Original Investigation

Association of Exercise With Lower Long-term Risk of Olfactory Impairment in Older Adults

Carla R. Schubert, MS; Karen J. Cruickshanks, PhD; David M. Nondahl, MS; Barbara E. K. Klein, MD; Ronald Klein, MD; Mary E. Fischer, PhD

IMPORTANCE The prevalence of olfactory impairment is high in older adults, and this decline in olfactory ability may pose health and safety risks, affect nutrition, and decrease quality of life. It is important to identify modifiable risk factors to reduce the burden of olfactory impairment in aging populations.

OBJECTIVE To determine if exercise is associated with the 10-year cumulative incidence of olfactory impairment.

DESIGN, SETTING, AND PARTICIPANTS Observational longitudinal population-based Epidemiology of Hearing Loss Study. Participants without olfactory impairment (n = 1611) were ages 53 to 97 years at baseline and were followed for up to 10 years (1998-2010).

MAIN OUTCOMES AND MEASURES Olfaction was measured with the San Diego Odor Identification Test at 3 examinations (1998-2000, 2003-2005, and 2009-2010) of the Epidemiology of Hearing Loss Study. The main outcome was the incidence of olfactory impairment 5 (2003-2005) or 10 (2009-2010) years later and the association of baseline exercise with the long-term risk of developing olfactory impairment.

RESULTS The 10-year cumulative incidence of olfactory impairment was 27.6% (95% CI, 25.3%-29.9%) and rates varied by age and sex; those who were older (hazard ratio [HR], 1.88 [95% CI, 1.74-2.03], for every 5 years) or male (HR, 1.27 [95% CI, 1.00-1.61]) had an increased risk of olfactory impairment. Participants who reported exercising at least once a week long enough to work up a sweat had a decreased risk of olfactory impairment (age- and sex-adjusted HR, 0.76 [95% CI, 0.60-0.97]). Increasing frequency of exercise was associated with decreasing risk of developing olfactory impairment (*P* value for trend = .02).

CONCLUSIONS AND RELEVANCE Regular exercise was associated with lower 10-year cumulative incidence of olfactory impairment. Older adults who exercise may be able to retain olfactory function with age.

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Author Affiliations: Department of Ophthalmology and Visual Sciences, University of Wisconsin, Madison (Schubert, Cruickshanks, Nondahl, B.E.K. Klein, R. Klein, Fischer); Department of Population Health Sciences, University of Wisconsin, Madison (Cruickshanks).

Corresponding Author: Carla R. Schubert, MS, Department of Ophthalmology and Visual Sciences, University of Wisconsin, 610 Walnut St, Room 1087 WARF, Madison, WI 53726-2336 (schubert@episense.wisc.edu).

Regular exercise has been shown to reduce the risk of many age-related conditions, including impaired physical functioning,[1] cardiovascular disease,[2] Alzheimer disease,[3] and dementia.[4] In addition, exercise has been associated with maintaining good health[5] and cognition in older age and increased survival.[2,6] It is not known if these health benefits extend to sensory changes common in aging. A significant proportion of older adults have impairment in their ability to identify odors.[7-10] The prevalence of olfactory impairment was 25% in a population of older adults, and the incidence rate for developing an olfactory impairment in 5 years was 12.5%; the long-term incidence rate is unknown.[7,11]

The sense of smell is an important early warning system for identifying danger and toxins in the environment (eg, smoke, natural gas, spoiled food, chemicals), and a loss or decline in olfactory ability may pose health and safety risks as well as affect quality of life.[12-14] Many older adults are unaware they have had a decline in their sense of smell.[7,15] Because of the high prevalence,[7-10] low awareness,[7,15] and the impact that a decline in olfactory function may have on safety, nutrition, and quality of life in older adults,[12-14] it is important to identify modifiable factors associated with olfactory function and aging. Previously, we reported that regular exercise was associated with a lower 5-year risk of developing olfactory impairment in a population of older adults.[11] The purpose of the present study was to determine the cumulative incidence of olfactory impairment over 10 years and determine if exercise remained associated with a lower risk of developing olfactory impairment over a longer time period.

