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Original article

# Association between intake of dairy products and short-term memory with and without adjustment for genetic and family environmental factors: A twin study



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Soshiro Ogata <sup>a, b, \*</sup>, Haruka Tanaka <sup>a, b</sup>, Kayoko Omura <sup>b</sup>, Chika Honda <sup>b</sup>, Osaka Twin Research Group<sup>1</sup>, Kazuo Hayakawa <sup>a, b</sup>

<sup>a</sup> Department of Health Promotion Science, Osaka University Graduate School of Medicine, Suita, Osaka, Japan
<sup>b</sup> Center for Twin Research, Osaka University Graduate School of Medicine, Suita, Osaka, Japan

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#### SUMMARY

*Background & aims:* Previous studies have indicated associations between intake of dairy products and better cognitive function and reduced risk of dementia. However, these studies did not adjust for genetic and family environmental factors that may influence food intake, cognitive function, and metabolism of dairy product nutrients.

In the present study, we investigated the association between intake of dairy products and short-term memory with and without adjustment for almost all genetic and family environmental factors using a genetically informative sample of twin pairs.

*Methods:* A cross-sectional study was conducted among twin pairs aged between 20 and 74. Short-term memory was assessed as primary outcome variable, intake of dairy products was analyzed as the predictive variable, and sex, age, education level, marital status, current smoking status, body mass index, dietary alcohol intake, and medical history of hypertension or diabetes were included as possible covariates. Generalized estimating equations (GEE) were performed by treating twins as individuals and regression analyses were used to identify within-pair differences of a twin pair to adjust for genetic and family environmental factors. Data are reported as standardized coefficients and 95% confidence intervals (CI).

*Results:* Analyses were performed on data from 78 men and 278 women. Among men, high intake of dairy products was significantly associated with better short-term memory after adjustment for the possible covariates (standardized coefficients = 0.22; 95% CI, 0.06–0.38) and almost all genetic and family environmental factors (standardized coefficients = 0.38; 95% CI, 0.07–0.69). Among women, no significant associations were found between intake of dairy products and short-term memory. Subsequent sensitivity analyses were adjusted for small samples and showed similar results.

*Conclusions:* Intake of dairy product may prevent cognitive declines regardless of genetic and family environmental factors in men.

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## 1. Introduction

\* Corresponding author. Department of Health Promotion Science, Osaka University Graduate School of Medicine, 1-7 Yamadaoka, Suita, Osaka 565-0871, Japan. Tel./fax: +81 6 6879 2556.

E-mail address: sob0405@sahs.med.osaka-u.ac.jp (S. Ogata).

<sup>1</sup> Osaka Twin Research Group, Kazuo Hayakawa, Yoshinori Iwatani, Jun Hatazawa, Shiro Yorifuji, Mikio Watanabe, Chika Honda, and Kayoko Omura, Center for Twin Research, Osaka University Graduate school of Medicine. As a component of cognition, short-term memory maintains small amounts of information in a usable condition for a short period of time [1–3]. Assessment of short-term memory is used as a screening tool for mild cognitive impairment (MCI) and Alzheimer's disease [4], and poor short term memory is a clinical feature of Alzheimer's disease [5].

The influence of dietary factors on cognitive ability has been reported and reviewed [6,7], and the intake of dairy products in the context of a balanced diet has been positively associated with better

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Abbreviations: BDHQ, brief-type self-administered diet history questionnaire; BMI, body mass index; CI, confidence interval; DZ, dizygotic; GEE, generalized estimating equations; MCI, mild cognitive impairment; MZ, monozygotic.

cognitive ability [8]. Previous longitudinal studies have also shown that high intake of dairy products prevented cognitive decline, including dementia [9,10]. In addition, cross-sectional studies have shown associations between high intake of dairy products and improved cognitive status [11–13], including short-term memory [13]. In contrast, another longitudinal study has shown no significant association between cognitive function and consumption of dairy products such as milk, yogurt, and cheese [14].

However, these studies failed to adjust for genetic and family environmental (such as childhood family environment) factors despite their reported influences on cognitive ability [15], food intake [16], and the metabolism of the dairy nutrients calcium [17] and vitamin B12 [18]. Moreover, of the few studies that have investigated the association between short-term memory and consumption of dairy products, none were adjusted for genetic and family environmental factors.

In the present study, we investigated the association between dairy product intake and short-term memory, and performed additional analyses with adjustment for almost all genetic and family environmental (environment shared within a twin pair such as childhood family environment) factors in twin pairs, which are naturally matched for genetic and family environmental factors. Accordingly, specific genetic and environmental factors were identified to improve screening methods and contribute strategies for the prevention of cognitive decline [19].

