

Mucosal symptoms elicited by fragrance products in a population-based sample in relation to atopy and bronchial hyper-reactivity

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Summary

Background Exposure to perfume and fragrance products may, in some individuals, cause symptoms from the eyes and airways. The localization, character and risk factors of such symptoms in the general population are unknown.

Objective To investigate both the localization and character of symptoms from the eyes and airways elicited by fragrance products, and the associations between such symptoms and skin prick test reactivity (atopy), methacholine bronchial hyper-reactivity (BHR), allergic rhinitis and asthma.

Methods A questionnaire on mucosal symptoms elicited by fragrance products was posted to 1189 persons who had participated in a Danish population-based study of allergic diseases in 1997/1998. The study included measurement of BHR, atopy, forced expiratory volume in 1 s (FEV₁), and serum eosinophilic cationic protein (serum ECP).

Results The response rate was 79.6%. Symptoms from the eyes or airways elicited by fragrance products were reported by 42%. BHR (adjusted odds ratio 2.3, 95% confidence interval 1.5–3.5) was independently associated with symptoms from the eyes and airways elicited by fragrance products. There were no significant associations between these symptoms and atopy, FEV₁ or serum ECP.

Conclusions Mucosal symptoms from the eyes and airways were common in this population. BHR was a significant and independent predictor of these symptoms. The lack of association with atopy suggested that IgE-mediated allergic mechanisms do not play a major role in the development of these symptoms.

Keywords allergic rhinitis, asthma, atopy, bronchial hyper-reactivity, epidemiology, fragrance, multiple chemical sensitivity, perfume

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Introduction

A perfume is a blend of odiferous ingredients composed of a diluent, usually ethanol, and a mixture of 10–300 different fragrance ingredients [1]. The ingredients of a perfume are volatile; thus, many people are exposed daily to airborne perfume ingredients. This exposure may be intentional, by using perfumed cosmetics and household products, or unintentionally, by evaporation from persons or objects.

Exposure to fragrance products can cause symptoms in individuals with asthma and rhinitis [2]. Anaphylaxis has also been reported following spraying of perfume in the eyes [3]. Despite estimates indicating that sensitivity to fragrance products is common [4,5], the frequency of mucosal symptoms elicited by exposure to these products in the general population is unknown. The localization, character and severity of these symptoms are unexplored and systema-

tic investigations exist of the relationship to objective measures only in confined groups of patients [6–10].

The aims of this study were to describe the localization and character of mucosal symptoms elicited by fragrance products in a population-based sample, and to investigate the associations between these symptoms and previously recognized atopy, bronchial hyper-reactivity (BHR), allergic rhinitis (AR) and asthma, in order to identify the characteristics of individuals with mucosal symptoms and find indications of possible mechanisms.

Material and methods

Study population and design

The study population had previously participated in a population-based study of allergic diseases in Copenhagen, Denmark (The Copenhagen Allergy Study) [11]. A screening questionnaire about respiratory symptoms had been sent to random samples of the general population. Random samples of responders ($n = 868$) and those who had reported

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symptoms of respiratory disease on exposure to pollen or furry animals ($n = 348$) participated in the study. Thus, individuals with IgE-mediated allergy were somewhat over-represented [12]. The study included measurement of skin prick test (SPT) reactivity, methacholine BHR, and serum eosinophilic cationic protein (serum ECP) [13]. The participation rate was 60.4%; the clinical examinations were between October 1997 and November 1998.

The current part of the study was based on a questionnaire about symptoms related to fragrance products, posted in October 2002 to 1189 persons still alive (97% of the baseline participants).

The results from the questionnaire about symptoms related to fragrance products were considered as outcome variables and compared with data collected during the health examination at baseline 1998 (predictor variables).

Questionnaire

Questions were formulated based on interviews with individuals who reported mild-to-severe discomfort when exposed to fragrance products. A preliminary questionnaire, which consisted of 100 questions, was tested in a pilot group of 24 individuals with self-reported perfume-related symptoms. There was a telephone interview 2 months later using the same questionnaire but without knowledge of the participant's initial answers. Ambiguous questions were omitted or changed, which left 67 questions in the final questionnaire. The mean κ value from the retest validation was 0.6.

