Fluctuating Olfactory Sensitivity and Distorted Odor Perception in Allergic Rhinitis

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Objective: To characterize the relationship between allergic rhinitis, the severity and duration of nasal disease, olfactory function, and self-reported olfactory symptoms, including fluctuations or distortions in odor perception.

Design: Assessment of olfactory function and symptoms of 90 patients with allergic rhinitis.

Setting: A clinic of a university teaching hospital and research facility.

Patients: Sixty patients who presented to the Taste and Smell Clinic who had positive allergy test results and 30 patients who presented to the Allergy-Immunology Clinic. The Taste and Smell Clinic patients were grouped by nasal-sinus disease status (30 without chronic rhinosinusitis or nasal polyps, 14 with chronic rhinosinusitis but without polyps, and 16 with nasal polyps).

Main Outcome Measures: Subjective olfactory symptom questionnaire and objective olfactory function tests.

Results: The Allergy-Immunology Clinic patients were diagnosed as being normosmic and the Taste and Smell Clinic patients as being hyposmic or anosmic with olfactory loss that increased significantly with nasal-sinus disease severity. Comparisons with normative data confirm that olfactory scores observed in all groups were significantly lower than expected because of the aging process alone. The self-reported duration of olfactory loss increased significantly with nasal-sinus disease severity. The Taste and Smell Clinic patients without chronic rhinosinusitis or nasal polyps reported the greatest incidence of olfactory distortions and olfactory loss associated with upper respiratory tract infections.

Conclusions: There appears to be a continuum of duration and severity of olfactory loss in allergic rhinitis that parallels increasing severity of nasal-sinus disease. As a result of the increased frequency of respiratory infection associated with allergic rhinitis, these patients are at risk for damage to the olfactory epithelium.


A RECENT study of topical corticosteroid nasal spray treatment of anosmia in patients with severe nasal-sinus disease suggests that nasal airway obstruction is not the only cause of olfactory loss in these patients.1 Following treatment, signs of disease (mucosal thickening, polypoid changes, and polyps) decreased significantly for all patients in the study. While olfactory function likewise improved significantly for 59% of the patients, the sense of smell in the remaining 41% did not change at all.1 Interestingly, one indicator of the successful olfactory response to treatment was a self-reported history of fluctuations in olfactory sensitivity, which could be interpreted as an indication of a functioning olfactory epithelium in an otherwise anosmic patient.1

The distortion of odors is another symptom reported by patients with olfactory loss, particularly those patients whose olfactory problems began with head trauma or upper respiratory tract infections.2-5 In the case of patients who were rendered anosmic by head trauma, these odor distortions have been interpreted as reflecting the regeneration of damaged or severed olfactory connections and can precede recovery of function.2,3 Distortions in olfactory function have also been associated with smell loss secondary to upper respiratory tract infection.3 Since there is evidence that the olfactory epithelium has been damaged in these patients,2 presumably as a result of the viral infection, it is possible that the odor distortions represent malfunction of a damaged epithelium and/or a phase of regeneration of the olfactory receptors.

Allergic rhinitis is associated with a loss of smell6-10 that is less severe than the smell loss associated with chronic rhinosinusitis and nasal polyps.10 The present
SUBJECTS AND METHODS

SUBJECTS

This study was approved by the Institutional Review Board of the University of Connecticut Health Center, Farmington. All subjects gave informed consent for participation.

Taste and Smell Clinic Patients

Study subjects included 60 Taste and Smell Clinic (TASC) patients with self-described olfactory loss and confirmed allergic rhinitis. Of 363 consecutive new patients evaluated at the TASC, 103 presented with complaints of olfactory dysfunction, had a history of nasal symptoms, and were referred for allergy testing. Seventy (68%) of these patients were considered to have allergic rhinitis and were therefore eligible for inclusion in this study; they reported episodic or continuous nasal congestion, rhinorrhea, postnasal drip, and sneezing and had at least 1 positive allergy skin test result that was relevant to their history, as described below. Ten patients were excluded from the study either because they were involved in litigation (n = 7) or because congenital anosmia could not be ruled out (n = 3).