Methods

Study Population

The data were collected as part of the Epidemiology of Hearing Loss Study (EHLS), a longitudinal population-based study of sensory health and aging in Beaver Dam, Wisconsin.[16-18] In 1987 to 1988, a private census was conducted in the city and township of Beaver Dam. All residents ages 43 to 85 years were invited to participate in the Beaver Dam Eye Study (BDES), a study of vision and ocular diseases of aging.[19] Of the 5924 people eligible for the study, 4926 (83%) participated in the baseline BDES examination in 1988 to 1990.[19] In 1993 to 1995, all BDES participants who were alive as of March 1, 1993, were invited to participate in the EHLS.[16] Of the 4541 eligible participants, 3753 (82.6% of eligible) participated in the EHLS baseline examination (1993-1995), 2800 (82.2% of eligible) in the 5-year examination (1998-2000), 2395 (82.5% of eligible) in the 10-year examination (2003-2005), and 1812 (80.8% of eligible) in the 16-year examination (2009-2010).[16-18] 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. Examination and interview data were obtained by trained and certified examiners following similar standardized protocols at each examination.

Olfactory Examination

Olfaction was measured at the 5-, 10-, and 16-year EHLS examinations (1998-2000, 2003-3005, and 2009-2010, respectively) using the San Diego Odor Identification Test (SDOIT).[7,11] The SDOIT is a standardized odor identification test that consists of 8 common odors (eg, chocolate, coffee).[7,20,21] A picture array with the 8 test odorants and 12 distracters is available to use during the test to aid the participant with identification and to allow for a nonverbal response to overcome any issues related to naming. 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, he or she is told the correct name of the odorant, and it is presented a second time later in the test sequence. The SDOIT score is the number of odorants correctly identified (0-8) after 2 trials. Olfactory impairment was defined as identifying fewer than 6 odorants correctly.[7] The SDOIT is very reliable, with a concordance correlation coefficient of 0.85 (95% CI, 0.79-0.91), and it has a test-retest agreement of 96% for olfactory impairment over an average of 3 weeks.[21]

Assessment of Exercise

Data from 2 interview questions obtained in the concurrent BDES examinations were used to determine the frequency of current exercise: "Do you exercise at least once a week long enough to work up a sweat?" and "How many times per week to you do this?" The data were analyzed as a dichotomous variable (none vs any), and as a 3-level variable (none, 1-2 times per week, and ≥3 times per week).

Assessment of Covariates

Height and weight were measured, and body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Participants brought their current medications to the examinations, and name and frequency of use were recorded. Nonfasting blood samples were obtained for measurement of hemoglobin A_{1C} (HbA_{1C}), and participants were classified as having diabetes mellitus based on self-report of a physician diagnosis, an HbA_{1C} level of 6.5% or higher or report of possible diabetes mellitus and taking medication for diabetes mellitus. Demographic (years of education, longest-held occupation), lifestyle, and medical history were obtained by interview; self-reported medical history included a history of stroke, Alzheimer disease, Parkinson disease, epilepsy, head injury, and allergies. Participants were considered to have a history of nasal conditions if they reported ever having been told by a physician they had nasal polyps or a deviated septum. Other nasal health information included a report of upper respiratory or sinus problems the week before, and nasal congestion on, the day of examination. Participants were asked about smoking history (current; past, quit <5 years ago; past, quit ≥5 years ago; never), weekly alcohol consumption, and history of ever consistently drinking 4 or more drinks per day.

Statistical Analysis

Analyses were conducted using SAS software (version 9.2; SAS Institute Inc) and were restricted to participants who did not have olfactory impairment at the baseline olfactory examination (SDOIT score ≥6 at 1998-2000 examination) and were therefore at risk for incident olfactory impairment. Incident olfactory impairment was defined as a SDOIT score lower than 6 at 1 of the follow-up examinations. Kaplan-Meier estimates[22] were used to calculate the 10-year cumulative incidence of olfactory impairment among those at risk for impairment at baseline. Cox proportional hazard models were used to evaluate the association between potential risk factors and the initial occurrence of olfactory impairment over 10 years.[23] Reported nasal congestion on the day of the examination, or a cold or sinus problems in the week before examination, was tested in models as a time-varying covariate. Age and sex were included in all models and interactions with sex were explored. Linear regression was used to explore the association between exercise and the SDOIT score as a continuous measure.

