



Evaluation of olfactory function in children with allergic rhinitis and nonallergic rhinitis



Seyhan Kutlug^{a,*}, Emre Gunbey^b, Ayhan Sogut^a, Mehmet Halil Celiksoy^a, Semsettin Kardas^b, Ugur Yildirim^b, Rifat Karli^b, Naci Murat^c, Recep Sancak^a

^a Department of Pediatric Allergy and Immunology, Faculty of Medicine, Ondokuz Mayıs University, Samsun, Turkey

^b Department of Otorhinolaryngology, Faculty of Medicine, Ondokuz Mayıs University, Samsun, Turkey

^c Industrial Engineering, Faculty of Engineering, Ondokuz Mayıs University, Samsun, Turkey

ARTICLE INFO

Article history:

Received 18 February 2016

Received in revised form 28 April 2016

Accepted 29 April 2016

Available online 4 May 2016

Keywords:

Allergic rhinitis

Children

Nonallergic rhinitis

Olfactory dysfunction

Olfactory function

Sniffin' sticks

ABSTRACT

Objectives: Allergic rhinitis (AR) occurs when the symptoms of rhinitis arise as a result of allergen-induced nasal mucosal inflammation. In the presence of rhinitis symptoms without infection or an allergic reaction in the nose, non-allergic rhinitis (NAR) is considered. Adults with these diseases have increased frequency of olfactory dysfunction. The aim of the present study is to assess olfactory function in children with AR and NAR.

Methods: A total of 77 children (aged six to 18 years) with AR and NAR were included in the study. The control group consisted of 45 healthy children. Sniffin' Sticks test was applied to both groups. The association between odor scores and demographic, clinical, and laboratory results was investigated.

Results: Forty two patients had allergic rhinitis. No significant difference was observed between patients with rhinitis and healthy controls with respect to odor scores. No association was observed between odor scores and the severity of rhinitis and the laboratory results of the patient groups. Odor identification and total odor scores of the patients with rhinitis lasting for longer than three years were significantly lower than those in the patient group with rhinitis lasting for one to three years. In the AR and control groups, the odor scores were found to increase with age.

Conclusions: When compared with healthy children, children with allergic rhinitis and non-allergic rhinitis were not found to have reduced olfactory function. The duration of rhinitis may be associated with the olfactory dysfunction in children with rhinitis.

© 2016 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Rhinitis is defined as the inflammation of the nasal mucosa, which is characterized by nasal congestion, nasal discharge, sneezing, and nasal itching [1]. Allergic rhinitis (AR) is an IgE-mediated inflammation of the nose caused by airborne allergens. It is the most common form of noninfectious rhinitis [1,2]. Allergic rhinitis is the most common allergic disease seen in children, and it is often accompanied by other allergic diseases. Non-allergic rhinitis (NAR) does not involve infectious agents or signs of atopy in the skin or blood. This disease is thought to be characterized by sensory nerve dysregulation or autonomic dysfunction in the nose [2]. Patients with AR and NAR compose the majority of chronic rhinoconjunctivitis cases [2]. The frequency of non-infectious rhinitis is 8.5% in chil-

dren aged six to seven years and 14.6% in those aged 13–14 years [3]. This disease may negatively affect the social lives of children [4].

Olfactory dysfunction may emerge in some situations, such as in upper respiratory tract infections, sinonasal diseases, aging, and head trauma [5,6]. Olfactory dysfunction has been reported to be more common in adults with AR and NAR than in healthy subjects [6–10]. Although the mechanism remains unclear, nasal congestion had been previously thought to be responsible for the olfactory dysfunction [10,11]. Later, it was suggested that the olfactory dysfunction was due to nasal inflammation [10,12]. Olfactory dysfunction studies in patients with allergic rhinitis mostly involve adults [13]. The frequency of olfactory dysfunction in adults with allergic rhinitis is 20–40% [13]. In population-based studies, the frequency is 19% [14].

