Associations between taste genetics, oral sensation and alcohol intake

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Abstract

Alcohol produces a range of oral sensations, some of which have been shown to vary with the perceived bitterness of 6-*n*-propylthiouracil (PROP), one marker for genetic variation in taste. Some studies report that offspring of alcoholics are most likely to be PROP nontasters [*Physiol. Behav.* 51 (1992) 1261; *Physiol. Behav.* 64 (1998) 147], yet others report the offspring as more responsive to sodium chloride (NaCl) and citric acid, which appears to contradict the taste genetic hypothesis. We predicted alcohol sensation and intake from measures of taste genetics (PROP bitterness and number of fungiform papilla), NaCl and citric acid intensity, and spatial taste pattern in 40 females and 43 males. Subjects used the general Labeled Magnitude Scale (gLMS) [*Chem. Senses* 18 (1993) 683; *J. Food Qual. Pref.* 14 (2002) 125] as an intensity and hedonic scale. Those who tasted PROP as most bitter or had highest numbers of fungiform papilla reported greatest oral burn from an alcohol probe; those who tasted least PROP bitterness consumed alcoholic beverages most frequently. Although higher NaCl and citric acid ratings associated with more frequent consumption of alcoholic beverages, the findings could be explained by lower intensity of tastants on the tongue tip (chorda tympani nerve) relative to whole mouth perception. In multiple regression analyses, PROP bitterness and the spatial pattern of taste perception were independent contributors to the prediction of alcohol intake. In summary, the results support that variation in oral sensation associates with alcohol intake. Those who taste PROP as least bitter and have low chorda tympani relative to whole mouth taste intensity appear to have fewest oral sensory hindrances to the consumption of alcoholic beverages.
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1. Introduction

Numerous studies support a familial component in the etiology of alcoholism (see Ref. [1] for review). A study of more than 3500 male twins in the United States [2] suggests both direct and indirect mechanisms in the heritability of alcoholism. Although direct mechanisms could include specific gene loci that control alcohol metabolism (e.g., alcohol dehydrogenase [3]), they are more likely to involve multiple chromosomes [4]. Indirect mechanisms include comorbid conditions, such as affective and conduct disorders [5] as well as personality disorders [6]. One direct mechanism could involve genetic variation in taste and oral sensation. This paper explores associations between genetic variation in taste, oral responses to an alcohol probe and consumption of alcoholic beverages.

Bitterness of phenylthiocarbamide (PTC) or the chemically related compound, 6-*n*-propylthiouracil (PROP), pro-vides a phenotypic marker for genetic variation in taste and oral sensation. Historically, researchers have used detection thresholds to classify individuals as nontasters or tasters of these bitter compounds (e.g., Refs. [7,8]). Family studies have shown that individuals who are nontasters have two recessive alleles, while tasters may carry one or both dominant alleles [9,10]. Insensitivity to PTC or PROP is estimated at 30% of the Caucasian population; the percentages vary with sex and race [11].

Scaling the intensity of PROP bitterness allows separation of tasters into "medium tasters" (those who taste PROP as bitter) and "supertasters" (those who taste PROP as exceptionally bitter) [12]. Supertasters cannot be identified via thresholds [13] and thus, effects due to supertasters cannot be revealed in studies classifying subjects by PROP threshold only. Responses to PTC/PROP associate with allelic variation on chromosome 5 [14] and 7 [14,15], regions that contain genes for putative bitter receptors (e.g., Refs. [16,17]). Single nucleotide polymorphisms in putative bitter receptors TAS2R3, TAS2R4 and TAS2R5 do not explain variation in PROP bitterness [18]. Supertasting

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may result from increased density of fungiform papilla as well as allelic variation that results in the presence or absence of a specific PROP receptor as proposed [19] and supported by preliminary data [20].

PROP bitterness influences oral sensations from alcohol, a relationship that appears to be mediated through fungiform papilla. Greater PROP bitterness associates with more bitterness from ethanol [21] and some types of beer [22], more bitterness, astringency and acidity from red wines [23], and greater irritation from ethanol [21,24]. A PROP bitterness and fungiform papilla relationship was first shown by Miller and Reedy [25]; PROP supertasters have, on average, the greatest number of fungiform papillae and taste buds as assessed with videomicroscopy [11]. A positive relationship between PROP bitterness and fungiform papillae number is also observed using lower magnification for papillae counting [26,27]. Fungiform papillae hold taste buds that are innervated for taste by the chorda tympani branch (CTN) of the facial nerve (cranial nerve VII). These taste buds are surrounded by fibers of the trigeminal nerve (cranial nerve V), which are believed to mediate oral burn [28–30].

Oral sensory differences in alcohol sensation with PROP tasting may explain some of the variability in alcohol preference and drinking behaviors [31]. Nontasters of PROP may experience the least bitterness/oral burn from alcohol and thus have greater preference for and consumption of alcoholic beverages. By scaling PROP bitterness, Intranuovo and Powers [22] found that those who tasted PROP as least bitter consumed significantly more beers in their first year of drinking. Guinard et al. [32] also reported that high users of beer (greater than 3.6 L per week) were more likely to be PTC/PROP nontasters than were low users (less than 720 ml per week). However, the method for PROP and PTC was described as a screening procedure without clear indication of how nontasters were defined. Mattes and DiMeglio [33] did not find differences in intake of alcoholic beverages between PTC tasters and nontasters. In this study, subjects tasted filter papers without PTC and those saturated with PTC. Nontasters were those who reported both papers as tasteless; tasters were those who rated the PTC-saturated paper as bitter. Differences in psychophysical methodologies used to define PROP/PTC may explain some differences across these studies (see discussion below).

