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Impact of Bitter Taste Receptor Phenotype upon Clinical Presentation in Chronic Rhinosinusitis

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Abstract

Background: Genetic variation of the bitter taste receptor T2R38 has been associated with recalcitrant chronic rhinosinusitis (CRS). Specific T2R38 polymorphisms, correlating with bitter taste sensitivity to phenylthiocarbamide (PTC), have been identified as an independent risk factor for surgical intervention in CRS patients without polyps; however, the exact role of PTC tasting ability in clinical practice remains unknown. This investigation characterizes PTC taste sensitivity in a tertiary care rhinology practice with pertinent clinical measures of disease and quality of life (QOL).

Methods: Adult CRS patients were prospectively assessed for their ability to taste PTC and categorized as nontasters, tasters or supertasters. Objective taste was assessed with strips for bitter, sweet, sour and salty, while olfactory testing was measured with Sniffin' Sticks. Correlation was performed between PTC tasting ability and patient demographics, endoscopy scores, validated QOL surveys, and both subjective and objective measures of taste and olfaction.

Results: Sixty-seven patients were enrolled. Fifty-two percent were identified as nontasters, 34% tasters and 13% supertasters. Nontasters were more likely to be non-Hispanic ($p=0.018$) Caucasians ($p=0.027$), without nasal polyposis ($p=0.004$) and non-asthmatics ($p=0.019$). There were no other statistical differences in patient demographics, QOL measures, subjective or objective olfactory and taste scores when compared against the patient's oral PTC-sensing ability.

Conclusions: Oral PTC-sensing ability may serve as a convenient marker of increased disease severity in Caucasian CRS patients without polyps and vary amongst regional populations. PTC

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tasting ability appears to provide unique phenotypic information not obtained using other subjective or objective measures of smell and taste.

Keywords

sinusitis; smell; taste; innate immunity; quality of life; genetic variation

Introduction:

Chronic rhinosinusitis (CRS) is described as persistent sinonasal inflammation that is multifactorial in nature, resulting from a variety of dysfunctional host-environmental interactions such as ciliary impairment, allergy, reactive airway disease, genetic factors, immune dysfunction, microbial infection/biofilms, environmental and iatrogenic factors, among others.¹ There is mounting evidence that the classification and treatment of CRS should be tailored to each individual patient based on the underlying pathophysiology, endotype or cluster.^{2,3} A burgeoning area of interest, is the bitter taste receptor gene family and its relation to innate immune immunity.⁴ Expression of the T2R bitter taste receptors have been shown to extend beyond the oral cavity, involving multiple areas of the body, including the sinonasal epithelium.⁵⁻⁷

At this time, T2R38 is the most well-studied of the CRS-related bitter taste receptors and has been shown to activate local innate immune responses by increased mucociliary clearance and bacterial killing.⁸⁻¹¹ Polymorphisms in the T2R38 receptor may render the receptor less functional, or nonfunctional, a phenomenon that occurs with relatively balanced distribution.¹²⁻¹⁶ Though genetic testing will directly identify a patient's T2R38 polymorphism, the use of a taste test for phenylthiocarbamide (PTC), a synthetic compound specific for the T2R38 receptor, can quickly assess T2R38 functionality, a measure that may be more relevant to clinicians¹⁷ and more reflective of T2R38 functionality.⁴ Examining the genotype and phenotypic expression of T2R38 in CRS patients, several pioneering studies have demonstrated a direct correlation between expression of these receptors with both the clinical manifestations and disease severity in CRS.^{4,17-21}

In this study, we sought to assess the functional expression of the T2R38 receptor with a PTC taste test in a unique, regional CRS population. Similar to prior studies, we prospectively examined the relationship between functional expression of T2R38, by PTC tasting ability, with clinical demographics and objective measures of CRS disease severity in a tertiary care patient population. Moreover, we investigated the relationship between PTC sensitivity and patient reported quality of life (QOL). In addition, given the clinical importance of olfactory and gustatory dysfunction in the CRS patient population^{20,22}, we compared PTC tasting ability with patient reported measures of smell and taste as well as traditional measures of olfaction and gustation. We hypothesized that differences in PTC tasting ability would provide further insight into clinical differences and QOL disparities in an advanced CRS population.