Although there are studies assessing olfactory function in adult patients with AR and NAR, olfactory function has not been studied in children with AR and NAR. The aim of this study is to compare olfactory function in children with non-infectious rhinitis with that in healthy children after measuring sensitivity via the skin test.

* Corresponding author at: Department of Pediatric Allergy and Immunology, Faculty of Medicine, Ondokuz Mayıs University, Kurupelit, Samsun 55139, Turkey. Tel.: +90 362 3121919; fax: +90 362 457 60 41.

E-mail address: seyhankutlug@hotmail.com (S. Kutlug).

2. Material and methods

2.1. Study group

Children (aged six to 18 years) who were admitted to the allergy and immunology clinic with reversible symptoms of rhinitis between April, 2014 and April, 2015 were included. Rhinitis diagnosis was performed according to Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines [1]. The following patients were excluded from the study: those with asthma (those with a history of asthma symptoms or evidence of asthma according to a pulmonary function test) or with a nasal anatomic structure disorder or active rhinosinusitis, those who had been receiving steroids, antihistamines, thyroid medication and/or anti-depressants for a month or longer, those who had undergone nasal surgery, and smokers. The irritant odors during smell test would trigger the asthma attacks so we have preferred to study on children without asthma. Seventy-seven patients meeting the aforementioned criteria were included in the study. Forty-five children aged six to 18 years without any ear-nose-throat symptoms and without clinical history of atopic disease were enrolled in the control group. Patients and control subjects were evaluated by an otorhinolaryngologist using nasal endoscopy. We did not include the control subjects and patients with nasal congestion or rhinorrhea to exclude the infection and obstructive factors. The current exclusion criteria were also applied for the control group.

The relationship between the symptoms and seasonality, severity, and duration of the symptoms were recorded. Hemogram and serum total IgE were measured, and a skin prick test was performed. The patients demonstrating sensitivity in the skin prick test were considered AR patients, and those without sensitivity were considered NAR patients.

This prospective study was approved by the Ethics Committee of Ondokuz Mayıs University with the protocol no. 2014/691. Written informed consent was obtained from parents of the children who participated in the study.

2.2. Allergy and laboratory testing

For atopy measurement, a skin prick test was performed. Histamine (10 mg/ml) was used as a positive control in the skin prick test, whereas physiological serum was used as negative control. The wheal was measured 15–20 minutes after the allergen was applied to the skin. According to the physiological serum response, a wheal of 3 mm or greater was considered significant [15]. The following allergens were used in the skin prick test: tree mix (*Castanea vulgaris*, *Quercus robur*, *Fagus sylvatica* ACE), grass mix (*Anthoxanth odoratum*, *Dactylis glomerata*, *Lolium pere me*, *Phleum protein France*, *Poa pratensis*), weeds (*Chenopodium album*, *Amaranthus retroflexus*), *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, *Alternaria Alternate*, *Aspergillus mix*, *Blattella Germanica*, and cat feathers (Stallergenes SA, 92160 Antony, France). Hemogram measurements were performed using the Advia 2120 hematology system (Siemens, Germany). Serum IgE levels were measured using the nephelometry method (Nephelometry BN2 Siemens, Germany). Eosinophil count on the hemogram was recorded.

2.3. Olfactory testing

Patients and control subjects were evaluated by an otorhinolaryngologist, and a Sniffin' Sticks test was performed (Burghart GmbH in Wedel, Germany) [16]. The validity of this test in the Turkish adult population was confirmed, although it was not confirmed in Turkish children [5]. However this test was validated in German children [17]. The test includes a total of 12 odors. An odor identification (OI) score (0–12) and an odor discrimination (OD) score (0–12) were generated for all individuals, with 12 representing the highest score and

Table 1

Demographic and clinical characteristics of the patients.

