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Retronasal Olfaction in Chronic Rhinosinusitis

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Abstract

Objective—The goals of this study were to assess retronasal olfaction in patients with chronic rhinosinusitis (CRS) and describe clinical factors that influence retronasal olfaction. This study sought to investigate the influence of retronasal olfaction on patient-perceived outcomes and examine the relationship between retronasal and orthonasal olfaction.

Methods—Retronasal olfactory function was tested using odorized powders in the oral cavity while Sniffin' Sticks Tests were used to assess orthonasal function prospectively in 69 adult CRS patients. Endoscopic evaluation of the olfactory cleft was scored using the Olfactory Cleft Endoscopy Scale (OCES). Several quality of life (QOL) instruments relating to sinonasal, olfactory and chemosensory functions were used to assess the interactions between patient-reported outcome measures and retronasal olfaction.

Results—There was strong correlation between retronasal and total orthonasal olfaction scores ($r=0.77$, $p<0.001$) as well as retronasal scores with orthonasal subscores. Retronasal scores were worse in patients with nasal polyposis ($p=0.002$), asthma ($p=0.04$) and aspirin-exacerbated respiratory disease (AERD) ($p=0.02$), while OCES was the only independent predictor of retronasal olfaction ($r=-0.42$, $p<0.001$). Significant correlation existed between retronasal olfaction and olfactory-specific QOL and chemosensory smell scores.

Conclusion—Few studies have examined retronasal olfaction in CRS patients. In this cohort, CRS patients demonstrated deficits in retronasal olfaction with worse scores in patients with nasal polyposis, asthma and AERD. Retronasal olfaction scores correlate with degree of inflammation of the olfactory cleft. Retronasal olfaction correlated strongly with orthonasal olfaction and

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patient-reported smell and taste metrics, though orthonasal olfaction may have a stronger correlation with these metrics.

Keywords

chronic rhinosinusitis; olfaction disorders; smell; taste; quality of life

Introduction

Most people are familiar with orthonasal olfaction which occurs during sniffing, wherein odorant-containing air passes in an anterior-to-posterior direction over the olfactory mucosa. Traditional psychophysical olfactory tests assess orthonasal olfaction and are utilized in the vast majority of olfactory research in chronic rhinosinusitis (CRS). However, retronasal olfaction is felt to be a critical component to the overall experience of food. Retronasal olfaction refers to odorant containing air moving from the oral cavity into the nasal cavity and over the olfactory mucosa. Odorants emanating from food particles would thus be smelled and this information combined with taste and physical perception to inform an overall “flavor” for that food or drink. Studies have shown retronasal olfaction to be distinct from orthonasal testing utilizing magnetic resonant imaging¹ and both electrophysiological^{2,3} and psychophysical testing.³ This distinction has been attributed to possible differences at the olfactory bulb and even at cerebral levels.³ In the setting of CRS, Landis et al. reported better retronasal olfaction than orthonasal olfaction in patients with CRS with nasal polyps (CRSwNP), attributing differences to mechanical obstruction of the anterior olfactory cleft from polyp burden⁴. However, studies simultaneously exploring both orthonasal and retronasal olfaction and their association with patient perceptions are lacking.

The meaning of the terms “taste” and “flavor” are often interchanged in the lexicon of the general population. Taste, or gustatory function, formally refers to the ability to detect sweet, sour, salty, bitter or umami substances when placed into the mouth. On the other hand, flavor can be defined as the blend of taste, smell, and physical sensations evoked by a substance when placed in the mouth. Patients with CRS often complain of alterations in the “taste” or “flavor” of food and drink, commonly interchanging these descriptors. Considering that olfactory dysfunction is a cardinal symptom of CRS, it is logical that loss of smell may be the main underlying driver in the subjective experience of food and drink for these patients.

The overall goal of this study was to better understand the contribution of retronasal olfactory dysfunction to patient-perceived alterations in the experience of foods. Specifically, we hypothesized that retronasal olfaction might better correlate with patient experience of “taste/flavor” than orthonasal olfaction. The specific objectives of this study were to 1) assess retronasal olfaction in patients with CRS, 2) determine the relationship between orthonasal and retronasal olfaction, 3) assess the influence of demographics, comorbid conditions, and disease severity on retronasal olfaction, and 4) determine the effect of retronasal olfaction on patient-perceived outcomes.

