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ARTICLE

Health issues and nutrition in the elderly

Exploratory dietary patterns and cognitive function in the "Seguimiento Universidad de Navarra" (SUN) Prospective Cohort

M. I. Muñoz-García[1,2] · M. A. Martínez-González[1,3,4] · C. Razquin[1,3] · M. Fernández-Matarrubia[1,5] · F. Guillén-Grima[1,5,6] · E. Toledo[1,3]

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Abstract

Background Dementia is projected to affect 135 million by 2050. Diet is a pertinent target for primary prevention, but firm recommendations for dementia prevention are not available yet. Our aim was to address the association between exploratory (empirically derived) dietary patterns (DP) and changes in the Spanish Telephone Interview for Cognitive Status (STICS-m, maximum score = 41 points) over 6 years.

Method Information on diet was collected with a validated 136-item food-frequency questionnaire from 803 participants in the Mediterranean cohort "Seguimiento Universidad de Navarra." We used principal component analysis to derive exploratory DP. The derived DP were associated with change in STICS-m scores over 6 years, through adjusted multiple linear regression models.

Results Two main DP were identified. The first DP resembled a Western dietary pattern (WDP)—high in sugar, fat, processed foods, and red meat—and the second DP resembled a Mediterranean dietary pattern (MDP)—high in vegetables, fruits, nuts, fish, and olive oil. Adherence to the WDP (tertile 3 vs tertile 1) was significantly associated with negative STICS-m changes after 6 years (between-tertile difference in changes: –0.80 points; 95% confidence interval [CI] –1.51, –0.08, p value = 0.03). Meanwhile, the MDP showed a positive +0.71 point (95% CI 0.15, 1.26, p value = 0.01) between-tertile difference in changes in the STICS-m score.

Conclusions A healthy, prudent, MDP was associated with less decline in cognitive function and, thus, could help to lower dementia incidence. Western-type diets were associated with a greater decline in cognitive performance and could increase dementia incidence.

Introduction

Dementia afflicted an estimated 44 million persons in 2016 with projections reaching 135 million by 2050 [1, 2]. Although recent evidence indicates that the incidence of dementia has declined by 13% between 1988 and 2015 in the United States and Europe [3], the forecasted ageing of the population worldwide [4] paired with an estimated increase in modifiable risk factors associated with dementia [5] indicates that somber projections are likely to come true. Currently, disease-modifying treatments designed to delay the progression of cognitive decline are not available and development of new drugs has been extremely slow [6]. Therefore, the need to focus on dementia prevention is clear [7].

Nutrition-related interventions are ideal for prevention of cognitive decline, as diet has been implicated in direct and indirect mechanisms that modify the risk of incident dementia [8]. A whole-diet approach through the study of

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✉ E. Toledo
etoledo@unav.es

[1] Department of Preventive Medicine and Public Health, School of Medicine, University of Navarra-IdiSNA, Pamplona, Spain

[2] Department of Neurology, Hospital Universitario 12 de Octubre, Madrid, Spain

[3] CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III, Madrid, Spain

[4] Department of Nutrition, Harvard T. H. Chan School of Public Health, Boston, MA, USA

[5] University of Navarra, Clínica Universidad de Navarra, Pamplona, Spain

[6] Department of Health Sciences, Public University of Navarra, Pamplona, Spain

dietary patterns (DP) versus single nutrients is able to capture the synergistic effects among individual components to better understand the impact of food-habits on health outcomes, allowing for more solid public health recommendations [9]. Initially, as DP could not be obtained directly from collected dietary data, they were derived empirically or “a posteriori” using statistical methods as an exploratory approach [10]. With the expansion of nutritional epidemiology, “a priori”-defined DP were used to study their relationship with various health outcomes, including dementia. Today, both methods are combined in order to better understand how nutrition affects neurocognition [11].

The main “a priori”-defined DP related to neuroprotection include the Mediterranean DP (MDP), the Dietary Approaches to Stop Hypertension (DASH), or a combination of the two, in the Mediterranean–DASH intervention for neurodegenerative delay diet [12], with the strongest evidence supporting the potential role of the MDP for dementia prevention [8, 13]. However, studies assessing exploratory DP are less numerous and coincide in two profiles: a prudent or healthy profile, associated with less risk of cognitive impairment and a Western or unhealthy DP (WDP) associated with a higher risk of cognitive impairment. Some studies have assessed exploratory DP in Australia, Sweden, and France [14–17]. Thus, the number of studies conducted in Mediterranean areas using exploratory DP to assess their association with changes in cognitive function is scarce. Our objective was to address the association between empirically derived DP and changes in cognitive function in a well-defined Spanish cohort of university graduates.