Methods:

Enrollment:

Adult patients, 18 years of age or older, with CRS were prospectively enrolled from a tertiary care rhinology practice into this cross-sectional study. All patients fulfilled diagnostic criteria for CRS according to the Clinical Practice Guideline of the American Academy of Otolaryngology–Head and Neck Surgery and the European Position Paper on Rhinosinusitis and Nasal Polyps.^{1,23} Patients with sinus surgery within the last 3 months, currently pregnant, or neurologic conditions such as Parkinson’s disease, multiple sclerosis and Alzheimer’s disease were excluded. This study was approved by the Medical University of South Carolina institutional review board and written informed consent was obtained from all participants.

PTC tasting ability

The ability to detect PTC was assessed with PTC taste strips as previously described (Sensonics International, Haddon Heights, NJ).²⁴ Using an odorless filter paper soaked in PTC, patients were instructed to categorize the taste strip as “like paper,” “somewhat bitter,” or “strongly/unpalatably bitter” as compared to a control. Similar to Farquhar et al.’s methodology, patients were categorized as nontasters, tasters or supertasters based on their perceived taste as bland, bitter or unpalatably bitter respectively as compared to a control test strip.²⁴

CRS disease severity:

Nasal endoscopy and patient-reported outcome measures were used to classify sinus disease severity. Sinonasal endoscopy was performed and scored using the Lund-Kennedy and Olfactory Cleft Endoscopy Scoring (OCES)²⁵ systems by treating physicians who were blinded to the patient’s data. Patients were also classified as having CRS with nasal polyps (CRSwNP) or CRS without nasal polyps (CRSSNP) based on nasal endoscopy. Participants rated their sinus-specific QOL using the 22-item Sino-Nasal Outcome Test (SNOT-22).²⁶ The SNOT-22 contains 22 questions each scored 0–5 (total score range 0–110), with higher scores representing worse QOL. Patients also completed a Patient Health Questionnaire-9 (PHQ-9) survey, which is a brief validated tool to screen for depression.²⁷

Taste measures:

Taste testing was performed using validated taste strips (“Taste Strips”, Burghart, Wedel, Germany).²⁸ Sixteen strips impregnated with four different concentrations of four tastants: sweet, sour, salty and bitter were assessed in comparison to a control. The following concentrations were used: sweet: 0.4, 0.2, 0.1, 0.05 g/ml sucrose; sour: 0.3, 0.165, 0.09, 0.05 g/ml citric acid; salty: 0.25, 0.1, 0.04, 0.016 g/ml sodium chloride; bitter: 0.006, 0.0024, 0.0009, 0.0004 g/ml quinine hydrochloride. Testing was performed from the lowest to highest concentrations in a pseudorandom fashion. The taste strips were placed in the anterior mid-tongue, and patients were allowed to close their mouth and move the strip around. Patients identified the tastes in a forced choice paradigm. Scores for each subgroup ranged from 0–4 with lower scores indicating worse performance. Subgroup scores were

added to give the total taste score. Gustatory dysfunction was determined using ideal cut-offs previously reported by Mueller et al. based on a $\leq 10^{\text{th}}$ percentile each of the four taste groups.²⁸ A score of <2 was considered hypogeusia for the sweet, sour and salty taste subgroups and less than 1 for the bitter subgroup. An overall score of <9 was considered hypogeusia.²⁸

Olfactory measures:

Olfactory testing was performed using the Sniffin' Sticks test (Burghart Instruments, Wedel, Germany). The test battery included odor threshold, odor discrimination, and odor identification. The threshold test was performed using dilution of n-butanol in a single-staircase, triple-forced choice procedure and scored from 1–16. In the discrimination test, subjects were asked to identify the different odor after randomly being presented with 16 sets of triplet pens with two containing the same odorant. This was scored from 0 to 16. The identification test used a multiple-choice procedure where sixteen odorants were presented at supra-threshold intensity. A “composite threshold-discrimination” (TDI) score, which ranged from 1 to 48, was then obtained by summing up all three scores.²⁹ Olfactory specific quality of life was assessed using the previously validated, short, modified version of the Questionnaire of olfactory disorders (QOD).³⁰ This instrument consists of 17 negative statements graded from 0 to 3 for maximum score of 51 (higher scores reflected worse QOL).