Perfume and fragrance products were defined as 'any cosmetic, skin-care lotion, cleansing agent, washing soap or air-freshener that is perfumed, e.g. fine fragrances, after-shave, eau de cologne, deodorant, moisturizers, powder, toothpaste, soap, shampoo, shaving foam, detergents, fabric softeners, toilet cleanser, etc.'

The questionnaire included items about symptoms from mucous membranes elicited by fragrance products including target organ, type of symptoms, duration, exposure time, severity and sources of fragrance products that triggered symptoms.

Outcome variables

Outcome variables were derived from the questionnaire and divided in two categories: organ-related variables, and more general variables describing frequency and severity. The questions were formulated in Danish. The questions in English reported here have not undergone any linguistic or cultural validation.

1. Organ-related symptoms comprised four variables, defined as at least one symptom, elicited by fragrance products, from the eyes, nose, mouth (or throat) or lungs, within the last 12 months (see Table 2 for details).
2. The following variables regarding frequency and severity of symptoms were defined:
'Affecting daily activity' was defined as an affirmative answer to the question 'Is your everyday life troublesome as a result of symptoms from your eyes, nose, mouth, throat or lungs elicited by perfume or fragrance products (e.g. by choice of shopping places, means of transportation or adjustment of working situations)?'.

'Affecting application pattern' of personal use of fragrance and cosmetics was defined from the questions 'Do you ever apply perfume, deodorant or after-shave', and 'If no, is this a consequence of symptoms from eyes, nose, mouth, throat or lungs?'.

'Frequent symptoms' was defined as at least one organ-related symptom occurring at least once a week.

'Several elicitors' was defined as mucosal symptoms elicited in at least three of the following situations: (1) when other persons are perfumed, (2) when other persons' clothing is washed in fragrant fabric softener, (3) when entering places with air fresheners and (4) when entering recently cleaned places.

'Extensive target organs' refers to symptoms elicited by fragrance products from all mucous-membrane areas (eyes, nose, mouth/throat and lungs).

Skin prick tests

The Soluprick SQ[®] system (ALK Abelló, Hørsholm, Denmark) was used for the SPT as previously described [11]. The panel of allergens comprised: birch, grass (timothy), mugwort, horse, cat, dog, mites (*Dermatophagoides pteronyssinus* and *D. farinae*) and moulds (*Cladosporium* and *Alternaria*). A negative control diluent and a positive control (10 mg/mL histamine) were included [11]. The largest and the smallest diameters (at the widest point and at the midpoint at 90°) of the weals were measured with a transparent ruler, and the mean weal diameter was calculated. A positive SPT was defined as giving a mean weal diameter of 3 mm or more.

Methacholine bronchial hyper-reactivity

Forced expiratory volume in the first second (FEV₁) was measured with a dry bellow spirometer (Vitalograph[®], Vitalograph Ltd, Buckingham, UK) as the higher of two measurements within 100 mL. The spirometer was checked each study day with a 3 L calibration syringe [14]. Volumes were reported at body temperature, atmospheric pressure and saturated with water vapour. Methacholine bronchial responsiveness (BHR) was measured with a modification of the method of Yan et al. [15]. Participants inhaled three puffs of saline from an Acorn[®] nebulizer (Medic-Aid, Pagham, UK) while breathing in slowly from functional residual capacity to total lung capacity, followed by increasing doses of methacholine (acetyl- β -methylenchloride, Unikem, Copenhagen, Denmark). The nebulizers were operated via a Morgan[®] dosimeter (P. K. Morgan, Kent, UK). The dosimeter was pre-set to an inhalation time of 500 ms and the doses were delivered 0.2 s after beginning inhalation. A maximal cumulative dose of 1200 μ g methacholine was inhaled beginning with 9.39 μ g and ending at a dose of 600 μ g, each inhalation represented a doubling of the cumulative dose. Lung function was measured 1 min after each dose and the test was stopped if FEV₁ was 20% below the post-saline value. The provocative dose of methacholine required to cause a 20% fall in FEV₁ (PD₂₀) was calculated by linear interpolation between the last two readings on the log dose-response plot. Participants were instructed to withhold bronchodilator medication for 12 h before the study visits, which were at the same time of day.

