



# Prospective association between adherence to the MIND diet and subjective memory complaints in the French NutriNet-Santé cohort

Moufidath Adjibade<sup>1</sup> · Karen E. Assmann<sup>1</sup> · Chantal Julia<sup>1,2</sup> · Pilar Galan<sup>1</sup> · Serge Hercberg<sup>1,2</sup> · Emmanuelle Kesse-Guyot<sup>1</sup>

Received: 21 September 2018 / Revised: 25 January 2019 / Accepted: 28 January 2019 / Published online: 31 January 2019  
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

## Abstract

**Objectives** Our objective was to examine whether adherence to the Mediterranean–DASH diet intervention for neurodegenerative delay (MIND) was associated with SMC (as measured by the cognitive difficulties scale; CDS) in the NutriNet-Santé cohort.

**Methods** The study sample consisted of 6011 participants aged  $\geq 60$  years at baseline, without SMC at the beginning. SMC were defined by a CDS score  $\geq 43$  (corresponding to the 4th CDS quartile) and SMC cases were participants with SMC at least once during follow-up. The MIND diet score (0–15 points) is a hybrid of the Mediterranean Diet and the Dietary Approaches to Stop Hypertension (DASH) scores, which includes ten brain healthy food groups and five unhealthy food groups. We used Cox proportional hazards models to estimate Hazard Ratios (HR) and 95% confidence intervals (95% CI).

**Results** Over a mean follow-up of 6 years, approximately 15% and 30% cases of SMC were identified among participants aged 60–69 and  $\geq 70$  years, respectively. The MIND diet score was not significantly associated with SMC in the full sample and among participants aged 60–69 years. Among participants aged  $\geq 70$  years, a significant inverse association was observed between adherence to the MIND diet and SMC ( $HR_{\text{tertile 3 vs tertile 1}} = 0.69$ , 95% CI = 0.47–0.99). This relationship was strengthened after exclusion of participants with depressive symptoms ( $HR_{\text{tertile 2 vs tertile 1}} = 0.69$ , 95% CI = 0.49–0.97;  $HR_{\text{tertile 3 vs tertile 1}} = 0.62$ , 95% CI = 0.41–0.93).

**Conclusions** These findings suggest that the MIND diet could help to prevent or delay SMC among older adults without depressive symptoms.

**Keywords** Aging · Cognition · Subjective memory complaints · Nutrition · MIND diet

## Abbreviations

BMI Body mass index ( $\text{kg}/\text{m}^2$ )  
CDS Cognitive difficulties scale  
CI Confidence interval

CU Consumption unit  
HR Hazard ratios  
IPAQ International physical activity questionnaire  
MIND Mediterranean–DASH diet Intervention for neurodegenerative delay  
mPNNS-GS Modified French Programme National Nutrition Santé-Guideline Score  
SD Standard deviation

**Electronic supplementary material** The online version of this article (<https://doi.org/10.1007/s00415-019-09218-y>) contains supplementary material, which is available to authorized users.

✉ Moufidath Adjibade  
m.ajibade@eren.smbh.univ-paris13.fr

<sup>1</sup> Equipe de Recherche en Epidémiologie Nutritionnelle (EREN), Centre d’Epidémiologie et Statistiques Sorbonne Paris Cité, Université Paris 13, Inserm (U1153), Cnam, Inra (U1125), COMUE Sorbonne Paris Cité, 74 rue Marcel Cachin, 93017 Bobigny, France

<sup>2</sup> Département de Santé Publique, Hôpital Avicenne, Bobigny, France

## Introduction

Subjective memory complaints (SMC) are strongly associated with age and represent self-identified changes in memory [1, 2]. They may be considered as an early marker of subsequent cognitive decline, and are a possible precursor of mild cognitive impairment (MCI) and neurodegenerative disease such as

Alzheimer disease (AD) [2–5]. SMC have also been related to medication side effects, personality traits and psychological factors such as depression and anxiety [5, 6]. Given the increase in life expectancy, and consequently, the growing proportion of older individuals in societies across the world, prevention of memory problems is a major public health challenge. Although SMC do not systematically predict future cognitive decline or neurodegenerative disease, they are associated with increased health care costs, poor quality of life, and impairment in Activities of Daily Living among older people [5, 7, 8].

Epidemiological evidence suggests that modifiable lifestyle factors, including diet, could play an important role in maintaining brain and cognitive health. Indeed, a “healthy diet” characterized by high consumption of plant foods, whole grains, olive oil and fish, and ensuring an adequate intake in various vitamins and minerals could help to strengthen cognitive abilities by stimulating memory [9, 10]. In particular, the Mediterranean Diet (MD) has been associated with a better cognitive function and a lower risk of cognitive impairment, AD [11, 12] and subjective cognitive function [13]. The Dietary Approaches to Stop Hypertension (DASH), initially designed to reduce elevated blood pressure, has also been associated with a better cognitive function in a number of studies [14–16].

Recently, a new concept of diet aimed at protecting the brain, namely the Mediterranean–DASH diet intervention for neurodegenerative delay (MIND), was developed [17]. The MIND diet includes many dietary components from the MD and DASH, as well as specific components such as green leafy vegetables and berries known for their neuroprotective role [18]. The MIND diet score was found to be a better predictor of cognitive decline than either the MD or DASH diet scores in the Rush Memory and Aging Project [17]. To date, a few studies have specifically investigated the association between this brain-health dietary score and cognition [17, 19–21], but none has focused on SMC. Among the existing studies, two included a relatively small sample of the same population [17, 21], another is cross-sectional [20] and another included only women [19]. Overall, these studies showed that adherence to the MIND diet was associated with a better cognitive health [17, 19, 20] and a lower risk of AD [21].

In the present study, we, thus, aimed to investigate the prospective association between adherence to the MIND diet and SMC among elderly adults (aged  $\geq 60$  years) in a large French cohort.

## Methods

### Study population

The NutriNet-Santé study is a large web-based observational cohort launched in France in 2009, which aims to investigate the relationship between nutrition and health, as well as the determinants of dietary behaviors and nutritional status. The design and methodology of the study have been fully described elsewhere [22]. Briefly, participants are Internet-using adult volunteers (aged  $\geq 18$  years) who were recruited from the general population by a vast multimedia campaign. To be included into the study, participants are invited to complete a set of validated self-administered questionnaires (sociodemographic, economic conditions, physical activity, dietary intake, anthropometrics, and health status) using a dedicated website [23–26]. The NutriNet-Santé study was conducted according to the guidelines in the Declaration of Helsinki, and was approved by the ethics committee of the French Institute for Health and Medical Research (IRB Inserm no. 0000388FWA00005831) and by the National Commission on Informatics and Liberty (CNIL no. 908450 and no. 909216). Electronic informed consent was obtained from each participant. The NutriNet-Santé study is registered in ClinicalTrials.gov (NCT03335644).