## 2. Materials and methods

#### 2.1. Participants

In the present cross-sectional study of twin pairs, data were collected from the Osaka University Center for Twin Research, which was founded in 2009 [20], and twin pairs were searched for using several methods, such as newspapers and posters placed in hospitals. Selected twin pairs participated in comprehensive medical examinations after providing informed consent. Eligibility criteria for analyses of the present study were the following: 1) receipt of medical examination between January 2009 and July 2014; 2) aged between 20 and 74 according to the normative sample of Japanese version of the Wechsler Memory Scale-Revised (WMS-R; [21]); 3) same-sex twin pairs; 4) participation in memory assessments; 5) participation in a dietary assessments without dietary control by doctors, dieticians, or other specialists; 6) no dementia; and 7) daily energy intake estimates between 600 and 4000 kcal [22]. The present study was performed by the Osaka University Center for Twin Research, and was approved by the Research Ethics Committee of Osaka University and the Institutional Review Board for Clinical Research at Osaka University Hospital.

Zygosity was determined on the basis of 15 loci of short tandem repeat markers [23], and twin pairs were classified as monozygotic (MZ) if the short tandem repeats were completely consistent within the twin pair, and as dizygotic (DZ) if any short tandem repeats differed between individuals of the twin pair.

## 2.2. Measurements

#### 2.2.1. Short-term memory

In the present study, trained interviewers assessed short-term memory using Logical Memory I of the Japanese version of WMS-R [21,24,25]. Participants were asked to listen to two short stories and immediately recall the details. The total score of the Logical Memory I score was calculated on the basis of the number of correct parts of the stories recalled, and ranged from 0 (worst performance) to 50 (best performance). In subsequent analyses, Logical Memory I scores were used as a quantitative variable.

#### 2.2.2. Intakes of dairy product and other food groups

Daily intakes of dairy products and other food groups, such as cereals, pulses, confectioneries, oil, fruits, green and yellow vegetables, other vegetables, alcoholic beverages, fish and shellfish, meat, and egg, were assessed using a brief-type self-administered diet history questionnaire (BDHQ) that included questions regarding the consumption frequency of selected foods and beverage items [26], and food group intakes during the preceding month were estimated [26]. Food and beverage items in BDHQ are commonly consumed in Japan, and were predominantly selected from a food list that was used in the National Health and Nutrition Survey of Japan [26]. The validity of BDHQ has already been established [26], and the dairy product intake was used as a quantitative variable in subsequent regression models.

Dairy product intake was assessed in BDHQ using items of fullfat milk and yogurt (the same item) and low-fat milk and yogurt (the same item) [26]. Definitions of other food groups were as follows [26]. Cereals were assessed in using items of rice, buckwheat noodles, Japanese wheat noodles, instant noodles and Chinese noodles, spaghetti and macaroni, breads. Pulses were assessed in using items of tofu (i.e. soybean curd) and tofu products, natto (i.e. fermented soybeans). Confectioneries were assessed in using items of rice crackers and rice cakes and Japanese-style pancakes, Japanese sweets, cakes and cookies and biscuits, ice cream. Oil were assessed in using items of mayonnaise and salad dressing, oil used during cooking. Fruits were assessed in using items of citrus fruit (including oranges), strawberries, persimmons and kiwifruit, other fruits. Green and yellow vegetables were assessed in using items of carrots and pumpkins, tomatoes, tomato ketchup, boiled tomato and stewed tomato, green leafy vegetables (including broccoli). Other vegetables were assessed in using items of raw vegetables used in salad (cabbage and lettuce), cabbage and Chinese cabbage, radishes and turnips, other root vegetables (onions, burdock and lotus root). Alcoholic beverages were assessed in using items of beer, sake, shochu and shochu mixed with water or a carbonated beverage, whiskey, wine. Fish and shellfish were assessed in using items of dried fish and salted fish (including salted mackerel, salted salmon and dried horse mackerel), small fish with bones, canned tuna, oily fish (including sardines, mackerel, saury, amberjack, herring, eel and fatty tuna), non-oily fish (including salmon, trout, white meat fish, freshwater fish and bonito), squid, octopus, shrimp and clam. Meat were assessed in using items of chicken (including ground chicken), pork and beef (including ground pork and beef), liver, ham, sausages and bacon.

### 2.2.3. Possible confounders

Age, sex, marital status, education level, current smoking status, body mass index (BMI), dietary alcohol intake, and medical history of hypertension or diabetes were included as potential confounders. Subjects reported data pertaining to these variables during comprehensive medical examinations. Marital status was dichotomized into current marriage and others. Education level was dichotomized into more than 16 years and 16 years or less on the basis of elementary school (6 years), junior high school (3 years), high school (3 years), junior college (2 years), professional training college (3 years), university (4 years), and graduate school (2 years and more). Current smoking status was dichotomized into current smoking and others. Body height and weight were measured to the nearest 0.1 centimeters and 0.1 kilograms respectively with participants wearing light clothing and no shoes. BMI was calculated as body weight in kilograms divided by the square of height in meters (kg/m<sup>2</sup>). Dietary alcohol intake was also estimated using the BDHQ [27]. Age, dietary alcohol intake, and BMI were entered into statistical models as quantitative variables, and

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