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Original Article

Phantom Smells: Prevalence and Correlates in a Population-Based Sample of Older Adults

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Abstract

Loss of olfactory function is common in old age, but evidence regarding qualitative olfactory dysfunction in the general older population is scarce. The current study investigates the prevalence and correlates of phantom smell experiences (phantosmia) in a population-based study (Swedish National Study on Aging and Care in Kungsholmen [SNAC-K]) of Swedish adults (n = 2569) aged between 60 and 90 years. Phantosmia was assessed through a standardized interview and defined as reporting having experienced an odor percept in the absence of any stimuli in the surrounding environment that could emit the odor. The relationships between phantosmia and demographic, genetic, health-related, and behavioral variables were analyzed with hierarchical logistic regression analyses. The overall prevalence of phantom smells was 4.9%, and was associated with female gender, carrying the met allele of the *BDNF* gene, higher vascular risk burden, and reporting distorted smell sensations (parosmia). Olfactory dysfunction was, however, not related to phantosmia. The most frequently reported phantom smell was smoky/burnt. A novel finding was that some individuals reported phantom smells with an autobiographical connotation. The results from this study indicate that the prevalence of phantosmia in the general older population is not negligible and that some factors that are beneficial for preserved olfactory function, such as female gender and the *BDNF* met allele, are also associated with the occurrence of phantom smells.

Key words: aging, genetic polymorphisms, hallucinations, olfactory perception, phantosmia, population based

Introduction

Olfactory dysfunction is common, especially among older individuals. Between 32% and 62% of the older population are estimated to have an impaired sense of smell compared with 6–17% in younger age groups (Murphy et al. 2002; Brämerson et al. 2004; Landis et al. 2004; Wehling et al. 2011). Olfactory dysfunction significantly impacts on quality of life; individuals with an impaired sense of smell often report nutritional and interpersonal problems as well as negative mood changes and depression (Temmel et al. 2002; Hummel and Nordin 2005). Age-related olfactory impairments are also associated with cognitive decline and can predict later occurrence of dementia in elderly adults (Olofsson et al. 2009; Stanciu et al. 2014; Devanand et al. 2015).

Previous research has mainly focused on quantitative olfactory dysfunctions in old age, such as reduced olfactory sensitivity and identification ability. However, olfactory dysfunctions may also involve qualitatively distorted odor sensations such as parosmia and phantosmia. Individuals with parosmia experience odors that

are incongruent with the olfactory environment. Fresh fruit smells may, for example, be perceived as rotten. An individual with phantosmia suffers from olfactory "hallucinations," experiences of odors when no odor source is present (Leopold 2002; Frasnelli et al. 2004). Qualitative olfactory dysfunctions are in fact often experienced as more disturbing than a reduction of smell function because the individual is repeatedly reminded of the problem (Leopold 2002). A person with a reduced sense of smell, on the other hand, may remain unaware of the olfactory deficit (Mackay-Sim et al. 2006).

Phantosmia has previously been documented in individuals with epileptic seizures, schizophrenia, depression, migraine, and otorhinolaryngology problems (Fuller and Guiloff 1987; Nordin et al. 1996; Leopold 2002; Chen et al. 2003; Frasnelli et al. 2004; Landis et al. 2004; Coleman et al. 2011). The prevalence has been estimated to range between 0.8% and 25% depending on the clinical group studied (Nordin et al. 1996; Landis et al. 2004), yet little is known about the prevalence of phantosmia in healthy individuals. One study on self-reported chemosensory alterations in a population-based US sample of adults 40 years and older found the prevalence of phantosmia to be 6% (Rawal et al. 2016). In another study investigating the frequency of various hallucinations (olfactory, gustatory, visual, auditory, haptic, out-of-body experiences, hypnopompic, and hypnagogic) in samples of healthy participants in 3 different countries, olfactory hallucinations were the most common hallucination, reported by 8.6% of the participants, with 3.5% experiencing phantosmia at least once a month (Ohayon 2000).

A related area of research addresses olfactory dreams, which also constitute a subjective experience of smell in the absence of actual stimulation. In one study, 31.7% of the sample reported having had olfactory sensations in a dream (Stevenson and Case 2004). The olfactory sensations described were often related to odors frequently encountered in the environment such as food, drinks, body odors, and odors occurring in nature. A large proportion (21%) of those experiencing olfactory sensations in dreams reported odors with a "smoky" or "burnt" quality (Stevenson and Case 2004). This is in line with the olfactory experiences reported by phantosmic patients. Phantom smells are frequently reported to be negative in valence and are often described as burnt, foul, unpleasant, spoiled, or rotten (Leopold 2002; Chen et al. 2003; Velakoulis 2006; Coleman et al. 2011), although neutral and positive phantom smells have also been reported (Acharya et al. 1998).

Olfactory hallucinations and phantosmias are reported more often by women than men (Ohayon 2000; Leopold 2002). Typically, the first episode occurs between the ages of 15 and 30 years, lasts for about 5–20 min and resolves spontaneously with no lingering effects. Also, evidence indicates that the hallucinations often become gradually more frequent and persistent following the year of onset (Leopold 2002).