Materials and methods

Study population

The participants represent a sub-cohort of the “Seguimiento Universidad de Navarra” (SUN) project, a prospective and dynamic cohort study composed of university graduates, ongoing since 1999 [18]. The recruitment questionnaire for the SUN cohort gathered self-reported information about anthropometric data, physical activity, or prevalent disease at recruitment. The validity of self-reported data has been evaluated in subsamples of the cohort [19]. For the subproject, 1921 participants older than 55 years and without self-reported cognitive impairment completed the Spanish version of the Telephone Interview for Cognitive Status (STICS-m) in 2008 [20]. Information regarding genetic variants associated with dementia performed through analysis and DNA extraction of saliva samples was gathered through the commercial kit Oragene DNA OG-500 from DNA Genotek in Ottawa, Canada [18].

Dietary assessment

The information on dietary habits was obtained from a repeatedly validated 136-item semi-quantitative food frequency questionnaire, completed at recruitment for the SUN Project [21]. The methods for derivation of nutrient composition have been published elsewhere [22]. The initial 136 items were then grouped into 31 predefined categories (the specific foods in each category can be found in Supplementary Table 1) [23]. We performed a principal component analysis on the food groups to identify distinct DP. The number of factors to be extracted was determined with a scree plot and with a cut-off eigenvalue >2. Only factor loadings >|0.25| were considered as relevant contributions for the DP and included in the tables. Each participants’ score was obtained by adding up each standardized food group consumption multiplied by its specific weighted scoring coefficient. The quantitative score of each DP was divided into tertiles.

Cognitive evaluation

The Telephone interview for Cognitive Status (TICS) is a validated telephone adaptation of the Mini-Mental State Examination to be performed over the phone [24], later modified (TICS-m) but still valid to discriminate Alzheimer’s disease patients and cognitively normal subjects (85% sensitivity and 83% specificity) [25]. The Spanish version was based on the TICS-m, evaluating four cognitive domains (orientation, memory, attention/calculation, and language) through 11 items, with a maximum score of 41. The change in STICS-m over 6 years was able to discriminate participants with greater subsequent risk of developing dementia in a validation study [20].

The baseline STICS-m was completed by 1069 participants who were contacted after 2 and 6 years to repeat the screening test. The mean (±SD) follow-up time until first cognitive evaluation in the SUN cohort was 6 ± 3 years. The number of participants who completed evaluations at year 2 was 1015 (5% of loss to follow-up), and at year 6 was 924 (14% loss since the baseline evaluation, 9% since year 2).

Due to missing items in the baseline STICS-m (12 participants had one missing item, one had two missing items, and 1 had three missing items), we imputed these values based on the participant’s sex, age, and attained scores in other items of the baseline STICS-m, as well as scores in the 2- and 6-year STICS-m. The same process was used to impute these items for one missing value in the 2-year STICS-m and one missing value in the 6-year STICS-m. We excluded 145 participants who did not complete the 6-year STICS-m and 1 participant with implausible STICS-m scores (defined as >4 SD from mean change over 6 years). Furthermore, 103 participants did not provide saliva samples and 14 subjects reported daily energy intakes outside predefined limits (1st–99th percentiles). A total of 806 participants were analyzed.

Statistical analyses

Characteristics of the participants in tertiles of each pattern were described with percentages for categorical variables and with means and standard deviations for continuous variables. Linear regression models were used to evaluate the association between adherence to the derived DP and change in STICS-m. The dependent variable was the change in STICS-m from baseline to the 6-year cognitive evaluation. The main independent variable was the adherence to each DP classified in tertiles, with the lowest adherence as reference category. In addition, we carried out linear trend tests using the median score of each category as a continuous variable. The covariates used for adjustment were chosen based on the association between covariates and diet, cognitive function, or both, based on previous research.

