

Role of physical exercise type in olfactory deterioration in ageing*

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Abstract

Background: Although ageing and neurodegenerative diseases, including Alzheimer disease, have been associated with olfaction impairment, studies exploring how to ameliorate this impairment are limited. The aim of the present study was to determine the effect of various types of physical exercise on olfaction decline in ageing.

Methodology: 99 healthy community-dwelling participants (85 women; mean [SD] age, 62.5 [5.7] years) were included. All the participants were required to complete the tests consisting of a questionnaire, cognitive test and olfaction test.

Results: Odor identification scores for participants who exercised regularly for more than 1 year (>3 times/wk; >30 min each time) were significantly higher than those for non-exercisers, and odor detection threshold scores were significantly higher in the exercisers. Both odor threshold and odor identification scores for those who exercised by practicing taiji (tai chi), dancing, or running were significantly better than those for participants who exercised by walking or who did not exercise.

Conclusion: Compared with those among older people who did not exercise, measures of olfaction among older adults who exercised were better, and the type of physical exercise mattered. Therefore, if physical exercise intervention is suggested to prevent or delay olfactory deterioration in older adults, the type of physical exercise should be considered.

Key words: ageing, Alzheimer disease, physical exercise, odor identification, odor threshold

Introduction

As suggested by Martzke et al., odor identification and the olfactory threshold sensitivity belong to different olfactory processing systems, the former is a function of the central nervous system, whereas the latter is a function of the peripheral nervous system⁽¹⁾. Both odor identification and odor sensitivity impairment are highly associated with neurodegenerative diseases, such as Alzheimer disease (AD). Numerous studies have demonstrated that odor identification is significantly impaired in persons with AD compared with that in their healthy counterparts⁽²⁾. The olfactory threshold sensitivity is also profoundly affected in AD⁽³⁾, with the degree of threshold deterioration correlated with the degree of dementia⁽⁴⁾.

Although much research has been conducted examining olfactory function as a biomarker of AD, studies investigating how to

prevent further decline of olfaction are limited. The few studies demonstrating that regular physical exercise improves olfactory function have focused on odor identification^(5,6), but the effect of regular physical exercise on the odor detection threshold was not robust. Schubert et al.⁽⁷⁾ found that regular physical exercise was correlated with a reduced risk of having a higher threshold, but suggested that physical exercise may not have a linear relationship with the olfaction threshold. In addition, to the best of our knowledge, none of the previous studies took into account the type of physical exercise. Therefore, the aims of the present study were twofold: 1) to determine whether physical exercise affects measures of olfactory function and 2) to examine whether different types of physical exercise play a role in the amelioration of olfactory function decline in older persons.

Material and methods

Participants

Because the ability of humans to identify odors begins to decline in the fifth decade of life⁽⁸⁾, we recruited participants who were more than 50 years old for the present study. Individuals reporting a history of any of the following conditions were excluded from the study: neurologic disease (e.g., brain tumor, Parkinson disease), local respiratory tract disorder (e.g., nasal surgery, active rhinitis or sinusitis), and psychiatric disorder (e.g., depression). All participants were asked about their history of alcohol use and cigarette smoking.

Candidates who exercised more than 3 times per week (>30 min/episode) were assigned to the exercise group, and those who did not engage in any exercise were assigned to the no-exercise group.

All procedures were performed according to the Declaration of Helsinki and approved by the Shanghai University of Sport Ethics Committee (Shanghai, China). Written informed consent was obtained from all participants prior to any examination.

Procedure

The procedure consisted of a questionnaire, cognitive tests, and olfactory tests and took 1 to 2 hours for each participant to complete. Participants could break at any time after a test. The order in which the 3 tests - the Mini-Mental State Examination (MMSE) cognitive test, the odor identification test, and the odor threshold test - were conducted was counterbalanced, but the order in which the participant personal information questionnaire was given was not counterbalanced.

Participant personal information questionnaire

Participant sex, age, height, weight, smoking and drinking history, educational level, history of surgical procedures and drug use, regular physical exercise habits, and years engaged in regular physical exercise were collected using a questionnaire. For details about the questionnaire, see the Supplementary Material online.

Cognitive test

The Chinese version of the MMSE⁽⁹⁾ was administered to examine the cognitive function of the participants. The MMSE is a 30-point questionnaire that takes 5 to 10 minutes to complete. It examines the following functions: registration (via repeating named prompts), attention and calculation, recall, language, ability to follow simple commands, and orientation.