Demographic and clinical characteristics	Patients (n = 77)
Age (years)	
Median (min–max)	11 (6–18)
Male gender, [n (%)]	41 (53)
Atopy in skin prick test, [n (%)]	
Allergic rhinitis	42 (54)
Nonallergic rhinitis	35 (46)
Classification, [n (%)]	
Seasonal	34 (44)
Perennial	43 (56)
Severity, [n (%)]	
Mild	47 (61)
Moderate–Severe	30 (40)
Symptom duration, [n (%)]	
≤1 year	13 (17)
1–3 years	21 (27)
>3 years	43 (56)
Sensitivity [n (%)]	
Mite	33 (42)
Pollen	20 (25)
Other	2 (2.5)
Negative	35 (45)
Eosinophils (/mm ³) [median (min–max)]	330 (30–2430)
Total IgE (IU/mL) [median (min–max)]	149 (17–1350)

IgE: immunoglobulin E.

0 representing the lowest. A total odor (TO) score (0–24), which is sum of these two scores, was also generated.

2.4. Statistical analysis

Data were analyzed by using the Statistical Package for Social Sciences (SPSS for Windows 20.0 Chicago, USA) program. Normality was assessed using the Kolmogorov–Smirnov test. Groups were compared using an independent t-test and the one-way ANOVA for normally distributed quantitative data. Data not showing normal distribution were analyzed using the Mann–Whitney U-test and Kruskal–Wallis test. Pearson's chi-squared test was used for the analysis of categorical data. For non-normally distributed data, the correlation between the variables was analyzed via Spearman correlation analysis. Results were presented as frequency, mean ± standard deviation and median (min–max). $p < 0.05$ was considered as significant difference. The Spearman rank correlation test was used to analyze the correlation.

3. Results

The median age in both patient (41 males, 36 females) and control groups (21 males, 24 females) was 11 years (ranging from six to 18 years in the patient group and seven to 18 years in the control group). Clinical and laboratory features of the patients are specified in Table 1. There was no statistically significant difference with respect to age or gender among groups (Table 2). The numbers of patients with a history of rhinitis for nearly one year, one to three years, and longer than three years were 13, 21, and 43, respectively. In the skin prick test, 20 patients had sensitivity only against mites, seven only

Table 2

Comparison of the demographic data and odor scores of patient and control groups.

	Patients (n = 77)	Controls (n = 45)	p
Age (years) [median (min–max)]	11 (6–18)	11 (7–18)	0.250
Gender (male/ female)	41/36	21/24	0.483
OI score [median (min–max)]	3 (0–7)	4 (0–9)	0.484
OD score [median (min–max)]	9 (1–12)	9 (2–11)	0.567
TO score (mean ± SD)	11.6 ± 3.1	11.5 ± 3.6	0.820

OI: odor identification OD: odor discrimination TO: total odor SD: standard deviation.

Table 3

Comparison of the demographic data and odor scores of the Allergic Rhinitis (AR), Nonallergic Rhinitis (NAR), and Control groups.

	AR group n = 42	NAR group n = 35	Control group n = 45	p
Age (years) [median (min–max)]	12 (6–18) ^A	9 (6–17) ^B	11 (7–18) ^A	0.007
Gender (male/female)	25/17	16/19	21/24	0.377
OI score [median (min–max)]	3 (0–7)	3 (0–7)	4 (0–9)	0.298
OD score [median (min–max)]	8.5 (1–12)	9 (3–12)	9 (2–11)	0.847
TO score (mean ± SD)	11.9 ± 3.5	11.4 ± 2.5	11.5 ± 3.6	0.782

AR: allergic rhinitis NAR: nonallergic rhinitis OI: odor identification OD: odor discrimination TO: total odor SD: standard deviation.

A, B: There is no difference between the groups with the same letter.

against pollen, and 13 against both mites and pollen. Two patients developed a reaction against other allergens. The remaining 35 patients showed no sensitivity (Table 1).