Materials and Methods

Recruitment and study population

Following institutional review board approval and informed consent, adult CRS patients, 18 years or older were prospectively enrolled. All participants fulfilled diagnostic criteria for CRS according to the Clinical Practice Guideline of the American Academy of Otolaryngology–Head and Neck Surgery.⁵ Exclusion criteria included pregnancy, sinus surgery within the last 3 months, and neurologic conditions.

Olfactory measures

Orthonasal olfaction—Orthonasal olfactory testing was performed using the Sniffin' Sticks test (Burghart Instruments, Wedel, Germany). The test battery included odor threshold, odor discrimination, and odor identification, each scored out of a possible 16 points.⁶ A "composite threshold-discrimination" (TDI) score, which ranged from 1–48 was then obtained by summing up all three scores.

Retronasal olfaction—Retronasal olfaction was tested using odorized powders presented to the oral cavity, as previously described.^{4,7} The retronasal test consisted of twenty grocery store condiments and food items that were available in powder form or odorized powders used in the food industry (Givaudan Flavors Corporation, IL, Chicago). The majority of items overlapped with those utilized in prior studies; however, given expected cross-cultural differences, several items were replaced with foods common to the southern United States (Table 1). These flavors were applied to the mid-posterior tongue using 50–90mg polystyrene mini scoops (Liftmode, Illinois, Chicago). Prior to application, patients pinched their nose, and were only allowed to unblock it after the powder was placed in the oral cavity and mouth closed. The mouth was kept closed until selection of the powder's odor was done using a forced multiple-choice paradigm with three distractor items. Patients rinsed their mouths with tap water after identification of each odor. Total retronasal scores were obtained by adding the number of correct identifications. This ranged from 0–20.

Nasal endoscopy

Sino-nasal endoscopy was performed and scored using the Olfactory Cleft Endoscopy Scale (OCES) as previously described,⁸ by physicians who were blinded to the patient's olfactory data. Patients were classified as having CRS with nasal polyps (CRSwNP) or CRS without nasal polyps (CRSSNP) based on nasal endoscopy.

Patient-reported outcome measures

Participants rated their overall sinus-specific quality-of-life (QOL) using the 22-item Sino-Nasal Outcome Test (SNOT-22), which includes a single question related to the sense of "smell/taste". The SNOT-22 contains 22 questions each scored 0–5 (total score range, 0–110), with higher scores representing more severe QOL impact.⁹ Olfactory-specific QOL was assessed using the previously validated, short, modified version of the Questionnaire of olfactory disorders (QOD-NS).¹⁰ This instrument consists of 17 negative statements graded from 0–3 for maximum score of 51 (higher scores reflected a worse QOL). The overall QOD-NS score was also broken down into subdomains, including social, eating, anxiety,

and annoyance. Perceived chemosensory dysfunction was assessed using the Chemosensory Complaint Score questionnaire (CCS).¹¹ This survey consists of questions pertaining to taste and smell. Scores ranged from 0–10 for the taste component and 0–6 for the smell component. Both scores were added to give the total chemosensory complaint score, with higher scores representing worse taste/smell.

Statistical Analysis

Data analysis was performed using SPSS 23.0 (IBM Corporation, Armonk, NY). Descriptive statistics (means, standard deviations, percentages, etc.) were used where applicable. Pearson correlation coefficients were used to characterize the associations between orthonasal and retronasal olfactory scores. Differences in retronasal olfaction across subgroups were compared using independent t-tests followed by multivariable regression. *p* values of 0.05 were considered statistically significant.

Results

Demographics

A total of 69 patients were enrolled of which 42% were CRsNP and 58% CRSwNP (Table 2). The average age of the cohort was 51.8 (range 20–77) and just under half were female (44.9%). Total SNOT-22 scores averaged 39.8 (SD = 24.8, range 0 – 97), indicating an overall moderate level of severity and a range including both asymptomatic and very symptomatic patients. See Table 2 for baseline demographics.

Retronasal olfaction and its relationship with orthonasal function

The average retronasal olfaction score for the cohort was 11.45 ± 4.12 (range 3 – 20). There was a strong correlation between retronasal score and orthonasal score as determined by total TDI (Figure 1). Similarly, there were strong correlations between retronasal score and orthonasal subscores, including threshold, discrimination, and identification (Figures 1a–d). Statistically significant differences were seen in retronasal scores when divided into anosmic, hyposmic and normosmic categories using TDI cut-offs (Figure 2).

