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## Exercise Is Associated with Lower Long-Term Risk of Olfactory Impairment in Older Adults

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### Abstract

**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.

**Objectives**—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 53-97 years at baseline and were followed for up to ten years (1998-2010).

**Interventions**—None

**Main Outcome and Measures**—Olfaction was measured with the San Diego Odor Identification Test at three examinations (1998-2000, 2003-2005, 2009-2010) of the Epidemiology of Hearing Loss Study. The main outcome was the incidence of olfactory impairment five (2003-2005) or ten (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% confidence interval =25.3, 29.9) and rates varied by age and sex; those who were older (Hazard Ratio =1.88, 95% Confidence Interval=1.74, 2.03, for every 5 years) or male (Hazard Ratio=1.27, 95% Confidence Interval=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

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Study concept and design: Schubert, Cruickshanks

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of olfactory impairment (age and sex adjusted Hazard Ratio= 0.76, 95% CI= 0.60, 0.97). Increasing frequency of exercise was associated with decreasing risk of developing olfactory impairment (p for trend = 0.02).

**Conclusion 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.

## Keywords

Olfaction; Exercise; Aging; Epidemiology; Longitudinal

## Introduction

Regular exercise has been shown to reduce the risk of many age-related conditions including impaired physical functioning<sup>1</sup>, cardiovascular disease<sup>2</sup>, Alzheimer's disease<sup>3</sup> and dementia.<sup>4</sup> In addition, exercise has been associated with maintaining good health<sup>5</sup> and cognition in older age and increased survival.<sup>2, 6</sup> 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.<sup>7-10</sup> The prevalence of olfactory impairment was 25% in a population of older adults and the incidence rate for developing an olfactory impairment in five years was 12.5%; the long term incidence rate is unknown.<sup>7,11</sup>

The sense of smell is an important early warning system for identifying danger and toxins in the environment (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.<sup>12-14</sup> Many older adults are unaware they have had a decline in their sense of smell.<sup>7,15</sup> Because of the high prevalence,<sup>7-10</sup> low awareness<sup>7, 15</sup> and the impact a decline in olfactory function may have on safety, nutrition and quality of life in older adults,<sup>12-14</sup> 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.<sup>11</sup> 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, WI.<sup>16-18</sup> In 1987-88 a private census was conducted in the city and township of Beaver Dam, WI. All residents aged 43-85 years were invited to participate in the Beaver Dam Eye Study (BDES), a study of vision and ocular diseases of aging.<sup>19</sup> Of the 5924 people eligible for the study, 4926 (83%) participated in the baseline BDES examination in 1988-1990.<sup>19</sup> In 1993-1995, all BDES participants who were alive as of March 1, 1993 were invited to participate in the EHLS.<sup>16</sup> 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).<sup>16-18</sup> 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, 2003-2005, 2009-2010 respectively) using the San Diego Odor Identification Test (SDOIT).<sup>7, 11</sup> The SDOIT is a standardized odor identification test that consists of eight common odors (chocolate, coffee, etc).<sup>7, 20,21</sup> 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, they are 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 two trials. Olfactory impairment was defined as identifying fewer than 6 odorants correctly.<sup>7</sup> The SDOIT is very reliable with a concordance correlation coefficient = 0.85 (95% confidence interval = 0.79, 0.91) and it has a test-retest agreement of 96% for olfactory impairment over an average of three weeks.<sup>21</sup>

### Assessment of Exercise

Data from two interview questions obtained in the concurrent BDES examinations were utilized 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 versus any), and as a three level variable (none, 1-2 times per week and 3 or more times per week).

### Assessment of Covariates

Height and weight were measured and body mass index (BMI) was calculated ( $\text{kg/m}^2$ ). Participants brought their current medications to the examinations and name and frequency of use were recorded. Non-fasting blood samples were obtained for measurement of Hemoglobin A1C and participants were classified as having diabetes mellitus based on self-report of a physician diagnosis, an A1C of 6.5% or higher or report of possible diabetes and taking medication for diabetes. 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's disease, Parkinson's disease, epilepsy, head injury and allergies. A participant was considered to have a history of nasal conditions if they reported ever having been told by a doctor 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, past - quit 5 or more years, never), weekly alcohol consumption and if there was ever a time when they consistently drank 4 or more drinks per day.