No significant differences were observed between the two groups in terms of the three odor scores (OI score, $p = 0.484$, OD score, $p = 0.567$, and TO score, $p = 0.820$) (Table 2). The AR, NAR, and control groups were compared in terms of odor scores, and no statistically significant difference was observed (Table 3). No correlation was detected between serum IgE levels, eosinophil count, and odor scores among the patient groups. The odor scores were not significantly related to seasonality, severity of rhinitis, or sensitivity to allergens ($p > 0.05$). However, the group with rhinitis symptoms lasting longer than three years and that with symptoms lasting for one to three years significantly differed in terms of odor discrimination and total odor scores. Accordingly, OD and TO scores of the group with rhinitis symptoms for longer than three years were found to be lower than those of the group with rhinitis symptoms for one to three years ($p = 0.008$ for both groups). We could not find any difference between the group with symptoms duration shorter than one year and that with symptom duration lasting for one to three years or lasting than three years according to odor scores ($p > 0.05$).

The correlation between age and odor scores was analyzed using the Spearman correlation. The median age of the NAR group was lower than those of the AR and control groups. The median ages of the control and AR groups were similar (Table 3). In the NAR group, no relationship was observed between age and any of the three odor scores. In the AR and control groups, OD and TO scores significantly increased with age (Table 4). However, no relationship was observed between OI score and age in the AR or control groups. We did not find difference between rhinitis symptom duration groups according to age either in children with AR and NAR ($p = 0.067$, $p = 0.591$, respectively).

Odor scores were compared in terms of gender in both patients and healthy controls using the Mann–Whitney U-test. Odor scores in the patient and control groups did not significantly differ with respect to gender ($p > 0.05$).

Table 4

The correlation between odor scores and age in the Allergic Rhinitis (AR), Nonallergic Rhinitis (NAR), and Control groups.

Odor scores		AR group n = 42	NAR group n = 35	Controls n = 45
Odor identification score	r	0.291	0.185	0.277
	p	0.062	0.288	0.065
Odor discrimination score	r	0.624 ^a	0.185	0.531 ^a
	p	<0.001	0.287	<0.001
Total odor score	r	0.504 ^a	0.243	0.436 ^a
	p	0.001	0.159	0.003

AR: allergic rhinitis NAR: nonallergic rhinitis r: spearman's correlation coefficient.

^a Correlation is significant at the 0.01 level (2-tailed).

4. Discussion

This is the first study in the literature investigating olfactory function in children with AR and NAR with no other risk factors for olfactory dysfunction. Study results revealed no significant differences in the olfactory function of children with AR and NAR and that of healthy controls. Atopy (as measured by a skin prick test) and severity of rhinitis did not seem to be related to olfactory function. However, the odor scores of the patients with rhinitis symptoms lasting for longer than three years were found to be lower than those of patients who had experienced rhinitis symptoms for one to three years.

Upper respiratory tract infections and sinonasal diseases are the primary causes of olfactory dysfunction [5,6,18]. Olfactory dysfunction was found to be more common in almost all the studies investigating the olfactory dysfunction in adult patients with AR and NAR [13]. Olfactory dysfunction is more common when allergic rhinitis is accompanied by rhinosinusitis [7,19]. Yet another study reported that patients with allergic rhinitis did not experience olfactory dysfunction [20]. The mean olfactory dysfunction frequency in AR varies from 20% to 40% [13]. In our study, individuals with upper respiratory tract infection were excluded because it is known that temporary olfactory dysfunction may occur in the presence of infection [11,12,18].