### Subjective memory complaints (SMC)

SMC were measured using the French version of the validated self-administered cognitive difficulties scale (CDS) [27, 28]. From 2 years of follow-up, this questionnaire was sent to participants every 2 years until 2017 (maximum of four validated questionnaires). The CDS is a 37-item questionnaire designed to describe daily deficiencies, lapses of attention or memory, and related functions noticed by the people themselves, using a five-point frequency scale (ranging from 0 for never to 4 for very often). All the items are summed to yield a total score between 0 and 148 points, with a higher score indicating more frequent and severe cognitive difficulties. In the present study, CDS scores were converted to binary variables (low level of complaints vs a high level) using a cut-off value of 43 (corresponding to the fourth quartile of the score distribution) [27]. Participants considered to have SMC were those who had a high level of memory complaints at least once during follow-up. We focused our analyses on participants with a low level of complaints at the first CDS measurement (i.e., those free of SMC at the first assessment), to ensure a prospective design.

### Dietary data and the MIND diet score

All participants included in the NutriNet-Santé cohort were invited to complete at baseline and twice a year thereafter

three non-consecutive 24-h dietary records, randomly assigned over a 2-week period (2 weekdays and 1 weekend day). All foods and beverages consumed at each eating occasion were reported via a validated web-based 24-h dietary record tool designed for the self-administration [24, 29, 30]. The consumed portions were indicated using the validated photographs of portion sizes [31], household measures, or by indicating the exact quantity (grams) or volume (milliliters). In this study, usual dietary intake was obtained using data from the first 2 years of follow-up (corresponding to the time window between baseline and the first CDS assessment), and then converted to the frequency of consumption or number of servings, according to the recommendations for each component of the MIND diet. Daily mean food consumption and the NutriNet-Santé composition table were used to estimate energy and nutrient intakes [32].

The description and scoring of the MIND diet score are presented in Supplemental Table 1. Briefly, the MIND diet is a mix of components of the MD and the DASH diet, with some modifications to optimize brain health. It includes ten “brain healthy” food groups (green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine) and five unhealthy food groups (red meats, butter and margarine, cheese, pastries and sweets, and fast fried foods) [17]. For each component (except for olive oil), 0, 0.5, or 1 point was assigned using fixed cut-off points, with a maximum of points attributed for high consumption of “healthy” components. For olive oil consumption, 1 point was assigned if it was the primary oil usually used and 0 otherwise. The MIND diet score was the sum of all components, and the total score ranged from 0 point (no adherence) to 15 points (complete adherence) [17].

### Baseline covariates

At baseline, self-administered sociodemographic questionnaires provided information on sex, date of birth, marital status (living alone, cohabiting, and separated/divorced/widowed), educational level (less than high school diploma, high school diploma, and university level), occupational category (never-employed/other activity, self-employed, employee, intermediate profession and managerial staff, and superior intellectual profession), smoking status (never, former, and current smoker), and monthly household income (< 1200, 1200–1800, 1800–2700, > 2700 euros per consumption unit and a category of participants who refused to disclose their income). Monthly household income was estimated per consumption unit according to a weighting system where one consumption unit (CU) is attributed for the first adult in the household, 0.5 CU for other persons aged 14 or older, and 0.3 CU for children under 14 [33].

Weight and height data were collected and body mass index (BMI) was calculated as the ratio of weight to squared

height ( $\text{kg}/\text{m}^2$ ). Participants were classified as underweight or normal weight ( $\text{BMI} < 25$ ), overweight ( $25 \leq \text{BMI} < 30$ ), or obese ( $\text{BMI} \geq 30$ ). Physical activity was assessed using a short form of the French version of the International Physical Activity Questionnaire (IPAQ) [23] and classified as low physical activity (< 30 min of physical activity; equivalent to brisk walking/day), moderate physical activity ( $\geq 30$  and < 60 min), or high physical activity ( $\geq 60$  min), according to the French guidelines for physical activity [34].

Prevalent and incident cases of cancer and cardiovascular diseases were self-reported during follow-up and validated by a medical committee through medical and/or hospitalization reports. Type 2 diabetes and hypertension were also self-reported. In addition, depressive symptoms were measured at the same time as SMC using the French version of the validated self-administered Center for Epidemiologic Studies Depression (CES-D) scale [35]. Depressive symptoms at the end of follow-up (CES-D questionnaire at the first report of high SMC, and last completed questionnaire if the participant did not report high SMC) were defined by a CES-D score  $\geq 17$  for men and  $\geq 23$  for women [35].

