Olive Oil and Cognition: Results from the Three-City Study

Claudine Berr^{a, b} Florence Portet^{a, b} Isabelle Carrière^a
Tasnim N. Akbaraly^{a, f} Catherine Feart^c Véronique Gourlet^d Nicole Combe^e
Pascale Barberger-Gateau^c Karen Ritchie^a

^aINSERM U888, Université Montpellier 1 and ^bCHU Montpellier, CMRR Languedoc Roussillon, Montpellier,

^cINSERM U897, Université Bordeaux 2, Bordeaux, ^dINSERM U708, Université Paris 6, Paris, and

^eITERG, Département de Nutrition & Santé, Université Bordeaux 1, Talence, France; ^fDepartment of Epidemiology and Public Health, University College London, London, UK

Key Words

Olive oil • Fatty acids • Cognition-dementia

Abstract

Background: Olive oil is a major component of the Mediterranean diet suggested to be beneficial to counteract Alzheimer's disease. **Aim of the Study:** Our objective was to examine the association between olive oil use, cognitive deficit and cognitive decline in a large elderly population. **Methods:** We followed 6,947 subjects with a brief baseline food frequency questionnaire and repeated cognitive tests. Olive oil intake was categorized as none (22.7%), moderate (use for cooking or dressing, 39.9%) and intensive (use for both cooking and dressing, 37.4%). Associations between olive oil and cognitive outcomes were examined taking into account socio-economic factors, health behaviors, health measures and other dietary intakes. **Results:** Participants with moderate or intensive use of olive oil compared to those who never used olive oil showed lower odds of cognitive deficit for verbal fluency and visual memory. For cognitive decline during the 4-year follow-up, the association with intensive use was significant for visual memory (adjusted OR = 0.83, 95% CI: 0.69–0.99) but not for verbal fluency (OR = 0.85, 95% CI: 0.70–1.03) in multivariate analysis. **Conclusions:** This olive

oil-cognition association needs to be confirmed by further studies. However, our findings already shed light on the potential importance of olive oil in the Mediterranean diet and on its beneficial effects on health.

Copyright © 2009 S. Karger AG, Basel

Introduction

A recent meta-analysis showed that a greater adherence to the Mediterranean diet was associated with lower overall mortality, mortality from cancer and cardiovascular diseases [1]. In 2006, in a northern Manhattan cohort, findings on overall diet and cognition suggest that high adherence to the Mediterranean diet decreases the risk of cognitive decline and Alzheimer's disease (AD) in a non-demented elderly population [2] and decreases the risk of mortality in AD patients [3]. More recently in the same cohort, higher adherence to the Mediterranean diet was associated with a trend for reduced risk of developing mild cognitive impairment (MCI) and with reduced risk of MCI conversion to AD [4]. Furthermore, when investigating the combined association of diet and physical activity [5], it showed that both factors are independently associated with a reduced risk for AD. In a subsample of

1,410 subjects included in the Three-City Bordeaux cohort [6] with 5-year follow-up after a 24-hour dietary recall, higher adherence to Mediterranean diet was not associated with the risk for incident dementia but was associated with a slower MMSE cognitive decline. In an associated editorial, Knopman [7] suggests that the Mediterranean diet may act on cognition through cerebrovascular mechanisms or by affecting the metabolism of the β -amyloid or the tau protein and that the effects may be brought about by some components of the Mediterranean diet.

The so-called Mediterranean diet is characterized by a high intake of vegetables, legumes, fruits and cereals, a moderate to high intake of fish, a high monounsaturated-to-saturated fatty acids ratio and a low intake of dairy products and meat [8]. While several studies have focused on the association between intake of fruits and vegetables or fish and cognitive outcomes or on other dietary habits which have been previously associated with dementia or cognitive decline (fish or omega-3 oil, fruits and vegetables) [9–20], little is known about the association between olive oil, a major component of the Mediterranean diet, and cognitive functioning.

Thus, our objective is to examine this association in a large population-based study of persons aged >65 years with a 4-year follow-up of cognitive functioning.

Methods

Participants

The Three-City (3C) study is a multi-centre cohort study, conducted in 3 French cities – Bordeaux (South-West), Montpellier (South-East), and Dijon (North-East) – and designed to estimate the risk of dementia and cognitive impairment attributable to vascular factors. Persons eligible for recruitment into the study had to be (i) living in these cities or their suburbs and registered on the electoral rolls, (ii) aged 65 years and over, and (iii) not institutionalized. Between March 1999 and March 2001, 9,294 individuals randomly drawn from electoral rolls agreed to participate in this project. The practical organization of the different components of the data collection varied slightly between centres and during follow-up. Participants were invited to the study examination centre or in a mobile center in a specially equipped vehicle or examined and interviewed at home. The detailed description of the study protocol has been published elsewhere [21]. The study protocol was approved by the Ethics Committee of the University Hospital of Kremlin-Bicêtre. Each participant signed an informed consent.