Allergy-Immunology Clinic Patients

A group of 30 University of Connecticut Health Center Allergy-Immunology Clinic (AC) patients, all of whom had a diagnosis of allergic rhinitis and none of whom had chronic rhinosinusitis or nasal polyps, served as a comparison group. These patients were sampled in late spring and summer.

study compares patients with allergic rhinitis whose primary complaint is olfactory dysfunction with those whose primary complaints are of nasal and respiratory symptoms. This comparison is made to characterize the relationship between the severity and duration of nasal disease and the possible damage to the olfactory system.

RESULTS

HISTORY AND PHYSICAL EXAMINATION

The 60 TASC patients included 35 men and 25 women aged 18 to 74 years (mean ± SD, 51.4 ± 12.4 years). The 30 AC patients included 10 men and 20 women aged 27 to 70 years (mean ± SD, 39.5 ± 10.0 years). Table 1 shows the results of the nasal-sinus disease classification of the TASC patients (TASC-0, n = 30; TASC-S, n = 14; and TASC-P with [n = 12] or without [n = 4] chronic rhinosinusitis, n = 16). The AC patients were significantly younger than the TASC patients (P < .001). There were no differences in age among the 3 TASC patient groups, but there was a significant difference in sex distribution (X² = 9.95, P = .007); only 2 (12%) of the 16 patients with polyps were women, compared with 5 (36%) of the 14 patients with chronic rhinosinusitis and 12 (40%) of the 30 patients with neither chronic rhinosinusitis nor polyps.

MEASURES

Patient History

The questionnaire administered to all patients included subjective assessment of olfactory function, duration of olfactory problem, history of perceiving distorted odors, fluctuations in olfactory sensitivity, and presence of phantom odors (perceiving odors in the absence of any external odor stimulus). Subjects were questioned about problems associated with olfactory loss, including a history of nasal polyps, sinus surgery, head trauma, toxic exposures, or loss of olfactory function associated with upper respiratory tract infections. Subjects were asked to estimate the date of onset of their symptoms of allergic rhinitis. They were also questioned about their history relevant to allergic rhinitis, including exposure to perennial allergens (eg, dogs, cats, mites, and fungi) or irritants (eg, tobacco and volatile organic compounds) or a history of asthma.

Physical Examination

All TASC patients underwent examination of the nasal cavity with a speculum followed by endoscopic rhinoscopic examination. Visibility of the olfactory clefts was noted. Computed tomographic (CT) scans of the paranasal sinuses were obtained when chronic rhinosinusitis was suspected; it was confirmed if the patient had at least 2 of the clinical signs (rhinorrhea, postnasal drip, or cough for more than 3 months) and if the CT scan showed mucosal thickening or opacification of 1 or more sinuses. The results of the rhinoscopic examination and CT scan were used to classify the TASC patients into 3 groups by increasing severity of nasal-sinus disease (TASC-0 patients had no evidence of sinusitis or nasal polyps, TASC-S patients had

OLFACTORY FUNCTION

Average olfactory function decreased significantly with increasing signs of nasal disease, as reflected in the odor identification scores (F3,84 = 44.83, P < .001) and the butanol threshold scores (F3,84 = 27.10, P < .001) (Figure 1). As expected, there was a significant correlation between the left and right nostril olfactory scores (r = 0.90, P < .001). The AC patient group was normosmic (mean ± SE composite score, 6.00 ± 0.22), although the 9 AC patients who complained of olfactory dysfunction were diagnosed as being mildly hyposmic (mean ± SE composite score, 5.67 ± 0.43). The TASC patients, who all complained of olfactory dysfunction, were severely hyposmic (mean ± SE TASC-0 score, 3.11 ± 0.45) and anosmic (mean ± SE TASC-S score, 0.93 ± 0.48; mean ± SE TASC-P score, 0.52 ± 0.28), with olfactory loss significantly increasing with nasal-sinus disease severity (P = .05).

Among the TASC patients, there was a weak association between the presence of nasal sinus disease and the lack of olfactory cleft visibility (X² = 4.36, P = .04). The frequency of visible olfactory clefts was significantly lower among the TASC patients with signs of nasal-sinus disease (TASC-S and TASC-P groups combined). One or both clefts were visible in only 19 (63%) of these patients, compared with 26 patients (87%) in the TASC-0 group (Table
evidence of sinusitis from either the CT scan or rhinoscopic examination but no polyps, and TASC-P patients had evidence of polyps on rhinoscopic examination).