Odor identification test

To reduce the influence of cultural differences on the results, we used the Special Identification Test of the "Sniffin' Sticks" test (Burghart, Wedel, Germany), which is the Chinese version, to exam olfactory identification among the participants. The test

was conducted as described by Hummel et al.⁽¹⁰⁾. Both nostrils were assessed for each participant in a well-ventilated room. The test included 16 odorants. Because people in China may not be familiar with 3 of the odorants in the original test, they were replaced by more familiar odorants: (No. 3) chocolate replaced cinnamon; (No. 8) ginger replaced turpentine; and (No. 12) soya sauce replaced cloves. Possible scores ranged from 0 to 16, with lower scores indicating a lower ability to identify odors.

Odor threshold test

Odor threshold was examined among the participants using the Sniffin' Sticks test with n-butanol as the odorant. The test was conducted for both nostrils in a well-ventilated room as described by Hummel et al.⁽¹⁰⁾. We prepared 16 dilutions of n-butanol in a geometric series. Three pens - 1 with odorant and 2 without any odorant (blank pens) - were presented to the participants for each dilution of n-butanol. Participants were scored using a 3-alternative forced-choice staircase paradigm. Possible scores ranged from 0 to 16, with lower scores indicating a high smell detection threshold.

Statistical analysis

Data were analyzed using SPSS, version 22.0 (SPSS Inc., Chicago, IL, USA). For continuous variables (e.g., age, MMSE score, odor identification score, and odor threshold score), independent-sample t tests were conducted to evaluate the difference between scores in the exercise group and those in the no-exercise group. The chi-squared test was used to analyze dichotomous (categorical) variables (e.g., male or female sex; smoking or no smoking) when examining the differences in scores between participants in the exercise group and those in the no-exercise group. An analysis of variance (ANOVA) followed by Dunnett post hoc tests were applied to compare the main effect of different physical exercise types on odor identification and odor threshold. Pearson correlation coefficient was used to assess correlational analyses. Data are displayed as mean \pm SD. A 2-sided $P < 0.05$ was considered statistically significant.

Results

Study population

In total, 108 healthy community-dwelling participants were enrolled in this study. Among the 108 enrolled participants, 99 were included in the final analysis, of which 85 (85.8%) were women and the mean (SD) age was 62.5 (5.7) years. We exclude 9 participants from the analysis because 3 participants did not complete all of the tests, 3 participants admitted that they had an upper respiratory tract infection after completing all the tests, and 3 participants reported that they had a cold during the testing. Thus, 57 participants were included in exercise group, and 42 participants were included in the no-exercise group. There were no significant differences in age, sex, educational level,

Table 1. Demographic characteristics and mmse, odor identification, and odor threshold scores among participants in the exercise and no-exercise groups

Variable	Exercise (n = 57)	No Exercise (n = 42)	P Value
Age (mean \pm SD), y	62.5 \pm 5.2	62.4 \pm 6.4	0.93
Female, No. (%)	50 (87.7%)	35 (83.3%)	0.53
Smoker, No. (%)	1 (0.02%)	1 (0.02%)	>.99
Educational level, mean \pm SD, y	7.9 \pm 4.1	7.4 \pm 3.6	00.50
MMSE score, mean \pm SD	25.6 \pm 3.8	25.5 \pm 3.0	0.37
Odor identification score, mean \pm SD	12.0 \pm 2.0	9.9 \pm 2.9	<0.001
Odor threshold score, mean \pm SD	7.3 \pm 2.3	4.9 \pm 2.3	<0.001

Note. MMSE represents Mini-Mental State Examination.

MMSE score, or smoking status either between the exercise and no-exercise groups or among the different exercise types (Table 1). None of the participants reported heavy alcohol use, and all the participants in the exercise group reported exercising for more than 1 year.

In the exercise group, 20 participants (35.1%) practiced taiji (also known as tai chi), 14 participants (24.6%) were dancers, 11 participants (19.3%) were walkers, and 12 participants (21.0%) were runners.