Two adjusted models were carried out. Model 1 was adjusted for sex, age at time of baseline STICS-m (linear and quadratic term), follow-up time from recruitment to the SUN Project until baseline cognitive evaluation, years of university education, and presence of a dominant APOE-ε4 allele. Model 2 was additionally adjusted for total energy intake (kcal/day), body mass index (kg/m^2), physical activity (METs-h/week), smoking (categories of never, former and current smoker, and number of package-years), alcohol intake (grams/day), prevalent cardiovascular risk factors at recruitment (hypertension, high total cholesterol >200 mg/dL, low HDL cholesterol <35 mg/dL, and type 2 diabetes), and prevalent disease at recruitment (depression, atrial fibrillation, or cardiovascular disease).

In addition, we calculated adjusted mean change in 6-year STICS-m scores for each tertile of the derived exploratory patterns using a factorial ANOVA model, adjusted for the variables in model 2. We also carried out a sensitivity analysis, with a more restrictive definition of "implausible" STICS-m scores, defined as >3.5 SD, resulting in the elimination of three participants.

All *p* values presented are two-tailed; *p* values <0.05 were considered statistically significant. Analyses were performed using STATA/SE version 12.1 (StataCorp., College Station, TX, USA).

Results

The principal component analysis yielded two predominant factors, which explained 14% of the total variability among the 31 food groups (consumption variability). Factor loadings with a correlation coefficient >|0.25| for each of the two DP obtained are presented in Table 1. The first component was characterized by high consumption of refined cereals, whole-fat dairy products, eggs, sweets, sugar-sweetened beverages, commercial bakery, sauces, precooked meals, fast food, processed and non-processed red meat, and potatoes (baked or fried). Thus, we labeled the first component as a "WDP." The second component was characterized by high consumption of vegetables, both natural and canned/dried fruits, nuts, fish, natural fruit juices, and olive oil. We labeled this pattern as a "MDP."

Table 1 Component loadings for the Western and Mediterranean dietary patterns identified with principal component analyses in the cognitive function sub-cohort of the SUN Project.

Food group	Western dietary pattern	Mediterranean dietary pattern
Vegetables		0.67
Fruit		0.65
Refined cereals	0.33	
Whole-fat dairy products	0.35	
Nuts		0.41
Eggs	0.37	
Fish		0.38
Sweets[a]	0.31	
Sugar-sweetened beverages	0.26	
Natural fruit juices		0.34
Commercial bakery	0.34	
Sauces[b]	0.46	
Processed/ precooked meals	0.46	
Fast food	0.45	
Processed red meat	0.38	
Red meat	0.47	
Olive oil		0.35
Potatoes	0.50	
Other fruits[c]		0.44

Only component loadings >|0.25| are displayed in the table.

[a] Including cookies, cakes, nougat, chocolate, and marzipan.

[c] Including canned fruit, dried fruit, avocado, and olives.

[b] Ketchup and mayonnaise.

Table 2 shows the main characteristics of the 806 participants analyzed, according to tertiles of adherence to the WDP and the MDP. The cohort was composed of 70% men, with a mean age at recruitment of 67 ± 5 years at time of the first cognitive evaluation. Those with higher adherence to the WDP were significantly more likely to be male (*p* value = 0.02), have a higher total energy intake (ANOVA *p* value < 0.001) and higher average alcohol consumption (ANOVA *p* value < 0.0001), and a lower prevalence of high total

Table 2 Baseline characteristics of the cognitive function sub-cohort of the SUN Project participants according to quartiles of adherence to the Western or the Mediterranean dietary pattern.