### Statistical analysis

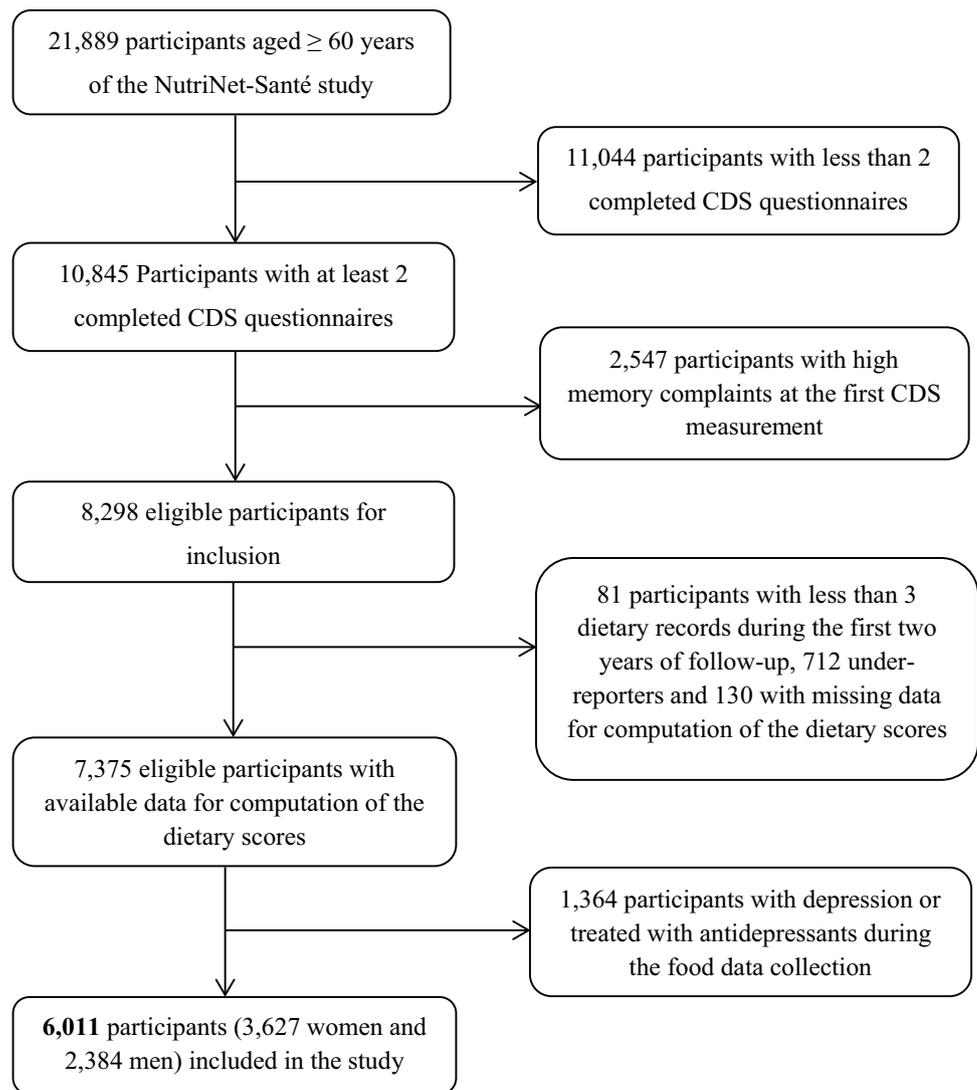
#### Selection of the study sample

Among the volunteers aged 60+ years included in the NutriNet-santé study (approximately 16% of the participants included in the cohort), 8298 were eligible for inclusion in this study (participants with at least two completed CDS questionnaires and not reporting high SMC at the first CDS measurement). Of these eligible participants, we included only participants who had available and valid data for the computation of the dietary scores and who had not reported depression or treatment with antidepressants during the dietary data collection. Finally, 6011 men and women were included in this prospective study (Fig. 1).

#### Characteristics of the participants

We compared participants included in the study with excluded eligible participants (participants aged 60+ years without valid dietary data among those who were free of SMC at the first CDS assessment and who had at least two completed CDS questionnaires during follow-up) using Chi-square tests or *t* tests as appropriated. Baseline characteristics and nutritional factors were presented as means  $\pm$  standard deviations (SD) or numbers (percentages), and were compared across tertiles of the MIND diet score using linear contrast or Cochran–Mantel–Haenszel tests. For descriptive purposes, nutrient intakes were energy-adjusted using the residual method [36].

**Fig. 1** Flowchart of participant selection. *CDS* cognitive difficulties scale



## Statistical models

Cox proportional hazards regression models for interval censored data were used to estimate Hazard ratios (HR) and 95% confidence intervals (CI) for the association between the dietary scores (modeled as continuous variables and as tertiles to simplify the interpretation of results as low, medium, and high adherence) and SMC. Age was used as the primary time-scale variable, with entry time defined as age at the first CDS measurement. For cases, exit time was defined as the average of (a) the age at the first report of SMC and (b) the age at the previous measurement with no SMC, while, for non-cases, it was defined as the age at the last completed CDS questionnaire [37]. Model 1 was adjusted for age, sex, marital status, educational level, occupational category, monthly household income per consumption unit, inclusion month, number of

recording days, and energy intake without alcohol. Model 2 (main model) was further adjusted for smoking status, physical activity, and BMI (continuous variable). Model 3 was further adjusted for comorbid conditions during follow-up (cancer, type 2 diabetes, hypertension, and cardiovascular events). Since the previous studies suggested a strong association between depressive symptoms and SMC [5], we presented a model 4 further adjusted for depressive symptoms at the end of the follow-up. An additional model (model 5) was also performed to additionally account for the baseline CDS score. Linear trend across tertiles of the MIND diet score was estimated by modeling the tertiles as ordinal variables.

Since memory complaints increase with age, we also tested the interaction between the MIND diet score and age, and conducted stratified age analyses.

## Sensitivity analyses

Supplementary analyses were performed to test the robustness of our findings. First, we investigated the association between the MIND diet score and SMC among participants without depressive symptoms at the end of the follow-up, to better control for the role of depression. Second, to evaluate the differential effect, compared to the MIND diet, of adherence to national dietary recommendations on brain health, we investigated the association between a modified version of the French Programme National Nutrition Santé-Guideline Score (mPNNS-GS) and SMC. The PNNS-GS is a validated a priori score reflecting adherence to the French nutritional guidelines developed for the general population [34], and it includes 1 physical activity component and 12 dietary components (eight refer to food serving recommendations and four refer to moderation in consumption). A penalty for overconsumption was assigned to individuals whose energy intake exceeded their energy needs by at least 5%, based on basal metabolic rate (using Schofield equation) and physical activity level. In this study, we used a modified version of the index, the mPNNS-GS, which takes into account only the dietary components. The maximum score was 13.5 and negative scores are theoretically possible due to the penalty system.

All statistical analyses were conducted using SAS (version 9.4; SAS institute Inc., Cary, NC, USA) with a significance level of 0.05 for two-sided tests.

## Results

### Sample characteristics

The analyses included 6011 women and men with a mean (SD) age of 64.4 (4.3) years at baseline. Compared to excluded participants from the eligible population ( $n=2287$ ), included participants were better educated, physically active, and more likely to be men and cohabiting. They were also more likely to have a BMI value in the normal-weight range, a household income per unit consumption  $\geq 1800$  euros, and less likely to have a chronic disease (Supplemental Table 2).

We identified 1053 (17.5%) cases of SMC during follow-up (mean follow-up = 6.1 years, SD = 1.7), with, respectively, 826 (15.7%) and 227 (30.6%) among participants aged 60–69 years and  $\geq 70$  years. Baseline characteristics of participants are presented across tertiles of the MIND diet score in Table 1. Participants with higher adherence to the MIND diet (third tertile) compared to those with lower adherence (1st tertile) were more likely to be women, better educated, more physically active, to have a household income per unit consumption  $\geq 2700$  euros (or not having

provided their income), and less likely to have a BMI  $\geq 25$  and chronic disease. In addition, a higher MIND diet score was associated with a lower daily energy intake, lower energy intake from lipids, and lower intake of saturated fatty acids, but with a higher intake of fibers, monounsaturated and polyunsaturated fatty acids, and most vitamins and minerals (Table 2).

### Association between the MIND diet score and SMC

A trend towards an inverse association, although not significant, was found between the MIND diet score and SMC in the full sample (Table 3). In analyses stratified according to age ( $P$  value for the interaction term = 0.02), an inverse significant relationship was observed between the MIND diet score and SMC only among older participants ( $\geq 70$  years). In the main model, a one-point increase in the MIND diet score was associated with a 14% (95% CI 4%; 23%,  $p=0.01$ ) reduction in the risk of SMC. When the score was modeled as tertiles, the highest adherence to the MIND diet was associated with a 31% (95% CI 1%; 53%,  $p=0.04$ ) reduction in the risk of SMC compared with the lowest adherence. These associations were attenuated after additional adjustment for health events during follow-up, depressive symptoms at the end of the follow-up, and the baseline CDS score, but remained significant in the analyses with the score modeled as a continuous variable. The associations were not significant in any model among participants aged 60–69 years.

