Association of olfactory and gustatory function with memory among community-dwelling independent older adults

A short running title: olfactory and gustatory function

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Ethical approval statement
This study is approved by the Kagoshima University (Faculty of Medicine) Ethics Committee (no.190090). All the participants provided informed consent.

Declaration of Conflicting Interests

The authors declare that they have no conflict of interest.

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Abstract

Background: This study examined the association between memory function and reduced olfactory and gustatory function among independent community-dwelling older adults.

Methods: This cross-sectional study included 127 older adults (65.4% women). We assessed their memory, odor, and taste identification skills. Open essence (OE) test and taste strips (TS) were used to identify hyposmia (OE test \( \leq 6 \)) and hypogeusia (TS test \( \leq 8 \)), respectively.

Results: Participants with severe hyposmia had significantly poorer memory functions compared to participants without severe hyposmia. After adjusting for covariates, multivariate logistic regression models revealed a significant association between immediate recognition performance and a decreased likelihood of severe hyposmia (odds ratio = 0.65, 95% confidence interval = 0.47—0.90). We observed no significant association between taste function and memory.

Conclusions: Memory function may be associated with olfactory impairment but not with gustatory function in older adults.

Keywords: Odor identification, Taste ability, Memory
Introduction

Impairments in sensory functions, such as olfactory function and taste, are features of several neurodegenerative disorders. Poor olfactory function occurs in patients with mild cognitive impairment (MCI) and Alzheimer’s disease (AD)\(^1\). A longitudinal study with 5-year follow-up indicated that olfactory tests in patients with MCI could help predict AD conversion\(^2\). Gustatory disorders also occur in AD\(^3\). However, studies on gustatory disorders in patients with MCI have yielded inconsistent results\(^4,5\). Thus, gustatory function may be maintained during the early stages of AD\(^6\).

Olfactory and taste abilities decrease with advancing age\(^7\), and many neurodegenerative conditions and health statuses may be associated with olfactory or gustatory dysfunction\(^8,9\). Impairments in odor and taste identification are features of several neurodegenerative disorders. Although moderate or severe reductions in olfactory and gustatory function may correlate with cognitive impairment\(^7\), few healthy older adults are aware of slight reductions in olfactory and gustatory function. Thus, the assessment of hyposmia and hypogeusia may be useful for identifying early cognitive deficits in independent older adults.

Memory deficits are early symptoms of AD and other types of dementia. Older adults without dementia but with problems related to memory have an increased risk for dementia compared with those with challenges in other cognitive dimensions, attention, and executive function\(^10\). Memory plays a specific role in olfactory perception;\(^11\) however, few studies have assessed gustatory function, with conflicting results. For instance, a previous study that included patients with MCI, AD, and controls did not
identify group differences in olfactory threshold, gustatory function, or food preferences

12. In contrast, poor memory, rather than other domains of cognitive function, was
associated with poor odor discrimination and identification12.

The association of memory with olfactory and gustatory functions remains unclear,
particularly in independent community-dwelling older adults. This cross-sectional study
investigated the association between memory function and reduced olfactory as well as
gustatory function in the sample population.

Methods
Participants
This study included cross-sectional data from 134 independent older adults who
participated in community-based blood pressure management classes after participating
in the Tarumizu Study 2019 a health check survey. The Tarumizu Study was conducted
in collaboration with Kagoshima University’s, Faculty of Medicine, Tarumizu City
Office, and Tarumizu Chuo Hospital 13. Participants aged ≥40 years were recruited via
mail reply-paid postcards from Tarumizu City, Japan, a residential suburb of Kagoshima
City. Totally, 1024 citizens participated in the Tarumizu Study 2019, conducted between
June and December 2019, of which 687 were older adults. Of the participants aged ≥65
years who had participated in blood pressure management classes after a health check
survey, 137 participated in additional assessments of odor and taste function. Flyers
were distributed to those who were participating in the blood pressure management
class to recruit them for this study. Participants who required support in activities of
daily living and those with missing data on odor and taste assessments were excluded. This study was approved by the Ethics Committee of Kagoshima University Faculty of Medicine (no. 190090). All participants provided informed consent.