Following the screening procedure described below, we excluded 217 participants with prevalent dementia at baseline. The initial study sample was thus composed of 9,077 participants. At the second round of the 3C study (2001–2002), 7,919 (87.2%) were examined again, 217 were deceased, and 941 refused or were lost

to follow-up. At the third round (2003–2004), 7,053 were examined (79.6% of the survivors after the second round), the cumulated number of deaths was 551, and 1,473 refused or were lost to follow-up. A total of 8,083 (89.1%) participants had at least one follow-up examination over the 4 years. Of these 8,083 subjects, 1,136 did not have a dietary questionnaire ($n = 55$) or one of the covariates, leaving 6,947 subjects for statistical analysis (of which 86.0% had made 2 visits).

Dietary Assessment

A brief food frequency questionnaire (FFQ) was administered at baseline to assess the dietary habits of the participants for 9 broad categories of food: (1) meat and poultry, (2) fish (including seafood), (3) eggs, (4) milk and dairy products, (5) cereals (including bread and starches), (6) raw fruits, (7) raw vegetables, (8) cooked fruit or vegetables, and (9) pulses. Frequency of consumption was recorded in 6 classes: never, less than once a week, once a week, 2–3 times a week, 4–6 times a week, or daily. Dietary habits of the sample have been described elsewhere [22]. Participants were also invited to indicate the dietary fats that they used at least once a week for dressing, cooking, or spreading among the following list: butter, margarine, corn oil, peanut oil, sunflower or grape seed oil, olive oil, mixed oil, duck or goose fat, lard, 'Vegetaline'® shortening (mainly saturated fat), colza oil, walnut oil, soya oil. Three categories of olive oil consumption were then defined: 'no use', 'moderate use': using olive oil for cooking or dressing alone or 'intensive' use: using olive oil both for cooking and dressing.

Neuropsychological Evaluation

The cognitive tests were administered by trained psychologists at baseline and then regularly repeated during the 4 years of follow-up. The 30-item Mini Mental State Examination (MMSE) [23] was used as an index of global cognitive performance. The recognition form of the Benton Visual Retention Test (BVRT), which evaluates immediate visual memory, consists in the presentation of a stimulus card displaying a geometric figure for 10 s after which individuals are asked to identify the initial figure among 4 possibilities [24]. Fifteen figures are successively presented and scores range from 0 to 15. The Isaacs Set Test (IST) [25], consisting of generating words belonging to semantic categories in 30 s, measured mostly semantic verbal fluency abilities but also speed of verbal production.

Deficit in global cognitive functioning, visual memory and verbal fluency were defined respectively by a score below the first quartile of its distribution: 26 for the MMSE, 10 for the BVRT and 40 for the IST. Cognitive decline was defined as being in the lowest 15% of the difference between baseline score and either follow-up visit for the 3 tests assessed at each wave, corresponding to a loss of 3 points on the MMSE score, 9 points on IST and 3 points on BVRT. Diagnosis of prevalent cases of dementia at baseline and incident cases during the follow-up was based on a 3-step procedure, with an independent committee of neurologists reviewing all potential cases of dementia, and is fully detailed elsewhere [21, 26].

Covariates

Socio-demographic information recorded at baseline include age, gender, marital status, educational level (no or primary/secondary/high school/university) and income level per month (EUR <750, 750–1,500, 1,500–2,250, >2,250). Health behaviours were assessed by smoking status (non/former/current) and diet. Di-