### Sensitivity analyses

In sensitivity analyses excluding participants with depressive symptoms at the end of the follow-up, the associations between the MIND diet score and SMC were strengthened (Table 4). In the main model, a one-point increase in the MIND diet score was associated with an 18% (95% CI 7%; 27%,  $p=0.001$ ) reduction in the risk of SMC. When the score was modeled as tertiles, the highest and medium adherence to the MIND diet was, respectively, associated with a 31% (95% CI 4%; 51%) and 38% (95% CI 7%; 59%) reduction in the risk of SMC compared with the lowest adherence. Additional adjustment for health events during follow-up did not substantially modify the associations (model 3). Associations were non-significant in any model in the full sample and among participants aged 60–69 years.

The use of the mPNNS-GS to measure diet quality provided similar results for the stratified analyses according to age (Supplemental Table 3). In addition, in the full sample, a significant inverse association was found between the mPNNS-GS and SMC, but this association was no longer significant after an additional adjustment for the baseline CDS score. The Pearson correlation between the MIND diet score and the mPNNS-GS was 0.37 ( $p < 0.0001$ ).

**Table 1** Baseline characteristics of 6011 participants according to the tertiles of the MIND diet score, NutriNet-Santé study

Baseline characteristics	Tertile 1	Tertile 2	Tertile 3	<i>P</i> <sup>a</sup>
MIND, range	1.0–5.0	5.5–6.5	7.0–11.5	
<i>n</i>	1674	2573	1764	
Age, years	64.5 ± 4.7	64.3 ± 4.2	64.3 ± 4.0	0.25
Sex, <i>n</i> (%)				< 0.0001
Male	822 (49.1)	1009 (39.2)	553 (31.3)	
Female	852 (50.9)	1564 (60.8)	1211 (68.7)	
Marital status, <i>n</i> (%)				0.24
Living alone	80 (4.8)	118 (4.6)	94 (5.3)	
Cohabiting	1308 (78.1)	1988 (77.3)	1326 (75.2)	
Separated/divorced/widowed	286 (17.1)	467 (18.1)	344 (19.5)	
Educational level, <i>n</i> (%)				< 0.0001
< High school diploma	642 (38.3)	868 (33.7)	483 (27.4)	
High school diploma	251 (15.0)	392 (15.3)	277 (15.7)	
University level	781 (46.7)	1313 (51.0)	1004 (56.9)	
Occupational categories, <i>n</i> (%)				0.38
Never-employed/other activity	5 (0.3)	16 (0.6)	11 (0.6)	
Self-employed	109 (6.5)	162 (6.3)	85 (4.8)	
Employee	279 (16.7)	487 (18.9)	303 (17.2)	
Intermediate profession	523 (31.2)	756 (29.4)	552 (31.3)	
Managerial staff	758 (45.3)	1152 (44.8)	813 (46.1)	
Household income per consumption unit, <i>n</i> (%)				0.10
Not answered	150 (9.0)	234 (9.1)	169 (9.6)	
< 1200 euros	98 (5.8)	125 (4.9)	87 (4.9)	
1200–1800 euros	316 (18.9)	512 (19.9)	304 (17.2)	
1800–2700 euros	530 (31.7)	729 (28.3)	499 (28.3)	
≥ 2700 euros	580 (34.6)	973 (37.8)	705 (40.0)	
Smoking status, <i>n</i> (%)				0.05
Former smoker	869 (51.9)	1213 (47.1)	872 (49.4)	
Current smoker	120 (7.2)	148 (5.8)	97 (5.5)	
Never-smoker	685 (40.9)	1212 (47.1)	795 (45.1)	
Physical activity, <i>n</i> (%)				0.003
Low	257 (15.4)	342 (13.3)	221 (12.5)	
Moderate	317 (18.9)	451 (17.5)	299 (17.0)	
High	1100 (65.7)	1780 (69.2)	1244 (70.5)	
Body mass index, <i>n</i> (%)				< 0.0001
Underweight	29 (1.7)	48 (1.8)	52 (2.9)	
Normal weight	842 (50.3)	1448 (56.3)	1074 (60.9)	
Overweight	607 (36.3)	838 (32.6)	489 (27.7)	
Obesity	196 (11.7)	239 (9.3)	149 (8.5)	
Prevalence of chronic diseases <sup>b</sup> , <i>n</i> (%)	1216 (72.7)	1793 (69.9)	1178 (66.9)	0.0002

Values are means ± standard deviation or numbers (percentages) as appropriate

*MIND* Mediterranean–DASH Diet Intervention for Neurodegenerative Delay

<sup>b</sup>*P* values are based on linear contrast or Cochran–Mantel–Haenszel tests

<sup>c</sup>Incident cases of cancer, type 2 diabetes, hypertension, and cardiovascular diseases

## Discussion

To our knowledge, this is the first study that has investigated the relationship between the MIND diet and SMC. In this prospective study including men and women aged

60+ years, we found that adherence to the MIND diet was inversely associated with SMC among older adult aged 70+ years over a mean follow-up of 6 years.

Noted that when we investigated the evolution of the CDS score in a supplementary analysis (CDS score over

**Table 2** Baseline nutritional factors of 6011 participants according to the tertiles of the MIND diet score, NutriNet-Santé study

