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Olfactory impairment in older adults: 5-year incidence and risk factors

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Abstract

Objectives/Hypothesis—The objective of this study was to determine the 5-year incidence of olfactory impairment and associated risk factors in a general population of older adults.

Study Design—Longitudinal population-based study.

Methods—Participants (n=1556) in the population-based Epidemiology of Hearing Loss Study had olfaction measured at the 5- and 10-year examinations (1998–2000 and 2003–2005, respectively). Olfactory ability was measured by the San Diego Odor Identification Test.

Results—The 5-year incidence of olfactory impairment was 12.5%. Incidence rates increased with age for men and women. In a multivariate model, age (OR = 1.79, 95% CI= 1.61, 2.00; for every 5-year increase), a history of nasal polyps (OR=2.33, 95% CI 1.13, 4.59), a history of deviated septum (OR=2.05, 95% CI 1.14, 3.56), and a history of heavy alcohol use (OR=1.84, 95% CI 1.13, 2.93) were associated with an increased risk of olfactory impairment, while use of lipid lowering agents (OR=0.68, 95% CI 0.46, 0.99; yes vs. no), exercising at least once a week (OR=0.69, 95% CI 0.48, 0.98), and oral steroid use (OR=0.37, 95% CI 0.11, 0.94) were associated with a decreased risk.

Conclusions—The 5-year incidence of olfactory impairment is high in this population of older adults. Modifiable risk factors associated with impairment suggest some impairment could be amenable to prevention or treatment.

Keywords

Olfaction; Smell disorders; Epidemiology; Aging

INTRODUCTION

Olfactory impairment is a common condition that exhibits an increased prevalence of impairment with age. Two population-based studies have found similar levels of olfactory impairment. The prevalence of olfactory impairment in the Epidemiology of Hearing Loss Study (EHLS) was 25% in participants aged 53 years and older and the overall prevalence of olfactory dysfunction was 19% in participants aged 20 years and older in the Skovde study.

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^{1,2} Both studies found the prevalence of olfactory impairment increased with age and was more common in men than women. ^{1,2} Additional factors associated with olfactory impairment were current smoking, a history of stroke or epilepsy, and nasal congestion or upper respiratory infection in the EHLS and nasal polyps and a history of diabetes in the Skovde study. ^{1,2}

These cross-sectional studies have provided important information on the prevalence of olfactory impairment in adults but longitudinal data are needed to measure the rates of new cases and identify factors associated with the development of olfactory impairment in the general population. Poor olfactory function may affect quality of life, food choices and the ability to detect smoke, natural gas or other toxins in the environment. ^{3,4} The purpose of this study was to measure the 5-year incidence of olfactory impairment and determine risk factors associated with the development of impairment.

MATERIALS AND METHODS

Population

The data were collected as part of the Epidemiology of Hearing Loss Study (EHLS), a longitudinal population-based study of sensory loss and aging in Beaver Dam, WI. The details of the study have been published elsewhere. ⁵⁻⁷ In 1993–1995, participants in the population-based Beaver Dam Eye Study (BDES) baseline examination (1988–1990; n=4926) were invited to participate in the EHLS. ⁵⁻⁷ Of the eligible 4926 baseline BDES participants, 3753 (82.6%) participated in the EHLS baseline examination (1993–1995).⁵ Subsequently, 2800 (82.2% of remaining eligible) participated in the 5-year examination (1998–2000) of the EHLS and 2395 (82.5% of remaining eligible) participated in the 10-year examination (2003–2005) of the EHLS. Olfaction was measured at the 5- and 10-year EHLS examinations (1998–2000 and 2003–2005, respectively). [1,6,8] There were 1881 participants without olfactory impairment at the 5-year examination which was the baseline for olfactory testing. Of those, 1556 (82.7%) were tested five years later, 142 (7.5%) died prior to a second examination, 90 (4.8%) refused and 93 (4.9%) were not tested at follow-up. Participants at risk for olfactory impairment who were not re-tested were more likely to be older, have fewer years of education and have cognitive impairment at baseline. There was no difference in smoking status between those with and without follow-up olfactory data. Written informed consent was obtained from all participants prior to each examination and approval for this research was obtained from the Health Sciences Institutional Review Board of the University of Wisconsin.