Serum eosinophilic cationic protein

UniCAP[®] ECP (Pharmacia Diagnostics AB, Uppsala, Sweden) measured serum ECP according to the manufacturer's instructions. The measuring range was 2–200 µg/L in undiluted serum and the cross-reactivity with other granulocyte proteins was less than 0.1%.

Definition of predictor variables

Atopy was defined as a positive SPT to at least one of the allergens in the panel. Participants who reacted to the negative control with a weal greater than 3 mm were excluded from analysis where SPT was involved.

BHR was expressed as PD₂₀, transformed into a dichotomous variable with a cut-off value of 1200 µg. The cut-off limit was defined as that below which participants could be expected to experience symptoms related to hyper-reactive pulmonary airways [16]. Values of serum ECP were transformed into a dichotomous variable with a cut-off value of 20 µg/L. FEV₁ values were expressed as percentages of predicted value [17] and transformed into a dichotomous variable with a cut-off value of 85% of predicted values. Age was dichotomized using mean age as the stratification point: 20–45, and 46–82-year-olds. *Smoking* status was expressed as either currently or not smoking in 1998.

AR was defined as whether the participant had had an itchy or stuffy nose or had been sneezing within the last 12 months: (1) when near grass, trees, or flowers; (2) after exposure to furry animals, e.g. horse, dog, cat, rabbit, guinea pig, or hamster; or (3) after exposure to dust when cleaning rooms or making beds, or when in bed, concurrent with a positive SPT to an allergen relevant to the symptoms [18].

Allergic asthma: shortness of breath or trouble breathing within the 12 months after the above-mentioned exposure, concurrent with a positive SPT to an allergen relevant to the symptoms.

Non-allergic asthma: affirmative answer to the question 'Within the last 12 months have you experienced wheezing?' and no positive SPT.

No respiratory atopic disease: no positive SPT, no AR and no asthma.

Statistical analysis

Statistical analyses were performed with SPSS version 11.0 for Windows. The χ^2 test and the *t*-test were used to compare differences between responders and non-responders in 2002. Associations were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). The associations between various predictors and outcome variables were further analysed by multivariate logistic regression.

Results

The overall response rate to the questionnaire about mucosal symptoms elicited by fragrance products was 79.6% of the 1189 participants still alive. Forty-two questionnaires (3.5%) were returned because the address was unknown. Twelve individuals (1%) declined to participate for various reasons.

One hundred and eighty-nine individuals (15.9%) did not respond. The mean age among responders was 45.8 (range: 20–82) years. Non-responders were younger but otherwise similar to responders (Table 1). The percentage of predicted FEV₁ was significantly lower in the deceased (mean 89.5%). Symptoms were most frequently reported from the nose followed by the eyes, lungs and mouth or throat (Table 2). The frequency of reporting at least one mucous membrane symptom elicited by fragrance products within the last 12 months was 42% in the total population (50% in women and 30% in men). Fourteen per cent had symptoms at least once a week, 5% reported that the symptoms influenced their choice of shopping places, means of transportation or resulted in adjustments of working situations, and 4% avoided personal use of perfume and perfumed cosmetics because of their mucosal symptoms. In those who reported symptoms they occurred as follows: other persons' wearing of perfume in 56%, air-fresheners in 32% and other persons' wearing of newly washed clothes in 28%. Tables 3 and 4 shows the relationship of predictor variables to the prevalence of organ-related symptoms and severity of symptoms. All symptoms were consistently associated with BHR and female gender.

In logistic regression models the results were adjusted for atopy, BHR, serum ECP, FEV₁, sex, age and smoking, which did not substantially change the crude ORs given in Tables 3 and 4.

