were presented twice each.

Results

The results showed that average log-mean ratings of taste intensity were once again higher for TTs \( F(1,22) = 7.6, P < 0.05 \) for all six stimuli tested (group x stimulus interaction \( F(1.22) = 0.66, P > 0.05, \text{n.s.} \)). However, the magnitude of the TT advantage varied considerably for the different stimuli (Figure 4), ranging from a ratio of 1.8:1 for the (again) weakly perceived MSG, to 4.2:1 for NaCl. Perception of bitterness from PROP differed between groups by a factor of 2.3 to 1, which was similar to the difference found previously on the tongue tip.

**Figure 4** Shown are the log-means of the perceived intensities of the principal taste qualities for the six stimuli of experiment 4 that were tested on the soft palate in groups of TTs and TnTs. The principal qualities for the respective tastes were sweetness for sucrose, saltiness for sodium chloride, sourness for citric acid, bitterness for quinine and PROP and ‘other’ for MSG. Ratings of all these qualities were significantly higher for TTs. Details of the graphs are the same as Figures 1–3.

### Experiment 5: whole mouth taste and flavor perception

The large and reliable group differences across all three gustatory regions indicated that TTs were more responsive to tastes throughout the mouth and thus should show a similar advantage in perception of whole-mouth taste stimulation. The gustatory ubiquity of the individual differences also raised the possibility that TTs might be more responsive to odors perceived retronasally. Retronasal odors are routinely misperceived as tastes and can become perceptually associated with tastes (Murphy et al., 1977; Frank and Byram, 1988; Frank et al., 1993; Stevenson et al., 1999). This close perceptual association with taste implies that retronasal olfactory and taste stimulation are integrated centrally. An obvious question is whether this integration occurs at a level in the CNS that is prior to the source of the TT advantage. If so, retronasal odors and odor-taste mixtures (i.e. flavors) should also be perceived more strongly by TTs.

**Procedure**

The perception of whole-mouth taste stimulation was compared for the two groups using a sip-and-spit-paradigm. The taste stimuli were 0.56, 0.32, 0.18, 0.10 and 0.056 M sucrose and 18, 10, 5.6, 3.2 and 1.8 mM citric acid. A single concentration of PROP (0.056 mM) was also included. The odorant vanillin (1.8 mM) was presented retronasally in aqueous solution by itself and with two concentrations of sucrose (0.056 and 0.56 M). A brief practice block of trials was given in which subjects were familiarized with tasting and rating the sucrose and citric acid stimuli in the form of 10 ml aqueous samples. Subjects practiced rating the sweetness, saltiness, sourness, bitterness and ‘other’ sensations on the gLMS. Just as the category ‘other’ was added in experiment 3 to accommodate the taste of MSG, it was used in this experiment to accommodate the odor of vanillin (vanilla), which some subjects might not be able to identify. Following the practice trials and water rinses, thermal taste was assessed as in previous experiments.

The procedure in the main part of the experiment was as follows: subjects tasted five concentrations of sucrose and five concentrations of citric acid presented as 10 ml samples in one of six pseudo-randomized orders. The order tested in a given session was randomly selected at the beginning of each session. Each taste sample was sipped and gently swished for ~3 s, after which it was expectorated. Intensity ratings of sweetness, saltiness, sourness, bitterness and ‘other’ were made immediately thereafter, with instructions to base ratings on the peak intensity experienced while the solution was in the mouth. The subjects were also instructed that while tasting the samples it was important to inhale and exhale normally through the nose at least once. This practice ensured retronasal delivery of vanillin on trials when it was presented.
After all of the taste samples except PROP had been presented, vanillin was presented as an orthonasal stimulus by holding a 5 ml sample of 1.8 mM vanillin directly under the subjects nose for ~3 s, during which time they inhaled once through the nose. Subjects then rated the total perceived odor intensity on the gLMS. This procedure was repeated with a fresh sample after a 1 min ISI. Subjects were unaware they were receiving the same solution twice.

Following the orthonasal odor rating, subjects sipped the PROP solution, expectorated it and rated its taste intensity in the same manner as the other chemical tastes.

Results
Consistent with the data from local taste stimulation, TTs rated whole-mouth stimulation from sucrose and citric acid significantly stronger than did TnTs [group effect, \( F(1,40) = 8.0, P < 0.01 \)]. Figure 5a,b shows that the group effect was consistent throughout the concentration range for both stimuli, although the mean difference was much larger for sucrose than for citric acid. Whole-mouth responsiveness to PROP (Figure 6) was also markedly higher for TTs \( [t(40) = 2.54, P > 0.05] \). Perceived bitterness for the single concentration we tested was rated 3.9 times stronger by TTs than by TnTs (a log-mean difference of +0.59).