Different results have been reported about the relationship between olfactory dysfunction and seasonality of rhinitis. Olfactory dysfunction has been found to be more frequent in perennial allergic rhinitis (PAR) than in seasonal allergic rhinitis (SAR) [8,21]. However, Moll et al reported that olfactory dysfunction is more common in patients with SAR than in those with PAR in the pollen season and that patients with PAR are more likely to have olfactory dysfunction in other seasons [22]. Another study showed that olfactory dysfunction is present in patients with SAR only in the beginning of the pollen season but not at other times of the year [12]. In our study, no significant relationship was observed between odor scores and seasonality of rhinitis or allergen sensitivity. Becker, S. et al used the Sniffin' Sticks test for the first time in patients with AR to assess olfactory function [10]. As in our study, they did not observe any differences between the odor scores and seasonality of rhinitis. We believe that these different literature results may be due to differences in the methods of measurement. Although Becker, S. et al did not find any correlation between odor scores and nasal eosinophilic mediators, they observed worse odor scores in patients with AR than in healthy controls. We did not measure nasal eosinophilic mediators, and we found no correlation between odor scores and serum eosinophil count and serum total IgE levels. Contradictory results have been reported in some studies using different methods [8,12].

Olfactory dysfunction was not severe in most of the studies involving patients with AR [13]. The percentage of those with constant olfactory dysfunction is lower than that of those with temporary olfactory dysfunction [20]. The frequency and the severity of olfactory dysfunction probably worsen due to intervening infections. We did not find a correlation between the severity of rhinitis and odor scores in our study. This is probably due to exclusion of the cases with infection. However, Rhee, C.S. et al reported a positive correlation between severity of rhinitis and olfactory dysfunction [23].

In general, olfactory dysfunction in patients with NAR has been reported to be more severe than that in patients with AR; this is probably due to the inclusion of heterogeneous NAR groups that included polyposis cases [6,19,24]. The most important finding of our study is that the odor scores of patients with AR and NAR and healthy controls were similar. This finding is unexpected and different from those obtained in previous similar studies [13]. Because patients with rhinosinusitis were not included in our study, it is logical that we

observed no difference between the AR and NAR groups. Only one study reported no significant difference between AR and NAR groups with respect to olfactory dysfunction [9]. Our result may be due to the fact that children may not be able to distinguish mild olfactory dysfunction. Olfactory dysfunction in patients with AR is usually reported to be mild [13]. It was also shown that the ability of healthy children to discriminate between different odors (as measured by Sniffin' Sticks) is enhanced with age [17]. The same study also showed that the frequency of olfactory dysfunction in children increases with age [17]. This may be attributed to the fact that olfactory dysfunction can be more easily diagnosed as children develop their ability to distinguish odors. The frequency of olfactory dysfunction also increases with age in the healthy adult population [5,25]. Simola and Malmberg reported that aging is one of the most important factors negatively affecting olfactory function in patients with rhinitis [6]. However, there are also studies in the literature reporting no relationship between age and olfactory dysfunction in patients with AR [8,9]. In our study, we observed that OD score measured via Sniffin' Sticks test increases with age in both AR and healthy control groups. In other words, in contrast to adults, odor function increases with age in children. The median age of our patients was similar in the AR and control groups.

Although the frequency of olfactory dysfunction in healthy adult males has been found to be significantly higher than in females [5,25], no relationship has been observed between gender and olfactory dysfunction in adults with AR [6,8,9]. We did not observe a significant difference between the odor scores of males and females in either the healthy controls or the rhinitis groups.

The second most important finding of our study is that those with a longer duration of rhinitis have a decreased ability to distinguish odors. This finding is consistent with studies conducted with adults [13]. Duration of rhinitis can be expected to increase with age. However, we observed that the ability to distinguish odors increases with age. Therefore, we believe that odor discrimination dysfunction is proportional to the duration of rhinitis, independent of age, because we could not find difference between symptom duration groups according to age in the patient group. However we could not find any difference between the group with rhinitis symptoms lasting shorter than one year and that with symptoms lasting for one to three years or lasting than three years according to odor scores. This result may be due to a small number of patients in the group with rhinitis symptoms lasting shorter than one year (Table 1). Only one study reported no association between duration of rhinitis and olfactory dysfunction in adults with AR [6]. However, in the same study, olfactory dysfunction was reported to be greater in patients with polypectomy. Yet, development of polyps is more frequent in patients who have rhinitis symptoms for an extended period of time [8,19]. Our study has several limitations. The children can misjudge the smell test compared to the adults. Sniffin' Sticks test was not validated in Turkish children, although it was validated in German children. The odor thresholds of the individuals were not measured. Neither allergic nor non-allergic nasal inflammatory mediators were studied. Therefore further studies involving larger numbers of pediatric patients are needed.