There is inconsistent support for PROP as a genetic marker for risk of alcoholism. In studies with alcoholics compared with controls, some report an excess of nontasters among the alcoholics [34–36] while other studies do not [37–39]. DiCarlo and Powers [36] also found a higher proportion of PROP supertasters in college students who reported both problems with alcoholism and depression in themselves and their parents than in nontasters. In studies examining family history of alcoholism, Pelchat and Danowski [31] found significantly more PROP nontasters among children of alcoholics than among children of non-

alcoholics, whether or not the children themselves were alcoholic. Kranzler et al. [40] did not find a significant relationship between PROP threshold and parental history of alcohol dependence in nonalcoholic young adults or in those with alcohol dependency [41].

Some of the inconsistencies in PROP effects on alcohol consumption behaviors could relate to the measurement of PROP tasting. Some of the studies that fail to find a PROP–alcohol association have methodological problems as reviewed by Pelchat and Danowski [31], including inappropriate matches between alcoholics and controls [39] and procedures that may falsely classify nontasters through a "yes/no" response to a PTC-impregnated paper [37] or a single PTC solution [38]. Studies on alcohol ingestive behaviors that use a threshold procedure [31,34,35,40,41] will fail to reveal PROP effects if the behavioral differences are most apparent across those who vary most in PROP tasting (i.e., nontasters and supertasters). DiCarlo and Powers [36] used the bitterness of the PROP-impregnated paper [42] to examine PROP effects on alcohol ingestive behaviors. Subjects were defined as nontasters, medium tasters and supertasters based on their ratings of bitterness of PROP using a nine-point category scale. Methodological advances show that these category scales may not accurately classify supertasting [13,43]. Characterization of supertasters and related sensory behaviors requires scaling methods that permit valid comparisons across subjects. The methodological difficulties in identifying supertasting has been reviewed previously [13,43] and will be reviewed here briefly.

Adjective-labeled, self-rating scales (e.g., Likert, category and visual analogue) are commonly used in taste studies. They are valid for within-subject comparisons; however, they are invalid for across-subject/group comparisons unless the adjectives denote the same perceived intensity, on average, to all groups of interest. However, intensity adjectives denote different absolute perceived intensities within subjects, depending on the domain to which they are applied. For example, a "strong" oral burn from a chili pepper reflects a greater perceived intensity than a "strong" rose odor. Intensity adjectives also denote different absolute perceived intensities across subjects depending on the subject's experience with the domain of interest. For taste, supertasters experience greater perceived intensities than do nontasters (see Refs. [13,43,44] for reviews); thus, a "strong" bitter to a supertaster is more intense than a "strong" bitter to a nontaster. Using adjective-labeled scales to make across-group comparisons when the groups, on average, use the adjectives to refer to different perceived oral sensory intensities obviously invalidates the comparisons [45]. Most of the time, the invalid comparison will simply underrepresent the actual effect size (e.g., Ref. [46]). However, in some cases, the invalid comparison will produce apparent differences that are actually in the wrong direction (see Ref. [45] for a review). For example, suppose that the adjective "strong" reflects a

perceived intensity that is twice as great to supertasters as it is to nontasters. Suppose an alcoholic beverage were 10% more intense to supertasters. Treating "strong" as if it reflected the same perceived intensity to both groups effectively reduces all of the supertaster ratings by half. Thus, a beverage that is 10% more intense would be reduced so far that the reduced rating for supertasters would fall below that for nontasters. We call this a reversal artifact.

Environmental factors, which impact oral sensation, affect the study of taste genetic influences on alcohol ingestive behaviors [42]. Depressed taste from the cranial nerves can alter oral sensations by changing the interactions among taste nerves [47], between taste nerves and trigeminal nerves [48] and possibly between taste and retronasal olfaction [49]. For example, an individual with depressed CTN taste relative to density of fungiform papillae or PROP taster status may have altered taste and somatosensory sensations that appear as phantom taste or pain sensations [50] or intensified taste and somatosensory sensations in response to oral stimuli [48,51]. Otherwise healthy adults can show depressed CTN taste relative to whole mouth sensations because of common illnesses, such as otitis media, middle-ear infection [42]. The logic of these findings is that damage to the CTN releases the usual inhibition from other nerves to intensify oral sensations. In relation to taste and alcohol, some studies have reported that individuals with a paternal history of alcoholism rated greatest intensity to concentrated sodium chloride (NaCl) and citric acid [52,53]. If these individuals were more likely nontasters, following the taste genetic hypothesis, those with the paternal history should have lowest intensity ratings of NaCl and citric acid (e.g., Refs. [44,54,55]). The question remains if these opposing findings result from interactions between genetic taste and environmental influences, which affect oral sensations and alcohol ingestive behaviors. Intensification of NaCl intensity has been seen in aged versus young women and the intensification is thought to result from increased trigeminal sensations as the result of taste damage [51].

The primary goal of the present study was to examine relationships between markers of taste genetics (perceived bitterness of PROP, PROP threshold and fungiform papilla number) and sensory responses to ethyl alcohol as well as reported intake of alcoholic beverages in adults. Existing data afforded analysis of relationships between the alcohol variables, NaCl and citric acid intensity, and a measure of CTN taste functioning. Multiple regression analyses were used to determine the ability of taste genetic and other taste markers to predict alcohol variables.