Nutritional factors	Tertile 1	Tertile 2	Tertile 3	P-trend <sup>a</sup>
MIND, range	1.0–5.0	5.5–6.5	7.0–11.5	
<i>n</i>	1674	2573	1764	
Total energy intake, Kcal/d	1992 ± 472	1877 ± 447	1783 ± 456	<0.0001
Alcohol intake, g/d	13.6 ± 14.3	11.4 ± 12.5	8.8 ± 11.0	<0.0001
Energy intake without alcohol, Kcal/d	1897 ± 440	1797 ± 421	1721 ± 438	<0.0001
Carbohydrates, % energy <sup>b</sup>	42.6 ± 5.7	42.9 ± 6.0	42.6 ± 6.8	0.96
Lipids, % energy <sup>b</sup>	39.3 ± 5.3	38.1 ± 5.6	37.9 ± 6.4	<0.0001
Saturated fatty acids, g/d <sup>c</sup>	34.0 ± 6.5	31.2 ± 6.0	28.1 ± 6.6	<0.0001
Monounsaturated fatty acids, g/d <sup>c</sup>	29.0 ± 5.4	29.1 ± 5.8	30.5 ± 7.3	<0.0001
Polyunsaturated fatty acids, g/d <sup>c</sup>	10.9 ± 3.3	11.5 ± 3.5	13.1 ± 4.9	<0.0001
Omega-3 fatty acids, g/d <sup>c</sup>	1.4 ± 0.6	1.6 ± 0.7	1.8 ± 0.8	<0.0001
Protein, % energy <sup>b</sup>	17.8 ± 2.9	18.6 ± 3.4	19.1 ± 3.9	<0.0001
Beta-carotene, µg/d <sup>c</sup>	3197 ± 1638	3663 ± 1697	4511 ± 2263	<0.0001
Thiamin, µg/d <sup>4c</sup>	1.1 ± 0.3	1.2 ± 0.3	1.3 ± 0.5	<0.0001
Vitamin B6, µg/d <sup>c</sup>	1.6 ± 0.3	1.8 ± 0.4	2.0 ± 0.4	<0.0001
Folic acid, µg/d <sup>c</sup>	310 ± 69.3	347 ± 74.2	402 ± 91.8	<0.0001
Vitamin B12, µg/d <sup>c</sup>	6.2 ± 5.1	6.2 ± 4.4	6.3 ± 4.7	0.28
Vitamin C, mg/d <sup>c</sup>	103 ± 47.2	121 ± 48.9	143 ± 55.9	<0.0001
Vitamin D, µg/d <sup>c</sup>	2.6 ± 1.6	2.9 ± 1.7	3.2 ± 1.8	<0.0001
Vitamin E, mg/d <sup>c</sup>	11.2 ± 3.5	11.7 ± 3.3	12.9 ± 3.6	<0.0001
Magnesium, mg/d <sup>c</sup>	319 ± 78.3	352 ± 83.9	401 ± 98.2	<0.0001
Zinc, mg/d <sup>c</sup>	10.9 ± 2.4	11.2 ± 2.4	11.3 ± 2.4	<0.0001
Fiber, g/d <sup>c</sup>	18.9 ± 4.3	21.2 ± 4.5	24.7 ± 5.9	<0.0001

Values are means ± standard deviation

MIND Mediterranean–DASH diet intervention for neurodegenerative delay

<sup>a</sup>P-trend values are based on linear contrast

<sup>b</sup>Values are percentages of total daily energy intake without alcohol

<sup>c</sup>Values were adjusted for energy intake without alcohol using the residual method

time as a continuous variable) rather than the presence or absence of SMC at least once during follow-up (binary variable), we observed an increase in the CDS score over time (full sample and age subgroups) and an inverse association between adherence to the MIND diet and the CDS score only at baseline and in the full sample (data not shown). However, follow-up duration was relatively long, limiting probably the detection of an association with change in CDS.

The main findings of our study can be compared with those of studies that have evaluated the associations between diet quality and cognition or dementia. In agreement with our findings, the previous epidemiological studies showed that adherence to the MIND diet was associated with a better verbal memory score [19], better cognitive function [20], slower decline in cognitive abilities [17], and a lower risk of AD [21].

As the MIND diet also reflects an overall healthier diet, our findings are also consistent with those obtained by Bhushan et al., based on data from 27,842 men of the Health Professionals Follow-Up Study, which showed an inverse association between adherence to the MD and subjective

cognitive function (as measured by six yes/no questions relating to memory [13]). More precisely, the highest quintile of the MD score as compared to the lowest quintile was associated with 36% (95% CI 25%; 45%) lower odds of a poor subjective cognitive function (score ≥ 3) and 24% (95% CI 17%; 30%) lower odds of a moderate subjective cognitive function (score = 1 or 2) [13]. In addition, most others studies have shown that adherence to several dietary scores, differing in terms of components and scoring, such as the DASH, MD, Healthy Diet Indicator, Healthy Eating Index, and PNNS-GS or a “healthier diet” (derived from dietary patterns and characterized by high intake of plant food, whole grain, seafood, and olive oil) was associated with a better cognitive function and a decreased risk of dementia [11, 12, 38–40].

Another study using data from the Gallup telephone surveys of US residents also showed that participants who reported eating fruits and vegetable less than four times/week had 26% (95% CI 14%; 39%) higher odds of reporting memory problems compared to those who reported eating more [41].

**Table 3** Association between the MIND diet score and memory complaints, NutriNet-Santé study

	Tertile 1	Tertile 2	Tertile 3	P-trend	Continuous	P <sup>a</sup>
All participants ( <i>n</i> = 6011)						
MIND, range	1.0–5.0	5.5–6.5	7.0–11.5			
<i>n</i>	1674	2573	1764			
Number of cases	338	443	272			
Model 1 <sup>b</sup>	1 (ref)	0.92 (0.79; 1.06)	0.87 (0.74; 1.03)	0.11	0.96 (0.91; 1.00)	0.07
Model 2 <sup>c</sup>	1 (ref)	0.92 (0.80; 1.07)	0.88 (0.74; 1.04)	0.13	0.96 (0.91; 1.00)	0.08
Model 3 <sup>d</sup>	1 (ref)	0.92 (0.80; 1.07)	0.88 (0.75; 1.04)	0.13	0.96 (0.91; 1.00)	0.07
Model 4 <sup>e</sup>	1 (ref)	0.92 (0.80; 1.07)	0.89 (0.75; 1.05)	0.15	0.96 (0.92; 1.01)	0.10
Model 5 <sup>f</sup>	1 (ref)	0.97 (0.84; 1.12)	0.94 (0.79; 1.11)	0.46	0.98 (0.93; 1.02)	0.32
60–69 years ( <i>n</i> = 5270)						
MIND, range	1.0–5.0	5.5–6.5	7.0–11.5			
<i>n</i>	1454	2253	1563			
Number of cases	255	349	222			
Model 1 <sup>b</sup>	1 (ref)	0.96 (0.82; 1.14)	0.92 (0.76; 1.11)	0.39	0.98 (0.93; 1.03)	0.41
Model 2 <sup>c</sup>	1 (ref)	0.96 (0.82; 1.13)	0.92 (0.76; 1.11)	0.40	0.98 (0.93; 1.03)	0.42
Model 3 <sup>d</sup>	1 (ref)	0.96 (0.82; 1.13)	0.92 (0.76; 1.11)	0.40	0.98 (0.92; 1.03)	0.39
Model 4 <sup>e</sup>	1 (ref)	0.97 (0.83; 1.15)	0.93 (0.77; 1.12)	0.46	0.98 (0.93; 1.04)	0.54
Model 5 <sup>f</sup>	1 (ref)	1.00 (0.85; 1.18)	0.97 (0.80; 1.17)	0.74	1.00 (0.95; 1.05)	0.96
≥ 70 years ( <i>n</i> = 741)						
MIND, range	2.5–5.0	5.5–6.5	7.0–10.5			
<i>N</i>	220	320	201			
Number of cases	83	94	50			
Model 1 <sup>b</sup>	1 (ref)	0.73 (0.54; 1.00)	0.66 (0.46; 0.96)	0.03	0.85 (0.77; 0.95)	0.01
Model 2 <sup>c</sup>	1 (ref)	0.76 (0.56; 1.04)	0.69 (0.47; 0.99)	0.04	0.86 (0.77; 0.96)	0.01
Model 3 <sup>d</sup>	1 (ref)	0.77 (0.56; 1.06)	0.70 (0.48; 1.02)	0.05	0.87 (0.78; 0.97)	0.01
Model 4 <sup>e</sup>	1 (ref)	0.74 (0.54; 1.02)	0.70 (0.48; 1.01)	0.05	0.86 (0.77; 0.96)	0.01
Model 5 <sup>f</sup>	1 (ref)	0.84 (0.60; 1.17)	0.81 (0.55; 1.20)	0.28	0.87 (0.78; 0.98)	0.02