Dietary pattern	Western dietary pattern			Mediterranean dietary pattern		
Category	T1	T2	T3	T1	T2	T3
Frequency (*N*)	269	269	268	269	269	268
Mean baseline STICS-M score (range 0–41) (SD)	34.0 (2.6)	34.1 (2.3)	34.1 (2.2)	34.2 (2.4)	34.2 (2.5)	33.8 (2.3)
STICS-m score at year 6 (SD)	35.1 (2.8)	35.2 (2.8)	35.1 (2.5)	35.2 (2.7)	35.2 (2.6)	35.1 (2.8)
Age at time of baseline STICS-m (years) (SD)	67.3 (5.5)	66.4 (5.1)	67.0 (5.4)	67.0 (5.1)	66.5 (5.1)	67.2 (5.8)
Time until baseline STICS-m evaluation (SD)	5.4 (2.7)	5.7 (2.6)	5.8 (2.6)	6.0 (2.4)	5.6 (2.7)	5.2 (2.7)
Women (%)	35.7	30.5	24.7	14.9	27.2	48.7
Years of university education (SD)	5.3 (1.8)	5.3 (1.9)	5.4 (1.9)	5.7 (2.0)	5.2 (1.7)	5.2 (1.9)
APOE 4 dominant model (%)	21.9	18.2	19.8	14.5	20.5	25.0
Total energy intake (kcal/day) (SD)	1698 (442)	2307 (476)	3055 (707)	2150 (726)	2211 (702)	2697 (805)
Body mass index (kg/m^2) (SD)	25.8 (3.2)	25.7 (3.1)	25.8 (3.0)	26.2 (2.9)	25.7 (3.0)	25.3 (3.3)
Physical activity in METS-h/week (SD)	27.4 (20)	28.0 (23)	29.0 (25)	25.4 (21)	28.7 (23.3)	30.4 (23.8)
Alcohol (g/day) SD	5.7 (7.5)	8.8 (11.0)	14 (17.0)	13.2 (17.0)	8.3 (10.4)	7.1 (9.5)
Smoking (%)						
Never	34	29	33	26	32	38
Current	17	20	14	21	16	14
Former	46	48	48	49	50	43
Cumulative package-years smoked (SD)	15.3 (17)	15.2 (16)	15.0 (16)	17.2 (17)	14.0 (15)	14.4 (17)
Prevalent depression (%)	20.1	13.4	15.0	19.0	13.0	16.8
Prevalent atrial fibrillation (%)	4.8	3.7	3.4	2.6	3.7	5.6
Prevalent hypertension (%)	42.0	33.1	39.2	36.4	34.9	43.9
Prevalent cholesterol >200 mg/dl (%)	60.6	58.0	44.0	47.2	55.4	60.1
Prevalent HDL <35 mg/dl (%)	4.5	5.2	4.9	6.7	4.5	3.4
Prevalent cardiovascular disease (%)	11.5	4.8	4.9	6.0	6.3	9.0
Prevalent type 2 diabetes (%)	12.3	6.7	5.2	6.7	11.5	6.0

cholesterol (p value = 0.001), cardiovascular disease (p value = 0.002), and type 2 diabetes at recruitment (p value = 0.01). There seemed to be a lower prevalence of APOE ε4 in T2 and T3 of the WDP and a higher level of physical activity (measured in METS per hour in a week); however, these findings were not statistically significant (p value = 0.56 and ANOVA p value = 0.7, respectively).

Participants with higher adherence to the MDP were significantly more likely to be female (p value < 0.001), have more years of university education (ANOVA p value = 0.002), have a higher total energy consumption (but lower than those with high adherence to the WDP, ANOVA p value < 0.001), higher level of physical activity (ANOVA p value = 0.04), lower alcohol intake (ANOVA p value < 0.0001) and smoking (p value = 0.04), lower BMI (ANOVA p value = 0.005) and higher prevalence of high total cholesterol (p value = 0.01), diabetes type 2 (p value = 0.04), and APOE ε4 (p value = 0.01) at recruitment. There was no significantly higher prevalence of cardiovascular disease (p value = 0.334), or atrial fibrillation with higher adherence to the MDP (p value = 0.2).

Dietary patterns and cognitive function

The results of the linear regression models are shown in Table 3. The point estimates of the regression coefficients for the WDP, showing the differences in the change in 6-year STICS-m for tertile 3 and 2 as compared to changes in tertile 1, were entirely negative. The comparison between the highest tertile of adherence compared to lowest adherence to the WDP in model 2 was associated with greater cognitive loss after 6 years ($\beta = -0.80$, 95% confidence interval [CI] –1.51, –0.08, p value = 0.03). The linear trend tests were only statistically significant model 2. This suggests a detrimental association between higher adherence to the WDP and cognitive function.

Conversely, for the MDP, the regression coefficients were entirely positive and the p values for linear trend tests were statistically significant for both models. This finding supports a beneficial association between better baseline adherence to the exploratory DP labeled as an MDP and cognitive performance, indicating a better preservation of cognitive functions. In model 2, the comparison between

Table 3 Multivariable adjusted mean changes in baseline to 6-year STICS-m scores, according to tertiles of adherence to WDP and MDP ($n = 803$).

