

Short communication

Sense of smell in allergic and nonallergic rhinitis

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Hyposmia is a fairly common complaint in patients with long-continuing allergic or nonallergic rhinitis. Other factors such as aging, smoking, or nasal surgery may affect olfaction, but these have been little studied in rhinitis-related hyposmia. The purpose of this study was to measure and compare olfactory thresholds in 105 rhinitis patients and 104 healthy controls and to analyze possible relationships between the sense of smell and rhinitis, age, sex, smoking, prick-test results, nasal resistance, and history of nasal or paranasal surgery. The olfactory threshold was assessed with a commercially available kit of squeeze-bottle pairs. The most important variables associated with the sense of smell were determined with stepwise multiple regression analysis, and intergroup differences were assessed with analysis of variance. The reference interval of olfactory thresholds by age was estimated with regression analysis. Nasal resistance was measured by active anterior rhinomanometry. Age and rhinitis were the only variables with significant effect on the olfactory threshold in the whole series. Both the proportion of hyposmic persons and the degree of the impairment of the sense of smell were significantly higher in the rhinitis group than in the control group. The nonallergic patients' sense of smell was poorer than that of seasonal or perennial allergic rhinitis patients. A history of operations for nasal polyposis was associated with hyposmia, but operations for chronic maxillary sinusitis were not. Neither smoking habits nor sex were related to olfactory thresholds. In conclusion, hyposmia in rhinitis patients is partly attributable to age-related changes, but our results indicate that the disease itself impairs the sense of smell.

Key words: allergic rhinitis; hyposmia; nonallergic rhinitis; olfactory threshold; reference interval.

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Hyposmia is often reported in association with rhinitis in the literature (1, 2), though there are relatively few studies in which the sense of smell of rhinitis patients has been quantitatively assessed (3, 4). On the other hand, olfactory thresholds are known to be related to age, being markedly higher among elderly people (5). In studies of rhinitis patients, the influence of age has usually been neglected. Many other conditions affecting the upper respiratory tract may also influence the sense of smell; e.g., the duration of rhinitis symptoms, other present or earlier nasal disorders – which may require operations on the nose and paranasal sinuses – nasal airway resistance, atopy, smoking, habits, and asthma-like symptoms. In these conditions, the olfactory alteration is often caused by blockage of airflow to the olfactory receptors

(transport olfactory loss). Hyposmia can also be caused by destruction of the olfactory epithelium or damage of the olfactory nerves or the central olfactory pathways (sensorineural olfactory loss). Analyzing these items is essential when assessing the sense of smell in rhinitis patients. To determine the effect of these and other factors on the sense of smell, we have compared the olfactory thresholds of long-term rhinitis patients with those of healthy controls.

Material and methods

Subjects

Some 105 patients (61 women and 44 men, mean age 51 years, range 27–78 years) participated in the

study. The series was collected among patients enrolled in an earlier follow-up study of allergic or nonallergic rhinitis. All patients had initially been studied at our clinic in 1969–72 (6) because of chronic rhinitis, and 97 of them stated that they still had symptoms at the time of follow-up some 20 years later. The control group consisted of 104 subjects (56 women and 48 men, aged 17–71 years, mean 39 years) with no acute or chronic nasal complaints. Information on the onset and duration of rhinitis symptoms, present and past history of nasal disorders, operations on the nose and paranasal sinuses, smoking habits, and asthma-like symptoms was gathered with the help of a questionnaire completed by all subjects.

The study protocol was approved by the ethics committee of the clinic. All subjects gave their informed consent to participation in the study.

Sense of smell

The olfactory threshold was measured with a commercially available smell test kit (Olfacto-Labs, Berkeley, CA, USA). The method has been described in detail elsewhere (7, 8). In brief, sensitivity to odor was tested stepwise with phenylethyl methyl ethyl carbinol at 3.2 concentrations in nine pairs of polypropylene squeeze bottles, the control bottle in each pair containing the plain diluent. Subjects were asked to choose the bottle they thought contained the odorant, and the test was repeated three times at each step. The weakest concentration at which the subject picked the correct bottle all three times was accepted as the olfactory threshold. Numerically, the threshold was expressed as arbitrary logarithmic units (ALU), designated as "decismels" (dS) by the manufacturer, analogically with the audiologic decibel scale. The concentrations in use were –25, –15, –5, 5, 15, 25, 35, 45, and 55 ALU. In the statistical analyses, the value of 65 ALU was used for those who could not identify the strongest concentration. To avoid the possible effect of recent smoking on the result, an interval of at least 15 min was required between smoking and testing.