Values are hazard ratios (95% confidence intervals)

MIND Mediterranean–DASH Diet Intervention for Neurodegenerative Delay

<sup>a</sup>*P* for linear relation (dietary score as a continuous variable)

<sup>b</sup>Adjusted for age, sex, marital status, educational level, occupational categories, household income per consumption unit, energy intake without alcohol, number of recording days, and inclusion month

<sup>c</sup>Adjusted for all variables in model 1 + smoking status, physical activity, and body mass index

<sup>d</sup>Adjusted for all variables in model 2 + comorbid conditions during follow-up

<sup>e</sup>Adjusted for all variables in model 3 + depressive symptoms at the end of the follow-up

<sup>f</sup>Adjusted for all variables in model 4 + baseline CDS score

In this study, the mPNNS-GS, a priori score developed to measure adherence to dietary recommendations of the PNNS [34, 42], was significantly associated with SMC in our full study sample and among participant aged 70 + years. The PNNS was initially designed for the prevention of nutrition-related chronic conditions (such as obesity, cardiovascular disorders, and cancer) in the general population, and higher adherence to its dietary recommendations reflect a healthier diet, like the MIND diet. However, the mPNNS-GS and the MIND diet score differ according to the food components included as well as the allocation of the points, which could explain the relatively low correlation observed between these scores.

Overall, our findings show that, although national dietary recommendations were not initially designed to protect the brain, they could help to prevent or delay SMC.

Moreover, our results indicated a more pronounced association between adherence to the MIND diet and SMC among older participants (≥ 70 years) who were free of depressive symptoms at the end of the follow-up. This finding suggests a main role of depressive symptoms on memory complaints, as already documented in the previous studies [1, 5]. This interrelation may rely on subjective or objective cognitive disabilities among depressed individuals. Moreover, recurrent depression has been associated with changes in cognitive functioning such as

**Table 4** Association between the MIND diet score and memory complaints among participants without depressive symptoms at the end of the follow-up, NutriNet-Santé study

	Tertile 1	Tertile 2	Tertile 3	<i>P</i> -trend	Continuous	<i>P</i> <sup>a</sup>
All participants ( <i>n</i> = 5640)						
MIND, range	1.0–5.0	5.5–6.5	7.0–11.5			
<i>n</i>	1561	2416	1663			
Number of cases	289	384	238			
Model 1 <sup>b</sup>	1 (ref)	0.94 (0.80; 1.10)	0.90 (0.75; 1.08)	0.24	0.96 (0.92; 1.01)	0.15
Model 2 <sup>c</sup>	1 (ref)	0.94 (0.81; 1.10)	0.91 (0.76; 1.09)	0.30	0.97 (0.92; 1.02)	0.19
Model 3 <sup>d</sup>	1 (ref)	0.94 (0.81; 1.10)	0.91 (0.76; 1.09)	0.30	0.97 (0.92; 1.02)	0.18
Model 4 <sup>e</sup>	1 (ref)	1.00 (0.86; 1.17)	0.94 (0.79; 1.13)	0.54	0.98 (0.93; 1.03)	0.42
60 to 69 years ( <i>n</i> = 4953)						
MIND, range	1.0–5.0	5.5–6.5	7.0–11.5			
<i>n</i>	1353	2126	1474			
Number of cases	212	308	197			
Model 1 <sup>b</sup>	1 (ref)	1.02 (0.85; 1.21)	0.98 (0.80; 1.20)	0.87	1.00 (0.94; 1.06)	0.92
Model 2 <sup>c</sup>	1 (ref)	1.02 (0.85; 1.22)	0.99 (0.81; 1.21)	0.93	1.00 (0.94; 1.06)	0.99
Model 3 <sup>d</sup>	1 (ref)	1.02 (0.85; 1.22)	0.99 (0.81; 1.21)	0.92	1.00 (0.94; 1.06)	0.95
Model 4 <sup>e</sup>	1 (ref)	1.04 (0.87; 1.24)	1.01 (0.82; 1.24)	0.91	1.01 (0.95; 1.07)	0.77
≥ 70 years ( <i>n</i> = 687)						
MIND, range	2.5–5.0	5.5–6.5	7.0–10.5			
<i>n</i>	208	290	189			
Number of cases	77	76	41			
Model 1 <sup>b</sup>	1 (ref)	0.67 (0.48; 0.94)	0.60 (0.40; 0.90)	0.01	0.82 (0.72; 0.92)	0.001
Model 2 <sup>c</sup>	1 (ref)	0.69 (0.49; 0.96)	0.62 (0.41; 0.93)	0.02	0.82 (0.73; 0.93)	0.001
Model 3 <sup>d</sup>	1 (ref)	0.69 (0.49; 0.97)	0.63 (0.42; 0.94)	0.02	0.83 (0.74; 0.93)	0.002
Model 4 <sup>e</sup>	1 (ref)	0.85 (0.60; 1.20)	0.71 (0.46; 1.08)	0.10	0.85 (0.75; 0.96)	0.01

Values are hazard ratios (95% confidence intervals)

MIND Mediterranean–DASH Diet Intervention for neurodegenerative delay

<sup>a</sup>*P* for linear relation (dietary score as a continuous variable)

<sup>b</sup>Adjusted for age, sex, marital status, educational level, occupational categories, household income per consumption unit, energy intake without alcohol, number of recording days, and inclusion month

<sup>c</sup>Adjusted for all variables in model 1 + smoking status, physical activity, and body mass index

<sup>d</sup>Adjusted for all variables in model 2 + comorbid conditions during follow-up

<sup>e</sup>Adjusted for all variables in model 3 + baseline CDS score

decreases in performance, affecting attention, verbal fluency, executive functions, and memory [43, 44].

The beneficial effect of the MIND diet on SMC and cognitive functions or dementia could be attributed to healthy components such as vegetables (especially green leafy vegetables), nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine. Indeed, healthy foods accounted in the MIND diet provide high amounts of several nutrients, including carotenoids, vitamins B, C, D, E, and polyphenols [17, 18, 45]. Most of these nutrients have been shown to have anti-inflammatory properties and are required for normal physiological functioning of the brain [38, 46]. In addition, B vitamins (especially vitamin B1, B2, B6, B12, and folates) and antioxidant nutrients deficiencies have been associated with cognitive dysfunction in several epidemiological studies [47, 48]. Finally, dietary fibers also play an important role in cognition, in

particular via their influence on gut microbiota composition [49, 50].