	T1	T2	T3	p for trend
	Mean change in T1	Adjusted differences vs T1		
WDP				
Model 1	1.18	–0.24 (–0.72, 0.24)	–0.22 (–0.70, 0.26)	$p = 0.41$
Model 2	[0 (ref.)]	–0.49 (–1.03, 0.05)	–0.80 (–1.51, –0.08)*	$p = 0.03$
MDP				
Model 1	0.97	0.08 (–0.40, 0.57)	0.52 (0.01, 1.03)**	$p = 0.04$
Model 2	[0 (ref.)]	0.16 (–0.34, 0.66)	0.71 (0.15, 1.26)$^{¥}$	$p = 0.01$

Model 1 is adjusted for age at time of baseline STICS-m, sex, follow-up time until baselines STICS-m, years of university education, and APOE 4 (dominant model (yes/no).

Model 2 is adjusted for variables in model 1 and additionally for a quadratic term for age at time of baseline STICS-m, smoking (categories of: never, former, smoker and missing, and number of package-years), total energy intake (in kcal/day), physical activity (in METS-h/day), body mass index (height/m^2), alcohol intake (g per day), prevalent disease at time of recruitment [depression, hypertension, high cholesterol (>200 mg/dl), low HDL cholesterol (<35 mg/dl), cardiovascular disease, type 2 diabetes, and atrial fibrillation].

WDP Western dietary pattern, *MDP* Mediterranean dietary pattern.

$^*p = 0.03$, $^{**}p = 0.05$, $^{¥}p = 0.012$.

highest and lowest adherence was compatible with an almost 1-point difference in STICS-m ($\beta = 0.71$, 95% CI 0.15, 1.26, p value = 0.012).

As can be seen in the table, there is a substantial change between coefficients in model 1 and model 2 (for example, 73% change for the comparison between tertile 3 vs tertile 1 for the WDP). After a stepwise analysis, we found that adjustment for total energy intake and alcohol consumption accounted for most of the change of coefficients in the analyses of the WDP. Adjustment for alcohol intake was responsible for the largest change in coefficients when assessing the MDP.

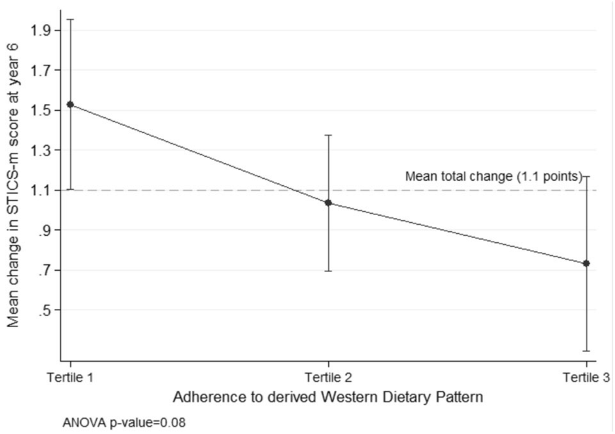

Fig. 1 Adjusted mean change in STICS-m score at year 6 for each tertile of the exploratory Western dietary pattern. Adjusted for age at time of baseline STICS-m (linear and quadratic term), sex, follow-up time until baselines STICS-m, years of university education, and APOE 4 (dominant model (yes/no), total energy intake (kcal/day), body mass index (kg/m^2), physical activity (METs-h/week), smoking (categories of non-smoker, former and current smoker, and number of package-years), alcohol intake (g/day), prevalent cardiovascular risk factors at recruitment (hypertension, high total cholesterol >200 mg/dL, low HDL cholesterol <35 mg/dL, and type 2 diabetes), and prevalent disease at recruitment (depression, atrial fibrillation, or cardiovascular disease).