Psychophysical test results for the exercise and no-exercise groups

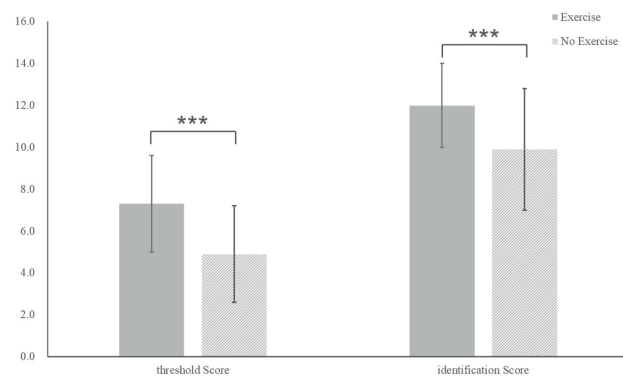
There was no significant difference in MMSE scores between the exercise group and the no-exercise group, although the MMSE scores were positively correlated with educational level ($r = 0.75$, $P < 0.001$). The mean (SD) odor identification score for the exercise group (12.0 [2.0]) was significantly higher than that for the no-exercise group (9.9 [2.9]) ($P < .001$). The odor threshold score was also significantly different between these 2 groups, with the mean (SD) odor threshold scores were higher in the exercise group (7.3 [2.3]) than in the no-exercise group (4.9 [2.3]) ($P < 0.001$) (Figure 1).

Olfactory test results for the types of physical exercise

Using ANOVA followed by Dunnett post hoc tests, a significant main effect of physical exercise type was found for odor identification and also for odor detection threshold (Figure 2).

The mean (SD) odor identification scores were 12.1 (1.3) for taiji practitioners, 12.3 (1.1) for dancers, 12.8 (1.5) for runners, 10.2 (3.2) for walkers, and 9.9 (2.9) for those who did not exercise. The mean odor detection threshold scores were 8.5 (1.6) for taiji practitioners, 8.1 (1.7) for dancers, 7.4 (2.0) for runners, 4.0 (1.2) for

Figure 1. Odor detection threshold scores and odor identification scores among participants who exercise regularly and those who do not exercise.



walkers and 4.9 (2.3) for people who did not exercise

The odor detection threshold and the odor identification scores for those who exercised by practicing taiji, dancing, or running were significantly higher than for those who exercised by walking or who did not exercise, indicating that compared with older people who walked for exercise or who did not exercise, those who practiced taiji, danced or ran for exercise had a lower threshold for detecting odors and were better able to identify odors (Table 2).

Discussion

Consistent with previous research^(5,6), the present study found that older people (approximately 62 years old) who exercised were better at odor identification than those who did not exercise. In addition, we found a positive influence of physical exercise on odor threshold. Altom et al.⁽¹¹⁾ had similar finding in dogs, revealing that suitable physical activity improves odor sensitivity in dogs. However, when we explored the impact of physical exercise type, we found that not all the types of physical exercise examined in this research had a positive effect on olfactory functions. Among the examined types of physical exercise, practicing taiji, dancing, and running significantly increased olfactory function in these older participants, whereas walking did not have the same effect. Previous studies have shown that physical exercise intensity or frequency might play an important role in the magnitude of the benefits for those with AD among an ageing cohort⁽¹²⁻¹⁶⁾. A longitudinal study reported that men with the lowest physical exercise intensity had 1.8 to 2.5 times worse 10-year cognitive decline than those with higher physical exercise intensity⁽¹²⁾. Interestingly, intensity and variation of physical exercise, rather than duration of time spent on physical exercise, have been positively correlated with cognitive function