This study has some potential limitations that should be noted. First, a large proportion of participants aged ≥ 60 years was excluded from the study, because they did not complete the SMC questionnaires, which could imply a potential bias in risk estimates. Second, participants were volunteers in a web-based nutritional cohort and, thus, had relatively healthier lifestyles and higher education as compared to the general population, which limits the generalizability of our results. In addition, although we have considered a wide range of confounders collected through validated questionnaires, we cannot exclude the possibility of residual confounding by unmeasured factors within this cohort.

The present study also exhibits a number of important strengths, including its large sample size (allowing for

stratified analyses), the prospective design, the repeated assessment of SMC data using a validated tool, and the quality of the dietary data.

In summary, this study indicated an inverse association between adherence to the MIND diet and SMC among older adults aged 70+ years, which was more pronounced among those who were free of depressive symptoms. These findings suggest that the MIND diet could help to prevent or delay high SMC, but an adequate treatment of individuals with depression or depressive symptoms remains a key element.

**Acknowledgements** We thank all the scientists, dietitians, technicians, and assistants for their technical contribution to the NutriNet-Santé study. We especially thank Younes Esseddik, Thi Duong Van, Frédéric Coffinieres, Mac Rakotondrazafy, Régis Gatibelza, and Paul Flanzly (computer scientists); and Nathalie Arnault, Véronique Gourlet, Dr. Fabien Szabo, Julien Allegre, Anouar Nechba, and Laurent Bourhis (data-manager/biostatisticians). We also thank all the volunteers of the NutriNet-Santé cohort. The NutriNet-Santé Study is supported by the French Ministry of Health (DGS), the French Public Health Agency, the French National Institute for Health and Medical Research (INSERM), the Medical Research Foundation (FRM), the French National Institute for Agricultural Research (INRA), the National Conservatory for Arts and Crafts (CNAM), the National Institute for Prevention and Health Education (INPES), and the Paris 13 University. MA was supported by a doctoral fellowship from the Ecole Doctorale Galilée, Paris 13 University, Sorbonne Paris Cité.

## Compliance with ethical standards

**Conflicts of interest** None of the authors declares any conflicts of interest.

## References

- Balash Y, Mordechovich M, Shabtai H et al (2013) Subjective memory complaints in elders: depression, anxiety, or cognitive decline? *Acta Neurol Scand* 127:344–350. <https://doi.org/10.1111/ane.12038>
- Jonker C, Geerlings MI, Schmand B (2000) Are memory complaints predictive for dementia? A review of clinical and population-based studies. *Int J Geriatr Psychiatry* 15:983–991
- Mitchell AJ, Beaumont H, Ferguson D et al (2014) Risk of dementia and mild cognitive impairment in older people with subjective memory complaints: meta-analysis. *Acta Psychiatr Scand* 130:439–451. <https://doi.org/10.1111/acps.12336>
- Kaup AR, Nettiksimmons J, LeBlanc ES, Yaffe K (2015) Memory complaints and risk of cognitive impairment after nearly 2 decades among older women. *Neurology* 85:1852–1858. <https://doi.org/10.1212/WNL.0000000000002153>
- Brigola AG, Manzini CSS, Oliveira GBS et al (2015) Subjective memory complaints associated with depression and cognitive impairment in the elderly: a systematic review. *Dement Neuropsychol* 9:51–57. <https://doi.org/10.1590/S1980-57642015DN9100009>
- Dux MC, Woodard JL, Calamari JE et al (2008) The moderating role of negative affect on objective verbal memory performance and subjective memory complaints in healthy older adults. *J Int Neuropsychol Soc JINS* 14:327–336. <https://doi.org/10.1017/S1355617708080363>
- Mol M, Carpay M, Ramakers I et al (2007) The effect of perceived forgetfulness on quality of life in older adults; a qualitative review. *Int J Geriatr Psychiatry* 22:393–400. <https://doi.org/10.1002/gps.1686>
- Waldorff FB, Siersma V, Waldemar G (2009) Association between subjective memory complaints and health care utilisation: a three-year follow up. *BMC Geriatr* 9:43. <https://doi.org/10.1186/1471-2318-9-43>
- Abate G, Marziano M, Rungratanawanich W et al (2017) Nutrition and AGE-ing: focusing on Alzheimer's disease. *Oxid Med Cell Longev* 2017:7039816. <https://doi.org/10.1155/2017/7039816>
- Smith PJ, Blumenthal JA (2016) Dietary factors and cognitive decline. *J Prev Alzheimers Dis* 3:53–64. <https://doi.org/10.14283/jpad.2015.71>
- Wu L, Sun D (2017) Adherence to Mediterranean diet and risk of developing cognitive disorders: an updated systematic review and meta-analysis of prospective cohort studies. *Sci Rep* 7:41317. <https://doi.org/10.1038/srep41317>
- Aridi YS, Walker JL, Wright ORL (2017) The association between the mediterranean dietary pattern and cognitive health: a systematic review. *Nutrients*. <https://doi.org/10.3390/nu9070674>
- Bhushan A, Fondell E, Ascherio A et al (2017) Adherence to Mediterranean diet and subjective cognitive function in men. *Eur J Epidemiol*. <https://doi.org/10.1007/s10654-017-0330-3>
- Tangney CC, Li H, Wang Y et al (2014) Relation of DASH- and Mediterranean-like dietary patterns to cognitive decline in older persons. *Neurology* 83:1410–1416. <https://doi.org/10.1212/WNL.0000000000000884>
- Berendsen AAM, Kang JH, van de Rest O et al (2017) The dietary approaches to stop hypertension diet, cognitive function, and cognitive decline in american older women. *J Am Med Dir Assoc* 18:427–432. <https://doi.org/10.1016/j.jamda.2016.11.026>
- Wengreen H, Munger RG, Cutler A et al (2013) Prospective study of dietary approaches to stop hypertension- and mediterranean-style dietary patterns and age-related cognitive change: the Cache County Study on Memory, Health and Aging. *Am J Clin Nutr* 98:1263–1271. <https://doi.org/10.3945/ajcn.112.051276>
- Morris MC, Tangney CC, Wang Y et al (2015) MIND diet slows cognitive decline with aging. *Alzheimers Dement J Alzheimers Assoc* 11:1015–1022. <https://doi.org/10.1016/j.jalz.2015.04.011>
- Morris MC (2016) Nutrition and risk of dementia: overview and methodological issues. *Ann N Y Acad Sci* 1367:31–37. <https://doi.org/10.1111/nyas.13047>
- Berendsen AM, Kang JH, Feskens EJM et al (2018) Association of long-term adherence to the MIND diet with cognitive function and cognitive decline in American women. *J Nutr Health Aging* 22:222–229. <https://doi.org/10.1007/s12603-017-0909-0>
- McEvoy CT, Guyer H, Langa KM, Yaffe K (2017) neuroprotective diets are associated with better cognitive function: the health and retirement study. *J Am Geriatr Soc* 65:1857–1862. <https://doi.org/10.1111/jgs.14922>
- Morris MC, Tangney CC, Wang Y et al (2015) MIND diet associated with reduced incidence of Alzheimer's disease. *Alzheimers Dement J Alzheimers Assoc* 11:1007–1014. <https://doi.org/10.1016/j.jalz.2014.11.009>
- Hercberg S, Castetbon K, Czernichow S et al (2010) The Nutrinet-Sante Study: a web-based prospective study on the relationship between nutrition and health and determinants of dietary patterns and nutritional status. *BMC Public Health* 10:242-
- Craig CL, Marshall AL, Sjostrom M et al (2003) International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 35:1381–1395
- Lassale C, Castetbon K, Laporte F et al (2015) Validation of a Web-based, self-administered, non-consecutive-day dietary record tool against urinary biomarkers. *Br J Nutr* 113:953–962