For intensity and hedonic ratings, subjects used the general Labeled Magnitude Scale (gLMS) [43,45], which is a generalization of the adjective-labeled, ratio scale devised by Green et al. [56,57]. The important change concerns the label at the top of the scale: "strongest imaginable sensation of any kind." The idea behind the choice of this label was to "stretch" the adjective-labeled scale to its maximum. To the extent that this maximal experience is equivalent across subjects, the gLMS will act as a universal sensory ruler. Even if this is not the case, this maximal experience is unlikely to be associated with taste. This means that the gLMS should produce valid comparisons, on average, across nontasters, medium tasters and supertasters of PROP. Previous research has shown that PROP taste functions for nontasters, medium tasters and supertasters produced by the gLMS are equivalent to those obtained by magnitude matching [13,58].

2. Methodology

2.1. Subjects and procedure

Subjects participated in an observational study designed to examine the relationship between genetic variation in taste and food/beverage sensations, dietary behaviors and nutritional status in adults. The goal of subject recruitment was to obtain diversity in genetic variation in taste in males and females and to minimize confounding factors that would affect the ability to examine taste genetic influences on dietary behaviors.

A telephone screening and the first visit served to recruit healthy adults who did not smoke tobacco or have a high level of dietary restraint. Because dietary restraint may influence accuracy of reporting dietary intake [59], potential subjects with high dietary restraint were identified by telephone with the concern for dieting subscale of the Restrained Eating Scale [60,61]. During the first visit, subjects completed the Three-Factor Eating Questionnaire [62]. Those who scored ≤ 12 on the "cognitive restraint of eating" [63] from this instrument were invited to participate in the complete study.

All subjects who met the screening criteria described above were accepted into the study. However, as subject recruitment continued, there was a need to oversample for nontasters and supertasters; this sampling occurred in the first visit. The PROP threshold procedure (described below) was a screen for nontasters; nontasters have a threshold of >0.2 mM PROP. The perceived bitterness of 0.32 mM PROP served as a screen for supertasting. This concentration was selected to be strong enough to allow relatively good separation of medium tasters from supertasters based on pilot data and previous studies (e.g., Ref. [11]). Higher PROP concentrations were avoided to minimize a context effect in later sessions (e.g., see Ref. [64]). Eight subjects who were suspected to be medium tasters were not invited to continue through the second and third visits.

Eighty-three adults (40 females, 43 males) participated in the present study. The subjects were primarily Caucasian (62 Caucasians, 11 Asians, 1 African American, 5 Hispanic and 4 Asian Indian) with a mean age of 26 ± 4 S.D. (range

21–39 years). Study subjects completed three visits that were approximately 1 week apart. The majority of the sample (60 of 80) had a normal body mass index [BMI; weight (kg)/height (m)^2 from 17 to 25]; 20 were overweight (BMI 25 to 30) and 3 were obese (BMI >30). There was no significant association between PROP bitterness and BMI in this sample. The University of Connecticut and Yale University Institutional Review Boards approved all study procedures. Subjects gave written consent and were paid for their participation.

Subjects used the gLMS to rate the intensity of oral stimuli and tones as well as the degree of liking/disliking of the alcohol probe. Subjects were instructed to consider the top of the scale across all sensory domains. For sensory intensity, the distances are treated as 0 for no sensation and as 100 for "strongest imaginable sensation of any kind." For hedonic ratings, subjects were instructed to consider the intensity of affective rather than sensory experiences. For pleasant experiences, the top of the scale was the "strongest imaginable pleasant experience of any kind" (i.e., +100); for unpleasant experiences, the top of the scale was the "strongest imaginable unpleasant experience of any kind" (i.e., −100).

Subjects made their ratings on a computer that displayed the gLMS and, through a basic program (Microsoft Basic, Version 2.43), converted the response into a whole number distance score visible to the subject. The experimenter was present to provide the samples and to assist the subjects in using the computer to make their ratings. Subjects pointed and clicked with the computer mouse to the location on the gLMS that represented the intensity of the sensation. The next screen showed the distance in whole numbers, which was recorded by the experimenter. The computer program then asked the subjects if they were ready for another sample; clicking "yes" provided a new gLMS to make the next rating. For hedonic ratings, subjects were instructed to first tell the researcher if they liked or disliked the alcohol stimulus. If they neither liked nor disliked the stimulus, a zero was registered.

2.2. Sensory responses to alcohol

During each of the three visits, subjects rated the intensity of tones as well as the intensity and the degree of liking/disliking of the 50% ethanol probe applied to the left tip of the tongue with a cotton-tipped applicator. The probe was selected as a measure of alcohol irritation and was prepared from dehydrated 200 proof ethyl alcohol diluted to 50% (volume/volume) with deionized water. Subjects extended their tongue and the alcohol was swabbed onto the left anterior tongue. They were asked to keep their tongue extended and wait until the burning sensation had reached the strongest point before making their ratings. Mean intensity and hedonic ratings were calculated for the three visits and associated with the taste genetic, NaCl and citric acid, and spatial taste measures.

2.3. NaCl and citric acid intensity and CTN taste functioning

These measures came from the spatial taste test during the first visit. The test measures taste functioning on areas innervated by chorda tympani and glossopharyngeal nerves as well as whole mouth perception. The procedures were those reported previously [65,66] except that subjects used the gLMS to rate the intensity of 1.0 M NaCl, 1.0 M sucrose, 32 mM citric acid and 1.0 mM quinine hydrochloride (QHCl). Stimuli were unilaterally painted with sterile cotton-tipped applicators onto fungiform papillae on the anterior tongue, the foliate papillae, the circumvallate papillae and the palate (quality and area presented in the order listed). Each taste stimulus was given in pairs, right and left side at each location (the initial side at each site varied). Whole mouth intensity was obtained following localized testing of all qualities. The experimenter asked subjects to fill their mouths sequentially with each tastant, swish, spit and then swallow the residual to stimulate the vagus nerve. Subjects rinsed with water before each presentation.