### Data analyses

Analyses were conducted using SAS version 9.2 software (SAS Institute Inc., Cary, NC, USA). Analyses were restricted to participants who did not have olfactory impairment at the baseline olfactory exam (SDOIT score  $\geq 6$ , 1998-2000) and were therefore at risk for incident olfactory impairment. Incident olfactory impairment was defined as a SDOIT score <6 at one of the follow-up examinations. Kaplan-Meier estimates<sup>22</sup> 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.<sup>23</sup> Reported nasal congestion on the day, 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 gender 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 aged 53-97 years of age 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 five- and/or 10-years later, 142 (7.5%) died prior to a second examination, 49 (2.6%) refused and 79 (4.2%) did not complete the olfaction test. The average follow-up time among those with follow-up olfactory data was 9.6 years (standard deviation = 2.22).

The 10-year cumulative incidence of olfactory impairment was 27.6% (95% confidence interval (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% Confidence Interval (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 under 80 years. The number of men aged 80 years and older at baseline who were at risk of developing olfactory impairment was small limiting our ability to estimate gender-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% Confidence Interval (CI) = 0.60, 0.97,  $p=0.03$  versus 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 versus none) than among those who only exercised 1-2 times per week (HR=0.84, 95% CI=0.60, 1.17 versus none). Additional factors that were significantly associated with the 10-year cumulative incidence of olfactory impairment included increasing age (HR = 1.88, 95% CI = 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 three 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 or more times per week) resulted in a 15% decrease in risk of developing olfactory impairment in 10 years ( $p$  for trend =0.02). 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 past smoker, quit < 5 years versus never smoked) which were all borderline non-significant in the multivariable model (Table 3). Including nasal congestion on the day of, 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 than participants who did not exercise, BMI, diabetes 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 three or more times per week had a higher mean SDOIT score (mean score 7.3 vs 7.2;  $p=0.008$ ) 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 ( $p=0.003$ )) than those who did not exercise; a similar but non-significant pattern was present at the 10-year follow-up (6.6 vs 6.4 ( $p=0.26$ )). 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 ( $p=0.02$ ), 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 that found a similar association between exercise and the 5-year incidence of olfactory impairment<sup>11</sup> 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 more than 70 years old, 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, though 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,<sup>24,25</sup> neurodegenerative disease<sup>26,27</sup>, and mortality.<sup>28,29</sup> Both Wilson et al<sup>28</sup> and Gopinath et al<sup>29</sup> suggest the association of olfactory impairment with mortality may be due to the presence of underlying neurodegenerative conditions. Pathological 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.<sup>30</sup> Exercise has been associated with less cognitive decline<sup>31</sup> lower risk of cognitive impairment and AD<sup>3,32,33</sup> and longer survival.<sup>2,6,34</sup> Cotman et al, in a review of animal and human studies, suggested exercise increases the availability of growth factors that in turn enhance cognitive function, plasticity, and neurogenesis.<sup>35</sup> Additionally, exercise has been shown to have positive effects on inflammation and cardiovascular health which may also affect cognition.<sup>2, 36</sup> Therefore, it is possible 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.<sup>37</sup> In the current study, participants who exercised had a lower BMI and were less likely to have diabetes 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 five years before the baseline exam had an increased risk for olfactory impairment that was borderline non-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. Additionally, 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 borderline non-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. Though 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- 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.<sup>38</sup> However, this fluctuation is less likely to occur in older adults<sup>38</sup> and exercise may still be associated with a decreased risk of developing an olfactory impairment regardless if 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 was available on participants.

## Conclusion

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. Further research is needed to identify the pathway of this association.