Data collection

Examination and interview data were obtained by trained and certified examiners following standardized protocols. Medical history, sensory health history (hearing, smell, taste), quality of life, lifestyle and demographic information were obtained by interview. Questionnaire data collected as part of the concurrent Beaver Dam Eye Study examinations were also available for analyses. ⁷

The San Diego Odor Identification Test (SDOIT), a standardized odor identification test that consists of eight common, natural odorants found around the home (chocolate, coffee, etc) was used to measure olfaction. ^{1,9,10} The odorants in the SDOIT are recognized name brand products that are prepared and maintained according to a standard scheduled. Prior to the presentation of odors, a picture board with the 8 test odorants and 12 distracters is presented. The participant is asked to name or identify each picture to assure they are familiar with the response choices. If unable to name or identify at least 18 of the pictures, the odorants are not presented. The picture array is available to use during the test to aid in identification and

to allow for a nonverbal response to overcome any issues with naming.^{1·9·10} The odors are presented in random order with a 45 second delay between odors to minimize adaptation. If a participant does not identify an odorant correctly, they are told the correct name of the odorant and it is presented a second time later in the test sequence. Participants were scored based on the number of odorants they correctly identified (0–8) after two trials. ¹ Incident olfactory impairment was defined as identifying fewer than six odorants correctly. ^{1·9·10} The SDOIT test-retest agreement for olfactory impairment over an average of three weeks was 95% and there was excellent agreement between olfaction impairment on the SDOIT and the Brief Smell Identification Test (96% agreement, kappa=0.81).¹¹

Data analyses

Confidence intervals for proportions used exact binomial methods. Potential risk factors were first tested in age and sex-adjusted logistic regression models. Multivariate logistic regression models were constructed by adding all variables significant at the 0.20 level in age and sex-adjusted models, and then eliminating variables that neither remained significant at the 0.05 level, nor substantially influenced the estimates of the remaining covariates in the model. Likelihood ratio confidence intervals and p-values were used. Interactions with age and gender were also explored.

Factors previously associated with the prevalence of olfactory impairment in this population (smoking (current, past or never), current nasal congestion or recent upper respiratory infection and a history of stroke) or reported to be associated with olfactory impairment in clinical studies (cognitive impairment (defined as a score < 24 on the Mini-Mental State Exam 12 or a report of Alzheimer's disease or dementia), a history of allergies, deviated septum, nasal polyps, diabetes, medication use, and a history of heavy alcohol use (defined as 4 or more drinks per day regularly for at least three months) were included in the models to determine their associations with the incidence of olfactory impairment. ^{1·13·14} In addition, cardiovascular disease and its risk factors (hypertension, obesity, exercise, snoring, cholesterol levels (total and high density lipoprotein (HDL)) and socioeconomic status (education and occupation) were considered as potential risk factors as we had previously found a cross-sectional association with stroke and hypothesized that vascular changes in the brain may contribute to olfactory changes. ¹ Medications reported to effect olfaction or taste were evaluated (chemotherapy and lipid lowering agents, diuretics, beta-blockers, anti-depressants, anti-anxiety medications, and anti-inflammatory medications, including nasal and oral steroids). ^{14–16} The antihyperlipidemic medications commonly referred to as statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (HMG-Co-A reductase inhibitors)) were analyzed together with all lipid lowering agents (LLA) and as a separate class. The statins were further classified as crossing the blood brain barrier (BBB) well (Lovastatin and Simvastatin) or not crossing the BBB well (Atorvastatin, Fluvastatin, and Pravastatin). ¹⁷

The effects of sinus or upper respiratory problems in the week prior to the 5-year follow-up olfactory examination and/or a stuffy nose the day of the examination were tested in the final model. Sensitivity analyses were performed excluding participants who correctly identified six odorants on the baseline olfaction test and five odorants at the follow-up five years later. ⁹ SAS version 9.1 software (SAS Institute Inc., Cary, NC, USA) was used to conduct most analyses; exact binomial confidence intervals were calculated using Stata version 10 (College Station, TX).

RESULTS

5-year incidence of olfactory impairment

There were 1556 participants at risk for olfactory impairment (Table 1) with olfactory testing at two examinations. The median baseline age was 66 years (range 53 to 91 years) and 598 (38%) were men and 958 (62%) were women. The overall 5-year incidence of olfactory impairment was 12.5% (Table 1). Incidence increased with age for both men and women. Incidence was similar for men and women in the younger age groups but higher for women in the older age groups, though the difference was not statistically significant and the numbers at risk in the highest age group were small, especially for men.