Olfactory Tests

The test of olfactory function that was developed and used by the TASC consists of 2 parts: a test of detection threshold sensitivity to n-butyl alcohol (up to 4% 1-butanol by volume) and a test of odorant identification using common household items (eg, baby powder, coffee, chocolate, and peanut butter).\(^{11}\) Nostrils are tested separately. The performance scores from the threshold and identification tests are reported on an 8-point scale (0-7); the diagnostic range is 0 to 1.75 for anosmia, 1.75 to 6.0 for hyposmia, and 6.0 to 7.0 for normosmia. Since previous studies have shown a significant correlation between nostrils on the TASC test,\(^{11,12}\) results are reported as the mean of the 2 nostral scores.

Allergy Tests

Skin testing included puncture tests and, if the results were negative, intradermal tests. For punctures, a bifurcated needle (ALO Laboratories, Columbus, Ohio) was used. Perennial allergens tested were Dermatophagoides farinae (10 000 allergenic units [AU] per milliliter), Dermatophagoides pteronyssinus (10 000 AU/mL), Alternaria (1.20 wt/vol), Aspergillus (1.20 wt/vol), Cladosporium (1.20 wt/vol), Penicillium mix (1.20 wt/vol), cat washings and pelt (50 000 AU/mL and later 5000 bioequivalent AU/mL), and dog epithelia (1.20 wt/vol). Seasonal allergens were those relevant to the northeastern United States: white birch (1.20 wt/vol), maple mix (1.20 wt/vol), white oak (1.20 wt/vol), timothy grass (1.20 wt/vol), June grass (1.20 wt/vol), and ragweed mix (short and giant, 138 antigen E units per milliliter, 1.20 wt/vol). The presence of a wheal diameter at least 3 mm larger than that of the saline control with surrounding erythema noted 20 minutes after placement of the test allergen was considered a positive puncture test result. When puncture test results were negative, intradermal injections of 0.02 mL (1:1000 wt/vol for fungi, pollen, and dog; 300 AU/mL for mite; and 500 AU/mL or 50 bioequivalent AU/mL for cat) were administered for relevant allergens. For intradermal tests, a wheal with a surrounding flare at least 5 mm in diameter and at least 3 mm in diameter larger than that of the saline intradermal control was considered a positive result.

Data Analysis

Descriptive statistics are reported as mean ± SE unless otherwise noted. Nonparametric tests (\(\chi^2\) analysis) were used to compare the frequency distributions of the subjective assessment of symptoms and the history of olfactory problems, rhinitis, other problems associated with olfactory dysfunction, and skin test results. Smell test scores (mean of the smell test scores of the left and right nostrils) used in the analyses included the threshold test score, odor identification test score, and a composite score based on the average of the threshold and odor identification scores. Analyses of variance and independent sample \(t\) tests were used to compare the TASC patients with the AC patients. In addition, the olfactory test results from patients in this study were compared with olfactory scores on the TASC odor identification and butanol threshold tests collected from 108 control subjects aged 25 to 84 years. Subjects who report normal olfactory ability have been recruited since 1981 to serve as controls for the TASC olfactory tests.

Figure 4 shows the frequency distribution of symptoms of olfactory dysfunction for the 30 AC patients, the 30 TASC-0 patients, and the 30 combined TASC-S and TASC-P patients. Compared with the other 2 patient groups, TASC-0 patients reported a greater incidence of olfactory distortions (14 [47%], compared with 3 [10%] of 30 patients in each of the other groups \(\chi^2 = 15.56, P<.001\)) (Figure 4). Fluctuations were reported significantly more frequently by the combined TASC-S and TASC-P group (22 patients [73%], compared with 10 patients [33%] in the AC group and 13 patients [43%] in the TASC-0 group \(\chi^2 = 10.40, P = .006\) (Figure 3). The incidence of reports of phantom odors was not significantly different among the patient groups.

For each of these symptoms of olfactory dysfunction, we explored the association of olfactory cleft visibility within nasal-sinus disease status and found that for TASC patients without nasal-sinus disease, odor distortions were reported significantly more often by patients with olfactory clefts visible than by those in whom neither cleft was visible \(\chi^2 = 4.04, P = .04\). In fact, only 4 (13%) of the TASC-0 patients had neither olfactory cleft visible and none of these patients reported olfactory distortions.