25. Lassale C, Peneau S, Touvier M et al (2013) Validity of web-based self-reported weight and height: results of the Nutrinet-Sante study. *J Med Internet Res* 15:e152-
26. Vergnaud AC, Touvier M, Mejean C et al (2011) Agreement between web-based and paper versions of a socio-demographic questionnaire in the NutriNet-Sante study. *Int J Public Health* 56:407–417
27. Derouesné C (1993) Empirical evaluation of the “Cognitive difficulties scale” for Assessment of memory complaints in General practice: a study of 1628 Cognitively normal subjects Aged 45–75 years. *Int J Geriatr Psychiatry* 8:599–607
28. McNair D, Kahn R (1983) Self-assessment of cognitive deficits. *Assess Geriatr Psychopharmacol Mark Powley* 137–143
29. Touvier M, Kesse-Guyot E, Mejean C et al (2011) Comparison between an interactive web-based self-administered 24 h dietary record and an interview by a dietitian for large-scale epidemiological studies. *BrJ Nutr* 105:1055–1064
30. Lassale C, Castetbon K, Laporte F et al (2016) Correlations between fruit, vegetables, fish, vitamins, and fatty acids estimated by web-based nonconsecutive dietary records and respective biomarkers of nutritional status. *J Acad Nutr Diet* 116:427–438
31. Le Moullec N, Deheeger M, Preziosi P et al (1996) Validation du manuel photos utilisé pour l’enquête alimentaire de l’étude SU.VI.MAX [Validation of the photo manual used for the dietary assessment of the SU.VI.MAX study]. *Cah Nutr Diet* 31:158–164
32. Etude NutriNet-Santé (2013) Table de Composition des Aliments de l’étude NutriNet-Santé [NutriNet-Santé Study Food Composition Database]. Economica, Paris
33. Institut National de la Statistique et des Etudes Economiques (INSEE) Website (2017) Définition des Unités de Consommation [Consumption Units definition]
34. Estaquio C, Kesse-Guyot E, Deschamps V et al (2009) Adherence to the French programme national nutrition sante guideline score is associated with better nutrient intake and nutritional status. *J Am Diet Assoc* 109:1031–1041
35. Führer R, Rouillon F (1989) The French version of the Center for epidemiologic studies-depression scale. *Psychiatr Psychol* 4:163–166
36. Willett W, Stampfer MJ (1986) Total energy intake: implications for epidemiologic analyses. *Am J Epidemiol* 124:17–27
37. Finkelstein DM (1986) A proportional hazards model for interval-censored failure time data. *Biometrics* 42:845–854
38. Solfrizzi V, Custodero C, Lozupone M et al (2017) Relationships of dietary patterns, foods, and micro- and macronutrients with Alzheimer’s disease and late-life cognitive disorders: a systematic review. *J Alzheimers Dis* 59:815–849. <https://doi.org/10.3233/JAD-170248>
39. van de Rest O, Berendsen AA, Haveman-Nies A, de Groot LC (2015) Dietary patterns, cognitive decline, and dementia: a systematic review. *Adv Nutr Bethesda Md* 6:154–168. <https://doi.org/10.3945/an.114.007617>
40. Yusufov M, Weyandt LL, Piryatinsky I (2017) Alzheimer’s disease and diet: a systematic review. *Int J Neurosci* 127:161–175. <https://doi.org/10.3109/00207454.2016.1155572>
41. Small GW, Siddarth P, Ercoli LM et al (2013) Healthy behavior and memory self-reports in young, middle-aged, and older adults. *Int Psychogeriatr* 25:981–989. <https://doi.org/10.1017/S1041610213000082>
42. Hercberg S, Chat-Yung S, Chaulia M (2008) The French national nutrition and health program: 2001–2006–2010. *Int J Public Health* 53:68–77
43. Marvel CL, Paradiso S (2004) Cognitive and neurological impairment in mood disorders. *Psychiatr Clin N Am* 27:19–36. [https://doi.org/10.1016/S0193-953X\(03\)00106-0](https://doi.org/10.1016/S0193-953X(03)00106-0) vii–viii.
44. Galecki P, Talarowska M, Anderson G et al (2015) Mechanisms underlying neurocognitive dysfunctions in recurrent major depression. *Med Sci Monit Int Med J Exp Clin Res* 21:1535–1547. <https://doi.org/10.12659/MSM.893176>
45. Vauzour D, Camprubi-Robles M, Miquel-Kergoat S et al (2017) Nutrition for the ageing brain: Towards evidence for an optimal diet. *Ageing Res Rev* 35:222–240. <https://doi.org/10.1016/j.arr.2016.09.010>
46. Meeusen R (2014) Exercise, nutrition and the brain. *Sports Med Auckl NZ* 44(Suppl 1):S47–S56. <https://doi.org/10.1007/s40279-014-0150-5>
47. Del Parigi A, Panza F, Capurso C, Solfrizzi V (2006) Nutritional factors, cognitive decline, and dementia. *Brain Res Bull* 69:1–19. <https://doi.org/10.1016/j.brainresbull.2005.09.020>
48. Solfrizzi V, Panza F, Capurso A (2003) The role of diet in cognitive decline. *J Neural Transm Vienna Austria* 1996 110:95–110. <https://doi.org/10.1007/s00702-002-0766-8>
49. Pistollato F, Sumalla Cano S, Elio I et al (2016) Role of gut microbiota and nutrients in amyloid formation and pathogenesis of Alzheimer disease. *Nutr Rev* 74:624–634. <https://doi.org/10.1093/nutrit/nuw023>
50. Simpson HL, Campbell BJ (2015) Review article: dietary fibre-microbiota interactions. *Aliment Pharmacol Ther* 42:158–179. <https://doi.org/10.1111/apt.13248>