The adjusted OR of having at least one mucosal symptom elicited by fragrance products from at least one organ and BHR was 2.3 (95% CI 1.5–3.5). However, the strongest association was observed between BHR and symptoms from the lungs elicited by fragrance products (adjusted OR 4.0 and 95% CI 2.5–6.5).

The associations between serum ECP and outcome variables were not statistically significant.

A statistically significant association was found between age (more than 46 years) and 'affecting application pattern' (Table 4), but age had no influence on reporting symptoms from various organs (Table 3).

Table 1. Characteristics of responders (*n* = 946), non-responders (*n* = 243), and deceased (*n* = 27)

	Responders (%)	Non-responders (%)	Deceased† (%)
Atopy	40	38	33
Bronchial hyper-reactivity	13	15	25
ECP (≥ 20 µg/L)	17	19	12
FEV ₁ (<85% of predicted)	19	24	38*
Sex (women)	56	50	41
Age (<46 years)	55	78*	33
Smoking status (current smoking)	36	42	42
Allergic asthma	10	10	7
Non-allergic asthma	12	14	22
AR	27	24	22
No respiratory atopic disease‡	48	48	44

ECP, eosinophilic cationic protein; FEV₁, forced expiratory volume in 1 s; AR, allergic rhinitis.

**P*-values <0.05, χ^2 test between responders and the group

†Include individuals that may have emigrated in the follow-up period

‡Individuals without atopy, without asthma, and without AR.

Table 2. The prevalence of various symptoms occurring within the last 12 months

	Participants with						
Do perfume or fragrance products induce any of the following symptoms?	Total (<i>n</i> = 946) (%)	Atopy (<i>n</i> = 378) (%)	Allergic rhinitis (<i>n</i> = 258) (%)	Bronchial hyper-reactivity (<i>n</i> = 118) (%)	Allergic asthma (<i>n</i> = 96) (%)	Non-allergic asthma (<i>n</i> = 109) (%)	No respiratory atopic disease (<i>n</i> = 456) (%)
Nose							
Sneezing	29	34	39	45	44	49	21
Runny nose	17	20	21	26	27	31	12
Itching	14	17	19	21	27	22	9
Pricking sensation	12	12	14	16	16	25	8
Irritation (stinging and dryness)	9	8	10	13	17	16	7
Stuffed-up nose	8	10	10	18	11	14	6
Eyes							
Itching eyes	15	18	20	27	30	29	9
Eye-irritation (stinging and dryness)	12	12	13	19	16	27	9
Tearful eyes	11	10	12	18	16	25	9
Swelling or flushing of eye surroundings	8	9	11	15	12	17	4
Lungs							
Troublesome breathing	11	11	13	32	25	29	7
Coughing	11	10	11	26	20	24	9
Wheezing	7	8	10	24	20	22	2
Phlegm when coughing	6	4	4	18	9	16	4
Chest tightness	5	4	4	12	9	15	3
Mouth or throat							
Discomfort	6	5	6	8	8	17	4
Irritation (stinging and dryness)	5	6	7	7	10	11	3
Pricking sensation	4	6	7	6	10	7	2
Itching	3	4	5	5	8	7	2

Table 3. Occurrence of symptoms elicited by fragrance products within the last 12 months in various subgroups