A measure of CTN taste functioning was calculated as the ratio of average intensities for CTN to whole mouth stimulation for all qualities. The ratio is thus a measure of CTN taste relative to oral sensory contributions from the glossopharyngeal, vagal and trigeminal nerves. Using the ratio versus absolute CTN allowed control for genetic taste effects on CTN ratings. That is, equal ratios would be seen in a PROP supertaster who reported higher CTN taste intensities relative to higher whole mouth intensities compared with a PROP nontaster who reported lower CTN taste intensities relative to lower whole mouth intensities. However, a lower ratio indicated lower CTN intensity, which may release the usual inhibition to taste from the glossopharyngeal and vagus nerves to produce higher whole mouth intensity. Intensities of NaCl and citric acid from the whole mouth stimulation and the CTN/whole mouth ratio were used to predict alcohol intensity and intake.

2.4. Measurement of PROP tasting

The ability to taste PROP was assessed by threshold and scaling methods. Both measures were compared with the sensory and hedonic responses to an alcohol probe and the frequency of alcohol intake.

2.4.1. Threshold

A PROP threshold test was determined on the first day of testing using a modified up–down procedure [67,68] with room temperature solutions ranging in quarter-log steps from 0.001 to 3.2 mM reagent grade PROP dissolved in deionized water (Hydro Picotech System, 18 MΩ/cc). Subjects tasted two samples (10 ml each, room temperature); one was water and the other was a given concentration of PROP. Each tasting was preceded with a water rinse. Subjects were instructed to choose the sample with the stronger taste. After
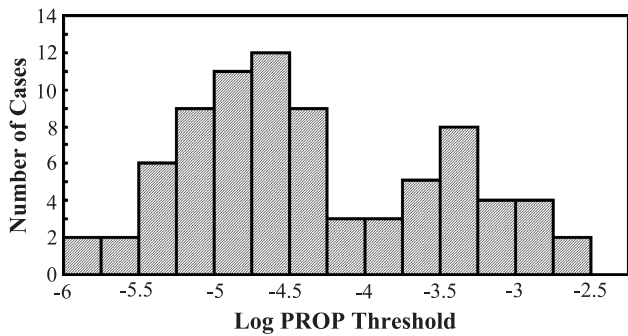
Fig. 1. PROP threshold distribution.

a correct choice, the same concentration was presented again. After two correct choices, the next lower concentration was presented (a reversal). After an incorrect choice, the next highest concentration was presented (a reversal). The first reversal was discarded and the threshold was considered to be the geometric mean of the next six reversals.

2.4.2. PROP scaling

Perceived bitterness of PROP was measured with the gLMS on the final day of testing, last within the session, using a protocol that included intensity ratings of sodium chloride (NaCl) and 1000-Hz tones [11]. Taste stimuli were presented in half-log steps: five NaCl solutions (from 0.01 to 1 M) and five PROP solutions (from 0.032 to 3.2 mM). Tones were presented in 12-dB steps (from 50 to 98 dB). Blocks of stimuli were presented in the following order: tones, NaCl, tones, NaCl, tones, PROP, tones, PROP, tones. The stimuli were randomized within each block. The PROP ratings were analyzed as raw gLMS ratings as well as normalized to tone ratings that preceded the tasting of PROP. For normalization, a factor was calculated for each subject from the geometric mean of 86- and 98-dB tones divided into the arithmetic mean of all geometric means. Each subject's raw data was then multiplied by that subject's normalization factor to provide comparable data for all subjects [69]. The NaCl data from the PROP scaling are part of an ongoing evaluation of standards in PROP studies and were not used in the analyses in the present study.

2.5. Fungiform papilla number

The number of fungiform papillae at the tongue tip was determined with videomicroscopy similar to the method of Miller and Reedy [25]. For this procedure, the subject's tongue was painted with blue food coloring to contrast between stained filiform and unstained fungiform papillae. Subjects reclined and steadied their stained tongues between two plastic slides attached with screws. Magnification ($\times 15$) easily distinguished fungiform from filiform papillae, which contain no taste buds. The images were recorded for 3 to 5 min to allow subsequent counting of the fungiform papillae in a 6-mm-diameter circle on the right and left tongue tips. For counting, images were

viewed on a high-resolution television and a circle template was placed on the image so that the edge touched the midline of the tongue as well as the tongue tip. The average of counts from the two sides was used to compare with the alcohol sensory and intake measures.