Influence of demographics, comorbid conditions, and CRS disease severity metrics on retronasal olfaction

The relationship between retronasal olfaction and demographic, comorbid and disease severity factors was explored using bivariate analysis (Table 3). There were no gender differences in mean retronasal scores (11.3 ± 4.4 in males vs 11.7 ± 3.7 in females, $p=0.7$). Similarly, retronasal scores did not correlate with age or race.

The average retronasal olfaction score was significantly worse in patients with asthma (10.3 ± 4.0 vs 12.4 ± 4.1 ; $p=0.04$), aspirin intolerance (8.4 ± 3.2 vs 11.9 ± 4.1 ; $p=.02$), and nasal polyp status (10.2 ± 4.1 vs 13.2 ± 3.5 ; $p=0.002$). There was no association with gastroesophageal reflux disease (GERD), diabetes, depression, allergic rhinitis, obstructive sleep apnea (OSA) or smoking history (Table 3). Retronasal olfaction correlated with Olfactory Cleft Endoscopy Score ($r=-.42$, $p<0.001$). This correlation was only significant in CRSwNP and not in CRsNP ($r=-0.35$, $p<0.03$ vs $r=-.16$, $p=0.43$ respectively; Table 4).

Multivariate regression analysis showed that OCES was the only independent predictor of retronasal olfaction, with both aspirin intolerance and nasal polyp status losing significance when combined with OCES in the model. For every point increase in the OCES, the retronasal score decreased by 0.43 points (95% CI= -0.66 to -0.20, $p<0.001$).

Retronasal olfaction and patient-reported outcome measures

Though there was no correlation between retronasal olfaction and total SNOT-22 scores, there was significant correlation between retronasal olfaction and olfactory-specific QOL as measured by the QOD-NS ($r=-0.41$; $p<0.001$) (Table 5). Similar correlation was found between retronasal olfaction and all the QOD subdomains, including the “eating” subdomain ($r=-0.43$; $p<0.001$), the “annoyance” subdomain ($r=-0.40$; $p=0.001$), the “social” subdomain ($r=-0.35$; $p=0.003$), and the “anxiety” subdomain ($r=-0.26$ ($p=0.032$)). Retronasal scores also strongly correlated with the smell/taste question of the SNOT-22 ($r=-0.60$; $p<0.001$) and the CCS smell score ($r=-0.49$ $p<0.001$), but not the CCS taste score ($r=-0.21$; $p=0.08$). Correlations between orthonasal testing (TDI) and patient-reported outcomes measures essentially mirrored those seen with retronasal olfaction (Table 5). In many instances, the point-estimates suggested greater correlation between orthonasal olfaction and the patient-reported smell and taste measures than between retronasal testing and those same measures.

Discussion

The ability to identify differences in food flavors is thought to depend mostly on the retronasal movement of air from the mouth into the olfactory cleft. Despite olfactory dysfunction being a cardinal feature of sinusitis, few studies have systematically examined retronasal olfaction in patients with CRS. In this cohort, patients with CRS were found to have deficits in retronasal olfaction, with worse scores in those with polyps, asthma, or AERD. Strong correlations between orthonasal olfaction and retronasal olfaction were seen, and retronasal olfactory scores correlated with patient-reported perception of smell using various survey instruments.

Differences might be expected between retronasal and orthonasal olfaction if the mechanism of olfactory loss is mainly related to nasal airflow. Specifically, inflammation or polyps located in the anterior nasal cavity might be more likely to impact orthonasal airflow as compared to retronasal, or vice versa. In a study by Landis et al., examining patients with nasal polyposis, retronasal function was better than orthonasal function, suggesting that polyps may differentially impede airflow into the olfactory cleft.³ However, in the current study, orthonasal and retronasal olfaction were highly correlated and there was no indication that retronasal olfaction was spared in patients with nasal polyps. Rather, olfactory cleft endoscopy scores independently correlated with retronasal olfaction, suggesting that inflammation or blockage of the olfactory cleft drives olfactory loss as opposed to changes in airflow alone. Mucosal inflammation of the olfactory cleft would be expected to impact orthonasal and retronasal olfaction to a similar degree, since it would be independent of nasal airflow directionality. Certainly, it should be kept in mind that the location of polyposis

was not specifically assessed. Therefore, it remains possible that focal polyp disease could differentially impact orthonasal versus retronasal olfaction.