Nasal resistance

In conjunction with testing the sense of smell, nasal resistance was measured on each side at 150 Pa pressure and total nasal resistance (TNR) calculated for all patients. We used a RhinoComp[®] computerized active anterior rhinomanometer. To achieve a fairly normal distribution, the values of nasal resistance were logarithmically transformed, and these values were used in statistical analysis.

Allergy tests

Skin prick tests were performed with Soluprick[®] allergen solutions (ALK, Denmark). Some 22–26 common allergens were tested on all patients. The patient was considered prick-test positive, if at least one allergen elicited a wheal whose diameter was at least 3 mm larger than that of the negative control.

Statistical methods

Stepwise multiple linear regression analysis was used to examine the associations between olfactory threshold and age, presence of rhinitis, sex, and smoking in all subjects and between olfactory threshold and age, diagnosed asthma, sex, ethmoidal and maxillary operations, prick-test positivity, nasal resistance, duration of rhinitis, actual rhinitis symptoms, and smoking in the patient group.

The age-related 95% reference interval for the olfactory threshold was calculated by the method of Isaacs et al. (9). A linear regression model was first fitted to the data of the control group. Another linear regression model was fitted to the standard deviations of the residuals about the first regression. For this purpose, the age range was divided into five 10-year brackets: 15–25, 25–35, 35–45, 45–55, and 55–65 years. In addition, the two persons aged over 65 years were consolidated with the 55–65 age group. The reference interval was calculated as

$$f_1(\text{age}) \pm 1.96 \times f_2(\text{age})$$

where f_1 and f_2 are the functions of age fitted to the threshold data and the residuals, respectively.

Comparison of groups was made with analysis of variance, the Scheffé test, and the chi-square test.

Results

The average olfactory threshold was 13.8 ALU (SD 11.2) in the control group and 23.9 ALU (SD 18.8) in the patient group. In the forward stepwise multiple regression analysis of all subjects, only age ($P < 0.0001$) and rhinitis ($P = 0.024$) showed significant association with olfactory threshold. In the patient data, past history of polyp operations ($P = 0.0032$) and age ($P = 0.0015$) were associated with poorer smell test results, whereas prick-test positivity ($P = 0.017$) was associated with better smell-test results. The detailed results are shown in Tables 1 and 2.

In the linear regression analysis of the control group, the equation of olfactory threshold as a function of age (in years) was as follows:

$$f_1(\text{age}) = 2.4 + 0.29 \times \text{age} \quad (P = 0.0001)$$

Table 1. Association of olfactory thresholds and age, sex, presence of rhinitis, and smoking habits in 105 rhinitis patients and 104 healthy controls. Results of forward stepwise multiple linear regression analysis: $R^2=0.210$, adjusted $R^2=0.202$, residual standard deviation=14.517

	Coefficient	SE	P value
Age (years)	0.42	0.078	<0.0001
Rhinitis history ^a	5.05	2.21	0.024
Variables which did not enter model			
Smoker ^b			
Smoking level ^c			
Sex ^d			
History of smoking ^b			

SE: standard error of coefficient.

^a No rhinitis history: 0, rhinitis history: 1.

^b No: 0, yes: 1.

^c Never smoked: 0, ex-smoker: 1, 1–5 cigarettes/day: 2, 6–10 cig./day: 3, 11–20 cig./day: 4, >20 cig./day: 5.

^d Female: 0, male: 1.

In the regression model fitted to the standard deviations of the residuals of the former regression, the function was as follows:

$$f_2(\text{age})=11.9-0.042 \times \text{age} \quad (P=0.46)$$

The equation of the olfactory threshold as a function of age fitted to the patient data was as follows:

$$f_3(\text{age})=-7.6+0.62 \times \text{age} \quad (P=0.0001)$$

The sense of smell deteriorated more rapidly in rhinitis patients than in the control group. The difference between the regression coefficients of the groups was 0.33 (95% confidence interval 0.017–0.639), $t=2.081$ ($P=0.039$). The data for the olfactory thresholds and the 95% reference intervals are depicted in Fig. 1.

According to the estimation of the age-related upper reference limit of the olfactory threshold, the number of hyposmic persons, i.e., subjects with olfactory threshold higher than $f_1(\text{age})+1.96 \times f_2(\text{age})$, was two (2%) in the control group and 16 (15%) in the rhinitis group ($\chi^2=11.77$, $P=0.0006$).

The natural logarithms of total nasal resistance and olfactory threshold showed no significant association (regression coefficient -5.50 , 95% confidence interval -12.58 to 1.57 , $P=0.13$). This was true also in the subgroup of hyposmic patients, where the coefficient was 3.97 , 95% confidence interval -3.20 to 11.13 , $P=0.26$.