2.6. Alcohol intake

The Block Food Questionnaire [70,71] version 98.1 was used to evaluate yearly intake of beer, wine/wine coolers and liquor/mixed drinks. In an interview during the second visit, subjects reported how often they consumed each beverage
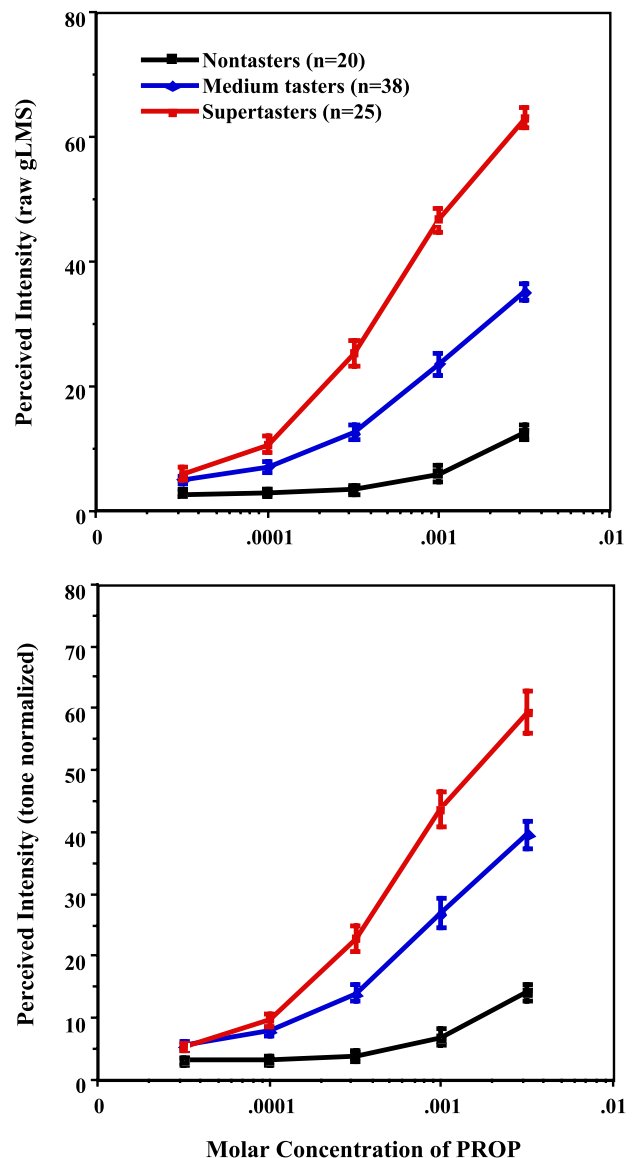

Fig. 2. Perceived bitterness ($\pm$SEM) PROP plotted against PROP concentration for nontasters, medium tasters, and supertasters using ratings from the gLMS (top graph) and those normalized to the intensity of 1000 Hz tones at 86 and 98 dB (bottom graph). Subjects were divided by bitterness of 3.2 mM PROP into 20 subjects who tasted PROP as less than "moderate," 38 who tasted PROP between "moderate and "very strong," and 22 who tasted PROP as "very strong" or greater.

(categories range from "every day" to "never") and the amount consumed per time. A yearly intake of each alcoholic beverage was calculated from reported frequency of intake multiplied by amount consumed each time. Total alcohol intake per year was the sum of beer, wine and liquor consumption.

2.7. Analysis

Data were analyzed using STATISTICA (Macintosh version 4.1, StatSoft, Tulsa, OK). Criterion for significance was $P \leq .05$. Simple regression was used to predict the alcohol data from the taste genetic, NaCl and citric acid intensity and measure of CTN taste functioning. These independent variables and sex were entered into standard multiple regression to predict alcohol intensity and intake. The Results section presents the multiple regression coefficient (r) and semi-partial correlations (sr) of significant contributors to the multiple r. Skewed variables were transformed to improve the normality of the distribution for this statistical procedure [72]. Univariate and multivariate outliers were removed by the standardized residual (≥ 2.5) and the Mahalanobis distance criteria (critical chi-square table with $P < .001$ and the degrees of freedom as the number of independent variables) [72].

3. Results

The sample had diversity in PROP tasting and fungiform papilla number. PROP threshold scores ranged from 0.0015 to 2.18 mM and had the usual bimodal distribution (Fig. 1). Fig. 2 shows PROP functions for subjects divided by bitterness of 3.2 mM PROP into 20 subjects who tasted PROP as less than moderate (≤ 22 on the gLMS), 38 who tasted PROP between moderate and very strong (>22 to 53 on the gLMS), and 25 who tasted PROP as very strong or greater (>53 on the gLMS); the normalized ratings produced similar functions. These subject groups are designated *nontasters*, *medium tasters*, and *supertasters*, respectively for the purpose of this manuscript. There was no significant average or distribution difference in 3.2 mM PROP bitterness ratings between females and males. The fungiform papilla number averaged from 11.75 to 42.50 papilla per 6-mm area and PROP bitterness showed significant correlation with fungiform papillae density in raw and tone normalized PROP bitterness ratings (Fig. 3). Women were more likely to have fungiform papilla numbers that exceeded 25 papilla in the circular template than were men ($\chi^2 = 4.966$, $P < .05$). Because raw and normalized PROP ratings produced similar functions and equivalent associations
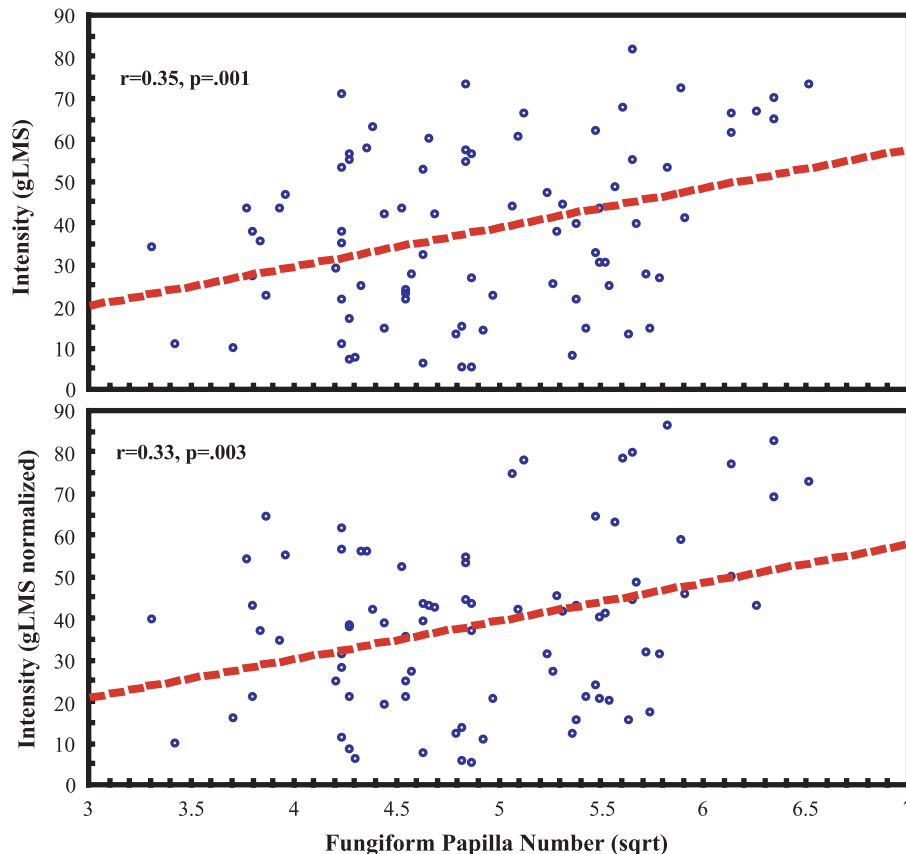