Items from patient medical histories that were associated with olfactory loss are shown in Figure 5. Patients in the combined TASC-S and TASC-P group had...
There was little difference in skin test results among the 3 patient groups. Allergy test results showed that there were no differences when allergens were grouped as perennial (on average, 87% of each patient group tested positive for mite, cat, dog, and/or fungi) or seasonal (on average, 84% of each patient group tested positive for grass, trees, and/or ragweed). However, there were significant differences for some individual tests. Fewer TASC patients tested positive for dog (16 [53%] TASC-0 and 8 [28%] TASC-S/TASC-P patients compared with 21 [70%] AC patients; \( \chi^2 = 10.75, P = .005 \)) and for ragweed (17 [57%] TASC-0 and 15 [50%] TASC-S/TASC-P patients compared with 26 [87%] AC patients; \( \chi^2 = 9.99, P = .007 \)).

**SKIN TESTS**

We examined the olfactory function of patients with allergic rhinitis. Our study sample included patients from an AC, whose primary complaint did not include olfactory dysfunction, and patients from a TASC, whose primary complaint was olfactory loss. We found that the TASC patients were older, had had nasal symptoms longer, had lower olfactory function scores, and were more likely to have histories of nasal-sinus disease than the AC patients. We also observed that men and women were not uniformly distributed among the TASC nasal-sinus disease...
and olfactory function is known to decline with age, a factory problems. Although the AC patients were younger patients with allergic rhinitis alone tend to have milder ol-
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degree of olfactory loss suffered by TASC patients (Fig-
consistent with our previously published studies; pa-
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chronic rhinosinusitis to those with nasal polyps (the ma-
us are also significantly lower than expected for their age
arily, the olfactory function scores for the AC patients
low the scores predicted for people their age. Interest-
groups. While there were slightly more women than men in the TASC-0 (allergic rhinitis only) group, men out-
numbered women 2 to 1 in the TASC-S (chronic rhino-
sinusitis) group and 7 to 1 in the TASC-P (nasal polyps) group. This finding is consistent with a previous study of 445 patients with nasal polyps in which men outnumbered women 2 to 1.12
Among all patients with allergic rhinitis, there appears to be a continuum of olfactory loss from patients without additional nasal-sinus disease to those who have chronic rhinosinusitis to those with nasal polyps (the majority of whom also have sinusitis). These findings are consistent with our previously published studies; patients with allergic rhinitis alone tend to have milder ol-
factory problems. Although the AC patients were younger and olfactory function is known to decline with age, a comparison with age-corrected predicted scores illus-
trates that the aging process alone cannot account for the degree of olfactory loss suffered by TASC patients (Fig-
ures 1 and 2). It is clear from Figure 1 that the olfactory
function scores of the TASC patients are substantially below the scores predicted for people their age. Interest-
ingly, the olfactory function scores for the AC patients are also significantly lower than expected for their age group (Figure 2), although their diagnostic category re-
ains normosmic.
Nasal obstruction, as measured by olfactory cleft vis-
ibility (Table 1), is significantly although weakly asso-
ciated with nasal-sinus disease. However, we did not find an association between cleft visibility and olfactory function in the present study or in our earlier study. At best, cleft visibility is a crude measure of nasal obstruction; however, other studies using other measures (eg, rhinomanometry) have also been unable to demonstrate an association between obstruction and olfactory dysfunction.
It is interesting that the duration and severity of ol-
factory loss is associated with the severity of nasal-sinus disease, whereas the duration of nasal symptoms alone is not. Since olfactory loss may be considered to be one of the signs of nasal-sinus disease, our results suggest that the 9 patients in the AC group who had already com-
plained of olfactory problems may be among the first in

**Figure 2.** Olfactory function test scores by age in the normal population. Regression equations for the butanol threshold (BA, solid line) and odor identification (ID, dashed line) test scores, based on data from normal control subjects (n = 108; age range, 25-84 years), are BA = 7.74 – 0.036 × age (years) and ID = 7.86 – 0.028 × age (years). Allergy-Immunology Clinic (AC) scores fell below the age-related norms, as indicated for both the BA (filled symbol) and ID (open symbol) tests.