Patient reported taste and smell

Perceived chemosensory dysfunction was assessed using the Chemosensory Complaint Score questionnaire (CCS).³¹ This survey consists of questions pertaining to taste and smell. The taste section consists of 8 questions addressing change in sense of taste, change in the way food tastes, presence and quality of a bad taste in mouth, effect of medications upon sense of taste and changes in quality of each taste subgroup (salt, sweet, sour, bitter). Any abnormality in those 8 questions is given one point. A ninth question asks for a rating of overall severity of taste abnormalities with one point given for mild or moderate dysfunction and two points for severe or incapacitating dysfunction. This results in a total taste score ranging from 0 (no taste complaints) to 10 (many/severe taste complaints). The smell section consists of four questions addressing change in sense of smell, change in the way food smells, effect of medication upon sense of smell and change in strength of odors. Each abnormality is given one point. A fifth question asks for an overall rating of severity of smell abnormality and is given one point for mild or moderate dysfunction and two points for severe dysfunction. This results in a total smell score ranging from 0 (no complaints) to 6 (many complaints). Both taste and smell scores were added to give the total chemosensory complaint score ranging from 0 to 16.

Statistical Analysis

Data analysis was performed using SPSS 23.0 (IBM Corporation, Armonk, NY). Descriptive statistics (means, standard deviations, percentages) were used to assess demographic information, comorbidities, and chemosensory metrics. One-way ANOVA tests were conducted between PTC-sensing categories and all normally distributed continuous variables. Post-hoc analysis was performed with the Holm-Bonferroni correction for

multiple comparisons. For non-normally distributed continuous variables, the Kruskal-Wallis Test was used. Differences between PTC groups by categorical variables were assessed using the Freeman-Halton exact test. For all assessments, other than post-hoc analysis, p values of ≤ 0.05 were considered statistically significant.

Results:

Patient demographics

This study prospectively enrolled 67 patients with CRS. The mean age of the cohort was 51.6 years and consisted of 55.2% men. Twenty-five percent of the patients were non-white and the cohort was predominantly non-Hispanic (95.0%). Three patients were current smokers (4.5%) while 21.0% were former smokers and 74.6% were never smokers. Asthma was present in 43.3% of the population while 61.2% had previously confirmed allergy testing and 10.4% had aspirin exacerbated respiratory disease (AERD). See Table 1 for a summary of baseline patient demographics. With regard to CRS-specific measures, patients were divided fairly evenly by polyp status (CRSwNP=56.7%, CRSsNP=43.3%) and most had undergone prior ESS (86.6%) (Table 2).

PTC tasting ability and patient characteristics

The distribution of nontasters, tasters and supertasters was 35 (52.2%), 23 (34.3%) and 9 (13.4%) respectively. Demographically, non-tasters were more often Caucasian ($p=0.027$), non-Hispanic ($p=0.018$), and likely to have been diagnosed with depression ($p=0.022$) (Table 1). Supertasters had the highest proportion of asthmatics ($p=0.019$) while tasters had the lowest proportion of migraineurs ($p=0.050$). There were no differences amongst the 3 PTC sensitivity groups in level of education ($p=0.343$), smoking history ($p=0.216$), allergies ($p=0.266$), alcohol consumption ($p=0.423$) or any of the other measured comorbidities listed in Table 1.

Regarding CRS-specific measures, nontasters more commonly had CRSsNP ($p=0.017$, Table 2). There were no differences in any other CRS-specific measure, including number of prior surgeries, olfactory cleft endoscopy score (OCES) or Lund-Kennedy endoscopy scores amongst the 3 groups at the time of study (Table 2). Post-hoc analysis of all demographic and CRS-specific factors using corrections for multiple comparisons identified non-Hispanic ethnicity, CRSsNP and depression as statistically different specifically between nontasters and tasters ($p=0.021$, $p=0.004$ and $p=0.016$ respectively).

Distribution and comparison of PTC tasting ability in this study was compared to prior investigations and reported in Table 3. There was a statistically significant difference in the distribution of tasting ability in this study compared to a prior study of healthy adults, assessed with the same taste strip protocol ($p=0.0002$). Furthermore, though the sensory ratings measured in this study cannot serve as an exact correlate for the precise genetic analysis measured in prior studies, the frequency of PTC tasting ability in our population was compared to the genotypic distribution of TAS2R38 diplotypes in past investigations and found to be significantly different (Table 3).

PTC tasting ability and patient reported outcome measures

Sinonasal quality of life as measured by the SNOT-22 and depression survey scores were similar amongst different PTC tasting abilities ($p=0.696$ and 0.125 respectively; Table 4). Despite differences in PTC tasting ability across the population, there were no correlations between total CCS scores, the smell section or the taste section of the survey (Table 4). The QOD negative statements survey (QOD-NS) was the only comparison that trended towards statistical significance with increasing mean QOD-NS scores across nontasters (8.49), tasters (11.57) and supertasters (17.11) respectively, but this did not reach predefined significance ($p=0.063$; Table 4).