Fig. 3. Scatterplots of 3.2 mM PROP bitterness on the general Labeled Magnitude Scale (top) and that normalized to the intensity of 1000 Hz tones at 86 and 98 dB (bottom) by the number of fungiform papilla (square root transformed).

Table 1
Correlation matrix: measures of taste genetics, NaCl and citric acid taste, spatial taste pattern, alcohol intensity/hedonics and intake

	PROP threshold	PROP bitterness	Fungiform papilla number	Whole mouth NaCl intensity	Whole mouth citric acid intensity	CTN/swallow intensity	Alcohol intensity	Alcohol hedonics	Alcohol intake
PROP threshold	1.00	−.72‡	−.17	.08	.02	−.13	.09	.15	.14
PROP bitterness		1.00	.37‡	.31*	.39‡	.06	.30†	−.27*	−.29†
Fungiform papilla number			1.00	.18	.18	−.07	.31†	−.26*	.09
NaCl intensity				1.00	.54‡	−.24*	.47‡	.09	.27†
Citric acid intensity					1.00	−.15	.36‡	.04	.23*
CTN taste/ swallow intensity (all qualities)						1.00	.28*	−.19	−.24*
Alcohol intensity							1.00	−.45‡	−.20
Alcohol hedonics								1.00	.19
Alcohol intake									1.00

* $P < .05$.
† $P = .01$.
‡ $P = .005$.

with fungiform papilla number, raw ratings are used for testing associations with alcohol and oral sensations.

Greater PROP bitterness associated with greater intensity from whole mouth NaCl and citric acid; fungiform papilla number only showed a modest association with the intensity of these tastes (Table 1).

The mean intensity rating of ethyl alcohol was 30.5 ± 1.6 S.E.M. (between moderate and strong) and mean liking/disliking rating was -10.42 ± 2.51 S.E.M. (between weakly and moderately dislike). Females were skewed toward higher intensities and more disliking (Fig. 4). Greater intensity from the alcohol probe was reported in those who rated the taste markers (PROP, NaCl and citric acid) as more intense, had greater CTN to whole mouth ratios and higher numbers of fungiform papilla (Table 1). Through multiple regression, significant variance in alcohol intensity ratings was explained by taste genetic measures, NaCl and citric acid intensities, sex and CTN to whole mouth ratio ($r=.65$, $P < .000005$). More intense sensations from the alcohol probe were reported by those who found PROP

(sr=.21, $P < .05$) and NaCl (sr=.33, $P < .001$) as more intense and had greater CTN to whole mouth ratios (sr=.27, $P < .01$).

Sixty-eight of 83 subjects reported consuming alcoholic beverages more often than once per month. The reported yearly consumption of alcoholic beverages did not differ significantly between males and females, either through testing mean or distribution differences (male average = 235.69 ± 39.49 S.E.M.; female average = 170.65 ± 28.87). The reported intake of alcoholic beverages correlated significantly with bitterness of PROP (Fig. 5), especially when those who "never" report drinking alcohol were removed from the analyses ($r=.36$, $P=.002$), but not with fungiform papilla number. Average yearly intake of alcoholic beverages for nontasters (300.75 ± 66.82 S.E.M.) was greater than that for medium (177.49 ± 32.62) or supertasters (118.17 ± 20.29). There was a consistent negative relationship between PROP bitterness and intake across the beer, wine and liquor. In multiple regression, PROP effects were separate from those of sex on alcohol intake.
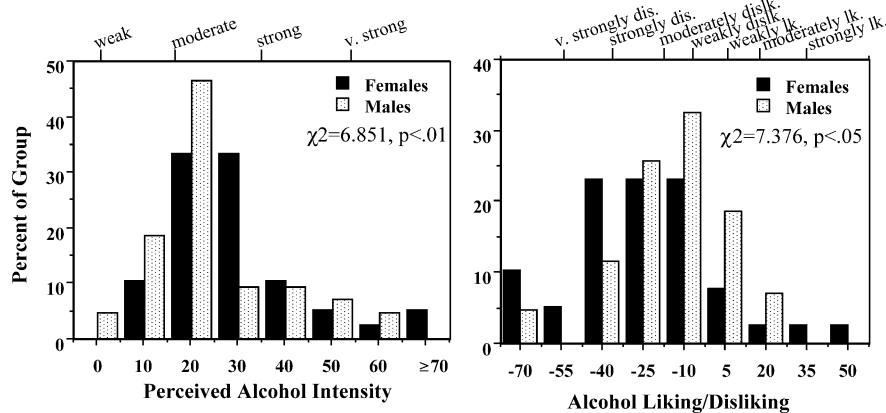