Phantosmia occurs in a variety of clinical conditions, and its causes are yet unknown. Prior accounts have suggested that the phantosmic sensations originate either in the peripheral olfactory nervous system or in central brain regions (Stevenson and Langdon 2012), such as the amygdala (Acharya et al. 1998; Chen et al. 2003) and the orbital frontal cortex (Arguedas et al. 2012). A recent study showed that patients who experienced phantosmia following head trauma were characterized by left frontal atrophy, suggestive of a cortical origin (Lötsch et al. 2016). However, a patient study reported successfully resolving phantosmia in 7 out of 8 patients through excision of the olfactory epithelium, suggesting also peripheral olfactory system involvement (Leopold et al. 2002). It is thus likely that phantosmias may originate from disruptions in the functional interactions of central and peripheral olfactory circuits.

Although aging is associated with diminished olfactory function (Brämerson et al. 2004; Landis et al. 2004; Larsson et al. 2004; Mackay-Sim et al. 2006), little is known about the role of aging in the occurrence of phantosmia or whether phantosmia is related to any of the variables that are typically associated with olfactory impairments. Genetic variation is one factor that may modulate olfactory ability. For example, Hedner et al. (2010) reported that carriers of the *BDNF* val allele exhibited a higher age-related olfactory decline compared with met allele carriers, perhaps due to the gene's role in neural plasticity (Poo 2001). Further, the apolipoprotein E (*APOE*) ε4 allele has been linked to olfactory deficits in older adults (Olofsson et al. 2010; Larsson et al. 2016; Olofsson et al. 2016). Olfactory impairments have also been associated with a number of other demographic, clinical, and behavioral variables (Murphy et al. 2002; Brämerson et al. 2004; Mackay-Sim et al. 2006). As phantosmia might be related to impaired olfaction (Frasnelli et al. 2004), it is important to further investigate variables that are known to play a role in old-age olfactory dysfunction and whether these may account for phantosmia.

The primary aim of this study was thus to investigate the prevalence of phantosmia in the general older population, and how phantosmia correlates with demographic, genetic, clinical, behavioral, olfactory, and cognitive variables. Furthermore, the qualitative (type of odor) and quantitative (e.g., duration, frequency) features of phantosmia in old age were examined.

Materials and methods

Participants

Participants were derived from the population-based longitudinal Swedish National Study on Aging and Care in Kungsholmen (SNAC-K). This study originally recruited 3363 randomly selected residents of the area of Kungsholmen in central Stockholm, Sweden, belonging to predefined age cohorts (60, 66, 72, 78, 81, 84, 87, 90, 93, 96, and 99 years or older). They took part in extensive baseline assessments of medical, psychological, and social factors. A subgroup of 2848 participants underwent cognitive assessment (Laukka et al. 2013), which included an interview on olfactory functions and an olfactory testing protocol. For the present study, 77 participants who did not respond to the questions regarding phantosmia were excluded. In addition, individuals with dementia ($n = 81$), Parkinson's disease ($n = 21$), and developmental disorder ($n = 1$), as well as individuals above 90 years of age ($n = 79$) or scoring < 24 ($n = 20$) on the Mini-Mental State Examination (MMSE) were excluded (see Figure 1). The final study sample included 2569 participants (61.6% women, mean age = 72.05 years, SD = 9.52). The SNAC-K study has been approved by the ethical committee at Karolinska Institutet. All participants provided written informed consent, and the study was performed in accordance with the ethical standards stated in the 1964 Declaration of Helsinki.

Assessment of phantosmia

Subjective assessments of olfactory abilities were acquired through a modified version of a standardized interview (Nordin et al. 2004), including questions regarding different olfactory functions and dysfunctions. Phantosmia was defined to the participants as an odor percept in the absence of any stimuli in the surrounding environment that could emit the odor. Specifically, phantosmia was assessed by the question "Have you in the last year experienced so called phantom smells?". The question was answered on a 5-point Likert-type scale, where 0 = "Never" and 4 = "Always." Participants were grouped as phantosmic (1–4) and nonphantosmic (0 = never).

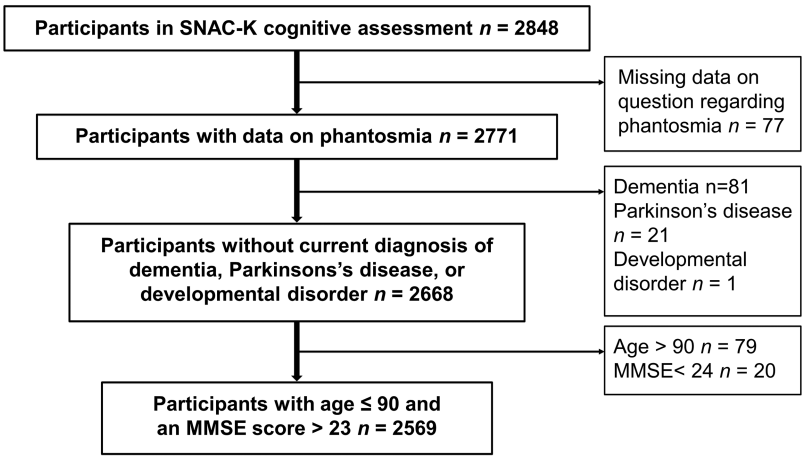

Figure 1. Exclusion flowchart. MMSE, Mini-Mental State Examination; SNAC-K, Swedish National Study on Aging and Care in Kungsholmen.