5. Conclusions

Olfactory function in children with allergic and non-allergic rhinitis was similar to that in healthy children. Odor discrimination function was poorer in patients who had suffered from rhinitis for longer than three years than in those who had suffered for a shorter period of time. The odor discrimination score was much more affected than the odor identification score in children with rhinitis.

Conflict of interest

None.

Funding source

No external funding was secured for this study.

Financial disclosure

The authors have no financial relationships relevant to this article to disclose.

Authorship

SK: Design of the work; acquisition, analysis and interpretation of the data for the work; writing the article; final approval of the article. EG: design of the work; acquisition, and interpretation of the data for the work; final approval of the article. AS: design of the work; interpretation of the data for the work; writing the article; final approval of the article. MHC: SK, UY, RK, RS: provided useful suggestion on the study design and carried out and collaborated on experiments, SK, NM: statistical analysis and interpretation of the data for the work, final approval of the article. All authors read and approved final manuscript.

References

- [1] J. Bousquet, N. Khaltaev, A. Cruz, J. Denburg, W. Fokkens, A. Togias, et al., Allergic rhinitis and its impact on asthma (ARIA) 2008 update [in collaboration with the World Health Organization, GA(2)LEN and AllerGen], *Allergy* 63 (86) (2008) 8–160.
- [2] J. Corren, F.M. Baroody, R. Pawankar, Allergic and nonallergic rhinitis, in: N.F. Adkinson, B.S. Bochner, A.W. Burks, W.W. Busse, S.T. Holgate, R.F. Lemanske, et al. (Eds.), *Middleton's Allergy: Principles and Practice*, Saunders, Philadelphia, 2014, pp. 664–685.
- [3] B. Björkstén, T. Clayton, P. Ellwood, A. Stewart, D. Strachan, ISAAC Phase Three Study Group, Worldwide time trends for symptoms of rhinitis and conjunctivitis: phase III of the international study of asthma and allergies in childhood, *Pediatr. Allergy Immunol.* 19 (2008) 110–124.
- [4] S.M. Nascimento, C. Naspitz, D. Sole, Evaluation of quality of life in children and teenagers with allergic rhinitis: adaptation and validation of the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), *Allergol. Immunopathol. (Madr)* 29 (2001) 111–118.
- [5] H. Tekeli, A. Altundağ, M. Salihoğlu, M. Cayönü, M.T. Kendirli, The applicability of the "Sniffin' Sticks" olfactory test in a Turkish population, *Med. Sci. Monit.* 19 (2013) 1221–1226.
- [6] M. Simola, H. Malmberg, Sense of smell in allergic and nonallergic rhinitis, *Allergy* 53 (1998) 190–194.
- [7] B.J. Cowart, K. Flynn-Rodden, S.L. McGready, Hyposmia in allergic rhinitis, *J. Allergy Clin. Immunol.* 91 (1993) 747–751.
- [8] B. Rydzewski, A. Prusiewicz, W.J. Sulkowski, Assessment of smell and taste in patients with allergic rhinitis, *Acta Otolaryngol* 120 (2000) 323–326.
- [9] J. Guss, L. Doghramji, C. Reger, A.G. Chiu, Olfactory dysfunction in allergic rhinitis, *ORL J. Otorhinolaryngol Relat. Spec.* 71 (2009) 268–272.
- [10] S. Becker, C. Pflugbeil, M. Gröger, M. Canis, G.J. Ledderose, M.F. Kramer, Olfactory dysfunction in seasonal and perennial allergic rhinitis, *Acta Otolaryngol* 132 (2012) 763–768.
- [11] D.A. Deems, R.L. Doty, R.G. Settle, V. Moore Gillon, P. Shaman, A.F. Mester, et al., Smell and taste disorders, a study of 750 patients from the University of Pennsylvania Smell and Taste Center, *Arch. Otolaryngol. Head Neck Surg.* 117 (1991) 519–528.
- [12] L. Klimek, G. Eggers, Olfactory dysfunction in allergic rhinitis is related to nasal eosinophilic inflammation, *J. Allergy Clin. Immunol.* 100 (1997) 158–164.
- [13] B.A. Stuck, T. Hummel, Olfaction in allergic rhinitis: a systematic review, *J. Allergy Clin. Immunol.* 136 (2015) 1460–1470.
- [14] A. Brämerson, L. Johansson, L. Ek, S. Nordin, M. Bende, Prevalence of olfactory dysfunction: the skövde population-based study, *Laryngoscope* 114 (2004) 733–737.
- [15] P. Demoly, F.B. Michel, J. Bousquet, In vivo methods for study of allergy: skin tests, techniques and interpretation, in: E. Middleton Jr., C.E. Reed, E.F. Ellis, N.F. Adkinson, J.W. Yunginger (Eds.), *Allergy, principles and practice*, Mosby Co, New York, 1998, pp. 430–439.
- [16] T. Hummel, B. Sekinger, S.R. Wolf, E. Pauli, G. Kobal, "Sniffin' sticks": olfactory performance assessed by the combined testing of odor identification, odor discrimination and olfactory threshold, *Chem. Senses* 22 (1997) 39–52.