etary habits include intake of fish/seafood (< once a week, once a week, $\geq$ twice a week), fruits and vegetables (<2 portions/day, 2 portions/day, $\geq$ 3 portions/day), intake of wine or other alcoholic beverages per week (0, 1–12, 13–36, >36 g/day), coffee consumption ($\leq$ 2 cups/day, 2–3 cups/day, >3 cups/day) and regular consumption (yes/no) of at least one oil rich in omega-3 polyunsaturated fatty acids (PUFA) (colza, walnut or soya oils). Health factors include history of cardiovascular diseases (yes/no), hypertension (defined as having systolic blood pressure $\geq$ 160 mm Hg or diastolic blood pressure $\geq$ 85 mm Hg or use of antihypertensive drugs) [27], diabetes (fasting glycaemia $\geq$ 7.0 mmol/l or having an anti-diabetic treatment), hypercholesterolemia (total plasma cholesterol $\geq$ 6.20 mmol/l or use of lipid-lowering drugs), and body mass index (BMI) categorised in 3 classes [normal (<25), overweight (25–30) and obese ($\geq$ 30)]. Depressive symptoms were assessed using the cut-off at 16 points on the Center for Epidemiological Studies-Depression scale (CES-D) [28]. Apolipoprotein E (APOE) genotype (at least 1 vs. no ϵ 4 allele) was also available and was carried out at the Lille Genopole.

Statistical Analyses

Differences in baseline characteristics according to olive oil consumption categories were tested using χ^2 tests. Logistic regression analyses were performed to estimate (1) the cross-sectional association between olive oil consumption and cognitive deficit at baseline and (2) the longitudinal association between olive oil consumption and cognitive decline during the follow-up. In these analyses, the adjustments for covariates were carried out in 3 steps. The basic model, model 0, was adjusted for sex, age, study centre, educational level, income and baseline cognitive score. Health behaviour and health status variables were added in model 1. Smoking status and dietary habits were further added in model 2. Interactions between olive oil consumption and covariates included in model 0 were tested and found to be non-significant.

Finally, a sensitivity analysis was carried out. The association between olive oil intake and cognitive decline was re-examined after excluding the 4-year incident dementia cases, as dietary changes or inaccurate reporting among demented participants are common. The results of logistic regression were expressed by odds ratios (OR) with their 95% confidence intervals (CI). Analyses were carried out using SAS software (version 9.1).

Results

Participants with at least one follow-up, with no diagnosis of dementia at baseline and for whom complete data on all covariates at baseline were available were included in this analysis ($n = 6,947$). Compared with those excluded ($n = 2,130$), participants included in the analyses were likely to be younger, with higher educational level and higher income. Controlling for these factors, a lower proportion of non-users of olive oil and of subjects with poor baseline cognitive functioning was observed in participants included compared to those excluded (online supplement 1, www.karger.com/doi/10.1159/000253483).

Fig. 1. Distribution of olive oil use according to level of education.

Baseline characteristics of the 6,947 participants as a function of olive oil consumption are described in table 1. Among them, 1,576 subjects declared no olive oil use (22.7% of total sample), 2,772 declared moderate use (39.9%) only for cooking (5.8%) or dressing (34.1%), and 2,599 both for cooking and dressing (intensive use, 37.4%).

Many factors were associated with olive oil use. The particular place of education is illustrated in figure 1. More educated participants were more likely to consume olive oil compared to less educated ones.

Cross sectional association between olive oil consumption and cognitive deficit at baseline is shown in figure 2, which presents odds ratio obtained with logistic regression (model 2). Compared to those who never used olive oil, participants with a high or moderate consumption of olive oil showed significantly lower odds of cognitive deficit in visual memory and verbal fluency while no significant association was shown for global cognitive functioning.

Table 2 shows the longitudinal association between olive oil consumption and cognitive decline. After adjustment for age, sex, centre, education, income and baseline cognitive score (model 0), participants who intensively used olive oil showed lower odds of cognitive decline in verbal fluency and visual memory compared to those who did not. No significant association was observed for global cognitive functioning. Further adjustment for health status (model 1) had little effect on these associations. When additionally controlling for dietary habits

Table 1. Baseline characteristics of the 6,947 participants as a function of olive oil use