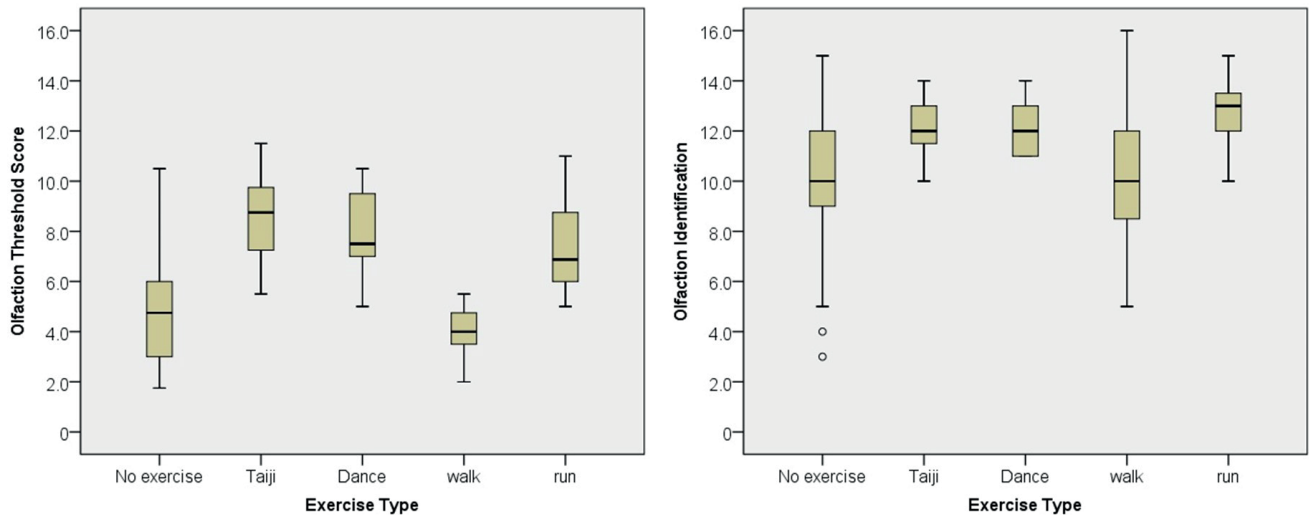


Figure 2. Odor detection threshold and odor identification scores stratified by exercise type. The boxes extend from the lower to the upper quartile values of the data, with a horizontal band at the median. The whiskers extend from the box to show the range of the data. Outlier points are those past the end of the whiskers.

Table 2. Comparison of odor threshold and odor identification scores between no exercise and 4 types of exercise.

Olfactory Function	Exercise	No Exercise	P Value
Odor threshold (mean ± SD), No. of participants	Taiji (8.5 ± 1.6), 20	4.9 ± 2.3, 42	<0.001
	Dance (8.1 ± 1.7), 14		<0.001
	Run (7.4 ± 2.0), 12		0.001
	Walk (4.0 ± 1.2), 11		0.55
Odor identification (mean ± SD), No. of participants	Taiji (12.1 ± 1.3), 20	9.9 ± 2.9, 42	0.003
	Dance (12.3 ± 1.1), 14		0.005
	Run (12.8 ± 1.5), 12		0.001
	Walk (10.2 ± 3.2), 11		0.99

⁽¹³⁾. The existence of a physical exercise intensity response on AD pathology has also been found in animal studies. Compared with high-intensity physical exercise for mice on a running wheel, mice who engaged in low-intensity physical exercise did not differ from controls in amyloid deposition ⁽¹⁴⁾. Both a significant reduction in soluble Aβ₄₂ levels and a significant increase in numerous Aβ clearance proteins occurred in a physical exercise training intensity-dependent manner in both the cortex and hippocampus of mice ⁽¹⁵⁾. A study in mice found that exercising 3 times per week for 12 weeks significantly ameliorated their inflammatory markers, whereas 1 time per week for 12 weeks did not have an effect, suggesting that physical exercise frequency plays a role ⁽¹⁶⁾. The present study included only participants who exercised more than 3 times per week and more than 30 minutes per episode; thus, exercise frequency was a factor for inclusion in the present study, but exercise intensity was not. Therefore, exercise intensity might have been a factor that caused walking to fail to positively influence olfactory function in elders although this hypothesis could not be explored in the present study. Abundant studies suggested that people in di-

verse occupations were benefited from regular physical exercise, they had lower all-cause mortality rate and better overall health ⁽¹⁷⁻²⁰⁾. In those people who has better overall health, better olfactory function has been repeated found ⁽²¹⁻²³⁾. Based on these, we assumed that physical exercise improved participants' overall health and then may promoted their olfactory function. Besides physical exercise, regular olfactory training has been found also could significantly increase olfactory ability regardless of age and health status ⁽²⁴⁻²⁷⁾. However, the present study only revealed the positive correlation between physical exercise and olfactory performance. In future research, the combination of physical exercise intervention and olfactory training should be employed to see the further relationship between them. Although several studies have demonstrated that poor olfactory function predicts cognitive impairment ⁽²⁸⁾, no significant difference was found in cognitive function as assessed using the MMSE between the participants in the exercise group and those in the no-exercise group in present study. This apparent discrepant finding may have occurred at least in part because we used a previous clinical diagnosis of a cognitive disorder as