PTC tasting ability and objective measures of olfaction and gustation

Similar to subjective olfactory and gustatory patient reported measures, there were no differences in objective measures of olfaction and gustation when compared amongst the 3 different PTC tasting groups (Table 5). There was no correlation when patients were compared amongst their PTC tasting ability and the individual bitter taste test of the taste strips test (nontasters= 2.49 ± 1.38 , tasters= 3.13 ± 1.18 , supertasters= 2.44 ± 1.24 , $p=0.155$; Table 5).

Discussion:

PTC tasting ability has been investigated since its discovery in 1931,^{13,32} but only recently, with the efforts of investigators at the University of Pennsylvania has this become an important area of focus in the rhinologic community.^{4,8,11} The present study contributes to the growing body of literature by supporting multiregional applicability of the clinical importance of T2R38 receptor activity (assessed by PTC taste ability) in CRS patients, and substantiates the correlation between the nontaster phenotype and CRS, especially Caucasian patients without nasal polyposis. Furthermore, this study suggests that differences in taste sensitivity to the bitter compound PTC provide unique information relating to patient attributes that other subjective or objective measures of smell and taste, or sinonasal quality of life do not provide.

In order to assess the influence of genetic variation of the gene that encodes the T2R38 receptor and its influence on CRS, prior studies have been conducted primarily in white patients of European descent given the characterization of this receptor in the literature.^{17,19} Subsequently, these findings were supported by a relatively large, retrospective, Canadian population based study, evaluating taste receptor gene single-nucleotide polymorphisms, that was comprised of 2 CRS populations with 85.2% and 94.1% white patients respectively.³³ Despite similar conclusions, all of the aforementioned studies along with small studies from Australia³⁴ and Italy³⁵, and the most recent report from Adappa and colleagues¹⁷, have reported genotypic heterogeneity across study populations (Table 3). Our cohort of patients demonstrated a different distribution of PTC tasting phenotypes as compared to earlier studies that examined the 3 main diplotypes that encode the T2R38 receptor. Furthermore, our results suggest that nontasters with CRS are more likely to be non-Hispanic white patients. These differences may be accounted for by the fact that 25% of our patient population was non-white, differences in regionality or differences between genotype and

phenotypic expression. The explanation of differences in distribution of PTC tasting phenotypes is veiled in this study by lack of genetic analysis or documented ancestry. It is worth noting that the incidence of nontasters varies around the world, from less than 5% in parts of Africa to greater than 40% in India^{13,36} and there can be significant genetic variation even within populations.³⁷ Given the heterogeneity of these findings, a diverse, large population based study would be needed to measure the true prevalence of T2R38 functionality in CRS patients and better understand its clinical relevance in this disease.

In addition to racial differences in PTC tasting ability, our study highlights the association of the nontaster phenotype with polyp status. Our results suggest that CRSsNP is a driving force behind this association, in particular the difference between nontasters and tasters, as this difference remained significant following post-hoc analysis. This is supported by two reports from the University of Pennsylvania demonstrating that in nonpolypoid patients, PTC tasting sensitivity is directly correlated with surgical quality of life outcomes and inversely correlated with biofilm formation.^{17,21} Though the genetic basis for these findings are beyond the scope of this report, these findings suggests that PTC tasting ability may be an informative clinical descriptor that would help inform both patient and clinician when discussing expectations and treatment strategies for CRSsNP. Furthermore, as many heterozygotes of the functional gene encoding T2R38 (TAS2R38) behave like nonfunctional homozygotes, this point of care taste test may be more clinically relevant than a genetic test.^{4,17}

Other unique findings in our study include the association of nontasters with physician-diagnosed depression and migraines as well as the increased prevalence of asthma in tasters and supertasters. Despite two of these associations remaining statistically significant on post-hoc analysis, we are cautious to attempt to explain the clinical importance of this finding, as we suspect that these associations are at least somewhat driven by polyp status as patients with nonpolypoid disease have been shown to have a higher prevalence of physician-diagnosed depression³⁸ and migraines³⁹, and a lower prevalence of asthma as compared to polyp patients.⁴⁰ Moreover, the literature examining the association between depression and PTC tasting ability is mixed. While a small study demonstrated a lower incidence of depression in supertasters⁴¹, other studies have demonstrated increased rates of depression in PTC tasters^{42,43} and an increased negative emotional response of supertasters.⁴⁴ Furthermore, a robust study of more than 12,000 patients failed to demonstrate a relationship between prevalence of depression and tasting ability.⁴⁵

