Title page

Title

Association of combined low physical activity and low dietary diversity with mild cognitive impairment among community-dwelling Japanese older adults

Running title

Physical activity, dietary diversity and cognition

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CONFLICT OF INTEREST
The authors declare no conflicts of interest.

Data Availability
The data supporting the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

AUTHOR CONTRIBUTIONS
Conceptualization, YK, HM; Data curation, YN, YT, MK, TT, TK, MO; Formal analysis, YK, HM; Investigation, YN, YT, SA, MT, MK, TT, TK, MO; Writing-original draft, YK, HM; Writing-review & editing, HM, YN, YT, SA, MT, MK, TT, TK, HS, MO.
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Abstract

Objective: This study aimed to investigate the potential association between the combination of low physical activity and low dietary diversity with mild cognitive impairment (MCI) in older Japanese adults.

Methods: Data from 600 older adults (mean age 74.1 ± 6.4 years; 62.0% women) were analyzed. We evaluated dietary variety based on the Food Frequency Score (FFS) (maximum 30 points) by assessing the one-week consumption frequencies of ten foods. An FFS of ≤ 16 indicated low dietary diversity. We assessed MCI using the National Center for Geriatrics and Gerontology (NCGG) Functional Assessment Tool. Physical activity levels was determined based on participant responses to two questions: “Do you engage in moderate levels of physical exercise or sports aimed at health?” and “Do you engage in low levels of physical exercise aimed at health?” Participants who responded “No” to both questions were classified as having low physical activity levels. We classified the participants into robust, low-dietary diversity, low-physical activity, and coexistence groups.

Results: The overall prevalence of MCI was 20.7%, with rates in the robust, low dietary diversity, low physical activity, and coexistence groups of 17.7%, 24.7%, 25.0%, and 41.9%, respectively. Multiple logistic regression analysis revealed that low dietary diversity and physical activity were associated with MCI in older adults (odds ratio [OR] 2.80, 95% confidence interval [CI] 1.22–6.28).

Conclusions: The results of the present study demonstrated the association of the co-occurrence of low dietary diversity and low physical activity with MCI. Older adults with both risk factors may require early detection, as well as physical activity and dietary interventions.

Keywords: aging, eating behavior, cognitive function, physical activity, older adults
Introduction

Mild cognitive impairment (MCI) is the intermediate state between normal cognitive aging and dementia [1, 2]. A previous longitudinal study showed that 28.2% of older adults with MCI at baseline had reverted to being cognitively intact at the two-year follow-up [3]. Thus, older adults with MCI can remain cognitively intact and are a target population for interventions aimed at preventing and delaying dementia onset.

The modifiable risk factors should be identified to develop interventions for MCI. Modifiable risk factors account for approximately 40% of dementia cases worldwide and can theoretically prevent or delay dementia onset [4]. The World Health Organization (WHO) reported that modifiable factors, such as low physical activity and an unbalanced diet, may be risk factors for MCI [5]. Another study indicated that nutritional factors and physical activity should be considered for MCI prevention and improvement [6]. A prospective study of 11,179 Chinese community-dwelling older adults revealed that low dietary diversity was associated with an increased risk of cognitive impairment [7]. Similarly, a study involving Japanese community-dwelling older adults demonstrated that diets rich in soy, vegetables, algae, and dairy products and low in rice were associated with reduced dementia risk [8]. Thus, previous studies have indicated that consuming a wide variety of foods may enhance or maintain cognitive function [9]. Moreover, several studies have also indicated that dietary diversity could be an important factor associated with modulating MCI.