In instances where a participant reported phantosmia, follow-up questions regarding the quality of the phantom smell were asked. The participants were first asked to indicate what type of phantom smell they had experienced. Seven predefined types of smells were provided: infected tissue, smoke, feces, rotten, musk, mold, and metallic. The participants could also generate their own label if the phantom smell did not match any of the predefined alternatives. They were allowed to select several categories if they had experienced more than one type of phantom smell. The answers generated by the participants were later grouped into 11 additional categories, consisting of similar responses. The grouping was conducted by 2 experts and was then compared and revised until a consensus was reached.

Another follow-up question addressed the intensity of the phantom smell ("How strong is the phantom smell?"). The participants indicated whether the phantom smell was perceived as faint, medium, or strong. They were also asked to assess for how long they had experienced the phantom smell (0 = "less than a year," 1 = "1–3 years," 2 = "4–5 years," 3 = "6–10 years," 4 = "more than 10 years," and 5 = "whole life") and how often the phantom smell appeared (0 = "every month," 1 = "every week," 2 = "daily," 3 = "always," and 4 = "other"). The duration of the phantom smell was assessed by the question "How long does the phantom smell last?" (0 = "fleeting," 1 = "a few minutes," 2 = "a few hours," and 3 = "all day"). Finally, the participants were asked to specify when the phantom smell last occurred (0 = "more than 6 months ago," 1 = "1–6 months ago," 2 = "2–4 weeks ago," 3 = "in the last few days," or 4 = "it is present right now").

Correlates of phantosmia

Demographic variables

Demographic variables included age, gender, and educational background. Age was dichotomized into 2 age groups; young-old (<75 years) and old-old (≥75 years). Educational background was measured as the number of years of formal schooling and was dichotomized into higher (≥12 years) and lower (<12 years) education.

Genetic variables

Genotyping was conducted via DNA extraction from peripheral blood samples. *APOE* (rs429358) and *BDNF* (rs6265) were genotyped using MALDI-TOF analysis on the Sequenom MassARRAY platform at the Mutation Analysis Facility, Karolinska Institutet (Darki et al. 2012). Hardy Weinberg Equilibrium was confirmed for both polymorphisms (*P*'s ≥ 0.10). For *APOE*, participants were grouped as carriers or noncarriers of the ε4 allele, and for *BDNF*, participants were dichotomized into homozygous val/val carriers and carriers of any met allele.

Vascular variables

Information on vascular variables was collected through self-report, clinical examination, medication lists, laboratory data, and the computerized Stockholm inpatient register (Welmer et al. 2014). Vascular conditions included in the study were cerebrovascular disease (stroke), number of cardiovascular diseases (heart failure, atrial fibrillation, and coronary heart disease), and number of cardiovascular risk factors (diabetes, hypertension, and high cholesterol). The indexes of both cardiovascular disease and cardiovascular risk burden ranged from 0 to 3.

Other clinical variables

Other clinical variables that potentially could be related to phantosmia included current diagnosis of depression (ICD-10 criteria), as well as self-reported lifetime history of head trauma, migraine, epilepsy, any form of cancer, hypothyroidism, and schizophrenia. Furthermore, dementia (DSM IV criteria) was diagnosed at each testing occasion. The potential effect of dementia conversion up to 6 years after baseline could therefore be investigated. Due to more rapid changes and higher attrition rates in the older cohorts, the follow-up interval was 3 years for older (>78 years of age) and 6 years for younger cohorts (60–72 years of age). Dementia conversion was treated as a dichotomous variable (dementia vs. no dementia).

Behavioral variables

Current smoking and alcohol consumption were assessed through a standardized interview conducted by a nurse. Alcohol consumption was based on self-rated estimations of frequency and amount of drinks on a typical drinking day, and categorized into no or occasional, light-to-moderate (1–14 drinks/week for men and 1–7 drinks/week for women), and heavy (>14 drinks/week for men and >7 drinks/week for women). No or occasional and light-to-moderate consumption were collapsed in the analysis. Physical activity was assessed by a self-administered questionnaire regarding both intensity and frequency. Physical inactivity refers to light, moderate, or intense exercise less or equal to 2–3 times per month and was compared with physical exercise more than 3 times per month. Furthermore, the longest held profession was assessed to investigate

the differences between unskilled or skilled manufacturing work ("blue collar") and intermediate or highly trained professionals ("white collar"). Weight and length for all participants were assessed and used to calculate their body mass index (BMI). Obesity was classified as BMI > 30.