Beyond patient and clinical demographics, we compared several CRS disease severity measures across the different PTC tasting sensitivities. We were unable to find any differences in CRS-specific quality of life using SNOT-22 scores based upon PTC classification. One prior study did demonstrate higher baseline SNOT-22 scores in patients with the supertaster genotype, however, these authors compared SNOT-22 scores between genotypic nontasters and tasters compared to supertasters, and did not compare SNOT-22 scores on the basis of phenotypic expression.¹⁷ When we regroup our analysis to mimic the prior study, the lack of statistical significance did not change ($p=0.652$). It is worth noting that there is no current common reporting standard for quick clinical tests of phenotypic expression of T2R38 functionality or PTC tasting ability. When examining endoscopy, we

found no statistical differences between Lund-Kennedy or olfactory cleft endoscopic scoring. Though these endoscopic measures have not been reported in prior investigations the University of Pennsylvania group has also demonstrated lack of association in objective radiographic measures of disease across PTC tasting ability.¹⁷

Most CRS-specific measures are quite broad and encompass a spectrum of symptoms and disease presentation, thus we also wished to study the association between PTC status and measures specifically focused upon taste and olfaction. Though prior works have demonstrated an association between PTC tasting ability and a variety measures including, overall taste qualities, oral somatosensation and retronasal olfaction⁴⁶ this study sought to assess the clinical utility and QOL influence of PTC sensitivity in CRS patients beyond direct smell and taste tests. In this report, objective olfaction measured by Sniffin' Sticks failed to demonstrate any differences. This corroborates a report that included 185 patients with nasal sinus disease and found similar results.⁴⁷ These authors hypothesized that though functional T2R38 receptors may be protective, once olfactory dysfunction occurs, PTC tasting ability has little effect on the degree of the loss. Doty and colleagues also suggested that T2R38 functionality is not protective against olfactory loss as olfactory receptor cells in the olfactory epithelium have nonmotile cilia.⁴⁷ Furthermore, the antimicrobial properties of the T2R38 receptor may be less influential on changes in smell if viral infection plays a role in a given patient's olfactory dysfunction.^{48–50} In order to study PTC status and patient reported olfaction, we examined QOD-NS and CCS-smell scores and were unable to find any differences, which is logical given their lack of objective differences.

We also examined the relationship between PTC status and both objective and subjective taste. Using taste strips for bitter, salt, sweet and sour, we were unable to find any differences in individual tastes. There was a trend towards statistical significance for the total taste scores across the 3 PTC tasting abilities, however, limited sample size of supertasters has made meaningful interpretation of these statistics difficult. Our findings are underpowered to compare this study to the previously mentioned investigation by Doty et al., that found that PTC tasters (both tasters and supertasters) with nasal sinus disease had improved suprathreshold taste identification.⁴⁷ Unfortunately, these authors did not distinguish supertasters from tasters and did not further characterize the extent of their patients' sinonasal disease. While there is a body of evidence that T2R38 taste receptors respond to tastants beyond bitter compounds^{51–54}, the mixed reports on the association between olfaction and gustation in CRS patients suggests that the answer to this question is not straightforward.^{55–58} Moreover, quinine hydrochloride, the compound used on taste strips, has been associated with several bitter taste receptor genes different than the TAS2R38 gene that is associated with PTC.⁵⁹ Similar to the lack of correlation between PTC status and objective taste, patient reported taste function does not correlate with PTC status, indicating that while PTC status is certainly something that can be differentiated with a simple taste strip, it is not readily apparent to patients in their daily lives.

Strengths/weaknesses

The strengths of this study include comprehensive prospective assessment of a unique CRS patient population that provides a more detailed analysis of CRS with measures of smell and

taste than previously reported. It will serve as an impetus to assess PTC tasting ability across different patient populations and provides further insight into the understanding of CRS at a genetic level. The limitations of this study include sample size, lack of a control population or comparative genetic analysis and its cross-sectional nature. Though this study did elicit differences in the CRS subgroups and polyp status, it is likely underpowered to explore all associations as the impact of PTC on any given measure may be present, but small in effect size. A larger, more definitive study will be needed to assess this disease process that afflicts 38 million Americans. In addition, this cross sectional study was not designed to measure the impact of medical or surgical outcomes. Future studies assessing taste receptors in CRS patients should longitudinally study a racially diverse patient population to better understand the clinical relevance of differences in PTC tasting ability across patient populations.