an exclusion factor and we assessed cognitive function only with the MMSE, which may lack sensitivity. In addition, olfactory function is largely independent of cognitive deficits in Parkinson disease⁽²⁹⁾, and olfaction dysfunction occurs at a very early stage of Alzheimer disease, even prior to the onset of the cognitive impairments typical with this disease⁽³⁰⁾. Moreover, olfaction threshold was able to distinguish the elderly patients of idiopathic Parkinson's diseases and controls⁽³¹⁾.

The exact mechanism responsible for physical exercise ameliorating, delaying, or preventing the deterioration of olfactory function in elders remains unclear. However, we speculate that one explanation might be physical-exercise-induced brain structural and processing changes that overlap with the olfactory pathway. As an integral part of the olfactory system, the hippocampus receives strong afferent input from the entorhinal cortex⁽³²⁾. A close relationship between hippocampal volume and odor identification has been detected by researchers⁽³³⁾. Physical-exercise-induced increases in hippocampal volume have been well documented⁽³⁴⁾. For example, that the size of the hippocampus increases by 12% to 16% with physical exercise was reported by Pajonk et al.⁽³⁴⁾. In addition, physical exercise boosts hippocampal blood volume⁽³⁵⁾ and increases brain-derived neurotrophic factor levels^(24,36) and the volume of its release from the brain⁽³⁷⁾. Moreover, the connectivity between frontal and hippocampal regions is significantly enhanced by physical exercise⁽³⁸⁻⁴⁰⁾.

There are some limitations that should be considered when interpreting the results of the present study. First, we used self-reported data rather than controlling the physical exercise intensity, frequency, or duration; however, we screened candidates to include those who exercised more than 30 minutes per episode, at least 3 times per week for more than 1 year. The use of self-reported data also limited our ability to categorize exercise intensity. Second, because the study population con-

sisted of mainly women, there might be sex differences in the associations observed between exercise and olfactory function that could not be explored in the present study. However, latest research showed there was no significant difference between male and female in ageing⁽⁴¹⁾. Third, we didn't take the number of daily drugs taken into consideration, since it was found that numbers of drugs taken were highly associated with olfactory threshold⁽⁴²⁾. Finally, we did not explore potential mechanisms to explain how physical exercise impacted odor detection threshold or odor identification.

Conclusion

Considering the high correlation between Alzheimer disease and olfactory function^(43,44), future studies should investigate whether physical exercise will improve olfactory function and the mechanism underpinning such a finding in participants with Alzheimer disease. Given that the present study found that the type of physical exercise may be important, when physical exercise intervention is applied to prevent, ameliorate, or delay olfactory deterioration in older adults, the type of physical exercise prescribed should be considered.

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Authorship contribution

XW and CZ designed the research protocol, CZ and DL conducted the research, CZ wrote the paper and XW had primary responsibility for the final content. All authors have read and approved the final manuscript.

Conflict of interest

All authors declared no conflict of interest.

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SUPPLEMENTARY INFO

Participant Personal Information Questionnaire

Dear Participants,

Thank you for your time completing this questionnaire. All the information will be strictly kept confidential. Please answer all the question with honest. Thank you again.

Q1. Gender: Male () Female ()

Q2. Date of Birth:

Q3. Height (cm):

Q4. Weight (kg):

Q5. Do you smoke or used to smoke? If yes, please specify.
Yes () Please specify how much cigarette taken. No ()

Q6. Do you drink or used to drink? If yes, please specify.
Yes () Please specify daily volume consumed. No ()

Q7. Have you got serious disease in recent 5 years (request surgery)?
Yes () Please specify. No ()

Q8. Are you taking drugs?
Yes () Please specify. No ()

Q9. How about your sleep ?
A Good B Not bad, may sleepless occasionally
C Very bad, sleepless most of the time

Q10. What's your education?
A ≤ 6years B 7-9 years C 10-12 years D ≥ 13 years

Q11. How many times you exercise in a week ? (≥ 30min/time)
A > 5 times B 3-5 times C 1-2 times D No regular exercise

Q12. How long have you been exercise?
A < 1year B 1-3 years C > 3 years