Olfactory functions

Olfactory performance was assessed using Sniffin' Sticks, a standardized 16-item odor identification test. The Sniffin' Sticks test battery is a well-validated and norm-referenced test set with high test–retest reliability (Hummel et al. 1997; Croy et al. 2015). The testing procedure has been described in detail elsewhere (Larsson et al. 2016). In short, odors were presented using felt tip-pens containing the following odors: apple, banana, cinnamon, cloves, coffee, fish, garlic, leather, lemon, licorice, mushroom, peppermint, petrol, pineapple, rose, and turpentine. Participants were first instructed to freely identify the odors. If they were unable to correctly identify an odor, they were asked to select 1 of 4 written response alternatives of which 1 was correct. The score of interest here was the proportion of correctly identified odors with free or cued identification. Participants with a score of 10 points or lower were classified as having olfactory dysfunction according to established clinical practice (Hummel et al. 2001).

Parosmia was defined as distorted odor perception where known odors are experienced as qualitatively different compared with how they are usually perceived (e.g., orange smells like mud). Parosmia was measured through self-reports with the question "Have you during the last year experienced a distorted sense of smell?". The question was answered on a 5-point scale, where 0 = "never" and 4 = "always." Participants were grouped as parosmic (1–4) and nonparosmic (0 = never).

Cognitive function

As a measure of global cognitive ability, MMSE (Folstein et al. 1975) was included.

Statistical analysis

Chi-square tests and *t*-tests were used to examine potential differences in the demographic, genetic, clinical, behavioral, olfactory, and cognitive variables between those with phantosmia and those without. The relationships between phantosmia and the included variables were analyzed by hierarchical logistic regression analyses. In the first step, gender, age group, and educational level were entered in the regression model (block 1). Subsequently, blocks containing genetic variables (block 2), vascular diseases and risk factors (block 3), other clinical variables (block 4), behavioral variables (block 5), olfactory functions (block 6), and cognitive ability (block 7) were entered. As a measure of model fit, Nagelkerke's pseudo-R^2 is reported for each step. The omnibus chi-square test of model coefficients was used to test whether entering a new block resulted in significantly improved model fit. Odds ratios (OR) including 95% confidence intervals and *P*-values for each contrast are reported. Potential interaction effects between individually contributing factors were assessed. Only statistically significant interaction effects ($P < 0.05$) were included in the final regression model.

An additional analysis was conducted to investigate whether participants with rare occurrences of phantosmia modulated the observed statistical associations. Here, the reported frequency of the phantom smell was used to separate between those with mild and more severe phantosmia. Those who experienced phantosmia at least once a month were compared with a reference group consisting of nonphantosmic individuals and individuals who experienced phantosmia less than once a month, using the same statistical procedure as above.

Results

Prevalence and correlates of phantosmia

The overall prevalence of phantosmia was 4.9% ($n = 125$). The prevalence of phantosmia across the demographic, genetic, vascular, clinical, behavioral, olfactory, and cognitive factors is presented in Table 1. Individuals with phantosmia were more likely to be women ($P = 0.038$), and *BDNF* met allele carriers ($P = 0.019$). They were also more likely to have parosmia ($P < 0.001$). No other significant differences between the 2 groups were observed. To reduce the number of variables in the regression analyses, variables that were nonsignificant at the univariate level and had few observations in the phantosmic group ($n < 10$, Table 1) were not included in the subsequent analyses.

Results from the blockwise hierarchical logistic regressions are presented in Table 2. The first block, with the demographic variables only, was not significantly associated with phantosmia ($P = 0.091$). Adding a genetic (Nagelkerke's pseudo-$R^2 = 0.02$; $P = 0.009$) and a vascular (Nagelkerke's pseudo-$R^2 = 0.04$; $P = 0.034$) block significantly improved model fit. Although overall model fit was better in the final model, including all 7 blocks (Nagelkerke's pseudo-$R^2 = 0.06$, χ^2 (19) = 39.48, $P = 0.004$), adding blocks including clinical, behavioral, olfactory, and cognitive variables did not result in significant model improvements.

In the final regression model, a number of significant individual correlates were identified. Among the demographic variables, only female gender showed an association with phantosmia. Independent of demographic information, a significant association was also observed with the *BDNF* met allele. Furthermore, cardiovascular risk burden, but none of the other clinical, behavioral, or cognitive variables, contributed significantly to phantosmia. Olfactory dysfunction was not related; however, prevalent parosmia showed a strong association to phantosmia. Examinations of potential interactions between variables revealed no significant effects and are therefore not included in Table 2.

In a follow-up analysis, we investigated the prevalence of severe phantosmia (defined as phantosmia experiences at least once a month) and found that it was experienced by 1.7% (48 individuals) of the sample. Adopting the same statistical procedure as above, we found that the final model resulted in a comparatively high model fit (Nagelkerke's pseudo-$R^2 = 0.12$, χ^2 (19) = 39.99, $P = 0.003$). In this analysis, female gender was no longer significantly related to phantosmia (OR = 1.78, $P = 0.140$, 95% CI = 0.83–3.83). However, the *BDNF* met allele (OR = 3.45, $P < 0.001$, 95% CI = 1.74–6.81), cardiovascular risk burden (OR = 1.77, $P = 0.020$, 95% CI = 1.09–2.87), head trauma (OR = 2.39, $P = 0.031$, 95% CI = 1.08–5.28), and parosmia (OR = 5.95, $P = 0.032$, 95% CI = 1.17–30.40) were all significantly related to severe phantosmia in the final model. Hence, the results indicate that the correlates of severe phantosmia are largely similar to those of overall phantosmia.