Risk factors

Baseline risk factors significantly associated with increased incidence of olfactory impairment in age and sex-adjusted models included history of nasal polyps, history of deviated septum, frequent snoring, and history of heavy alcohol use (Table 2). Use of LLA and exercise were associated with a decreased risk of olfactory impairment in age- and sex-adjusted models (Table 2). Epilepsy, Parkinson's disease and Alzheimer's disease were not included in the models due to small sample sizes.

In a multivariate logistic regression model, age (Odds ratio (OR) = 1.79, 95% Confidence Interval (CI)= 1.61, 2.00; for every 5-year increase), a history of nasal polyps (OR=2.33, 95% CI= 1.13, 4.59), a history of deviated septum (OR=2.05, 95% CI= 1.14, 3.56), and a history of heavy alcohol use (OR=1.84, 95% CI=1.13, 2.93) remained associated with the incidence of olfactory impairment, while use of LLA (OR=0.68, 95% CI= 0.046, 0.99; versus none) and exercising at least once a week (OR=0.69, 95% CI =0.48, 0.98) remained associated with a decreased risk (Table 3). Oral steroid use became a significant protective factor in the multivariate analyses (OR=0.37, 95% CI= 0.11, 0.94). Gender was retained in the final model but was not significant. Upper respiratory problems on the day or in the week prior to the 5-year follow-up olfactory test did not modify these results. Smoking status, frequent snoring, education, body mass index, hypertension, history of cardiovascular disease, total cholesterol, HDL cholesterol, allergies, diabetes, and nasal steroid use at baseline were not significant predictors of incident olfactory impairment in the multivariate model and no significant interactions with age or gender were found. The analyses were repeated excluding 49 participants whose olfaction scores declined by only one unit at the cut point (from a score of 6 to 5) and yielded similar results (Table 3).

LLA and the 5-year incidence of olfactory impairment

The results from the models analyzing LLA by class are shown in Table 4. The majority of participants (78%) on LLA were taking those classified as statins. There was a reduced risk of olfactory impairment for those taking statins as compared to participants not taking LLA. This association was not seen with non-statin LLA. Further analyses breaking down the statins by their ability to cross the BBB showed the reduced risk of olfactory impairment was associated only with those statins that cross the BBB well (OR= 0.46 95% CI= 0.21, 0.90).

DISCUSSION

To the authors' knowledge, this is the first population-based study to determine the 5-year incidence of olfactory impairment. The overall 5-year incidence rate was 12.5% in adults 53 years of age and older but this varied significantly by age and the incidence rate in those 70–79 years was over 20%. Previous studies have shown that the prevalence of olfactory impairment is high (25%) in older adults but the rate of new cases of impairment was

unknown.¹ One out of every eight older adults acquired an olfactory impairment over a five year period. A history of nasal polyps, a deviated septum and heavy alcohol use increased the risk for olfactory impairment while exercise and use of statins or oral steroids were associated with a decreased risk.

Although the reduced risk of olfactory impairment found with statins and exercise might be due to chance, these associations could be indicators that atherosclerosis may be part of the causal pathway for some olfactory impairments. Both statins and exercise have been reported to be associated with less atherosclerosis and better cardiovascular health.^{18–20} Additionally, statins have been reported to have a diverse range of effects including improving endothelial function and reducing oxidative stress and vascular inflammation.²¹ One of these mechanisms could result in statins having a direct neuroprotective effect on the areas of the brain related to central olfactory processing. Olfactory impairment has been associated with the development of cognitive impairment and neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease suggesting a strong link between brain health and olfactory ability.^{13, 22} Therefore, factors that improve or protect brain health may also improve or protect olfactory ability. This hypothesis would fit with the statin association being seen only with those statins that cross the BBB.

In addition to age, a history of nasal polyps or a deviated septum was associated with an increased risk for the incidence of olfactory impairment. Both conditions may cause a conductive olfactory impairment by blocking the nasal passages and preventing odors from reaching the olfactory neuroepithelium. Treatments for these conditions, either medication or surgery, are available though in the case of nasal polyps are not always long-term solutions.¹⁴ The reduced risk of olfactory impairment observed with oral steroid use may be the result of their ability to reduce inflammation and nasal polyps.^{23, 24} Although nasal steroids were not associated with olfactory impairment in this study, oral steroids have been reported to be more effective than nasal steroids treating nasal polyps and sinonasal disease or idiopathic smell loss in some studies.^{23–25}