One of the main hypotheses of this study was that retronasal olfactory scores would better correlate with patient-reported metrics that involve the concept of taste or flavor. Although retronasal scores did significantly correlate with the QOD eating domain and the CCS total score, the strength of these correlations appeared weaker than what was seen with orthonasal TDI scores though this was not compared statistically. These results were surprising and their explanation not entirely clear. It is possible that orthonasal olfaction contributes more to the experience of food than we had initially expected. One can imagine that orthonasal olfaction is important in anticipation of food. Irrespective of this, our data suggests that the addition of retronasal testing does not add much above and beyond TDI testing in this patient group.

The strengths of this study include simultaneous assessment of retronasal olfaction, orthonasal olfaction, and patient-reported metrics across a cohort of patients meeting criteria for CRS. However, several important caveats must be kept in mind. The study enrolled patients from a tertiary rhinology clinic, many of which had prior sinus surgery and nasal polyps. Patients may thus differ from those with less severe disease or those who have not had prior surgery. Although patient-reported metrics utilized in this study related to olfaction, taste and eating, they were not specifically designed to tease out subtle differences between taste, smell, and flavor. Additionally, specific questions related to food choices, overall diet, and weight were not assessed and thus one cannot say with certainty that orthonasal olfaction is always a better predictor than retronasal testing. Lastly, the study was cross-sectional in nature. It remains unknown how retronasal olfaction changes after specific treatments, such as sinus surgery.

Conclusion

Retronasal olfactory function is diminished in patients with CRS, particularly those with polyps, asthma, and AERD. The degree of inflammation visible on the olfactory cleft independently correlates with retronasal olfaction, including patients with and without polyps. Strong correlation was found between retronasal and orthonasal olfactory scores. Although retronasal olfaction correlated with several different patient-reported smell and taste metrics, these correlations appeared weaker than those seen with orthonasal testing.

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Figure 1.

a) Retronasal olfaction scores compared to total TDI and retronasal scores compared to individual b) threshold, c) discrimination and d) identification scores

Figure 2.
Comparison of Retronasal Olfaction Scores across the TDI subgroups

Table 1

Odorized powder used for retronasal olfactory testing.

	Target Items	Distractor Items
1	Grapefruit	Cherry, Lemon, Orange
2	Bread	Pizza, Garlic, Milk
3	Milk	Vanilla, Banana, Honey
4	Strawberry	Tangerine, Grape, Apple
5	Orange	Raspberry, Cherry, Strawberry
6	Onion	Smoked ham, Salami, Chives
7	Cinnamon	Cocoa, Caramel, Honey
8	Apple	Orange, Strawberry, Grape
9	Mushrooms	Bread, Fish, Wine
10	Banana	Mustard, Curry, Ginger
11	Coffee	Cocoa, Cinnamon, Honey
12	Smoked ham	Bread, Fish, Chives
13	Peach	Banana, Apple, Watermelon
14	Ginger	Mustard, Cinnamon, Curry
15	Grape	Orange, Lemon, Apple
16	Vanilla	Honey, Cherry, Banana
17	Curry	Cheese, Mustard, Cucumber
18	Cocoa	Caramel, Tea, Coffee
19	Garlic	Onion, Chives, Ham
20	Cheese	Grapes, Peach, Pineapple

Bold items – Substituted food items common to the Southern United States

Table 2

Baseline characteristics (N = 69)

		Mean $\pm$ SD	N (%)
Demographics			
Age		51.8 $\pm$ 16.7	
Gender	Male		38 (55.1)
	Female		31 (44.9)
Race	Black		17 (24.6)
	White		52 (75.4)
Ethnicity	Hispanic		4 (5.8)
	Non-Hispanic		65 (94.2)
Comorbid conditions			
Diagnosis	CRSsNP		29 (42.0)
	CRSwNP		40 (58.0)
Previous sinus surgery			60 (87.0)
Asthma			30 (43.5)
History of Allergies			49 (59.4)
AERD			8 (11.6)
GERD			24 (34.8)
Diabetes			6 (8.6)
Depression			19 (27.5)
OSA			16 (23.1)
Smoking history	Never Smoker		51 (73.9)
	Former Smoker		15 (21.7)
	Current Smoker		3 (4.3)
CRS Disease Severity			
OCES		4.0 $\pm$ 4.0 (0–14)	
SNOT22		39.9 $\pm$ 24.8 (0–97)	