Qualitative descriptions of phantom smells

Qualitative descriptions of frequency and intensity of phantom smell perception are summarized in Figure 2A–E. Among the individuals with phantosmia ($n = 125$), 16% had experienced phantosmia their entire life, 16% had experienced phantosmia for more than 10 years, and 17% had experienced phantosmia for less than a year. The majority of the phantosmics reported that the intensity of the

Table 1. Prevalence of phantosmia as a function of potential correlates ($n = 2569$)

Characteristic	*n*	Phantosmia, number (%)		
		No, 2444 (95.1%)	Yes, 125 (4.9%)	*P* value
Demographic				
Gender				0.04
Male		950 (38.9)	37 (29.6)	
Female		1494 (61.1)	88 (70.4)	
Age				0.30
<75		1510 (61.8)	83 (66.4)	
≥75		934 (38.2)	42 (33.6)	
Education				0.54
Low (<12 years)		1183 (48.4)	57 (45.6)	
High (≥12 years)		1261 (51.6)	68 (54.4)	
Genetic				
APOE (ε4 carrier)	2415	665 (29.0)	43 (36.1)	0.09
BDNF (Met carrier)	2283	692 (31.9)	48 (42.5)	0.02
Vascular conditions				
Heart failure		237 (9.7)	14 (11.2)	0.58
Coronary heart disease		405 (16.6)	25 (0.2)	0.32
Atrial fibrillation		367 (15.0)	17 (13.6)	0.66
Cerebrovascular disease		222 (9.1)	5 (4.0)	0.05
High cholesterol	2498	307 (12.9)	16 (13.0)	0.98
Hypertension	2565	1240 (50.8)	72 (58.0)	0.11
Diabetes	2507	222 (9.3)	13 (10.6)	0.64
Clinical, other				
Head trauma	2547	331 (13.7)	23 (18.4)	0.14
Migraine		77 (3.2)	6 (4.8)	0.31
Depression		97 (4.0)	8 (6.4)	0.18
Hypothyroidism	2556	211 (8.7)	15 (12.1)	0.19
Cancer	2556	370 (15.2)	23 (18.5)	0.32
Schizophrenia		9 (0.4)	1 (0.8)	0.45
Epilepsy	2564	19 (0.8)	2 (1.6)	0.31
Dementia at follow-up		184 (7.5)	5 (4.0)	0.14
Behavioral				
Heavy drinking	2559	419 (17.2)	24 (19.4)	0.54
Physical inactivity		619 (25.3)	38 (30.4)	0.20
Current smoking	2554	364 (15.0)	24 (19.2)	0.20
Manufacturing occupation	2565	479 (19.6)	32 (25.8)	0.09
Obesity (BMI > 30)	2515	321 (13.4)	24 (19.5)	0.06
Olfaction				
Olfactory dysfunction	2393	618 (27.1)	28 (24.3)	0.51
Parosmia	2557	26 (1.1)	8 (6.4)	<0.01
Cognition				
MMSE, mean ± SD		28.91 ± 1.29	29.05 ± 1.17	0.26

SD, standard deviation.

phantom smell was faint (48%) or of medium strength (43%); 9% experienced strong phantom smells. Phantom smells were experienced at least once a week by 20% of the phantosmic sample. However, a majority of those who selected the response alternative "other" reported that the phantom smell occurred less than once a month (54%). Phantom smells within the last few days were reported by 24% of the phantosmic group. The phantom smell was most commonly reported to last for a few minutes (43%) or to appear fleetingly (39%).

The different types of reported phantom smells are described in Figure 3. The most frequently reported phantom smell was smoky or burnt, reported by 54 of the 117 phantosmic individuals who had specified the type of the smell they had experienced. Other smell qualities reported were rotten ($n = 5$), mold ($n = 8$), metallic ($n = 6$), cooked food ($n = 5$), perfume ($n = 6$), flower ($n = 6$), and dusty and/or dirty ($n = 6$). Twenty-eight participants reported more than one type of phantom smell.

Nine individuals reported phantom smells with an autobiographical connotation. The autobiographical descriptions linked to each phantom smell are summarized in Table 3. Phantom smells that were associated with childhood memories were reported by 3 individuals, and 2 individuals reported smells that had been perceived during an incident of fire in their homes several years ago. Furthermore, 2 individuals reported phantom smells that were associated with their deceased spouses.