The mean olfactory threshold of prick-test-positive patients was 18.9 and that of prick-test-negative patients 33.9 ALU. In the analysis of variance with age as a covariate, the difference between the groups was significant ($P=0.0096$), the adjusted means being 21.2 and 31.5 ALU, respectively. There was a significant intergroup difference ($P=0.0097$) between different types of rhinitis (seasonal allergic, $n=28$,

Table 2. Association of olfactory thresholds and age, duration of rhinitis symptoms, sex, history of asthma and operations for nasal polyposis, presence of rhinitis symptoms, prick-test results, and smoking habits in 105 rhinitis patients. Results of forward stepwise multiple linear regression analysis: $R^2=0.452$, adjusted $R^2=0.403$, residual standard deviation=15.021

	Coefficient	SE	P value
Prick-test positivity ^a	-9.34	3.84	0.017
Operations for polyposis ^a	12.69	4.17	0.0032
Age (years)	0.62	0.19	0.0015
Asthma ^a	7.59	5.01	0.13
Duration of rhinitis (years)	-0.37	0.25	0.14
Smoker ^a	13.73	7.96	0.089
Smoking level ^b	-3.05	2.43	0.21
Variables which did not enter model			
Sex ^c			
Present rhinitis ^a			
History of smoking ^a			
Logarithm of TNR			
Operations for maxillary sinusitis ^a			

SE: standard error of coefficient; TNR: total nasal resistance.

^a No: 0, yes: 1.

^b Never smoked: 0, ex-smoker: 1, 1–5 cigarettes/day: 2, 6–10 cig./day: 3, 11–20 cig./day: 4, >20 cig./day: 5.

^c Female: 0, male: 1.

perennial allergic, $n=36$, nonallergic, $n=33$, according to skin-test results), and nonallergic patients demonstrated significantly higher thresholds than seasonal ($P=0.0006$) and perennial ($P=0.0006$) allergic patients, but no difference could be found between the types of allergic rhinitis ($P=0.97$) (Scheffé test). The average olfactory thresholds were 17.5, 18.6, and 35.0, and the age-adjusted means 20.4, 18.7, and 32.0, respectively. In nasal resistance, there was no difference between the groups.

Thirty patients (29%) reported that they had undergone surgery for nasal polyps. The need for polypectomy or ethmoidectomy appeared to be associated with impaired sense of smell: 10 of them were hyposmic, whereas only six of the 75 patients with no polyp operations had olfactory thresholds above the reference interval (Yates correction $\chi^2=8.78$, $P=0.0031$). Among the patients with and without prior maxillary sinus operations, the proportions of hyposmic subjects were similar ($P=0.37$, Fisher's exact test).

Twenty-nine control subjects (28%) and 18 patients (17%) were actual smokers, while 25 (24%) and 33 (31%), respectively, were ex-smokers. Neither sex nor smoking habits (earlier or present smoking) were significantly associated with smell-test results in patients or controls.

Discussion

As a rule, rhinitis patients whose sense of smell is studied are unselected with regard to duration of

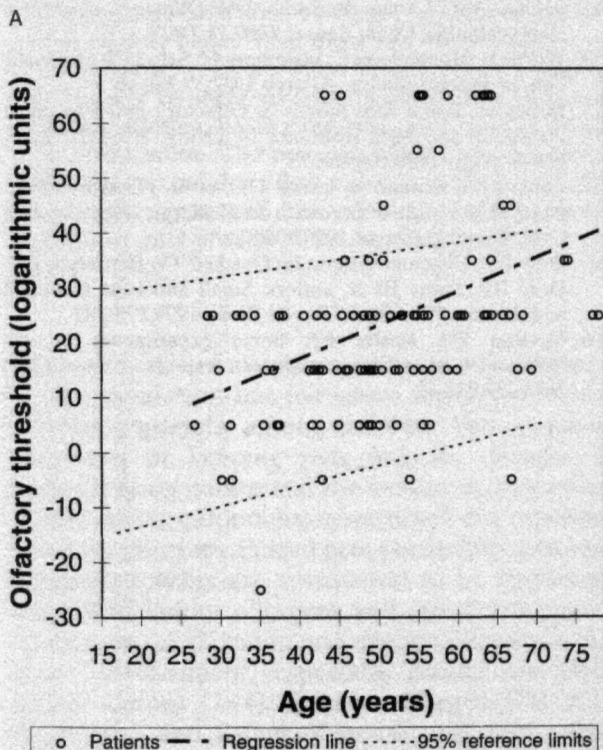
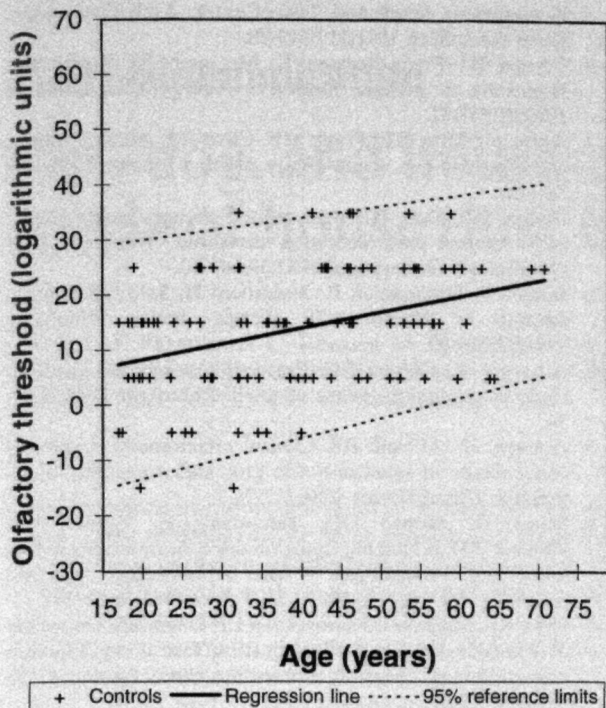