Conclusion:

Functionality of the T2R38 bitter taste receptor has increasingly been shown to play a role in the pathogenesis of CRS. This study assesses a unique CRS patient population, demonstrating that non-Hispanic Caucasians without nasal polyposis are more likely to be associated with the nonfunctional phenotype. PTC tasting ability is a simple point of care test of T2R38 functionality that may serve to better characterize CRS patients, particularly those without polyps, and inform both patient and physician alike. Despite the T2R38 receptor's known mechanisms that influence sinonasal innate immunity and are directly responsible for taste, tasting ability of the bitter compound PTC was not correlated with subjective or objective measures of olfaction and gustation and thus provides unique information.

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Table 1.

Patient demographics and comorbidities stratified by PTC tasting ability.

		Nontaster (n=35)	Taster (n= 23)	Supertaster (n=9)	p-value
Age (Mean $\pm$ SD)		54.86 ($\pm$ 16.48)	47.70 ($\pm$ 15.41)	49.22 ($\pm$ 19.36)	.250
Female, N (%)		13 (37.14)	10 (43.48)	7 (77.78)	.111
Race, N (%)	Non-White	5 (14.29)	7 (30.43)	5 (55.56)	.027 *
	White	30 (85.71)	16 (69.57)	4 (44.44)	
Ethnicity, N (%)	Hispanic	0 (0.00)	4 (17.39)	0 (0.00)	.018 *
	Non-Hispanic	35 (100.00) [#]	19 (82.61)	9 (100.00)	
Level of education (Mean $\pm$ SD)		15.39 ($\pm$ 2.37)	14.38 ($\pm$ 2.67)	15.00 ($\pm$ 2.24)	.343
Drinks per week (Mean $\pm$ SD)		2.09 ($\pm$ 2.98)	4.08 ($\pm$ 5.47)	1.61 ($\pm$ 3.01)	.423
Smoking history, N (%)	Never	22 (62.86)	20 (86.96)	8 (88.89)	.216
	Former	11 (31.43)	2 (8.70)	1 (11.11)	
	Current	2 (5.71)	1 (4.35)	0 (0.00)	
Asthma, N (%)		10 (28.57)	12 (52.17)	7 (77.78)	.019 *
Allergy by Testing, N (%)		23 (65.71)	11 (47.83)	7 (77.78)	.266
AERD, N (%)		2 (5.71)	3 (13.04)	2 (22.22)	.225
Diabetes Mellitus, N (%)		3 (8.57)	2 (8.70)	1 (11.11)	1.00
OSA, N (%)		10 (28.57)	3 (13.04)	3 (33.33)	.297
GERD, N (%)		13 (37.14)	8 (34.78)	3 (33.33)	1.00
Depression, N (%)		13 (37.14) [#]	2 (8.70)	4 (44.44)	.022 *
Migraines, N (%)		8 (22.86)	1 (4.35)	3 (33.33)	.050 *
Anxiety, N (%)		9 (24.29)	7 (30.43)	4 (44.44)	.571
Fibromyalgia, N (%)		1 (2.86)	0 (0.00)	1 (11.11)	.367

* indicates statistical significance

[#] indicates statistical significance following Holm-Bonferroni correction between non-taster and taster groups.

CRS_wNP, CRS with nasal polyposis; *CRS_sNP*, CRS without nasal polyposis; *AERD*, aspirin exacerbated respiratory disease; *OSA*, obstructive sleep apnea; *GERD*, gastroesophageal reflux disease; *N*, number of patients; *SD*, standard deviation.

Table 2.