A history of heavy alcohol use was another risk factor for the development of olfactory impairment in this study. Alcohol abuse has previously been reported to be a cause of olfactory impairment in studies conducted in alcohol-dependent cohorts.^{26, 27} Though the pathway for alcohol-related olfactory impairment is unknown, these studies have suggested that it may be due to alcohol-related changes in the brain in areas important for olfactory processing.^{26, 27} While information was not available on the length of time of heavy alcohol use or time since stopped, it is unknown how long olfactory ability might remain impaired after alcohol use has been discontinued.²⁷

Although cross-sectional studies have found the prevalence of olfactory impairment to be higher in men than women^{1,2} there was no gender difference in the incidence of olfactory impairment. The apparent greater difference in the rates by gender among those 80 years and older was not statistically significant and the number of participants at risk in this oldest age group was small, suggesting the estimate may be unstable. Additionally, the age-adjusted relative risk for olfactory impairment in men was not significantly different than in women. More men had prevalent olfactory impairment at baseline¹ but the similar incidence rates between men and women suggests that impairment in men may start earlier in life. This pattern was also noted in the Baltimore Longitudinal Study of Aging which reported that while women performed better than men in all age groups and men's scores declined significantly faster with age, the rate of decline in women's scores caught up to men at age 85.²⁸

Smoking history was not associated with the 5-year incidence of olfactory impairment in this study. Current, but not past smoking was associated with olfactory impairment in this population at baseline,¹ but less than 10% of the population at risk for olfactory impairment were current smokers, limiting our power to detect an association here in these longitudinal analyses.

There are some limitations in this study to note. The SDOIT uses only eight odorants and therefore rare, specific anosmias may be missed. As an odor identification test, the SDOIT utilizes suprathreshold levels of odorants and may not be as sensitive as a threshold test in detecting hyposmias. Also, the dose and duration of medication use were not known. The population of this study is largely non-Hispanic white and therefore these results may not be applicable to other groups. The strengths of this study include the longitudinal population-based design, the measurement of olfaction versus reliance on self-report and the extensive amount of information available on potential risk factors. The test-retest reliability of the SDOIT is high and it has been shown to be comparable to the Brief Smell Identification Test (B-SIT) for classifying olfactory impairment.¹¹

CONCLUSION

The 5-year incidence of olfactory impairment is high in this population of older adults. Modifiable risk factors associated with impairment suggest some impairment could be amenable to prevention or treatment. Treatments for other age-related diseases, such as cardiovascular disease, may be beneficial for olfactory impairment as well.

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Table 1

Five-Year Incidence of Olfactory Impairment by Age and Sex in the Epidemiology of Hearing Loss Study, 1998 – 2005

Age, years	Women			Men			All		
	n at risk	Incidence %	95% CI	n at risk	Incidence, %	(95% CI)	n at risk	Incidence, %	95% CI
53–59	272	3.7	1.8, 6.7	197	4.6	2.1, 8.5	469	4.1	2.5, 6.3
60–69	365	9.9	7.0, 13.4	249	8.8	5.6, 13.1	614	9.4	7.3, 12.0
70–79	270	19.3	14.7, 24.5	133	24.8	17.7, 33.0	403	21.1	17.2, 25.4
80–97	51	52.9	38.5, 67.1	19	31.6	12.6, 56.6	70	47.1	35.1, 59.4
All	958	13.0	11.0, 15.3	598	11.7	9.2, 14.6	1556	12.5	10.9, 14.3
Age-Adjusted Relative Risk		1.00			1.10 (0.84, 1.43)				

CI= Confidence Interval

Table 2

Selected Potential Baseline Risk Factors for 5-year Incident Olfactory Impairment in the Epidemiology of Hearing Loss Study, 1998–2005