Results

There were 1881 participants ages 53 to 97 years without olfactory impairment at the 5-year EHLS examination, which was the first examination that included olfactory testing. Of those, 1611 (85.6%) were tested again 5 and/or 10 years later, 142 (7.5%) died prior to a second examination, 49 (2.6%) refused to participate in the study, and 79 (4.2%) did not complete the olfaction test. The mean (SD) follow-up time among those with follow-up olfactory data was 9.6 (2.2) years.

Table 1. The 10-Year Cumulative Incidence of Olfactory Impairment in the Epidemiology of Hearing Loss Study

	Women			Men			All		
Baseline Age, y[a]	No. at Risk	Cases	10-y Cumulative Incidence[b] (95% CI)	No. at Risk	Cases	10-y Cumulative Incidence[b] (95% CI)	No. at Risk	Cases	10-y Cumulative Incidence[b] (95% CI)
53-59	279	20	7.5 (4.4-10.7)	204	24	12.4 (7.8-17.1)	483	44	9.6 (6.9-12.3)
60-69	381	74	21.0 (16.7-25.3)	257	58	25.1 (19.5-30.7)	638	132	22.6 (19.2-26.1)
70-79	276	112	52.2 (45.2-59.2)	139	66	56.9 (47.5-66.2)	415	178	53.8 (48.2-59.4)
80-97[c]	NR	NR	NR	NR	NR	NR	75	46	78.7 (66.3-91.1)
All	NR	NR	NR	NR	NR	NR	1611	400	27.6 (25.3-29.9)

Abbreviation: NR, not reported because the sample size was too small to make comparisons by sex.

[a] 1998-2000.

[b] Kaplan-Meier estimates of 10-year cumulative incidence.

Table 2. Selected Baseline Covariates and the 10-Year Cumulative Incidence of Olfactory Impairment

Baseline (1998-2000), Covariates	No. (%)	Age- and Sex-Adjusted HR (95% CI)	*P* Value
Age, every 5 y, adjusted for sex	1611	1.88 (1.74-2.03)	<.001
Sex, adjusted for age			
Women	992 (61.6)	1 [Reference]	
Men	619 (38.4)	1.27 (1.00-1.61)	.046
Exercise at least once a week	718 (44.5)	0.76 (0.60-0.97)	.03
Exercise, times per week			
0	872 (54.8)	1 [Reference]	
1-2	252 (15.9)	0.84 (0.60-1.17)	.30
≥3	466 (29.3)	0.73 (0.56-0.96)	.02
Education, y			
<12	202 (12.5)	1.46 (0.98-2.19)	.06
12	815 (50.6)	1.30 (0.94-1.80)	.12
13-15	276 (17.1)	1.16 (0.78-1.74)	.46
≥16	318 (19.7)	1 [Reference]	
Occupation[a]	458 (29.6)	1.31 (1.01-1.70)	.04
History of head injury	434 (26.9)	0.93 (0.71-1.21)	.56
Nasal polyps or deviated septum	154 (9.6)	1.56 (1.09-2.23)	.01
Nasal steroids	105 (6.6)	1.65 (1.07-2.55)	.02
Oral steroids	110 (6.9)	0.57 (0.31-1.05)	.07
History of stroke	18 (1.1)	1.70 (0.70-4.11)	.24
History of diabetes mellitus	175 (11.0)	1.08 (0.76-1.53)	.67
Smoking history			
Never	775 (48.7)	1 [Reference]	
Past; quit <5 y ago	48 (3.0)	1.92 (1.06-3.46)	.03
Past; quit ≥5 y ago	607 (38.2)	1.10 (0.85-1.42)	.46
Current	160 (10.0)	1.39 (0.90-2.15)	.13
History of heavy alcohol use	211 (13.3)	1.30 (0.92-1.84)	.14
BMI, mean (SD)	30.3 (5.9)	0.99 (0.97-1.01)	.32

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HR, hazard ratio.

[a] Longest-held occupation in manufacturing, production, farming, and forestry vs all others.

The 10-year cumulative incidence of olfactory impairment was 27.6% (95% CI, 25.3%-29.9%). The cumulative incidence rates increased dramatically for both men and women, with each decade increase in baseline age (**Table 1**). Although the overall 10-year cumulative incidence rates were similar between men (27.8% [95% CI, 24.0%-31.5%]) and women (27.5% [95% CI, 24.5%-30.4%]), the rates were slightly higher among men than women in all age groups younger than 80 years. The number of men aged 80 years or older at baseline who were at risk of developing olfactory impairment was small, limiting our ability to estimate sex-specific risks in this age range.