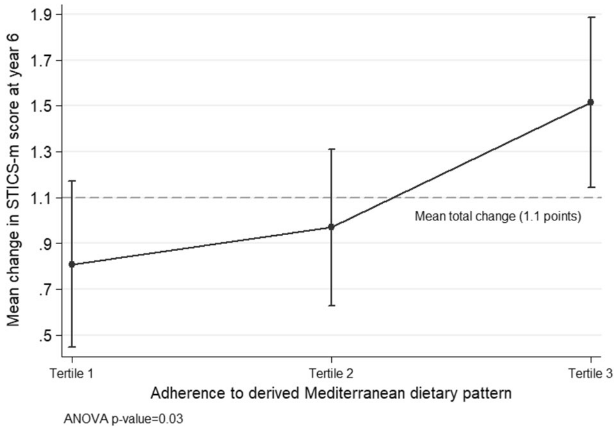

Fig. 2 Adjusted mean change in STICS-m score at year 6 for each tertile of the exploratory Mediterranean dietary pattern. Adjusted for age at time of baseline STICS-m (linear and quadratic term), sex, follow-up time until baselines STICS-m, years of university education, and APOE 4 (dominant model (yes/no), total energy intake (kcal/day), body mass index (kg/m^2), physical activity (METs-h/week), smoking (categories of non-smoker, former and current smoker, and number of package-years), alcohol intake (g/day), prevalent cardiovascular risk factors at recruitment (hypertension, high total cholesterol >200 mg/dL, low HDL cholesterol <35 mg/dL, and type 2 diabetes), and prevalent disease at recruitment (depression, atrial fibrillation, or cardiovascular disease).

The total mean change in STICS-m was 1.1 (±2.9) points. Figures 1 and 2 show the adjusted mean change for each tertile of adherence to the WDP and MDP, respectively. Figure 1 shows the decrease in mean change between tertile 1 and tertiles 2 and 3 for the WDP. Figure 2 shows, conversely, the increase in mean change across tertiles for the MDP. Furthermore, the sensitivity analysis with the elimination of three participants with >3.5 SD change in the STICS-m after 6 years ensued similar results, although the results for the WDP in model 2 were no longer statistically significant. The table with the results for the sensitivity analysis can be found in Supplementary Table 2.

Discussion

The principal component analysis performed in this sub-study of the SUN project yielded two main distinct exploratory DP. The first DP resembled a WDP, characterized by high sugar, high fat, and processed foods with red meat as the main source of protein [26]. The second DP was related to an MDP, a plant-based diet with olive oil as the principal source of fat and high consumption of fish, differing mostly from the traditional concept of a Mediterranean diet in the moderate consumption of red wine (usually present in definitions of the Mediterranean diet) [27]. High adherence to the derived WDP was associated with a significant negative change in STICS-m scores after 6 years of follow-up, when compared to those with lowest adherence. Conversely, high adherence to the derived MDP was associated with a significant positive change in STICS-m scores after 6 years, when compared to those with lowest adherence. Thus, an MDP appears to be beneficial toward preserving cognitive function while a WDP appears to be detrimental.

The evidence that supports the harmful effects on cardiovascular disease of a WDP is strong [28]. The negative association ostensibly extends to cognitive function and dementia. Similar observational studies with exploratory DP have shown that a Western-type DP was associated with higher declines in Mini-Mental State Examination scores in a Swedish population [14, 15], and higher decline in executive and visuospatial function domains in an Australian population [16]. Further studies associate high-sugar consumption with worse cognitive function [29], and high saturated fat diets with a higher incidence of dementia [30]. Our results are compatible with a deleterious effect of a WDP on cognitive function.

On the contrary, there is solid evidence that an MDP is beneficial for cognitive function, shown in systematic reviews of both observational and experimental studies [8, 13]. Most investigations have used "a priori"-derived DP with significant heterogeneity in the scales used for evaluation of adherence to the MDP [31]. Nonetheless, empirically derived DP that show a prudent profile (high in vegetables, fruits, whole grains, low-fat dairy and fish consumption), closely related to the MDP except for the high consumption of olive oil, have been associated with better cognitive performance [14–16].

The mechanisms through which the WDP can be damaging toward cognitive function can be indirect or direct. Experimental studies in animals, and fewer in healthy human controls, demonstrate how high sugar and fat diets specifically impair memory-related functions through damage to the hippocampus [32]. The mechanisms include inflammation, decrease of brain-derived neurothrophic factor, and alteration of the integrity of the blood–brain barrier, which increases the level of circulating pathogens that reach the brain. Damage to the hippocampus also restricts appetite control circuits, leading to higher consumption of harmful foods [33].

Indirect mechanisms include alterations of the gut microbiome that modify intestinal permeability, leading to increased circulation of inflammatory cytokines and bacteria endotoxins that impair the blood–brain barrier and lead to hippocampal dysfunction. Furthermore, gut microbiome alterations seem to be correlated with altered brain vascular physiology and structure, also contributing to neurodegenerative diseases [34]. Finally, WDP have been shown to increase the prevalence of modifiable risk factors of dementia, such as hypertension, obesity, depression, or diabetes [5, 28].