		Fragrance products elicit symptoms from the							
		Eyes (<i>n</i> = 199)		Nose (<i>n</i> = 325)		Mouth or throat (<i>n</i> = 107)		Lungs (<i>n</i> = 166)	
		Prevalence (%)	OR*	Prevalence (%)	OR*	Prevalence (%)	OR*	Prevalence (%)	OR*
Atopy	Yes	23	1.1	38	1.2	13	1.2	18	1.0
	No	21	(0.8–1.5)	33	(0.9–1.6)	11	(0.8–1.9)	18	(0.7–1.5)
BHR	Positive	35	2.3	47	1.8	19	2.0	40	4.0
	Negative	19	(1.5–3.4)	34	(1.2–2.6)	10	(1.2–3.4)	14	(2.6–6.1)
ECP	≥20 µg/L	27	1.5	39	1.2	17	1.7	23	1.4
	<20 µg/L	21	(0.9–2.1)	34	(0.8–1.7)	11	(1.0–2.7)	17	(0.9–2.2)
FEV ₁	≥85% of pred.	21	1.0	35	1.0	12	1.0	17	0.8
	<85% of pred.	21	(0.7–1.5)	36	(0.7–1.3)	12	(0.6–1.7)	21	(0.5–1.2)
Sex	Women	28	2.4	42	2.1	14	1.6	22	2.0
	Men	14	(1.7–3.4)	26	(1.6–2.8)	9	(1.0–2.4)	12	(1.4–2.9)
Age (years)	20–45	22	1.0	37	1.2	11	0.9	18	1.0
	46–82	21	(0.7–1.4)	32	(0.9–1.6)	12	(0.6–1.4)	18	(0.7–1.4)
Smoking	Current	21	0.8	36	1.1	12	1.1	20	1.3
	Not smoking	22	(0.7–1.3)	34	(0.8–1.4)	11	(0.7–1.7)	17	(0.9–1.8)
Allergic asthma	Yes	32	1.8	48	1.9	19	2.0	34	2.7
	No	20	(1.1–2.9)	33	(1.2–2.9)	11	(1.2–3.5)	16	(1.7–4.3)
Non-allergic asthma	Yes	42	3.1	53	2.3	25	3.1	38	3.4
	No	19	(2.1–4.8)	33	(1.5–3.5)	10	(1.9–5.1)	15	(2.2–5.3)
Allergic rhinitis	Yes	26	1.4	42	1.6	15	1.5	20	1.3
	No	20	(1.0–2.0)	32	(1.2–2.1)	10	(1.0–2.4)	17	(0.9–1.8)
No respiratory atopic disease	Yes	16	0.5	28	0.6	7	0.4	13	0.5
	No	27	(0.4–0.7)	41	(0.4–0.7)	16	(0.3–0.7)	23	(0.4–0.7)

BHR, bronchial hyper-reactivity; ECP, eosinophilic cationic protein; FEV₁, forced expiratory volume in 1 s; pred., predicted.

*Crude odds ratio (OR) (95% confidence interval). Statistically significant ORs are indicated in bold.