More surprising was the group difference in perception of vanillin sensed retronasally. Figure 7a shows that when vanillin was sipped and held briefly in the mouth, either by itself or in mixture with sucrose, ratings of ‘other’ (which were assumed to include the vanilla odor or flavor) were much higher for TTs than for nontasters \( [F(1,40) = 7.7, P < 0.01] \). Sweetness ratings (Figure 7b) were also significantly higher for TTs in all three conditions \( [F(1,40) = 21.5, P < 0.001] \). The latter outcome indicates that TTs perceived more ‘sweetness’ in the vanillin odor, which translated into higher ratings of sweetness for the mixtures as well as for vanillin itself (i.e. odor-taste enhancement; Frank et al., 1993). TTs also rated the odor of vanillin higher when it was sniffed orthonasally \( [t(40) = 2.4, P < 0.05] \), although the proportional difference between groups (1.8:1) was less than half what was found for retronasal delivery (3.8:1).

Discussion
The occurrence of the TT advantage for all taste qualities, for all three gustatory sites and for olfactory stimulation, strongly suggests that individual differences in thermal taste perception are associated with a generally higher responsiveness to both gustatory and olfactory stimulation. Assuming that thermal taste results from stimulation of a subset of temperature-sensitive gustatory fibers, individuals who are more responsive to gustatory stimulation would be more likely to perceive taste from this relatively weak sensory signal. A peripheral factor, such as higher innervation density, is unlikely to be the primary cause of the TT advantage, since the advantage holds for stimulation of three...
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different cranial nerves: the facial nerve (VII) (of which the chorda tympani and greater superficial petrosal nerves are separate branches), the glossopharyngeal nerve (IX), and the olfactory nerve (I). Moreover, if the TT advantage in perception of vanillin had a peripheral origin, the difference between groups would have been independent of the mode of stimulus delivery. Instead, retronasal stimulation yielded a two-fold larger group difference than did orthonasal stimulation.

A more parsimonious hypothesis is that the TT advantage arises from differences in the sensitivity or excitability of brain regions where olfactory and gustatory stimulation converge. Greater excitability in such regions would effectively produce a higher ‘gain’ within the afferent system, leading to stronger perceptual responses for a given level of gustatory or olfactory stimulation. CNS factors have been discussed as possible contributors to individual differences in normal taste perception only with respect to response bias (Ekman and Akesson, 1965; Ekman et al., 1968). However, there is no a priori reason to assume that CNS sensory processes vary less across individuals than do PNS sensory processes, and studies have begun to identify brain regions in humans where differences in excitability could potentially affect perception of both taste and flavor. A recent fMRI study in humans found that taste-olfactory mixtures activated the caudal orbitofrontal cortex, insular and anterior cingulate cortex, and the amygdala (de Araujo et al., 2003). Although it has yet to be determined with certainty which brain areas are most important for intensity perception (Small et al., 2003a), together these regions appear to form a functional system for flavor perception. The idea that the sensitivity of all or part of this ‘flavor system’ could vary across individuals receives indirect support from studies in other sensory systems which have shown that changes in the availability of and sensitivity to neuromodulators can affect cortical activation levels. Brain serotonin levels have been hypothesized to affect the intensity-dependence of auditory event-related potentials (Hegerl and Juckel, 1993; Hegerl et al., 1995) and in visual attention tasks the level of activation in the anterior cingulate cortex, a region also involved in taste and flavor perception (de Araujo et al., 2003), has been linked to genetic differences in expression of dopamine receptors (Fan et al., 2003). Interestingly, recent evidence has implicated dopamine in modifying either the motivation to eat palatable foods (Yamamoto et al., 1998) or their taste pleasantness (Small et al., 2003b).

However, the significant group difference in perception of vanillin sensed orthonasally could be taken as evidence against a flavor-system explanation of the TT advantage. Orthonasal odor sensations arise from stimuli outside the mouth, and thus are not part of the flavor signal per se. This seeming contradiction may be explained both by the ability of olfactory stimuli to become perceptually associated with gustatory stimuli (Murphy et al., 1977; Frank and Byram, 1988; Frank et al., 1993; Stevenson et al., 1999) and by evidence that orthonasal stimuli can be integrated with taste stimulation (Rozin, 1982). Vanillin is normally experienced in connection with foods and has a perceived sweetness (Figure 7) that gives its odor a complex, flavor-like quality. This combination of factors makes it less surprising that TTs perceived the vanillin odor to be stronger (though less so) when sensed orthonasally. Similarly, the small but significant difference between groups in perception of warmth on the tongue tip (Figure 1d) may reflect the ability of warming to evoke sweetness in TTs. Even though subjects were instructed to attend only to temperature on trials in which they rated warmth, the spatially and temporally correlated gustatory quality may have influenced the way the thermal stimulus was perceived. The absence of a difference in warmth (or cold) perception between groups when the

Figure 7 Log-mean perceived intensity ratings are shown for TTs and TnTs for sipped, aqueous solutions of vanillin and vanillin in mixture with two concentrations of sucrose: (a) contains ratings of ‘other’ sensations, which were expected to include perception of vanilla flavor; (b) contains ratings of sweetness. TTs rated both qualities much higher than TnTs, indicating that TTs advantage extends to perception of retronasal olfactory and taste-olfactory (flavor) mixtures. Details of the graphs are the same as Figures 1–5.