Low dietary diversity in older adults is associated with physical dysfunction [10], which contributes to low physical activity [11]. Furthermore, low physical activity leads to aging-related anorexia [12] [13] and is associated with low dietary diversity [14]. Previous studies have shown that low dietary diversity and low physical activity are highly prevalent and frequently occur at later ages.
Thus, the co-occurrence of low dietary diversity and low physical activity in older adults might result in a higher MCI risk than either condition alone. However, the association of these conditions in older adults with MCI remains unclear. Therefore, the present study investigated the potential association of concurrent low dietary diversity and physical activity with MCI in older Japanese adults.
2. Materials and Methods

2.1 Participants

This cross-sectional study analyzed data from the Tarumizu Study, a community-based health survey conducted in collaboration with Kagoshima University (Faculty of Medicine), the Tarumizu City Office, and Tarumizu Chuo Hospital since 2017 [15]. Participants were recruited from Tarumizu City, a residential suburb of Kagoshima City, Japan. In 2019, an invitation was mailed to all citizens aged ≥ 40 years in Tarumizu City to recruit residents for the study. Recruitment was also supported through local newspaper advertisements and community campaigns. This study used data from a health check survey conducted between June and December 2019. A total of 1,024 individuals aged ≥ 40 years participated in the 2019 Tarumizu Study. The exclusion criteria were: age < 65 years, a diagnosed history of severe neurological diseases (e.g., dementia or stroke), depression, certification for long-term care, inability to perform basic activities of daily living, and missing data. Finally, we analyzed data from 600 community-dwelling older adults (mean age, 74.1 ± 6.4 years; women, 62.0%) (Figure 1). The Kagoshima University (Faculty of Medicine) Ethics Committee (Ref no.170351) approved this study. Written informed consent was obtained from all participants before their inclusion in the study.

2.2.1 Assessment of diet variety

Diet variety was assessed using the Food Frequency Score (FFS) [16]. The FFS is a self-reported measure evaluating the one-week consumption frequencies of ten food groups: meat, fish/shellfish, eggs, milk and dairy products, soybean products, green and yellow vegetables, potatoes, fruits, seafood, fats, and oils. The FFS allots each food category a score ranging from 0 to 3 points based on the following responses: (1) I eat it almost every day (3 points); (2) I eat it 3–4 days/week (2 points); (3) I eat it 1–2 times/week (1 point); and (4) I hardly ever eat it (0 points). The FFS is the sum of the scores, with lower scores indicating low diet variety (range,
0–30). The FFS is a simple and valid method for assessing dietary variety in older adults [17]. Based on a previous study, we defined low dietary diversity in older adults as an FFS of ≤ 16 points [18].

2.2.2 Assessment of physical activity
We evaluated physical activity based on responses to two questions during face-to-face interviews: “Do you engage in moderate levels of physical exercise or sports aimed at health?” and “Do you engage in low levels of physical exercise aimed at health?” Participants who did not respond to either question were classified as having low physical activity [19].

2.2.3 Assessment of MCI
We evaluated MCI status using the National Center for Geriatrics and Gerontology-Functional Assessment Tool (NCGG–FAT), which consists of the following domains: (1) memory (word list memory I [immediate recognition] and word list memory II [delayed recall]), (2) attention (a tablet version of the Trail Making Test [TMT], Part A), (3) executive function (a tablet version of the TMT, Part B), and (4) processing speed (a tablet version of the Digit Symbol Substitution Test). The NCGG–FAT has demonstrated high test-retest reliability and moderate-to-high validity among community-dwelling older adults [20]. The advantages of the NCGG–FAT over traditional neurocognitive assessments include its easy administration using a tablet PC with onscreen instructions, eliminating the need for assessors’ in-depth knowledge of neurocognitive measures. This minimizes the influence of individual assessors on the results. The simplicity and portability of the application allow non-specialist assessment in community and non-clinical settings by non-specialists. Participants can complete the NCGG–FAT battery within 20–30 minutes, which is half the time required for an equivalent battery of traditional psychiatric tests. This efficiency makes the NCGG–FAT suitable for cognitive screening in population-representative samples to assess the risk of cognitive decline in multidimensional functions.
Data aggregation is facilitated by the digital format of tablet PCs, allowing quick data compilation and analysis from large populations compared with paper-based methods [21]. The tests used in the present study established standardized thresholds for the definition of MCI in the corresponding domain (score < 1.5 standard deviations [SDs] below age- and education-specific means based on our algorithm from a database including > 10,000 community-dwelling older Japanese individuals) for a population-based cohort of community-dwelling older adults [22]. Participants with lower NCGG-FAT scores in one or more tests were defined as having MCI [20].