**Figure 3.** Mean self-reported duration of olfactory loss and nasal symptoms for patients with allergic rhinitis. Duration of olfactory loss was significantly longer for Taste and Smell Clinic (TASC) patients with signs of nasal-sinus disease (TASC patients with chronic rhinosinusitis but without polyps [TASC-S] and TASC patients with nasal polyps with or without chronic rhinosinusitis [TASC-P]) than for TASC patients with no signs of nasal-sinus disease [TASC-O]). Duration of nasal symptoms was significantly shorter for Allergy-Immunology Clinic (AC) patients than for any TASC patient group. Asterisk indicates P = .05. T-shaped bars indicate S.E.

**Figure 4.** Frequency of olfactory symptoms reported by patients from the Allergy-Immunology Clinic (AC) or the Taste and Smell Clinic (TASC). TASC-0 indicates TASC patients without chronic rhinosinusitis or nasal polyps; TASC-S, TASC patients with chronic rhinosinusitis; and TASC-P, TASC patients with polyps. Distortions and fluctuations in olfaction were reported significantly more frequently by the indicated groups; asterisk indicates P = .002.

**Figure 5.** Frequency of positive findings in the medical history of patients from the Allergy-Immunology Clinic (AC) or the Taste and Smell Clinic (TASC). TASC-0 indicates TASC patients without chronic rhinosinusitis or nasal polyps; TASC-S, TASC patients with chronic rhinosinusitis; and TASC-P, TASC patients with polyps. Significant differences between TASC and AC patients are indicated (asterisk) for a history of polyps (P < .001), sinus surgery (P = .004), and viral upper respiratory infection (P < .001).

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this group to develop more serious signs of nasal-sinus disease in the future.

A significant number of TASC patients in this study reported a history of viral respiratory tract infections, which perhaps is to be expected, since allergic rhinitis has been shown to be associated with frequent respiratory tract infections.14 There is evidence from biopsy specimens of human olfactory mucosa5 that damage—perhaps irreversible damage—can occur as a result of these infections and that the degree of damage is correlated with olfactory dysfunction. Distortions in olfactory perception, which could be a consequence of epithelial damage, tend to be reported by patients whose olfactory loss is associated with viral respiratory tract infections.7,8

Among the patients in our study, the highest incidence of olfactory distortions and history of upper respiratory tract infection were reported by the patients with the lowest incidence of nasal obstruction, yet their olfactory function was significantly impaired. This suggests that the link between allergic rhinitis and olfactory loss may be caused in part by more frequent respiratory tract infections promoted by the pathophysiologic characteristics of allergic rhinitis, and not only by inflammatory diseases, such as nasal polypsis. This may also explain why, for a sizeable number of patients in our earlier study,1 topical nasal steroid treatment for olfactory loss associated with nasal-sinus disease failed.

Among our patients, the frequency of self-reported fluctuations in olfactory sensitivity increased with the increasing severity of nasal-sinus disease. However, the frequency of self-reported distortions in odor perception was highest in those with less serious disease (Figure 4). It is possible that odor distortions only occur during a phase of recovery following an upper respiratory tract infection (ie, perhaps a degenerating [or possibly regenerating] olfactory epithelium temporarily produces faulty odor perceptions).15 This might explain why the highest incidence of self-reported distortions was among patients in the TASC-0 group (Figure 4), which also had the highest incidence of olfactory loss associated with upper respiratory tract infections. The TASC-S/TASC-P group also reported histories of upper respiratory tract infections but not distortions. The distortions may have occurred in an earlier stage in the development of this group's nasal-sinus disease.

One of the limitations of our study is that the AC group in particular was a sample of convenience (ie, we offered olfactory function testing to everyone who came to the allergy clinic for treatment during the late summer). This could account for some of our results (eg, the younger age and the higher incidence of asthma in the AC group).

Our systematic examination of 90 patients with allergic rhinitis, including a series of 60 TASC patients, suggests that 2 details from a patient's history may help determine the most likely cause of their olfactory loss: patient reports of fluctuations in olfactory sensitivity are significantly associated with obstructive nasal-sinus disease, and patient reports of distorted olfactory perceptions are significantly associated with viral respiratory tract infections. In patients with allergic rhinitis, the duration and severity of olfactory loss are associated with more severe nasal-sinus disease. These patients are at increased risk for olfactory loss because allergic rhinitis promotes the development of repeated respiratory tract infections, which lead to damage to the olfactory epithelium.

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