Table 4. Occurrence of symptoms indicating severity in various subgroups

		Symptoms elicited by fragrance products									
		Affecting daily activity (<i>n</i> = 47)		Frequently (<i>n</i> = 132)		By several elicitors (<i>n</i> = 71)		In extensive target organs (<i>n</i> = 56)		Affecting application pattern (<i>n</i> = 33)	
		Prevalence (%)	OR*	Prevalence (%)	OR*	Prevalence (%)	OR*	Prevalence (%)	OR*	Prevalence (%)	OR*
Atopy	Yes	6	1.1	14	0.9	8	1.0	6	1.0	4	1.1
	No	5	(0.6–2.6)	15	(0.6–1.3)	8	(0.6–1.6)	6	(0.6–1.7)	4	(0.5–2.2)
BHR	Positive	12	3.0	24	2.0	14	2.1	12	2.5	7	2.5
	Negative	4	(1.5–5.9)	13	(1.3–3.3)	7	(1.2–3.9)	5	(1.3–4.7)	3	(1.1–5.6)
ECP	≥20 µg/L	4	0.8	21	1.8	10	2.0	9	2.1	6	3.2
	<20 µg/L	6	(0.3–2.4)	14	(1.0–3.1)	8	(1.0–3.9)	6	(1.0–4.4)	3	(1.4–7.2)
FEV ₁	≥85% of pred.	5	1.1	14	0.7	9	1.9	6	1.0	4	1.6
	<85% of pred.	5	(0.5–2.4)	18	(0.5–1.2)	5	(0.9–4.0)	6	(0.5–1.9)	2	(0.5–4.6)
Sex	Women	7	2.7	18	1.8	10	2.0	8	1.9	5	1.9
	Men	3	(1.4–5.4)	11	(1.2–2.6)	5	(1.2–3.4)	4	(1.0–3.3)	3	(0.9–3.9)
Age (years)	20–45	4	0.6	15	1.0	6	0.6	5	0.7	2	0.3
	46–82	6	(0.4–1.2)	15	(0.7–1.4)	10	(0.4–1.0)	7	(0.4–1.2)	6	(0.2–0.7)
Smoking	Current	5	1.0	15	1.1	7	0.9	6	0.9	3	0.8
	Not smoking	5	(0.5–1.9)	14	(0.7–1.6)	8	(0.5–1.5)	6	(0.5–1.5)	4	(0.4–1.6)
Allergic asthma	Yes	9	1.9	21	1.6	14	2.3	12	2.4	9	3.0
	No	5	(0.9–4.2)	14	(0.9–2.8)	7	(1.2–4.2)	5	(1.2–4.8)	3	(1.3–6.8)
Non-allergic asthma	Yes	13	3.3	30	3.0	14	2.1	11	2.3	5	1.4
	No	4	(1.7–6.5)	13	(1.9–4.8)	7	(1.1–3.9)	5	(1.2–4.5)	4	(0.6–3.6)
Allergic rhinitis	Yes	7	1.4	16	1.1	10	1.4	7	1.3	5	1.5
	No	5	(0.8–2.6)	14	(0.8–1.7)	7	(0.8–2.3)	6	(0.7–2.3)	3	(0.8–3.2)
No respiratory atopic disease	Yes	3	0.4	12	0.6	7	0.7	5	0.6	3	0.8
	No	7	(0.2–0.8)	17	(0.4–0.9)	9	(0.4–1.1)	7	(0.4–1.1)	4	(0.4–1.6)

BHR, bronchial hyper-reactivity; ECP, eosinophilic cationic protein; FEV₁, forced expiratory volume in 1 s; pred., predicted.

*Crude odds ratio (OR) (95% confidence interval). Statistically significant ORs are indicated in bold.

No associations were found between atopy and mucosal symptoms elicited by fragrance products. Smoking and FEV₁ were not associated with any of the outcome variables.

Consistent associations between allergic asthma, non-allergic asthma and organ-related outcome variables were found (Table 3). Sixty-seven percent of individuals with non-allergic asthma reported at least one mucosal symptom elicited by fragrance products within the last 12 months. The prevalence of symptoms among all other groups was lower, the lowest in individuals with no respiratory atopic diseases. The OR between non-allergic asthma and different outcome variables was generally higher than for allergic asthma. AR differed from asthma in relation to both pattern and degree of association. An association between AR and symptoms elicited by fragrance products from the nose, mouth or throat, only, was found (Table 3). No association was found between AR and outcome variables indicating severity of symptoms (Table 4).

Discussion

This is the first population-based study investigating objective measures of atopy or BHR in relation to mucosal symptoms elicited by fragrance products. Some clinical studies have focused on these symptoms and atopy in patient groups with asthma and rhinitis [2, 6, 8, 10]. Others have studied

pathophysiological mechanisms of airway symptoms elicited by fragrance products in confined groups of patients without atopy or asthma [7, 9]. Epidemiological studies have been carried out regarding the symptom complex of multiple chemical sensitivity (MCS) [4, 5, 19]; however, objective markers of atopy or asthma were not investigated. MCS is not a well-defined entity [19], but it causes various symptoms from multiple organs elicited by chemicals in low concentrations, not only fragrance products [20]. The current study focused on mucosal symptoms only; thus, no direct comparison can be made with results obtained from epidemiological studies on MCS.

The mucosal symptoms elicited by fragrance products were not associated with previously recognized atopy (defined as positive SPT) in the current study; therefore, pathways different from specific IgE-mediated immunological mechanisms are more likely.

