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Original Article

Olfactory identification ability in patients with mild cognitive impairment and Alzheimer's disease

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Abstract. [Purpose] To examine the olfactory identification abilities and specify the difficult-to-identify odors in community-dwelling individuals with mild cognitive impairment (MCI) and Alzheimer's disease (AD). [Participants and Methods] We included, 12 and 17 patients with MCI (MCI group) and AD (AD group), respectively, and 30 community-dwelling older adults with no history of MCI or a dementia diagnosis (control group). Scores on the Japanese odor stick identification test (OSIT-J), an olfactory identification ability test, were compared among the three groups with intergroup differences examined accordingly. Next, we performed intergroup comparisons of the ratios of correct responses for each odor, and the difficult-to-identify odors were examined. [Results] OSIT-J scores of the MCI and AD groups were significantly lower than those of the control group. There were no intergroup differences in the correct identification of pungent odors. No patients in the AD group could identify the odor of cooking gas. The ability to identify food-related odors was reduced in the MCI and AD groups. [Conclusion] Patients with MCI and AD had reduced olfactory identification abilities in comparison to community-dwelling older adults without cognitive decline. These findings suggest the importance of olfactory evaluation before providing patients with dementia with therapeutic interventions associated with olfactory stimuli.

Key words: Olfactory impairment, Alzheimer's disease, Mild cognitive impairment

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INTRODUCTION

The number of individuals with dementia and mild cognitive impairment (MCI) as a result of aging is increasing each year[1)], and the early detection and prompt intervention in dementia are important. Olfactory testing has attracted attention as a screening approach for the early detection of dementia. The olfactory sense deteriorates with age[2)]; however, it has been reported that the olfactory identification ability, which is the ability to identify types of odors, is reduced in patients with Alzheimer's disease (AD)[3)] in particular. Reduced olfactory identification ability has been reported to be associated with increased risks for progression to AD in individuals with MCI and the development of MCI in healthy older individuals[4)]. Authors of previous studies have stated that evaluating an individual's olfactory identification ability could aid in the early detection of an elevated risk for dementia[4)]. Meanwhile, olfactory stimuli have been used for therapeutic intervention in patients with MCI and AD because they are believed to promote the activation of brain function and are expected to improve

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cognitive function[5]. These previous findings suggest that dementia has a strong association with the olfactory sense; however, there are various odor types, and different odor stimuli are likely to evoke different responses. Therefore, before the provision of effective therapeutic intervention, it is important to test for and identify reduced cognitive function and reduced olfactory identification ability with regard to odor types. Previous studies on cognitive function and olfactory identification ability have examined the specific odors for which the olfactory identification ability is reduced in inpatients with MCI and AD[6]; however, no previous studies have included community-dwelling individuals with MCI and AD.

In this study, we examined the olfactory identification ability and specific odors that were difficult to identify in community-dwelling individuals with MCI or AD but who were receiving care from family.

PARTICIPANTS AND METHODS

To recruit participants for this study, we explained the objective and methods of the study to patients participating in an outpatient rehabilitation program (cognition/physical-revitalizing rehabilitation) conducted for people with reduced cognitive function at the Department of Rehabilitation, National Center for Geriatrics and Gerontology. Thirty-one willing patients provided written consent to participate in the study. Those who had difficulty understanding the study, such as patients with advanced AD, received a verbal, easy-to-understand explanation. We excluded individuals who could not fully understand the study even after receiving a verbal explanation. Finally, we included 12 patients with MCI (MCI group) and 17 patients with AD (AD group). AD was diagnosed at the National Center for Geriatrics and Gerontology according to the diagnostic criteria of the National Institute of Neurological and Communicative Disorders and Stroke AD and Related Disorders Association[7]. MCI was diagnosed according to the criteriadescribed by Petersen et al[8]. All participants in the MCI group had amnestic MCI. The MCI group consisted of three males and nine females in the age range of 68–85 (mean ± SD, 78.9 ± 6.0) years, and they had a history of education ranging from 9 to 16 (12.5 ± 2.2) years. The AD group consisted of nine males and eight females aged 62–85 (77.6 ± 6.3) years, and they had an education history of 9–16 (11.9 ± 1.8) years. Aside from the participants recruited from the cognition/physical-activating revitalizing program, to recruit additional participants, we also explained the objective and methods of this study to community-dwelling older adults who were participating in a local salon for older people. Of the 57 salon participants who consented to study participation, 30 who were independently capable of performing activities of daily living, had no history of MCI or dementia diagnosis, no signs in the medical interview of diseases affecting the olfactory sense, and a score of at least 26 points on the Japanese version of Montreal Cognitive Assessment (MoCA-J) were included as a control group. The control group consisted of 6 males and 24 females in the age range of 65–82 (72.8 ± 4.1) years, and they had an education history of 12–16 (13.3 ± 1.7) years.