AERD = aspirin exacerbated respiratory disease; CRSsNP = chronic rhinosinusitis without nasal polyps; CRSwNP = chronic rhinosinusitis with nasal polyps; GERD = gastroesophageal reflux disease; OSA = obstructive sleep apnea; OCES - Olfactory Cleft Endoscopy Score; SD = standard deviation; SNOT-22 = 22-item Sino-Nasal Outcome Test.

Table 3

Comparison of Retronasal Olfaction Scores across demographics, comorbidity, and disease characteristics (N=69)

Demographics		<i>r</i>	Mean ± SD	<i>p</i>
Age		-.07		.57
Gender	Male		11.3 ± 4.4	.70
	Female		11.7 ± 3.7	
Race	White		11.8 ± 4.4	.29
	Black		10.5 ± 3.2	
Comorbid Conditions		Present (Mean ± SD)	Absent (Mean ± SD)	<i>p</i>
Asthma		10.3 ± 4.0	12.4 ± 4.1	.04
Allergy (Testing Confirmed)		11.0 ± 4.2	12.2 ± 4.0	.23
AERD		8.4 ± 3.2	11.9 ± 4.1	.02
GERD		12.2 ± 4.1	11.0 ± 4.1	.27
Diabetes		11.0 ± 2.0	11.5 ± 4.3	.62
Depression		11.4 ± 4.0	11.5 ± 4.2	.97
OSA		12.4 ± 3.7	11.2 ± 4.2	.31
Former Smoker		11.3 ± 3.7	11.4 ± 4.4	.94
CRS Severity Measures		<i>r</i>	Mean ± SD	<i>p</i>
Olfactory Cleft Endoscopy Score		-.42		<.001
Diagnosis	CRSwNP		10.2 ± 4.1	.002
	CRSSNP		13.2 ± 3.5	

* Bold values are significant.

AERD = aspirin exacerbated respiratory disease; CRSSNP = chronic rhinosinusitis without nasal polyps; CRSwNP = chronic rhinosinusitis with nasal polyps; GERD = gastroesophageal reflux disease; OSA = obstructive sleep apnea; OCES - Olfactory Cleft Endoscopy Score; SD = standard deviation; SNOT-22 = 22-item Sino-Nasal Outcome Test.

Table 4

Retronasal and orthonasal olfaction vs. disease severity metrics by nasal polyp status

	Retronasal vs OCES $r(p)$	TDI vs OCES $r(p)$
All Participants N = 69	-.42(<.001)	-.52(<.001)
CRSwNP N = 40	-.35(.03)	-.54(<.001)
CRSsNP N = 29	-.16 (.43)	-.23 (.26)

* Bold values are significant.

OCES = Olfactory Cleft Endoscopy Score; CRSsNP = chronic rhinosinusitis without nasal polyps; CRSwNP = chronic rhinosinusitis with nasal polyps.

Table 5

Correlation between retronasal olfaction and overall sinus-specific Quality of Life

	Retronasal Olfaction $r(p)$	Orthonasal Olfaction (TDI) $r(p)$
CCS Taste Score	-.21 (.08)	-.43 (<.001)
CCS Smell Score	-.49 (<.001)	-.49 (<.001)
CCS Total Score	-.35 (.003)	-.49 (<.001)
QOD NS Total	-.41 (<.001)	-.56 (<.001)
QOD Eating Domain	-.42 (<.001)	-.58 (<.001)
QOD Social Domain	-.35 (.003)	-.44 (<.001)
QOD Anxiety Domain	-.26 (.03)	-.39 (.001)
QOD Annoyance Domain	-.40 (.001)	-.56 (<.001)
SNOT22 Total	-.16 (.18)	-.23 (.06)
Sense of smell/taste in SNOT-22	-.60 (<.001)	-.76 (<.001)

* Bold values are significant.

QOD = Questionnaire for Olfactory Disorders; NS = negative statements; QOD Eating Domain == Questionnaire for Olfactory Disorders Eating Domain; CCS = Chemosensory Complaint Score; SNOT-22 = 22-item Sino-Nasal Outcome Test.