2.2.4 Covariates

During the face-to-face interviews, the participants were asked about their sociodemographic characteristics (age, sex, body mass index [BMI], and educational level), number of current medications, and living arrangements (living alone or not). We assessed the presence of depressive symptoms using the 15-item Geriatric Depression Scale (GDS), which contains 15 ‘yes’ or ‘no’ questions and provides a score between 0 and 15, with higher scores indicating more depressive symptoms [23]. Gait speed was measured as participants walked through a designated location where a photoelectric sensor-type gait measuring instrument (YW; YAGAMI Inc., Aichi, Japan) automatically recorded their walking time. Participants were asked to walk 14 m (divided into two 2.0-m long end zones and a 10 m long middle zone) at their usual walking speed, after which their walking speed was calculated (m/s).

2.2.5 Statistical analysis

We performed statistical analyses using R Version 4.2.1, with statistical significance set at p < 0.05. First, participants were classified into the robustness, low dietary diversity, low physical activity, and combined low dietary diversity and low physical activity groups. These groups were compared using Student’s t-test and chi-square test for continuous and categorical variables, respectively. Second, logistic regression models were constructed to calculate the
odds ratios (ORs) with 95% confidence intervals (CIs) to determine the association between low physical activity combined with low dietary diversity and MCI. The logistic regression model was adjusted for age, sex, education, BMI, education, medication, GDS score, and gait speed. These confounding factors are associated with exposure, including dietary diversity and physical inactivity. Moreover, they are recognized risk factors for MCI and cognitive decline and were selected based on a detailed scrutiny of previous studies [24] [7]. The Mantel–Haenszel test was subsequently applied to examine the frequency of intake of the FFS components (almost every day, 3–4 days/week, and < 2 days/week) and the prevalence of MCI.
3. Results

This study analyzed data from 600 older adults (mean age 74.1 ± 6.4 years; 62.0% women). Table 1 presents the demographic characteristics of the participants. We classified the participants into the robust (n = 424 [70.7%]), low dietary diversity (n = 81 [13.5%]), low physical activity (n = 64 [10.7%]), and coexistence (n = 31 [5.1%]) groups. The overall prevalence of MCI was 20.7% (n = 124), with respective rates of 17.7%, 24.7%, 25.0%, and 41.9% among participants in the robust, low dietary diversity, low physical activity, and co-occurrence groups (p < 0.05).

Table 2 displays the results of the adjusted multiple logistic regression analysis examining the association between the coexistence of low dietary diversity, low physical activity, and MCI. After adjusting for confounding factors such as age, sex, education, medication, BMI, gait speed, and GDS, the co-occurrence of low dietary diversity and low physical activity was significantly associated with MCI (OR 2.80, 95% CI 1.22–6.28), whereas low dietary diversity (OR 1.36, 95% CI 0.73–2.46) and low physical activity (OR 1.29, 95% CI 0.65–2.44) alone were not.

The Mantel-Haenszel test revealed a higher prevalence of MCI among participants with less frequent consumption of meat (almost every day: 18.0%, 3–4 days/week: 16.7%, and < 2 days/week: 27.6%), eggs (almost every day: 18.0%, 3–4 days/week: 20.8%, and < 2 days/week: 27.3%), and milk and dairy products (almost every day: 19.0%, three or four days a week: 13.6%, and < 2 days a week: 29.6%) (p for trend p < 0.05). Although participants with less frequent consumption of fish (almost every day, 17.4%, 3–4 days/week, 19.4%; and < 2 days/week, 24.2%), green and yellow vegetables (almost every day, 19.1%, 3–4 days/week, 21.9%; and < 2 days/week, 25.8%), and fats and oils (almost every day, 17.5%, 3–4 days/week, 20.9%; and < 2 days/week, 23.7%) also had a higher prevalence of MCI, the differences were
not statistically significant.
4. Discussion

The results of this cross-sectional study suggest that the combination of low dietary diversity and physical activity is associated with MCI, whereas low dietary diversity or low physical activity individually were not. Furthermore, the prevalence of MCI was higher among participants with less frequent consumption of meat, eggs, milk, and dairy products.