The following tests were used to evaluate cognitive function:

1. MoCA-J: The MoCA-J is a cognitive function screening test consisting of items for visuospatial/executive function, naming, attention, language, abstraction, delayed recall, and orientation. Scores of less than 26 of 30 points are considered to indicate cognitive decline[9]. The MoCA-J has been shown to detect milder cognitive decline than the Mini-Mental State Examination-Japanese (MMSE-J)[9].

2. MMSE-J: The MMSE-J is a screening test of cognitive function that consists of items regarding orientation, memorization, attention, calculation, recall, and language. Of a possible 30 points, scores of less than 24 indicate suspected cases of dementia[10].

We used the OSIT-J (Daiichi Yakuhin Sangyo Co., Ltd., Tokyo, Japan) to test the olfactory identification ability of study participants.

In the OSIT-J, participants sniff pieces of scented paper to identify the following 12 odors: India ink, wood, perfume, menthol, Japanese orange, curry, gas leak, rose, Japanese cypress, sweaty socks/sweaty odor, condensed milk, and roasted garlic. For each question, one of the following six alternatives was chosen: “correct answer”, “different odor from the correct answer”, “detectable but unrecognizable”, and “odorless”. For each item, one point was given to the individual who selected the correct answer and zero points to those who selected any of the other options. Total scores of less than 8 of 12 points were considered to indicate a decrease in olfactory identification ability[11].

First, the OSIT-J total score was compared among the MCI, AD, and control groups. Subsequently, those odors that could not be identified correctly were examined.

We used JMP14 (SAS Institute Inc, Cary, NC, USA) for statistical processing. A significance level of 5% was used. One-way analysis of variance was used for intergroup comparisons of age and education history, and Tukey’s test was used when the analysis showed a significant difference. After removing the effects of age and education history, we used analysis of covariance to compare the MoCA-J, MMSE-J, and OSIT-J total scores with the correct answer rates for each of the odors among the three groups because age and education have effects on cognitive function and age has effects on olfactory identification ability.

This study was conducted with the approval of the Research Ethics Board of Kinjo University (2020-02) and the Ethics and Conflicts of Interest Board of National Center for Geriatrics and Gerontology (approval No. 1469).

RESULTS

Table 1 shows the age, years of education, the evaluation of the cognitive function, and the results of the olfactory identification tests of the MCI, AD, and control groups. Age of the MCI and AD groups differed significantly from the score of the control group ($p<0.01$ for both); individuals in the control group were the youngest, followed by those in the AD group, and then those in the MCI group. The number of years of education also differed significantly between the AD group and the control group, with the control group having a longer history of education ($p<0.05$). The total scores of both the MoCA-J and MMSE-J of the MCI and AD groups differed significantly from the score of the control group ($p<0.01$ for both) and between the MCI group and the AD group ($p<0.05$); the total scores were higher in the following order: control >MCI >AD groups. The OSIT-J total scores of the MCI and AD groups differed significantly from the score of the control group ($p<0.01$ for both); however, we found no significant differences between the MCI group and the AD group.

Table 2 shows the results of the comparisons of correct answer rates for each of the odors among the three groups. The comparisons of the correct answer rates for the 12 different odors used in the OSIT-J showed that the correct answer rates for perfume and sweaty socks/sweaty odor did not differ significantly among the three groups, whereas the rates for the other 10 odors exhibited a significant difference ($p<0.05$).