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stimuli were presented to nongustatory surfaces (Figure 2a,b) supports this interpretation.

Whatever its specific cause, centrally-mediated differences in taste and flavor responsiveness could help to explain inconsistencies in the published data on the relationship of PROP/PTC sensitivity to perception of other tastes. Classification of individuals as PROP/PTC ‘tasters’ and ‘nontasters’ has not been disputed, but the idea that tasters can be further subdivided into ‘supertasters’ and ‘medium-tasters’ and that responsiveness to all tastes can be predicted from responsiveness to PROP/PTC (Bartoshuk, 1993; Bartoshuk et al., 1994, 1996, 1998; Tepper and Nurse, 1998; Prescott et al., 2001), has not always been supported (Schifferstein and Frijters, 1991; Yokomukai et al., 1993; Delwiche et al., 2001; Horne et al., 2002). Some of the negative findings are undoubtedly attributable to use of psychophysical methods not well-suited for measuring individual differences (Lucchina et al., 1998; Bartoshuk, 2000; Bartoshuk et al., 2003). However, variation in a CNS process that is independent of PROP/PTC receptor expression would tend to lower the correlation between perception of PROP/PTC and other tastes. Although individuals with an abundance of PROP receptors and a high central responsiveness should be highly responsive to all tastes (‘supertasters’), individuals with fewer PROP receptors but a high central sensitivity should be also be highly responsive to other tastes. By this reasoning, perceived intensity should be more highly correlated among taste stimuli for which individual variation in receptor expression is not as extreme as it is for PROP/PTC. The present data are consistent with this expectation: sucrose sweetness on the front of the tongue in experiment 3 was significantly correlated (Pearson’s r, P < 0.05) with ratings for the primary taste qualities of all other taste stimuli, whether they were delivered to the front or back of the tongue (average r = 0.44), except for PROP (r = 0.26, n.s.). In contrast, PROP bitterness on the front of the tongue was significantly correlated only with citric acid sourness and quinine bitterness on the front of the tongue, and PROP bitterness on the back of the tongue. The same general pattern held for the soft palate (experiment 4) and for whole mouth stimulation (experiment 5). On the soft palate, correlations between ratings for sucrose and NaCl, citric acid, and quinine were 0.72, 0.85, and 0.68, respectively (Pearson’s r, all Ps < 0.05), compared to 0.03, 0.20, 0.13 (all Ps > 0.05) between PROP and the same three stimuli. In the whole mouth, the average correlation between intensity ratings for the five concentrations of sucrose and citric acid was 0.44, compared to only 0.20 between the same stimuli and the bitterness of PROP.

These relatively high correlations in intensity perception across taste stimuli raise an obvious question: why have they not been reported before? As was mentioned in the context of individual differences in PROP/PTC perception, the primary reason may be the prevalence in the past of psychophysical methods that are not well suited for identifying and quantifying individual differences. The two most widely used methods, magnitude estimation and category scales, both tend to obscure individual differences, but in different ways: magnitude estimation by confounding differences in perceived intensity with differences in number usage, and category scales by introducing ceiling effects that limit the ability to differentiate between moderately and highly responsive individuals. The gLMS is a category ratio scale (Borg, 1982) that was developed specifically for measuring individual differences in taste and somatosensation (Green et al., 1993, 1996). Subsequent studies have demonstrated the scale’s effectiveness for measuring individual and group differences within certain constraints (Lucchina et al., 1998; Bartoshuk, 2000; Bartoshuk et al., 2003). One of the chief constraints is the need to rule out differences in scale use that could be misinterpreted as evidence of sensory differences. This was accomplished in the present study by employing the same scale and instructions to measure temperature perception on the lip and hand, which revealed no differences in ratings between groups.

It is reasonable to ask whether the differences we have found here for perceived intensity are reflected in a greater sensitivity to threshold-level tastes and odors. While finding lower thresholds in TTs would buttress the suprathreshold findings and indicate that the TT advantage affects perception throughout the full perceptual range, not finding a difference would not contradict the suprathreshold results. This is because differences in suprathreshold responsiveness are not always associated with differences in threshold sensitivity (Bartoshuk et al., 1994; Bartoshuk, 2000). Indeed, a difference in central gain might be expected to have a lesser effect on the threshold for detection than on perceived intensity. A higher central gain should increase the background noise in the flavor system to about the same extent that it boosts a weak chemosensory signal. Without a significant change in the signal-to-noise ratio, little change in the detection threshold would be expected. This hypothesis is currently being tested.

In summary, the present results show that the ability to perceive thermal taste on the tongue tip is positively correlated with the responsiveness to chemical taste stimuli of all kinds throughout the mouth. The data also provide the first evidence of a significant association between the ability to perceive taste and smell at suprathreshold levels, particularly when olfactory stimulation is sensed retronasally. This implies that individuals differ in the ability to perceive the flavor of food as well as its taste and that these differences may arise in part from variation in the sensitivity or ‘gain’ of CNS processes that are involved in perception of the chemosensory attributes of foods.

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