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

	Women				Men				All			
	N at Risk	Cases	10-year Cumulative Incidence <sup>a</sup>	95% CI	N at Risk	Cases	10-year Cumulative Incidence <sup>a</sup>	95% CI	N at Risk	Cases	10-year Cumulative Incidence <sup>a</sup>	95% CI
Baseline Age, years (1998-2000)												
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 <sup>b</sup>									75	46	78.7	66.3, 91.1
All	992	245	27.5	24.5, 30.4	619	155	27.8	24.0, 31.5	1611	400	27.6	25.3, 29.9

CI=confidence interval

<sup>a</sup> Kaplan-Meier estimates of 10-year cumulative incidence;

<sup>b</sup> Sample size too small to make comparisons by sex

**Table 2**  
**Selected Baseline Covariates and the 10-year Cumulative Incidence of Olfactory Impairment**

Baseline (1998-2000) covariates	N (%)	Age & Sex Adjusted Hazard Ratios (95% Confidence Intervals)	p-value
Age, every 5 years (adjusted for sex)	1611	1.88 (1.74, 2.03)	<0.001
Sex (adjusted for age)			
Women (referent)	992 (61.6)	1.00	
Men	619 (38.4)	1.27 (1.00, 1.61)	0.046
Exercise at least once a week	718 (44.5)	0.76 (0.60, 0.97)	0.03
Exercise, times per week			
0 (referent)	872 (54.8)	1.00	
1-2	252 (15.9)	0.84 (0.60, 1.17)	0.30
3 or more	466 (29.3)	0.73 (0.56, 0.96)	0.02
Education			
< 12 years	202 (12.5)	1.46 (0.98, 2.19)	0.06
12 years	815 (50.6)	1.30 (0.94, 1.80)	0.12
13-15 years	276 (17.1)	1.16 (0.78, 1.74)	0.46
16 or more years (referent)	318 (19.7)	1.00	
Occupation <sup>a</sup>	458 (29.6)	1.31 (1.01, 1.70)	0.04
History of Head Injury	434 (26.9)	0.93 (0.71, 1.21)	0.56
Nasal polyps or deviated septum	154 (9.6)	1.56 (1.09, 2.23)	0.01
Nasal Steroids	105 (6.6)	1.65 (1.07, 2.55)	0.02
Oral Steroids	110 (6.9)	0.57 (0.31, 1.05)	0.07
History of Stroke	18 (1.1)	1.70 (0.70, 4.11)	0.24
History of Diabetes	175 (11.0)	1.08 (0.76, 1.53)	0.67
Smoking history			
Never (referent)	775 (48.7)	1.00	
Past - quit <5 years ago	48 (3.0)	1.92 (1.06, 3.46)	0.03
Past – quit 5 years ago	607 (38.2)	1.10 (0.85, 1.42)	0.46
Current	160 (10.0)	1.39 (0.90, 2.15)	0.13
History of heavy alcohol use	211 (13.3)	1.30 (0.92, 1.84)	0.14
BMI, kg/m <sup>2</sup> Mean (standard deviation)	30.3 (5.9)	0.99 (0.97, 1.01)	0.32

BMI= Body mass index; kg= kilogram; m= meter

<sup>a</sup>Longest held occupation in manufacturing, production, farming, forestry vs. all others

**Table 3**  
**Multivariable Model of Exercise and the 10-year Cumulative Incidence of Olfactory Impairment**

Baseline Risk Factor	Hazard Ratio (95% Confidence Interval)	p-value
Age, for every 5 years	1.88 (1.74, 2.04)	<0.001
Sex	1.21 (0.95, 1.56)	0.13
Exercise - times per week		
0 (referent)	1.00	
1-2	0.87 (0.62, 1.23)	0.43
3 or more	0.73 (0.56, 0.96)	0.02
Nasal polyps or deviated septum	1.47 (1.02, 2.13)	0.04
Using Nasal Steroids	1.53 (0.97, 2.42)	0.07
Taking Oral Steroids	0.54 (0.29, 1.00)	0.05
Smoking history		
Never (referent)	1.00	
Current	1.41 (0.91, 2.18)	0.13
Past, quit < 5 years ago	1.82 (0.99, 3.34)	0.05
Past, quit 5 years ago	1.11 (0.86, 1.44)	0.42