- [17] V.A. Schriever, E. Mori, W. Petters, C. Boerner, M. Smitka, T. Hummel, The “Sniffin’ Kids” test – a 14-item odor identification test for children, *PLoS ONE* 9 (2014) e101086.
- [18] D.A. Leopold, Physiology of olfaction, in: C.W. Cummings (Ed.), *Otolaryngology – Head and Neck Surgery*, Mosby Year Book, vol. 1, St. Louis, 1993, pp. 640–664.
- [19] A.J. Apter, J.F. Gent, M.E. Frank, Fluctuating olfactory sensitivity and distorted odor perception in allergic rhinitis, *Arch. Otolaryngol. Head Neck Surg.* 125 (1999) 1005–1010.
- [20] P. Olsson, N. Berglind, T. Bellander, P. Stjarne, Prevalence of self-reported allergic and non-allergic rhinitis symptoms in Stockholm: relation to age, gender, olfactory sense and smoking, *Acta Otolaryngol* 123 (2003) 75–80.
- [21] E. Binder, E. Holopainen, H. Malmberg, O. Salo, Anamnestic data in allergic rhinitis, *Allergy* 37 (1982) 389–396.
- [22] B. Moll, L. Klimek, G. Eggers, W. Mann, Comparison of olfactory function in patients with seasonal and perennial allergic rhinitis, *Allergy* 53 (1998) 297–301.
- [23] C.S. Rhee, J.H. Wee, J.C. Ahn, W.H. Lee, K.L. Tan, S. Ahn, et al., Prevalence, risk factors and comorbidities of allergic rhinitis in South Korea: the Fifth Korea National Health and Nutrition Examination Survey, *Am. J. Rhinol. Allergy* 28 (2014) e107–e114.
- [24] S.S. Mann, S. Maini, K.S. Nageswari, H. Mohan, A. Handa, Assessment of olfactory status in allergic and non-allergic rhinitis patients, *Indian J. Physiol. Pharmacol.* 6 (2002) 186–194.
- [25] M.M. Vennemann, T. Hummel, K. Berger, The association between smoking and smell and taste impairment in the general population, *J. Neurol.* 255 (2008) 1121–1126.