In contrast, a Mediterranean or prudent diet can positively influence modifiable cardiovascular risk factors, decreasing the probability of developing dementia [5, 35]. In addition, specific anti-inflammatory and antioxidant properties, as well as positive microbiome effects, have also been attributed to the Mediterranean diet [34]. Previous studies have evaluated the direct effect of the Mediterranean diet on brain structure, suggesting that this diet protects against brain tissue loss [36].

At the center of the beneficial properties of the MDP is the olive oil consumption, the main source of monounsaturated fatty acids, polyphenols, and other antioxidants [35]. Polyphenols, also found in fruits, vegetables, tea, and red wine, have been shown to modulate tau hyperphosphorylation and beta amyloid aggregation in animal models of Alzheimer's disease [37]. An important distinction between our derived MDP and the traditional definition of the MDP is the moderate consumption of red wine [27]. Moderate alcohol consumption (6 g/day), especially wine, has been associated with modest improvements in cognitive function [38]. Further studies have found no biological explanation for the probable protective effect of alcohol consumption [39]. In our study the beneficial properties of the MDP is independent of total alcohol consumption.

There are several limitations that constrain the conclusions of this study. First, the sample is not representative of a population at risk of developing dementia due to its high educational level and associated middle-high socioeconomic status. However, we focused our objective on the biological effect of diet, not on the generalizability of our results, and restriction to participants with a higher educational level partly removes confounding by these two factors. Second, the measure of exposure through the FFQ is self-reported and the measure of the outcome through the STICS-m has a degree of measurement error, both of which may lead to misclassification. Both the FFQ and STICS-m, however, have been previously validated in Spanish participants [20, 21]. Furthermore, the STICS-m is a screening test and, thus, an imperfect measure of cognition from which we cannot derive definite diagnosis of MCI or dementia. However, our work is focused on analyzing the impact of DP on ageing-related changes in cognition but not on MCI or dementia risk per se. This may be addressed in a future study on the same cohort after a longer follow-up period.

In addition, repeated measures of the STICS-m can lead to a "practice effect," as scores increase in successive evaluations, which was observed in our sample. This phenomenon can be found in both cognitively normal and impaired persons, which is why we focus on analysis of change in cognitive function. A recent review demonstrates how lower practice effects are consistently associated with current or future diagnosis of cognitive impairment [40]. We find it significant that we observed a negative change after 6 years with higher adherence to the WDP, even as the absolute mean overall change for the sample was positive. In this regard, a "practice effect" cannot be precluded given the repeated testing of our participants. Finally, derivation of exploratory DP involves arbitrary decisions based on data, which may need additional confirmatory analysis [10]. However, similar derived DP have been extracted from this cohort in other studies and have been found in previous investigations [23].

Apart from our efforts to counter possible limitations, the strengths of our study include the long period of follow-up and the extensive data obtained from each participant, which allowed adjustment for many potential confounders. Moreover, the repeated cognitive evaluation completed years after the recruitment questionnaire reduces the possibility of reverse causation bias and allows for a period of latency between dietary exposure and cognitive outcomes.

To conclude, the results of our study imply that an MDP may be beneficial toward cognitive function and a WDP could be harmful toward neurological health, which is both consistent with previous literature and biologically plausible. Thus, promoting a Mediterranean-style pattern and encouraging straying away from a Western-style diet could decrease dementia incidence. Messages such as this could be included in future dietary recommendations and aid in decreasing the impact of an ageing population. Further studies could focus on how to make a Mediterranean-style diet more accessible and a Western-style diet less readily available.

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Author contributions MAM-G and ET designed research, MIM-G did the literature search and wrote the first draft. MIM-G, ET, and CR were responsible for data analysis. MAM-G, CR, and ET were responsible of conducting research. MAM-G, ET, and CR had primary responsibility for final content. MF-M and FG-G, together with the other authors, contributed to data interpretation and critical review of the manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

Ethical approval To obtain informed consent, we suitably informed the candidates of their right to refuse to participate in the SUN study or to withdraw their consent at any time without reprisal, according to the Declaration of Helsinki. Their voluntary completion of the baseline questionnaire was understood as freely given informed consent. Participants in the cognitive function subproject provided a specific written informed consent. These methods were accepted by the Institutional Review Board of the University of Navarra.

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