To investigate whether any specific feature of the phantom smell was associated with other features, Spearman's rank correlation coefficients were calculated. This revealed a significant positive correlation between the last occurrence of the phantom smell and how often the phantom smell is perceived ($r = 0.40$, $n = 91$, $P < 0.001$). This indicates that

Table 2. Blockwise hierarchical logistic regression analysis for correlates of phantosmia ($n = 2003$)

Characteristic	Nagelkerke's pseudo-R^2	Model parameters		Model parameters, all factors included	
		OR	95% CI	OR	95% CI
1. Demographic	0.01				
Gender (female)		1.63*	1.04–2.54	1.68*	1.04–2.69
Age (≥75 years)		0.79	0.50–1.25	0.78	0.46–1.33
Education (≥12 years)		1.19	0.78–1.82	1.40	0.88–2.22
2. Genetic	0.02**,[a]				
APOE (ε4 carrier)		1.38	0.90–2.10	1.39	0.90–2.13
BDNF (Met carrier)		1.76**	1.17–2.64	1.81**	1.19–2.74
3. Vascular	0.04*				
CVD burden		1.25	0.93–1.69	1.25	0.92–1.69
CVR burden		1.37*	1.01–1.85	1.36*	1.00–1.86
Cerebrovascular disease		0.57	0.22–1.45	0.57	0.22–1.47
4. Clinical, other	0.04				
Head trauma		1.59	0.94–2.69	1.63	0.96–2.77
Hypothyroidism		1.21	0.62–2.37	1.14	0.57–2.25
Cancer		1.34	0.79–2.27	1.30	0.76–2.22
5. Behavioral	0.05				
Heavy drinking		0.99	0.58–1.67	1.01	0.59–1.71
Physical inactivity		1.29	0.80–2.08	1.29	0.80–2.08
Smoker		1.10	0.63–1.92	1.09	0.63–1.91
Manufacturing profession		1.60	0.96–2.71	1.65	0.98–2.79
BMI > 30		1.09	0.62–1.94	1.09	0.61–1.94
6. Olfaction	0.06				
Olfactory dysfunction		0.83	0.48–1.42	0.87	0.51–1.50
Parosmia		3.71*	1.17–11.76	3.88*	1.21–12.43
7. Cognition	0.06				
MMSE		1.14	0.93–1.40	1.14	0.93–1.40

CVD, cardiovascular disease; CVR, cardiovascular risk.

[a]Significance was based on the omnibus chi-square test of model coefficients.

*$P < 0.05$, **$P < 0.01$.

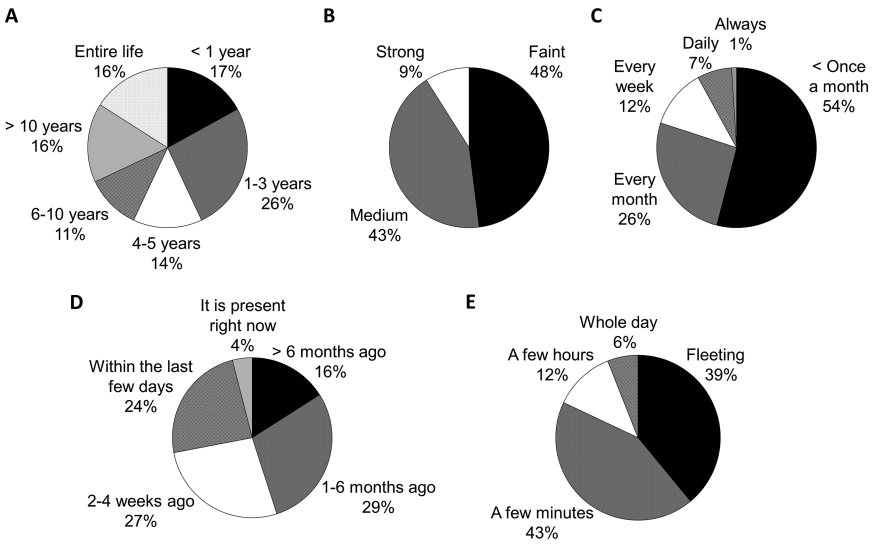

Figure 2. The distribution of answers to the following questions regarding the qualitative features of the phantom smell ($n = 125$). (A) How long have you had the phantom smell? (B) How strong is the phantom smell? (C) How often does the phantom smell appear? (D) When did the phantom smell last appear? (E) How long does the phantom smell last?

individuals who have experienced their phantom smell more recently also tend to experience the smell more often. An association was also observed between how often the smell occurs and how long it lasts ($r = 0.24$, $n = 91$, $P = 0.022$), indicating that the phantom smell lasts longer in individuals who experience phantom smells more often. The associations between duration, frequency, and recency indicate that the severity of phantosmia varies systematically among affected individuals. Correlation coefficients between all variables are presented in Table 4.