In an age- and sex-adjusted Cox proportional hazards model, exercising at least once a week was associated with a reduced risk (hazard ratio [HR], 0.76 [95% CI, 0.60-0.97]; *P* = .03 vs no exercise) of developing an olfactory impairment over 10 years (**Table 2**). The association with exercise was more robust among those who exercised 3 or more times per week (HR, 0.73 [95% CI, 0.56-0.96] vs no exercise) than among those who exercised only 1 or 2 times per week (HR, 0.84 [95% CI 0.60-1.17] vs no exercise). Additional factors that were significantly associated with the 10-year cumulative incidence of olfactory impairment included increasing age (HR, 1.88 [95% CI,

Table 3. Multivariable Model of Exercise and the 10-Year Cumulative Incidence of Olfactory Impairment

Baseline Risk Factor	Hazard Ratio (95% CI)	*P* Value
Age, for every 5 y	1.88 (1.74-2.04)	<.001
Sex	1.21 (0.95-1.56)	.13
Exercise, times per week		
0	1 [Reference]	
1-2	0.87 (0.62-1.23)	.43
≥3	0.73 (0.56-0.96)	.02
Nasal polyps or deviated septum	1.47 (1.02-2.13)	.04
Using nasal steroids	1.53 (0.97-2.42)	.07
Taking oral steroids	0.54 (0.29-1.00)	.05
Smoking history		
Never	1 [Reference]	
Current	1.41 (0.91-2.18)	.13
Past; quit <5 y ago	1.82 (0.99-3.34)	.05
Past; quit ≥5 y ago	1.11 (0.86-1.44)	.42

1.74-2.03], for every 5 years, adjusting for sex) and being male (HR, 1.27 [95% CI, 1.00-1.61], adjusting for age), and in age- and sex-adjusted models, a history of nasal conditions (nasal polyps or a deviated septum), taking nasal steroids, occupation, and smoking history (Table 2).

In a multivariable model adjusted for age, sex, and a history of nasal conditions, exercising 3 or more times a week was significantly associated with a lower risk for developing an olfactory impairment (HR, 0.73 [95% CI, 0.56-0.96). In this model, each increase in exercise level (none to 1-2 times per week and 1-2 times per week to ≥3 times per week) resulted in a 15% decrease in risk of developing olfactory impairment in 10 years (*P* value for trend = .02). Exercise remained an independent predictor (HR, 0.73 [95% CI, 0.56-96]) when also controlling for nasal steroids (HR, 1.53 [95% CI, 0.97- 2.42]), oral steroids (HR, 0.54 [95% CI, 0.29-1.00]), and smoking (HR, 1.82 [95% CI, 0.99-3.34] for a past smoker who quit <5 years previously vs never smoked), which were all nonsignificant in the multivariable model (**Table 3**). Including nasal congestion on the day of the examination, or a cold or sinus problems in the week before examination, as a time-varying covariate did not affect the association between exercise and olfactory impairment. Although participants who reported exercising at least once a week had a lower mean BMI and were less likely to be current smokers or have diabetes mellitus than participants who did not exercise, BMI, diabetes mellitus, and current smoking were not significantly associated with developing olfactory impairment over 10 years (Table 2).

Among the 1611 at risk for olfactory impairment at baseline, participants who reported exercising 3 or more times per week had a higher mean SDOIT score (mean score, 7.3 vs 7.2; *P* = .008) at baseline than participants who did not exercise. Adjusting for age, sex, and nasal conditions, those who exercised at baseline also had a higher mean SDOIT score at the 5-year follow-up (7.1 vs 6.9; *P* = .003) than those who did not exercise; a similar but nonsignificant pattern was present at the 10-year follow-up (6.6 vs 6.4; *P* = .26). In addition, participants who reported exercising regularly at the 10-year follow-up had less decline in SDOIT score between baseline and 10 years than participants who reported no exercise at 10 years (decline in mean SDOIT score of 0.7 vs 0.9 [*P* = .02], respectively).