Consistent associations between mucosal symptoms elicited by fragrance products and BHR were found. This indicates that such symptoms would be more prevalent in persons with asthma, and when investigating the epidemiological definitions of asthma used in this study, this assumption was confirmed. Allergic asthma and non-allergic asthma were both associated with symptoms elicited by fragrance products. In contrast, smoking and low FEV₁ were not associated with outcome variables. This suggests that symptoms related to fragrance products are not more common in individuals with chronic obstructive pulmonary disease.

Mucosal symptoms elicited by fragrance products were most frequently reported from the nose. The prevalence of symptoms from the nose in individuals with AR was in accordance with a study including 315 patients with rhinitis [2]. Unexpectedly, the association between reporting fragrance-elicited symptoms from the nose and having AR was weak and severity of the fragrance-elicited symptoms was not more common among individuals with AR than those without.

A decline in lung function after perfume inhalation has been reported in individuals with severe asthma [10] and in cases after occupational exposure to perfume [21, 22]. It has, however, been disputed whether respiratory symptoms elicited by fragrance products in persons with asthma could be attributed to bronchial obstruction [8]. Sensory reflex mechanisms have been suggested as alternative mechanisms [7, 9]. Increased sensitivity to inhaled capsaicin indicating an alteration of chemosensory perception as suggested by Millqvist et al. [23] was proposed to be involved when symptoms were elicited by perfume in the eyes and airways [9]. This phenomenon known as sensory hyper-reactivity seems to be frequent among individuals with unclear respiratory symptoms [24]. Future studies may reveal if symptoms from mucous membranes other than in the lungs can be predicted by sensitivity to inhaled capsaicin. It has been suggested that airway inflammation in asthmatics could up-regulate the sensitivity to inhaled capsaicin [25]. In persons with severe asthma, bronchial obstruction has been elicited by exposure to perfume [10]. We explored the effect of elevated serum ECP as a marker of inflammation in persons with asthma, but no consistent association between mucosal symptoms and serum ECP was found. This might be explained by serum ECP having been measured 4 years earlier than the assessment of symptoms from mucous membranes elicited by fragrance products. The possible effects of different medication could have given additional valuable information, e.g. a positive effect of inhaled steroids could have supported airway inflammation playing a role in elicitation of the symptoms. However, the questionnaire was focused on only the symptoms.

Atopy and methacholine responsiveness were measured 4–5 years earlier than odour sensitivity; theoretically this may have influenced the results. However, asthma is a chronic disease and the importance of follow-up time is probably of minor relevance for the results. Recall bias could be a problem: participants with a positive test for SPT and/or BHR may be more aware of mucosal symptoms, and therefore report more symptoms. However, individuals with atopy did not report more symptoms.

This study is not intended to equate the subjective attribution of mucosal symptoms on exposure to volatile fragrances with proven causal relationship. To evaluate whether the relationship between the reporting of mucosal symptoms elicited by fragrance products and BHR is causal, data from objective measurements of the former symptoms and BHR should be collected in a prospective study. Experimental studies are needed to investigate the mechanisms of exposure to fragrances and elicitation of various mucosal symptoms.

Women, as opposed to men, reported more frequent and more severe mucosal symptoms after exposure to fragrance

products (Tables 3 and 4). The threshold of mucosal sensitivity in the eyes and airways may depend on gender. To support this hypothesis, the cough threshold measured by inhaled capsaicin is significantly lower in healthy women compared with healthy men [26]. Another explanation of the difference between men and women could be related to a heavier exposure in women to fragrances from personal cosmetic usage [27].

In conclusion, symptoms from the eyes and/or airways elicited by fragrance products were frequent in this population-based sample. The reported symptoms were not associated with atopy. This suggests a mechanism of action different from IgE-mediated allergy. Female gender and BHR were strong and independent predictors of reporting symptoms from eyes and/or airways elicited by fragrance products. Consistent with the results of BHR, a significant association was found between all mucous membrane symptoms elicited by fragrance products and subgroups of asthma. The results of this study indicate that persons with asthma are more frequently and more severely bothered by exposure to fragrance products than those without asthma. However, considering the frequency of reported symptoms to fragrance products in the total population sample, other risk groups must exist – a subject for future investigation.

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