**Olfactory functioning**

We assessed olfactory functioning using the Open Essence (OE) test (Wako Pure Chemical Industries)\(^4\), which included 12 odor items known to people in Japan (Indian ink, perfume, wood, orange, menthol, curry, rose, cooking gas, Japanese cypress "hinoki," sweaty clothes, condensed milk, and roasted garlic). Each of the 12 cards contained one odorant and was folded into halves. Microencapsulated test odorants were applied to the left half of the card instead of glue. Six choices, including four alternative odor names, “detectable, but not recognized,” and “no smell detected” were printed in Japanese on the opposite side of the card. The participants chose their answers after opening each card. **One of the four odor names was the correct choice, with one point awarded for each correct answer.** Herein, we defined hyposmia as participants with an OE test score of ≤6 out of 12\(^5\).

**Gustatory functioning**

We used Taste Strips (TS)\(^6\) to assess the gustatory function of the whole mouth. Sixteen TS were impregnated with sweet, sour, bitter, and salty solutions at four different concentrations (sweet: 0.05, 0.1, 0.2, and 0.4 g/mL sucrose; sour: 0.05, 0.09, 0.165, and 0.3 g/mL citric acid; bitter: 0.0004, 0.0009, 0.0024, and 0.006 g/mL quinine-HCl; and salty: 0.016, 0.04, 0.1, and 0.25 g/mL NaCl)\(^7\). The strips were presented in a predetermined order: sweet, salt, sour, and bitter, starting with the weakest
concentration. Each TS was placed on the tongue and the participants were asked to close their mouths. The participants then categorized each strip as sweet, salty, sour, bitter, unidentified, or tasteless. The participants rinsed their mouths with water before tasting each strip. Each taste score ranged from 0 to 4 points (1 point for each correct answer). Thus, the total TS score ranged from 0–16. A total TS score ≤8 indicated hypogeusia in this study.

Memory assessment
We applied a subitem (word-list memory) of the National Center for Geriatrics and Gerontology Functional Assessment Tool (NCGG-FAT) to assess memory function. The wordlist memory tasks involved immediate recognition and delayed recall of a 10-word target list. The participants were asked to memorize 10 words. Each target word was presented for 2 s on a tablet computer. Subsequently, 30 words, including 10 and 20 target and distraction words, respectively, were presented. We requested that the participants choose 10 target words immediately, and the trial was repeated three times. The average number of correct answers in the three trials yielded the total score for the immediate recognition task. For the delayed recall score, we asked the participants to recall the 10 target words after approximately 20 min. The high test-retest reliability and moderate-to-high validity of the NCGG-FAT have been confirmed in community-dwelling older adults.

Statistical Analysis
All data were analyzed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Since the data were not normally distributed, we used the
Mann–Whitney U and chi-square tests (for sex and smoking status) to compare data between participants with and without hyposmia (OE test ≤6 and ≥7, respectively). We also tested the differences between participants with (TS test ≤8) and without (TS test ≥9) hypogeusia. Spearman's correlation coefficients were calculated to test the simple associations between age, olfactory function, gustatory function, and memory test performance. We tested the associations of hyposmia and hypogeusia with memory function using logistic regression analyses, with hyposmia (OE test ≤6) and hypogeusia (TS test ≤8) as dependent variables, and memory performance scores (immediate recognition and delayed recall) as independent variables. The odds ratios (ORs) for hyposmia and hypogeusia in the memory performance tests were adjusted for age, sex, education, and smoking status. Statistical significance was set at $p < 0.05$.

Results

The participant demographics are reported in Table 1. The mean (interquartile range) age of the participants was 74.0 (70.0—79.0) years and 66.4% were female.

Participants with hyposmia (OE test ≤6) were significantly older and had lower memory performance scores for immediate recognition and delayed recall compared with participants without hyposmia. Sex and smoking status but not memory performance differed significantly between participants with (TS test ≤8) and without hypogeusia (Table 2).

Table 3 shows the correlations among age, olfactory function, gustatory function, and
memory. We observed significant simple correlations between OE test scores and age (Spearman's $\rho = -0.292, p < 0.001$), immediate recognition (Spearman's $\rho = 0.327, p < 0.001$), and delayed recall (Spearman's $\rho = 0.295, p < 0.001$). TS test scores were not significantly correlated with age, immediate recognition, or delayed recall. In addition, we observed no significant correlation between OE and TS test scores (Spearman's $\rho = 0.150, p = 0.083$).