In the present study, the combination of low dietary diversity and low physical activity was significantly associated with MCI. A previous study including 43,896 participants followed up for 9.5 years reported that a high level of leisure time and moderate-to-vigorous physical activity was associated with a decreased risk of disabling dementia in men [24]. Another study showed that physical activity is associated with a lower risk of cognitive impairment, Alzheimer’s disease, and dementia [25]. Makizako et al. reported that higher levels of moderate rather than light physical activity were associated with hippocampal volume in older adults with MCI. In addition, moderate physical activity was not directly associated with memory but was mediated through hippocampal volume [26]. Physical inactivity contributes to decreases in risk factors for cognitive decline such as chronic diseases, including diabetes mellitus [27], hypertension [28], cardiovascular disease [29], and antioxidants [30]. Previous studies have suggested that low levels of physical activity are a risk factor for cognitive decline. Dietary factors are also important for maintaining and improving cognitive function. A previous large cross-sectional study reported on dietary diversity and cognitive function in older Japanese adults [31]. The results of a longitudinal study with a 2-year follow-up suggested that increased dietary diversity is a protective factor against cognitive decline [32]. The present study used the FFS to evaluate dietary diversity, including meat, fish/shellfish, eggs, milk and dairy products, soybean products, green and yellow vegetables, potatoes, fruits, seafood, fats, and oils. Our results showed a lower incidence of MCI among community-dwelling older adults who consumed meat, eggs, milk, or dairy products. These foods have high protein and amino acid
levels, and the intake of amino acids, especially lysine, phenylalanine, threonine, and alanine, is positively associated with cognitive function in later life [33]. Therefore, the consumption of foods containing proteins and amino acids is important for maintaining and improving cognitive function. Hence, both physical activity and dietary factors are important for enhancing and maintaining cognitive function, and the lack of these factors may increase the risk of cognitive decline.

Lifestyle-focused multicomponent interventions and positive, healthy lifestyles favorably affect cognitive function. The results of a two-year randomized controlled trial showed that multidomain interventions, including diet and physical and cognitive activities, improved and maintained cognitive function in older adults [34]. A systematic review and meta-analysis showed that non-pharmacological, multidomain interventions (e.g., physical exercise and dietary supplements) were associated with small to medium effect sizes, indicating improvements in cognitive function in older adults with MCI compared with a single intervention [35]. Furthermore, a large cohort study reported that positive behaviors such as never or formerly smoking, never drinking, a healthy diet, regular physical exercise, active cognitive activity, and social contact were associated with a slower rate of memory decline [36].

Previous studies have suggested that multicomponent healthy behaviors are more important than single healthy behaviors for maintaining and improving cognitive function. The results of the present study demonstrated the association of low dietary diversity and physical activity with MCI, consistent with previous findings.

This study has several limitations. First, although we evaluated the frequency of food intake, the quantity of each food item could not be assessed. Future studies should consider the quantity of food consumed. Second, we subjectively assessed physical activity; future studies should evaluate more objective measures of physical activity. Third, the current study was
cross-sectional; thus, we were unable to determine the causal relationships between dietary diversity, physical activity, and MCI. Fourth, we excluded socioeconomic and economic status from the multivariate analyses. Other possible covariates (e.g., lifestyle activities and socioeconomic status) must also be investigated as they are likely also related to dietary diversity, physical activity, and MCI. Finally, owing to the large sample size and community setting, the assessment of physical activity using quantitative tools (e.g., accelerometer) was difficult.
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CONFLICT OF INTEREST
The authors declare no conflicts of interest.

Data Availability
The data supporting the findings of this study are available upon request from the corresponding author. The data are not publicly available because of privacy and ethical restrictions.

AUTHOR CONTRIBUTIONS
Conceptualization: YK, HM; Data curation: YN, YT, MK, TT, TK, MO; Formal analysis: YK, HM; investigation: YN, YT, SA, MT, MK, TT, TK, MO; writing–original draft: YK, HM; writing–review and editing: HM, YN, YT, SA, MT, MK, TT, TK, HS, MO.