Fig. 1. Scatter diagrams showing olfactory thresholds of control subjects by age, with 95% reference interval (A), and patients by age, with 95% reference interval (B).

the disease. The duration range can be very wide; therefore, assessment of the effect of chronic rhinitis on the olfactory threshold can be misleading.

Since our patients had been included in a follow-up study and all of them had a rhinitis history of more than 20 years, evaluation of long-term changes in the sense of smell is likely to be more reliable. In some patients, current symptoms were quite mild, but the disease had previously been active for a long time. The age distribution of the patients was wide, and age-related changes certainly played an important role. This is also seen in clinical practice, but it is not feasible to collect a representative patient series matched for age and duration of chronic rhinitis. The control group in this study was slightly younger than the patient group, but the subjects were distributed over all age groups, except for the oldest.

Investigators have developed several methods of assessing the sense of smell. Unfortunately, each method is used in one center only, and the results of different studies are poorly comparable. Commercially available methods, e.g., UPSIT (10) for smell identification and the kit used in this study for measuring olfactory threshold, may remedy this disadvantage in the future, as they are widely available. Scaling of the olfactory threshold is also an open question. The developers of the kit that we used have designated the logarithmic unit as "decismel", but the term has not gained wide acceptance. Thus, we preferred to use the descriptive term "arbitrary logarithmic unit".

The proportion of hyposmic subjects was larger in the rhinitis group than in the control group, even when age was taken into consideration. This was borne out by the regression-analysis results, indicating that the sense of smell deteriorates more rapidly in rhinitis patients than in persons with healthy noses. However, we could not find any significant direct association between the duration of rhinitis and the olfactory threshold. Our 15% proportion of hyposmics was smaller than the 35% reported by Seiden et al. (11), who used smell identification as their method, and the 23% reported by Cowart et al. (3), who used a phenyl-ethyl alcohol concentration series in paired squeeze bottles. In the primary follow-up study of our patients in 1982, impaired sense of smell was reported by 31–43% of the subjects, depending on the duration of rhinitis symptoms (12). These figures, however, were based on anamnestic information, and no objective assessments were made at the time. The lack of association between nasal obstruction and olfactory threshold demonstrated by our results has been shown in several earlier studies (3, 13, 14).

The olfactory thresholds of prick-test positive patients were lower than those of patients with nonallergic rhinitis. This result suggests that non-allergic disease could be more damaging to the

sense of smell than allergic rhinitis. Even in this comparison, nasal obstruction did not explain the difference. Nasal polyposis usually indicates severe chronic rhinitis, and it is not surprising that a disease requiring polyp operations had led to higher olfactory thresholds than other types of rhinitis. Chronic maxillary sinusitis, on the other hand, is not as persistent a disease as polyposis; in addition, the diseased mucosa is situated farther from the olfactory epithelium than in ethmoidal polyposis, and surgery involves less manipulation of the olfactory epithelium. This may explain why a history of maxillary sinus operations had less impact on olfaction.

Smoking habits did not affect the sense of smell in this study. Contrary to some earlier studies (15, 16), we found no differences between male and female olfactory thresholds.

Our findings indicate that even if age-related changes are considered, chronic rhinitis impairs the sense of smell. Today, treatment of rhinitis is both effective and safe. The question of whether these medications are effective in preventing loss of the sense of smell in the long run needs further study.

Acknowledgments

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