Table 4 presents the results of the multivariate logistic regression models. Improved performance scores for immediate recognition were significantly associated with hyposmia after controlling for age, sex, education, and smoking status (adjusted OR = 0.65, 95% confidence interval [CI] 0.47—0.90). An improved delayed recall performance score was associated with hyposmia, however the association was not statistically significant after controlling for covariates (adjusted OR = 0.89, 95% CI 0.72—1.10). The results of multivariate logistic regression analyses showed no significant association between hypogeusia and memory.

Discussion

The primary finding of this study was the association of poor memory scores with olfactory impairment. However, taste function and memory were not associated in independent community-dwelling older adults. Even in a relatively healthy aging stage, olfactory impairment may be associated with lower memory performance but not taste function.
Sensory systems, including taste and smell, are affected by aging. Sensory impairment progresses slowly with advancing age, and smell and taste deficits are highly prevalent in older adults. Impaired sensory function affects quality of life in older people. For instance, olfactory impairment complicates danger detection in our environment (e.g., gas, smoke, and spoiled food), while taste impairment increases the risk of foodborne illnesses, alters food choices to impair nutritional status, and elevates the risk of allergic reactions. Olfactory impairment may also be a marker related to age-associated frailty status, such as sarcopenia and brain shrinking. Our findings demonstrated an association between olfactory function and memory but not between gustatory function and memory. The current observational study could not assess these mechanisms, although olfactory loss could reflect age-related changes in the physiological system that are more sensitive than gustatory function.

A previous study analyzing data from a nationally representative sample of older adults reported that gustatory dysfunction was associated with dementia, while olfactory dysfunction was associated with MCI and dementia. In addition, middle-aged and older individuals with gustatory and olfactory dysfunction had worse global cognitive function than either alone. Herein, we observed no significant association between taste function and memory, while olfactory dysfunction was related to memory function. Those results confirmed the associations between poor memory function and olfactory impairment in the early stage of age-related sensory dysfunction.

Several interventional studies including older adults, MCI, and dementia have examined the effects of olfactory training on brain function. These intervention studies
demonstrated the positive effects of training the sense of smell to improve olfactory function; however, the interventions showed a limited effect on cognition. A randomized controlled trial that conducted intensive olfactory training twice daily for 15 d (30 sessions) to older adults with dementia reported improved memory. Neurofibrillary tangles in the olfactory bulb and the projection pathways from the olfactory bulb to the secondary olfactory brain regions are the earliest pathological features of AD and a damaged olfaction. Despite evidence from well-designed intervention studies, training and improvement in olfactory function may positively impact the prevention of cognitive decline.

Olfactory and gustatory functions are essential in the activities of daily living in older people. For instance, the loss of olfactory function may lead to poor flavor perception, reduced food enjoyment, reduced appetite, and difficulties with cooking as well as detection of spoiled food. The loss of gustatory function may lead to health consequences such as metabolic syndrome through unhealthy dietary patterns. In addition, olfactory function and physical activity are strongly related, with better olfactory performance observed in older adults with active lifestyles. An active lifestyle is an important protective factor that reduces the risk of cognitive deficits. Therefore, the interaction with lifestyle indicated an association between olfactory function and memory. Thus, the association between gustatory function and lifestyle may be limited in older adults.

This study has several limitations. First, causal inferences could not be made because of the cross-sectional study design. Future longitudinal studies should investigate how
changes in memory over time are associated with changes in olfactory and gustatory function. Second, other cognitive aspects such as attention, executive function, and spatial perception should be considered. Third, although specific tests for olfactory and gustatory functions were conducted, odor sensitivity and identification may have different characteristics and roles in older adults. Finally, more possible factors associated with order and taste function, such as comorbidities, socioeconomic status, and dietary intake should be considered to comprehensively understand the association of olfactory and gustatory function with memory.

In conclusion, community-dwelling, independent older adults with poor olfactory function had lower memory performance scores. However, we observed no significant association between gustatory function and memory. Our findings suggest that memory function may be closely associated with olfactory impairment but not with gustatory function in this population. Thus, older adults showing loss of olfactory function should be carefully observed. Additional research is needed to determine the specific role of olfactory and gustatory functions in memory in older adults.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, HM and SM; Data curation, HM, YN, SA, and YT; Investigation, HM, YN, SA, and YT; Methodology: HM and YN; Project administration: HM, YN, and SM; Supervision, TM and SM; Writing-original draft: HM; Writing-review and editing: YN, SA, YT, TM, and SM.