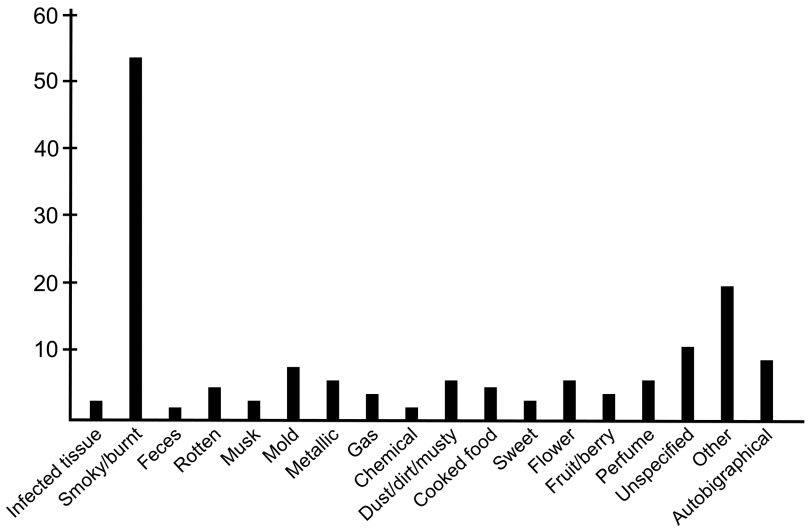

Figure 3. Type of phantom smells reported by the participants. *Y* axis represents the number of individuals who reported the smell.

Table 3. Personal descriptions of phantom smells with an autobiographical connotation

Description
The subject experienced phantom smells when she/he entered the apartment. This started when the subject moved to another house, and she/he associates the phantom smell with smells from the old house
Smells that are associated with childhood, for example "barn"
Childhood smells. Grandmother's place in the forest. House from the 1700 s
Smell of something dirty. Associated with a previous event that the subject experienced
The subject's childhood home burnt down when the subject was 2 years old. The subject sometimes wakes up and experiences the smell of smoke
A specific hospital smell. Associated with the death of the spouse
Mother's perfume
Smell of smoke. Started after a fire in the home
Aftershave used by the deceased husband

Table 4. Spearman rank correlation coefficients between the phantosmia-related questions

Factors	1	2	3	4
1. How strong is the smell?				
2. How long have you had the smell?	0.04			
3. When did the smell last appear?	0.04	−0.17		
4. How often does the smell appear?	0.18	−0.18	0.40**	
5. How long does the smell last?	0.12	−0.15	0.12	0.24*

*$P < 0.01$, **$P < 0.001$.

Discussion

Although qualitative perceptual distortions, or hallucinations, have been investigated in the auditory and visual senses, less is known about qualitative distortions in the olfactory sense. This is one of the first studies to investigate the experiences of phantosmia, the perception of an odor where the odor source is not present, in a large population-based sample of older adults. The overall prevalence of phantosmia was 4.9% and was mainly associated with female gender, the *BDNF* met allele, vascular risk burden, and reported experience of parosmia, another qualitative odor distortion.

Overall, the prevalence of phantosmia corresponds with prior reports conducted in healthy individuals, where phantosmia was reported by 6.0–8.5% of the sample (Ohayon 2000; Rawal et al. 2016). Studies of clinical groups have reported a wider range of prevalent phantosmia. Nordin et al. (1996) reported a prevalence of phantosmia of 25.6% in a group of chemosensory and nasal/sinus patients. However, Landis et al. (2004) investigated phantosmia in relatively healthy otorhinolaryngology outpatients and found that only 0.8% of those without olfactory loss experienced phantom smells. One explanation for the discrepancy could be ascribed to differences in how phantosmia has been operationalized and described to the participants. Another explanation could be that previous work has focused on different groups of patients with mixed pathogenesis.

In our sample, which included individuals between 60 and 90 years, age was not associated with the prevalence of phantosmia. Our finding that 32% of the phantosmics reported that they had experienced phantom smells for more than 10 years indicates that, at least for some individuals, phantosmia persists from middle age until old age. We observed a higher prevalence of phantosmia in women, which is in line with previous research. As women in general are better than men at naming odors (Larsson et al. 2004), and more often than men are negatively affected by environmental odors (Nordin et al. 2013), their heightened olfactory sensitivity might make them more prone to experiencing phantom smells. However, women were not more likely to experience phantom smells when only considering those with severe phantosmia. These results might be explained by a gender difference in criterion, such that women report phantosmia at a lower threshold compared to men.

Although the neurobiological basis of phantosmia is unknown, the present study suggests that phantosmia is linked to the presence of the *BDNF* met allele. This statistical relationship remained stable after all other variables had been accounted for. The *BDNF* (rs6265) gene is mainly responsible for neuronal survival, transmission, and synaptic plasticity (Poo 2001), and previous studies have reported that *BDNF* is implicated in cognitive and olfactory function. Most studies targeting the effect of *BDNF* on cognitive function suggests that met allele carriers are more cognitively impaired than homozygote val carriers (see for example Hariri et al. 2003). However, some studies have

found the opposite relationship, indicating that met allele carriers exhibited less age-related cognitive decline (Erickson et al. 2008). We previously reported that the met allele might be protective against age-related decline in olfactory function (Hedner et al. 2010). The *BDNF* gene expression is high in various parts of the central nervous system involved in olfaction, including the hippocampus and olfactory bulb (Zigova et al. 1998; Poo 2001; Hariri et al. 2003). Although not conclusive, our results are consistent with the notion that the met allele is associated with increased levels of plasticity in the olfactory system, which might result in preserved olfactory function, but also in an increased risk of "false alarms" when no odors are present.

