Supplemental information

Association of low meal frequency with decreased *in vivo* Alzheimer's pathology

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Supplemental Information

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This supplemental material has been provided by the authors to give readers additional information about their work.
**Figure S1.** Flow chart, related to STAR methods

- Excluded (n = 347)
  - Not fulfilled the inclusion criteria (n = 46)
  - Met one of the exclusion criteria (n = 63)
  - Withdrawal of consent (n = 55)
  - Loss of contact (n = 3)
  - Cognitively normal young & middle-aged adults (n = 74)
  - Alzheimer’s disease dementia (n = 87)
  - Missing data in dietary assessments (n = 19)

Assessment for eligibility (n = 758)

Baseline data Available for analysis (n = 411)

- CN (n = 278)
- MCI (n = 133)
Table S1. Assessment of dietary and food patterns, related to STAR methods

| Questions                                                                 | Answers                                      | Reference |
|--------------------------------------------------------------------------|----------------------------------------------|-----------|
| 1. Dietary pattern                                                       |                                              |           |
| 1) Meal frequency                                                       |                                              |           |
|    Have you regularly had three regular meals a day?                     | (a) always                                   | MDA       |
|                                                               | (b) not always                               |           |
| 2) Inter-meal snack                                                     |                                              |           |
|    Have you regularly eaten inter-meal snack a day?                     | (a) high (always)                            | MDA       |
|                                                               | (b) moderate (sometimes)                     |           |
|                                                               | (c) low (seldom)                             |           |
| 3) In terms of fluid (water, juice, coffee, tea, milk) intake            |                                              |           |
|    How much fluid have you consumed per day regularly?                  | (a) more than 5 cups                         | MNA       |
|                                                               | (b) 3 to 5 cups                               |           |
|                                                               | (c) less than 3 cups                          |           |
| 2. Dietary patterns including food types                                 |                                              |           |
| 1) Protein                                                              |                                              |           |
|    Have you regularly had at least one serving of dairy products per day?| (a) high (3 yes)                             | MNA       |
|    Two or more servings of legumes or eggs per week?                    | (b) moderate (2 yes)                         |           |
|    Meat, fish or poultry every day?                                     | (c) low (if 0 or 1 yes)                      |           |
| 2) Fruits & vegetables                                                  |                                              |           |
|    Have you regularly consumed two or more servings of fruit or vegetables per day? | (a) high (yes)                               | MNA       |
|                                                               | (b) low (no)                                 |           |
| 3) Fried foods                                                          |                                              |           |
|    Have you regularly eaten more than one serving of fried or stir-fried food every two days? | (a) high (always)                            | MDA       |
|                                                               | (b) moderate (sometimes)                     |           |
|                                                               | (c) low (seldom)                             |           |
| 4) Fatty foods                                                          |                                              |           |
|    Have you regularly eaten more than one serving of fatty foods every three days? | (a) high (always)                            | MDA       |
|                                                               | (b) moderate (sometimes)                     |           |
|                                                               | (c) low (seldom)                             |           |
| 5) Salty foods                                                          |                                              |           |
|    Have you regularly added salt or sauce to your food?                 | (a) high (always)                            | MDA       |
|                                                               | (b) moderate (sometimes)                     |           |
|                                                               | (c) low (seldom)                             |           |

● Trained research nurses should interview both participants and their informants semi-quantitatively to determine dietary and food patterns.
Table S2. Assessment of lifetime alcohol intake and smoking amounts, related to STAR methods

| Questions                              | Answers |
|----------------------------------------|---------|
| 1. Alcohol intake, lifetime            | □□□□ SD(s)/week |
|   How much alcohol have you regularly consumed weekly throughout your life? |         |
| 2. Smoking intake, lifetime            | □□□□ pack(s)/day |
|   How many cigarettes have you smoked daily throughout your life? |         |

- Trained research nurses should interview both participants and their informants semi-quantitatively to determine amounts of lifetime alcohol intake and smoking.
- One standard drink (SD) is defined as any drink that contains 10 grams of pure alcohol according to the World Health Organization (WHO) guideline (Available from: https://www.who.int/substance_abuse/publications/audit_sbi/en/).
Table S3. Results of multiple linear and logistic regression analyses for the associations between meal frequency categories and Aβ, AV-1451, AD-CM, AD-CT, or WMH volume in cognitively normal individuals, related to Table 2

| Meal frequencies | Aβ retention, SUVR | Aβ positivity |
|------------------|--------------------|--------------|
|                  | p                  | OR (95% CI)  | p  |
| Model 1 **       |                    |              |    |
| 3 meals per day  | Reference          | Reference    |    |
| < 3 meals per day| -0.135             | 0.048        | 0.362 (0.131 to 1.006) | 0.051 |
| Model 2 **       |                    |              |    |
| 3 meals per day  | Reference          | Reference    |    |
| < 3 meals per day| -0.141             | 0.050        | 0.258 (0.074 to 0.896) | 0.033 |
| Model 3 **       |                    |              |    |
| 3 meals per day  | Reference          | Reference    |    |
| < 3 meals per day| -0.128             | 0.087        | 0.187 (0.046 to 0.755) | 0.019 |

AV-1451, SUVR  AD-CM, SUVR  AD-CT, mm  WMH volume, cm³

|                  | p     | p     | p     | p     |
|------------------|-------|-------|-------|-------|
| Model 1 **       |       |       |       |       |
| 3 meals per day  | Reference | Reference | Reference | Reference |
| < 3 meals per day| -0.215 | 0.112 | 0.055 | 0.442 | -0.052 | 0.401 | 0.020 | 0.786 |
| Model 2 **       |       |       |       |       |
| 3 meals per day  | Reference | Reference | Reference | Reference |
| < 3 meals per day| -0.311 | 0.070 | 0.092 | 0.228 | 0.021 | 0.746 | -0.007 | 0.933 |
| Model 3 **       |       |       |       |       |
| 3 meals per day  | Reference | Reference | Reference | Reference |
| < 3 meals per day| -0.278 | 0.144 | 0.091 | 0.217 | 0.010 | 0.876 | -0.025 | 0.754 |

Aβ=beta-amyloid. OR=ods ratio. CI=confidence interval.

** Adjusted for age, sex, education, apolipoprotein ε4, and geriatric depression scale status.

* Adjusted for covariates in Model 1 plus, vascular risk score, body mass index status, lifetime physical activity score, lifetime cognitive activity score, occupational complexity, annual income status, fluid intake, alcohol intake, smoking, dietary pattern including food types (protein, fruits or vegetables, fried foods, fatty foods, and salty foods), and inter-meal snack.

^ Adjusted for covariates in Model 2 plus, serum nutritional markers (albumin, glucose, HDL-cholesterol, LDL- cholesterol, iron, ferritin, zinc, vitamin B₁₂, and folate).
The moderating effects of potential covariate on the relationships between lifetime meal frequency (3 meals per day versus < 3 meals per day) and Aβ retention (or Aβ positivity) were examined by multiple linear (or logistic) regression analyses including meal frequency × one potential covariate interaction term as well as meal frequency, and all potential covariates.