Fig. 4. Distributions of perceived alcohol intensity (left) and alcohol hedonics (right) for females and males. Frequencies are expressed as percentage of each sex. The distributions were tested with the chi square analyses; the categories were > or <30 on the gLMS for intensity ratings and <−23, ≥−23 and <−9, and ≥−9 on the gLMS for hedonic ratings.
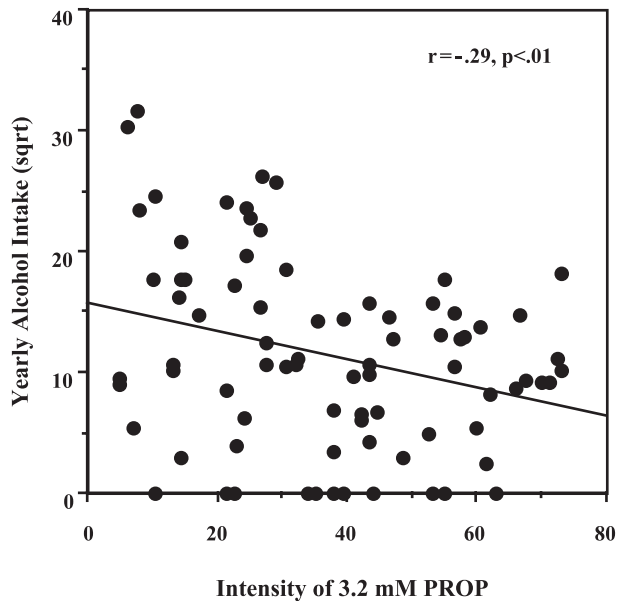
Fig. 5. Frequency of intake of alcoholic beverages over 1-year (square root transformed) by the bitterness of 3.2 M PROP rated on the general Labeled Magnitude Scale.

Multiple regression with sex, fungiform papilla number, PROP bitterness, NaCl and citric acid intensities and CTN/whole mouth ratio explained significant variance in intake of alcoholic beverages (r=.48, P < .002). Only PROP bitterness and CTN/whole mouth ratio were significant predictors: those who reported lower PROP bitterness (sr = − .26, P=.01) and lower CTN/whole mouth ratios (sr = − .24, P=.01) reported more frequent consumption of alcoholic beverages.

4. Discussion

This study of healthy adults showed significant associations between oral sensation and intake of alcoholic beverages. Those who tasted the least bitterness from concentrated PROP or had lowest numbers of fungiform papilla, as markers for genetic nontasters, reported less burn and disliking of a 50% alcohol probe painted on the tongue tip as well as more frequent consumption of alcoholic beverages. The spatial pattern of oral sensation also explained variation in burn from the alcohol probe and consumption of alcoholic beverages. Individuals who showed the most potential for chorda tympani nerve damage (low CTN to whole mouth ratio) reported the least intensity from the alcohol probe and the most frequent intake of alcohol beverages. Multiple regression analyses showed separate influences of taste genetics and spatial patterns of oral sensation on alcohol intake.

These findings support genetic taste influences on oral sensations from alcohol, which may influence the liking/disliking and ultimately consumption of alcoholic beverages. The present study and others suggest that genetic nontasters

have less deterrence for consuming alcoholic beverages because they experience less negative oral sensations. Negative responses to alcohol sensations have been shown to deter the initiation of drinking in adolescents [73] and positive oral sensations from alcohol are reported as a reason for drinking alcohol in adults [22]. One study reported that over 80% of alcoholics liked the taste of alcoholic beverages [41]. Genetic variation in taste may have less affect on consumption patterns of beverages where bitter and irritation sensations are minimized or in social and physical environments that support drinking alcoholic beverages.

Taste genetic influences on alcohol sensation are consistent with previous studies with PROP bitterness related to alcohol sensations most frequently reported. Through magnitude matching and the standardization of oral sensations to the intensity of sodium chloride, Bartoshuk et al. [21] found that PROP medium and supertasters report greater bitterness and irritation from 30% to 50% ethanol applied to the tongue tip than do nontasters. Using the Labeled Magnitude Scale [56,57] for measuring intensity of oral sensations, Itranuovo and Powers [22] extended these findings to sampled beer; PROP supertasters tasted the most bitterness in bitter ale (Pilsner Urquell). Note that the differences in the perceived intensities of alcohol sensations across taster groups are sufficiently large to produce significant differences even with these earlier scaling methods. Recent data show that the gLMS produces a more accurate assessment of PROP effects on oral sensations [43,45]. Pickering et al. [23] used the gLMS and showed that individuals who tasted 3.2 mM PROP as greater than very strong also reported significantly more bitterness, astringency and acidity in red wines; advances in psychophysical techniques [13,43,45] may have revealed these associations where previous attempts did not [74].

Liking/disliking of alcohol associates with alcohol sensations and measures of taste genetics according to findings from this study and others. The more irritating the alcohol probe (present study) as well as more bitter a beer [22], the less it was liked. Greater PROP bitterness and number of fungiform papilla associated with more dislike of the alcohol probe; this is consistent with previous studies associating PROP bitterness with level of liking from sampled beer [22].