In the present study, prevalent parosmia was associated with phantosmia. It is possible that the same biological mechanisms underlie these 2 qualitative olfactory distortions. In the study by Nordin et al. (1996), 9.6% of the participants reported both parosmia and phantosmia. In contrast to previous findings, olfactory impairments were not related to phantosmia in the current sample. Prior work on clinical populations has observed an association between smell loss and phantosmia, and these results have been interpreted as supporting a peripheral account of the origin of phantosmia (Leopold 2002; Hong et al. 2012). The lack of such an association in our sample suggests that previous findings might not generalize to the population of older individuals.

Furthermore, the present study revealed a significant relationship between the number of vascular risk factors and phantosmia. One possible explanation to this finding might be that certain medication alters the olfactory functions and changes olfactory perception (Doty and Bromley 2004). No relationship was observed between other clinical variables and phantosmia, suggesting that phantosmia is specifically linked to vascular conditions.

The relatively low value (0.06) of Nagelkerke's pseudo-R^2 for the final model suggest that a large proportion of the variance remained unexplained and that other variables, not covered by this study, are of importance for the occurrence of phantosmia. However, it should be noted that this value was comparatively larger (0.12) in the model for severe phantosmia. Restricting the sample of phantosmics to individuals with more frequent experiences of phantosmia resulted in more distinct group differences, where gender was no longer of importance and head trauma appeared as a correlate of phantosmia (Lötsch et al. 2016).

The present study also investigated qualitative descriptions of prevalent phantosmia, making it one of the first studies to investigate the perceived qualities of the phantom smells. The most commonly experienced phantom smells were unpleasant, specifically smoky or burnt sensations. This confirms previous findings regarding phantom smells as well as reports of smell sensations in dreams (Leopold 2002; Chen et al. 2003; Stevenson and Case 2004). Why negative odors are overrepresented is not yet known, but could be the result of an evolutionary history where detecting and avoiding fire smoke would be of particular adaptive value. It has been shown that combat veterans with posttraumatic stress disorder are sensitive to fire odors, which suggests an exaggerated response to threat-related odors as a result of previous experiences (Cortese et al. 2015). It has also been suggested that negative odor sensations are easier to access in memory (Konstantinidis et al. 2006; Larsson et al. 2009). However, a number of individuals in the present study reported positive phantom smell qualities such as flower, perfume, and fruit. Intriguingly, 9 individuals reported smells with an autobiographical connotation. This suggests that the phantom smells should not be characterized as merely neural noise originating in the peripheral olfactory system, but instead might be linked to personal and meaningful events or memories. These findings should be viewed in the context of autobiographical memories, which often are more vivid and emotional when generated by an odor compared with other sensory cues (Larsson and Willander 2009; Larsson et al. 2014).

Among the strengths of the present study are the population-based sample selection and the large sample size. This allows robust inferences to the general population. The study, however, also has some limitations to consider. Given that the results are based on cross-sectional data, the direction of the associations among the variables cannot be established, and any causal inferences on risk factors for phantosmia cannot be determined. Also, because the age range of the sample was restricted to 60–90 years of age, our findings cannot be generalized beyond this age span. Despite the large sample size, phantosmia is a relatively rare condition, which reduces the power and makes it difficult to clearly establish potential relationships between the variables of interest.

The subjective and retrospective nature of phantosmia assessment poses certain challenges. In the present study, data were collected through a structured interview. An advantage of this method over surveys is that it enables the interviewer to clarify potential uncertainties. However, it is difficult to exclude the possibility that some of the participants did not understand the meaning of phantosmia. As people's experiences are subjective, 2 individuals might classify the same olfactory sensation as 2 different types of phantom smells. A further limitation of the present study, and other studies, is that the information regarding phantosmia relies on retrospective self-reports. The participant might have forgotten or overestimated or underestimated how frequent and how intense their phantom smells were. To limit this type of bias, future studies should investigate phantosmia by using prospective diaries in which participants can write information about their phantom smell continuously. It should also be noted that it cannot be ruled out that a source of the odor was in fact present at the time the participant experienced the phantom smell. This is especially the case for odors where the source of smell might not be visible, for example, mold.

To conclude, the present findings suggest that the prevalence of phantosmia in the elderly general population is not negligible as about 5% reports such experiences. Phantosmia is mainly associated with female gender, the *BDNF* met allele, vascular risk factors, and parosmia. It is of interest to note that variables that are frequently reported to be beneficial for olfactory function, such as female gender and the *BDNF* met allele, are also associated with the experience of phantosmia. Given this pattern of results, it would be of interest for future research to determine whether olfactory experts (e.g., perfumers, wine experts) are more susceptible to phantosmia than nonexperts. Our results complement those of prior work on phantosmia in clinical populations with olfactory deficits. Further studies are needed to address the epidemiology and underlying biological mechanisms of phantosmia in healthy individuals as well as in clinical groups.

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