Discussion

In the current study, regular exercise was associated with a reduced risk of developing an olfactory impairment over 10 years in older adults. In addition, more frequent exercise was associated with a greater reduction in the risk of developing olfactory impairment. These results extend the previous finding in this population of a similar association between exercise and the 5-year incidence of olfactory impairment[11] and suggest that regular exercise may have a long-term benefit for olfactory health in older adults. The cumulative incidence of olfactory impairment was high in those older than 70 years, as more than half developed an olfactory impairment in the 10-year period, underscoring the need to identify modifiable risk factors to reduce the burden of olfactory impairment in older adults.

The pathway for an association of exercise with olfaction is unknown, although it might be through the effect of exercise on either brain function or overall general health. Olfactory impairment has been found to be associated with cognitive impairment,[24,25] neurodegenerative disease,[26,27] and mortality.[28,29] Both Wilson et al[28] and Gopinath et al[29] suggest the association of olfactory impairment with mortality may be due to the presence of underlying neurodegenerative conditions. Pathologic changes, specifically the number of neurofibrillary tangles, that occur with aging or neurodegenerative disease within the brain's olfactory center have been found to be correlated with odor identification performance.[30] Exercise has been associated with less cognitive decline,[31] lower risk of cognitive impairment and Alzheimer disease,[3,32,33] and longer survival.[2,6,34] Cotman et al,[35] in a review of animal and human studies, suggested that exercise increases the availability of growth factors that in turn enhance cognitive function, plasticity, and neurogenesis. In addition, exercise has been shown to have positive effects on inflammation and cardiovascular health, which may also affect cognition.[2,36] Therefore, it is possible that exercise may have a beneficial effect on the areas of the brain involved in olfactory processing similar to the suggested effects of exercise on cognition.

It is also possible that in this study, exercise is an indicator of overall health or a marker for a combination of several health, lifestyle, and behavioral factors that have a protective effect on the olfactory system. One study found olfactory impairment to be associated with disability and increased use of community services in older adults even after controlling for age and cognition.[37] In the current study, participants who exercised had a lower BMI and were less likely to have diabetes mellitus than participants who did not exercise, although individually these factors were not significantly associated with olfactory impairment. Current smoking was not associated with developing an olfactory impairment; however, participants who quit smoking in the 5 years before the baseline examination had an increased risk for olfactory impairment that was not significant in the multivariable model.

Although there is a chance that participants without olfactory issues were more likely to exercise, all participants included in this study had good odor identification scores at baseline. In addition, while a positive history of obstructive nasal conditions (nasal polyps or a deviated septum) and the use of nasal steroids were associated with an increased risk of developing olfactory impairment, these factors had no effect on the exercise estimate when included in the multivariable model. Similarly, the use of oral steroids was suggestive of a reduced risk for development of olfactory impairment, but was not significant in the multivariable model and did not affect the association between exercise and olfactory impairment.

To our knowledge, this is the first population-based study of the 10-year cumulative incidence of olfactory impairment in older adults. The high incidence rate seen in this population-based study illustrates the extent of this health condition in older adults. Although rates were slightly higher for men than women, the 10-year cumulative incidence rates more than doubled for both men and women with each decade increase in age from the 50s through the 70s.

This study has some limitations that should be noted. Exercise was based on self-report and the participant's self-perception of exercise. The type, length, and intensity of exercise were also not available. These analyses are indicative of an event that was measured at the 5-year and/or 10-year follow-up examination, and testing status on the day of examination may not reflect the participant's long-term olfactory status as some olfactory impairment does improve.[38] However, this fluctuation is less likely to occur in older adults,[38] and exercise may still be associated with a decreased risk of developing an olfactory impairment regardless of whether the impairment is temporary or permanent. It should also be noted that this study has several major strengths. First, this was a large, population-based study with high response rates at follow-up examinations. Second, the same standardized odor identification test was administered at each examination by trained study examiners. Third, the population is well-characterized, and extensive covariate data on participants were available.

In conclusion, the 10-year cumulative incidence of olfactory impairment was high in this population of older adults, but the reduced risk of impairment among those who exercised regularly suggests some olfactory impairment may be preventable. Additional research is needed to identify the pathway of this association.

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Study concept and design: Schubert, Cruickshanks.
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