The correct answer rates for India ink, wood, rose, condensed milk, and roasted garlic of the MCI group and the AD group were significantly lower than those of the control group ($p<0.05$ for all); however, these rates were not different between

Table 1. Comparisons of the results of the cognitive function test and olfactory identification test

	MCI (n=12)	AD (n=17)	Control (n=30)	
Age (years)	78.9 ± 6.0	77.6 ± 6.3	72.8 ± 4.1	** ##
Education (years)	12.5 ± 2.2	11.9 ± 1.8	13.3 ± 1.7	#
MoCA-J total score (points)	20.5 (17–23)	17 (7–22)	28 (26–30)	** ## §
MMSE-J total score (points)	25 (23–29)	19 (11–25)	30 (25–30)	** ## §
OSIT-J total score (points)	5.5 (0–9)	3 (0–8)	10 (2–12)	** ##

Mean ± SD, median (range).
MCI: mild cognitive impairment; AD: Alzheimer's disease; MoCA-J: Japanese version of Montreal Cognitive Assessment; MMSE-J: Mini-Mental State Examination-Japanese; OSIT-J: Odor Stick Identification Test for Japanese.
**$p<0.01$ MCI vs. control.
#$p<0.05$, ##$p<0.01$ AD vs. control.
§$p<0.05$ MCI vs. AD.
Age and educational group range: One-way ANOVA.
MoCA-J, MMSE-J, OSIT-J: analysis of covariance (ANCOVA).

Table 2. Comparison of correct answer rates for each of the odors among the three groups

(%)	MCI (n=12)	AD (n=17)	Control (n=30)	
India ink	16.7	17.6	73.3	*#
Wood	25.0	23.5	80.0	*#
Rose	25.0	17.6	73.3	*#
Condensed milk	25.0	52.9	93.3	*#
Roasted garlic	33.3	29.4	86.7	*#
Menthol	58.3	41.2	86.7	#
Orange	33.3	17.6	73.3	#
Japanese cypress	50.0	17.6	73.3	#
Gas leak odour	41.7	0.0	80.0	#§
Curry	50.0	11.8	96.7	*#§
Perfume	33.3	52.9	76.7	
Sweaty socks	50.0	58.8	46.7	

*$p<0.05$ MCI vs. control.
#$p<0.05$ AD vs. control.
§$p<0.05$ MCI vs. AD.
Analysis of covariance (ANCOVA).
MCI: mild cognitive impairment; AD: Alzheimer's disease.

the MCI and AD groups. The correct answer rates for menthol, Japanese orange, and cypress wood were significantly lower in the AD group than in the control group ($p<0.05$); however, these values did not differ from those in the MCI group. The correct answer rate for the odor of a gas leak in the AD group was 0% and differed significantly from the rates of the MCI and control groups ($p<0.05$ for both). However, no significant differences were found between the MCI and control groups. The correct answer rate for curry differed significantly among the three groups ($p<0.05$ for all).

DISCUSSION

The limbic system, which includes the entorhinal cortex, anterior piriform cortex, amygdala, and hippocampus, and the cerebral cortex, including the orbitofrontal cortex, is involved in olfactory sensation[12]. Odors tend to be associated with memory because the entorhinal cortex contains an abundance of neural connections with the hippocampus and interacts with the Papez circuit, which is associated with memory[6, 13]. MCI and AD lesions are also known to originate in the medial temporal lobe, including the hippocampus, in association with early-stage damage to the entorhinal cortex, and these lesions extend to other areas of the cerebral cortex as the disease progresses[14]. In this study, the comparison of the OSIT-J total scores confirmed the reduced ability of olfactory identification in the MCI and AD groups compared with the control group, as also reported in a previous study[3]. The possible mechanisms underlying the observed decreases in olfactory identification ability in patients with AD include difficulty in distinguishing odors due to an impairment in the entorhinal cortex involved in the olfactory sense and difficulty in linking the test odors and recalling memories of the previously experienced odors due to memory impairment caused by damage to the hippocampus[13]. Because participants with MCI in this study had amnestic MCI[15], a condition that can progress to AD, similar mechanisms are likely to underlie the reduced olfactory identification ability in MCI.