Associations between suprathreshold measures of PROP bitterness and alcohol intake are consistent with previous studies. Intranuovo and Powers [22] found that PROP nontasters had the highest intake of alcoholic beverages when they first started drinking; their findings did not extend to current alcohol consumption. The present study did find PROP effects on intake of alcohol during the year preceding the study; history of alcohol use and initiation of alcohol consumption was not determined. The sample size of the present study did not allow examination of relationships between PROP tasting and intake of specific alcoholic beverages. It may be that PROP effects would be less on alcoholic beverages that have less bitterness or irritation. The present study found that PROP bitterness was a better marker for alcohol intake than number of fungiform papilla;

that PROP shows significant and stronger correlation with alcohol intake than fungiform papillae number has also been found in preliminary data on middle-aged adults [75]. PROP bitterness may be a marker of all oral sensations from alcohol (e.g., taste, oral somatosensation and retronasal olfaction) whereas fungiform papilla number is more salient to the oral somatosensory properties.

The present study failed to find a significant relationship between PROP threshold and alcohol sensation, hedonics or intake. Although threshold showed a strong negative correlation with bitterness of 3.2 mM PROP (i.e., high threshold and low PROP bitterness), thresholds cannot consistently identify supertasters [11]. Factors not directly related to alcoholism (e.g., viral infection of the respiratory system and head trauma) damage taste, particularly bitterness [42], making an individual appear to be genetically less sensitive to PROP. Individuals who have depressed bitter taste perception on the anterior tongue show heightened response to burn from oral irritants [48] as well as phantom pain sensations [50]. It is not surprising that inconsistent findings exist on PROP tasting related to alcohol ingestive behaviors in studies that employ threshold as the measure of PROP tasting. A consistent relationship between history of alcoholism and PROP tasting may be more apparent with psychophysical techniques that clearly separate PROP nontasters, medium tasters and supertasters [13,23,43,45]; PROP supertasters may experience the most negative sensory cues from alcohol.

Females were skewed toward higher alcohol burn and more aversive ratings of this sensation. This sex difference cannot be explained by differences in PROP tasting across males and females; although previous studies show a sex difference in PROP tasting (see Ref. [11] for a review), females and males in the present study did not differ in PROP tasting. Women in the present study were skewed toward higher density of fungiform papillae; this has been reported previously [44]. The density of fungiform papilla and interactions between taste and trigeminal nerves influence the burn from alcohol. Because fungiform papillae are innervated by both taste and trigeminal fibers, individuals with highest density would likely experience greater burn from the alcohol probe.

Oral sensory responses to the 50% alcohol probe, intensity or hedonic ratings, did not correlate significantly with alcohol intake. This was expected as the probe provided primarily a measure of alcohol irritation that may not generalize to the full array of sensory and learned experiences associated with alcoholic beverages. Additionally, the probe was limited to the left tongue tip and drinking stimulates the entire mouth. Those who taste PROP as more bitter get more intensity and greater disliking from the probe of alcohol irritation, which might explain why these individuals consume alcohol less frequently. Intranuovo and Powers [22] did find that subjects reported the main reason for drinking beer was because they "liked the taste." Future investigations would benefit from testing the association between PROP intensity, oral sensations from alcoholic beverages and alcohol intake.

The NaCl and citric acid effects on alcohol intake appear to correspond with findings of Sandstrom et al. [53]; individuals who consumed alcoholic beverages most frequently (present study) or had a positive paternal history of alcoholism [53] perceived concentrated NaCl and citric acid as most intense. A direct comparison is difficult however because the studies employed different alcohol outcomes and the latter used a scaling methodology that limits ability to make valid across group comparisons. The present study revealed that the spatial pattern of taste (lower taste on the anterior tongue relative to whole mouth) explained some of the contribution of NaCl and citric acid to predict less burn from the alcohol probe and to predict more frequent intake of alcoholic beverages. Thus, it may be lower CTN taste functioning that leads to intensified whole mouth sensations from NaCl and citric acid. The concentrations of NaCl and citric acid in the Sandstrom et al. study would act as trigeminal stimuli: NaCl: 0.31, 0.62, 0.92, 1.23 and 1.54 M; and citric acid: 0.10, 0.19, 0.29, 0.38 and 0.48 M (correction of concentrations published in error, personnel communication from H. Kranzler—August 2003). Reductions of CTN taste intensify oral trigeminal sensations as shown by experimental [48] and clinical [50] evidence. It is unknown if the lower CTN taste is an antecedent or a consequence of the alcohol intake. As an antecedent, environmental insults (e.g., viral and trauma induced) could reduce oral sensations on the tongue tip and limit this barrier to consuming bitter and irritating alcoholic beverages. There may also be physiologic connections between salt sensations/hedonics and alcohol ingestive behaviors as suggested by preliminary evidence [53]. Low CTN taste could also be a consequence of disease and pathologies associated with high consumption of alcohol intake [76,77]. This deserves further evaluation.

The clinical significance of the intake data must be evaluated. While a greater percentage of the nontasters reported consuming alcohol daily than did supertasters, consumption of one to two alcoholic beverages per day can be part of a healthy diet as outlined in the 2000 edition of the Dietary Guidelines for Healthy Americans [78]. The subjects in the present study were recruited for a range of PROP tasting in both females and males and to control variables that could confound the ability to examine the influence of PROP tasting on dietary behaviors. The sample was diverse in PROP tasting; the bimodal distribution of PROP thresholds demonstrated both nontasters and tasters and the PROP functions suggested medium and supertasters (Fig. 2). Alcohol use in the sample approximated national statistics; according to the 1999 National Household Survey on Drug Abuse [79] data, approximately 60% of individuals aged 21–39 consumed alcohol in the month preceding the survey and that the rates of alcohol consumption were up to 70% in college students in New England. This compares to the present sample in which 65 of 80 subjects report consuming

alcoholic beverages greater than once per month. Inclusion of subjects with low levels of dietary restraint may have improved the accuracy of self-reported alcohol consumption as high dietary restraint has been shown to decrease the accuracy of dietary assessment [59].

Acknowledgements

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