Covariate, measured at baseline*	No Incident Olfactory Impairment (n=1361)	Incident Olfactory Impairment (n=195)	Age and Sex Adjusted OR *	95% CI
<u>Education</u>				
< 12 years	156 (11%)	36 (18%)	1.00	
12 years	675 (50%)	108 (55%)	1.19	0.77, 1.90
13–15 years	247 (18%)	27 (14%)	0.82	0.46, 1.46
16 or more years	283 (21%)	24 (12%)	0.67	0.37, 1.20
<u>Smoking</u>				
Never	653 (48%)	97 (50%)	1.00	
Past	560 (41%)	78 (40%)	1.03	0.72, 1.46
Current	135 (10%)	16 (8%)	1.42	0.76, 2.54
Manufacturing Occupation	347 (25%)	53 (27%)	1.04	0.72, 1.51
History of allergies	545 (40%)	78 (40%)	1.08	0.78, 1.49
History of nasal polyps	40 (3%)	17 (9%)	2.40	1.24, 4.49
History of deviated septum	87 (6%)	21 (11%)	2.08	1.19, 3.52
Frequent snoring	500 (37%)	76 (39%)	1.59	1.12, 2.25
Impaired Cognition	37 (3%)	10 (5%)	1.23	0.54, 2.60
Cardiovascular disease**	157 (12%)	31 (16%)	0.85	0.53, 1.33
Hypertension***	736 (54%)	121 (62%)	0.99	0.71, 1.39
Diabetes mellitus	134 (10%)	22 (11%)	0.96	0.56, 1.56
Total Cholesterol >240 mg/dl	311 (23%)	45 (23%)	0.97	0.66, 1.41
HDL Cholesterol <40 mg/dl	325 (25%)	45 (23%)	0.86	0.57, 1.28
Lipid lowering agent use	368 (27%)	45 (23%)	0.66	0.45, 0.96
<u>Statin Use</u>				
No statin use	1059 (78%)	159 (82%)	1.00	
Statins that cross the BBB well	120 (9%)	9 (5%)	0.44	0.20, 0.87
Statins that do not cross the BBB well	169 (12%)	23 (12%)	0.79	0.48, 1.28
Nasal steroid, yes	86 (6%)	14 (7%)	1.51	0.78, 2.74
Oral steroid, yes	102 (7%)	4 (2%)	0.42	0.13, 1.06
Chemotherapy, yes	30 (2%)	6 (3%)	0.96	0.33, 2.38
History of heavy alcohol use	175 (13%)	34 (17%)	1.94	1.21, 3.06
Body Mass Index ≥ 30 kg/m ²	665 (49%)	79 (41%)	0.83	0.60, 1.15
Exercise at least once per week	630 (46%)	63 (32%)	0.68	0.48, 0.95

BBB=Blood Brain Barrier; CI=Confidence Interval; OR = Odds Ratio

* missing data for each covariate comprised less than 5% of each outcome group with the following exceptions: snoring was unknown for 6% of participants without incident olfactory impairment and 8% of those with incident olfactory impairment; statin use was unknown for 5% of participants with incident olfactory impairment.

** Includes a history of doctor diagnosed angina, myocardial infarction or stroke.

defined as blood pressure $\geq 140/90$ or taking hypertension medications.

Table 3

Multivariate Logistic Regression Model Estimates for the 5-year Incidence of Olfactory Impairment in the Epidemiology of Hearing Loss Study, 1998–2005

Baseline Covariate	Using Full Data		Sensitivity Subset**	
	OR	95% CI*	OR	95% CI*
Age: effect of 5 year increase	1.79	1.61, 2.00	1.82	1.61, 2.06
Gender: Men vs. Women	0.98	0.67, 1.42	0.83	0.54, 1.26
History of nasal polyps	2.33	1.13, 4.59	2.50	1.13, 5.21
History of deviated septum	2.05	1.14, 3.56	2.49	1.35, 4.44
Lipid lowering agent: Yes vs. No	0.68	0.46, 0.99	0.64	0.41, 0.98
Oral corticosteroids used	0.37	0.11, 0.94	0.26	0.04, 0.86
History of heavy alcohol use	1.84	1.13, 2.93	1.88	1.08, 3.19
Exercise at least once per week	0.69	0.48, 0.98	0.84	0.57, 1.23

CI=Confidence Interval; OR = Odds Ratio

* Likelihood Ratio 95% Confidence Intervals

** Excludes participants who correctly identified 6 odorants at baseline and 5 odorants at follow-up

Table 4

5-Year Incidence of Olfactory Impairment by use of Lipid Lowering Agents in the Epidemiology of Hearing Loss Study, 1998–2005

	n	Adjusted OR*	95% CI**
No LLA	1126	1.00	-----
Non-statin LLA	92	0.78	0.39, 1.45
Statin LLA	321	0.65	0.41, 0.99
No Statin LLA	1218	1.00	-----
Statins that cross the BBB well	129	0.46	0.21, 0.90
Statins that do not cross the BBB well	192	0.81	0.48, 1.31

LLA = Lipid Lowering Agents; BBB= Blood Brain Barrier

* Odds Ratio: Adjusted for age, gender, history of nasal polyps, deviated septum, oral steroids, heavy alcohol use.

** Likelihood Ratio 95% confidence intervals