A reduction in the olfactory identification ability is difficult to detect because it usually does not directly interfere with daily life and often goes unnoticed[16]. However, comparisons of the correct answer rates for the various odors among the MCI, AD, and control groups showed that different odors were difficult to identify depending on the severity of cognitive impairment and that there were differences in which odors were difficult to identify.

There were no differences in the olfactory identification of “sweaty socks, sweaty odor” and “perfume” among the three groups. A previous study[6] also stated that olfactory identification ability is probably preserved for pungent odors, such as “sweaty socks, sweaty odor”, in people with MCI and mild AD. Isovaleric acid, whose odor is classified as pungent, is used for “sweaty socks, sweaty odor” in OSIT-J[17]. Isovaleric acid has a strong acid smell, consisting of odors of cheese, body, socks, among others; it has so offensive odor substance that is subject to control by the Offensive Odor Control Law of Japan[18]. Results of the present and previous studies suggest that cognitive dysfunction does not practically interfere with the olfactory identification ability for pungent odors, such as the isovaleric acid odor, and even individuals with advanced dementia can smell these odors.

The ability to identify the odor of a gas leak in the MCI group was lower than that in the control group, and patients with AD could not identify the odor at all. This result underpins the potentially life-threatening risk of gas leakage for noninstitutionalized people with MCI or AD who cannot smell gas[19]. Generally, MCI refers to a condition in which cognitive capacity is reduced but the individual remains capable of independent living. Our finding is essential in that even individuals with MCI are less likely to smell gas leaks than community-dwelling older adults without cognitive decline. Gas leak accidents are likely to cause major social problems. To address this risk, social environment changes, such as the dissemination of safety devices for detecting gas leaks and promotion of the shift to non-gas energy resources (e.g., use of induction cooking), are required as well as lifestyle guidance to families living together and social education activities.

We found that MCI and AD were also associated with the reduced olfactory identification ability for food-related odors, such as roasted garlic, curry, and Japanese orange. The olfactory sense affects the gustatory sense and is also involved in appetite control[20]. Therefore, reduced olfactory identification ability may be associated with the inability to sense food flavors, loss of enjoyment of eating, and difficulty in cooking. Individuals with MCI and AD cook less often[21] and are prone to losing their appetite[22]. These behavioral changes may be attributable to not just apathy and depression but also reduced olfactory identification ability. Moving forward, concerned individuals should be aware of the potential usefulness of olfactory assessments to specify the cause of such behavioral changes. Meanwhile, a previous study reported that patients with dementia like sweet foods more than they did before disease onset[22]. It is interesting that, in this study, the ability of patients with AD to identify the condensed milk odor was higher than that of individuals with MCI. The olfactory sense possibly has a strong association with eating. Moving forward, associations between the olfactory sense and changes in eating behavior, as well as reduced olfactory sense, in individuals with MCI and dementia should be studied.

An intervention strategy using olfactory stimuli is expected to activate the brain function in individuals with MCI and AD[5]. The results of the present study indicate that some odors are not recognized by some individuals and thus they may not effectively stimulate the brain. Therefore, before the olfactory stimulus can be used for effective intervention in patients with MCI and AD, olfactory assessments should be conducted to specify the odors that can be identified by patients and those that are not unpleasant to them.

In individuals with severe cognitive impairment, the OSIT-J cannot distinguish whether an incorrect answer is because of the lack of understanding of the test method or because of non-detection of the odor because participants select an answer

from among several options. Therefore, olfactory assessment methods suitable for patients with severe dementia represent a subject of future discussions. The olfactory sense is affected by habits and environmental factors[17] and varies substantially among individuals[13]. Future studies should also evaluate and analyze these factors.

We demonstrated that the olfactory identification abilities of individuals with MCI and patients with AD were lower than those of community-dwelling older adults without cognitive decline and that the ability varied depending on the odor. Because of their reduced olfactory identification abilities, individuals with MCI and AD may experience changes in their eating behavior and a decrease in the ability to sense dangers, such as gas leakage. Therefore, before providing lifestyle guidance at home, environmental improvements, and therapeutic interventions, performing olfactory assessments is believed to be essential.

Funding and Conflict of interest

The authors declare no conflict of interest.

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