CRS-specific measures

	Nontaster (n=35)	Taster (n= 23)	Supertaster (n=9)	p-value
	Mean ($\pm$ SD)	Mean ($\pm$ SD)	Mean ($\pm$ SD)	
CRS _w NP, N (%)	14 (40.00)	18 (78.26)	6 (66.67)	.017 *
CRS _s NP, N (%)	21 (60.00) [#]	5 (21.74)	3 (33.33)	
Prior Sinus Surgery (Mean $\pm$ SD)	1.86 ($\pm$ 1.77)	1.39 ($\pm$ 1.03)	2.56 ($\pm$ 1.67)	.156
Olfactory Cleft Endoscopy Score	3.35 ($\pm$ 3.57)	5.09 ($\pm$ 4.59)	3.78 ($\pm$ 4.15)	.361
Lund-Kennedy Endoscopic Score	5.20 ($\pm$ 3.62)	5.74 ($\pm$ 4.37)	5.22 ($\pm$ 3.27)	.865

* indicates statistical significance

[#] indicates statistical significance following Holm-Bonferroni correction between non-taster and taster groups.

CRS_wNP, CRS with nasal polyposis; CRS_sNP, CRS without nasal polyposis; N, number of patients; SD, standard deviation.

Table 3.

Distribution of PTC tasting ability and TAS2R38 diplotypes

	Nontaster	Taster	Supertaster	p-value
PTC tasting ability in healthy adults ^{24, a}	29.5%	34.1%	36.4%	.0002
PTC tasting ability in current study ^a (N=67)	52.2%	34.3%	13.4%	
Comparison of current study phenotypes to genotypes reported in CRS literature				p-value
	AVI/AVI	PAV/AVI	PAV/PAV	
Adappa et al. 2013 (N=28)	46.0%	50.0%	3.6%	<.0001
Adappa et al. 2014 (N=70)	37.0%	54.0%	8.5%	<.0001
Adappa et al. 2016 (N=207)	80.7%		19.3%	.2765
Gallo et al. 2016	18.9%	54.7%	15.1%	.0040
Rom et al. 2017 (N=25)	24.0%	48.0%	16.0%	<.0001

^aDid not assess genotype frequency, only phenotypic expression.

Table 4.

Patient reported outcome measures stratified by PTC tasting ability

	Nontaster (n=35)	Taster (n= 23)	Supertaster (n=9)	p-value
	Mean (± SD)	Mean (± SD)	Mean (± SD)	
CRS and depression measures				
SNOT-22 Total	38.57 (± 24.15)	43.43 (± 27.31)	36.25 (± 21.13)	.696
PHQ-9 Total	3.94 (± 4.39)	4.35 (± 3.54)	7.22 (± 5.40)	.125
Olfactory and taste measures				
QOD NS Total	8.49 (± 9.09)	11.57 (± 10.06)	17.11 (± 12.10)	.063
QOD PS Total	2.17 (± 2.43)	1.91 (± 1.88)	2.00 (± 1.50)	.901
CCS Taste Score	2.69 (± 2.86)	3.43 (± 2.71)	4.44 (± 2.83)	.219
CCS Smell Score	2.43 (± 1.96)	3.09 (± 2.13)	3.11 (± 1.90)	.406
CCS Total Score	5.11 (± 4.55)	6.52 (± 4.24)	7.56 (± 4.42)	.253

QOD NS, questionnaire of olfactory disorders negative statements; *QOD PS*, questionnaire of olfactory disorders positive statements; *CCS*, chemosensory complaint score questionnaire; *PHQ-9*, Patient Health Questionnaire-2

Table 5.

Objective smell and taste measures stratified by PTC tasting ability

	Nontaster (n=35)	Taster (n= 23)	Supertaster (n=9)	p-value
	Mean (± SD)	Mean (± SD)	Mean (± SD)	
Olfaction measures				
Threshold	4.37 (± 3.33)	3.79 (± 2.89)	3.50 (± 2.44)	.664
Discrimination	9.54 (± 3.17)	8.83 (± 3.37)	8.78 (± 2.77)	.648
Identification	10.77 (± 3.91)	9.65 (± 4.25)	8.22 (± 4.84)	.230
TDI Total	24.69 (± 9.23)	22.27 (± 9.51)	20.50 (± 9.52)	.402
Taste measures				
Sweet	2.83 (± .95)	3.22 (± .52)	2.67 (± .71)	.114
Sour	2.11(± .72)	2.35 (± .57)	1.78 (± .97)	.122
Salty	2.74 (± .95)	2.74 (± 1.29)	2.67 (± 1.22)	.982
Bitter	2.49 (± 1.38)	3.13 (± 1.18)	2.44 (± 1.24)	.155
Taste Strips Total Score	10.17 (± 2.61)	11.43 (± 2.15)	9.56 (± 2.79)	.083

TDI, summation of threshold, discrimination and identification scores