	n	Non-use %	Moderate use (cooking or dressing), %	Intensive use (both cooking and dressing), %	χ^2 test p ¹		n	Non-use %	Moderate use (cooking or dressing), %	Intensive use (both cooking and dressing), %	χ^2 test p ¹
Sex						APOE ϵ 4 carrier					
Men	2,755	23.2	39.9	36.9	0.69	No	5,582	22.8	40.1	37.1	0.59
Women	4,192	22.4	39.9	37.7		Yes	1,365	22.3	39.1	38.6	
Age						Alcohol, g/day					
65–69	1,778	17.5	41.7	40.8	<0.0001	0	1,375	29.6	39.4	31.0	<0.0001
70–74	2,334	22.0	39.3	38.7		1–12	3,141	20.8	39.9	39.3	
75–80	1,860	25.2	39.3	35.5		13–36	1,843	20.0	41.1	38.9	
80+	975	29.2	39.1	31.7		>36	588	25.0	37.4	37.6	
Education						Coffee, cups/day					
No or primary	1,654	28.9	38.2	32.9	<0.0001	<2	4,784	23.6	39.8	36.5	0.005
Secondary	2,510	24.5	40.2	35.3		2–3	1,449	21.5	40.9	37.6	
High school	1,419	18.5	40.8	40.7		>3	714	18.8	38.4	42.9	
University	1,364	16.1	40.5	43.4							
City						Fish					
Bordeaux	1,416	33.0	38.1	28.9	<0.0001	Less than once/week	782	33.6	36.7	29.7	<0.0001
Dijon	3,716	25.7	36.2	38.1		Once/week	2,630	28.4	39.8	31.8	
Montpellier	1,815	8.4	48.9	42.7		Twice or more/week	3,535	16.0	40.7	43.3	
Marital status						Fruits and vegetables					
Married	4,128	20.4	40.6	39.0	<0.0001	Less than twice/day	2,000	29.6	37.4	33.0	<0.0001
Divorced	515	20.8	37.9	41.3		Twice/day	2,549	22.3	39.6	38.1	
Widowed	1,774	27.2	39.0	33.8		3 times or more/day	2,398	17.3	42.4	40.3	
Single	495	28.7	38.2	33.1		Omega-3 oil					
Other	30	10.0	50.0	40.0		No	6,586	23.0	39.8	37.2	
Monthly income, EUR						Yes	361	17.5	42.1	40.4	0.05
<750	336	39.0	34.8	26.2	<0.0001	Butter					
750–1,500	2,122	28.6	39.0	32.4		No	2,633	21.6	40.3	38.1	0.24
1,500–2,250	1,976	21.9	40.2	37.9		Yes	4,314	23.3	39.6	37.0	
>2,250	2,513	16.1	41.1	42.8		Goose and duck fat					
Depressive symptoms						No	6,727	22.7	39.9	37.4	0.63
<16	5,369	22.2	40.3	37.5	0.18	Yes	220	20.0	41.4	38.6	
≥16	1,578	24.3	38.6	37.1		Corn oil					
Cardiovascular disease						No	6,762	22.7	39.6	37.7	0.008
No	6,336	22.5	40.0	37.5	0.45	Yes	185	21.6	50.3	28.1	
Yes	611	24.7	39.1	36.2		Peanut oil					
BMI						No	5,803	22.1	38.5	39.4	<0.0001
Normal	3,276	19.4	41.4	39.2	<0.0001	Yes	1,144	25.9	46.9	27.2	
Overweight	2,758	24.4	38.5	37.1		Sunflower oil					
Obese	913	29.1	38.9	32.0		No	3,665	16.5	35.8	47.7	<0.0001
Diabetes						Yes	3,282	29.5	44.5	26.0	
No	6,302	22.0	40.3	37.7	0.0003	MMSE baseline					
Yes	645	29.0	36.1	34.9		≥26	5,951	21.8	40.2	38.0	0.0002
Hypertension						<26	970	27.6	38.5	33.9	
No	3,044	19.9	40.7	39.4	<0.0001	IST 30 baseline ²					
Yes	3,903	24.9	39.3	35.8		>40	5,246	20.4	39.9	39.7	<0.0001
Hypercholesterolemia						≤40	1,624	29.9	39.9	30.2	
No	1,794	22.1	40.0	37.9	0.79	BVRT baseline ²					
Yes	5,153	22.9	39.9	37.2		>10	4,973	20.2	41.1	38.7	<0.0001
Smoking						≤10	1,893	28.8	37.3	33.9	
Never	4,230	22.7	39.9	37.4	0.08						
Former	2,339	22.0	39.6	38.5							
Current	378	26.7	42.1	31.2							

¹ p values are given for the global χ^2 test of heterogeneity. We have examined all comparisons between moderate use vs. no use and intensive use vs. no use.

For variables for which the heterogeneity test was significant at $p < 0.05$, all 2 by 2 comparisons were significant except when compar-

ing moderate use vs. no use for: coffee consumption ($p = 0.11$), corn oil use ($p = 0.13$), peanut oil ($p = 0.63$).

² Cut-off corresponding to the first quartile of the sample distribution.

Fig. 2. Cross-sectional association between olive oil use and cognitive deficit at baseline: risk of cognitive deficit in olive oil users expressed by the odds ratio value (OR) with its 95% CI calculated with logistic regression model (controlling for age, sex, centre, education, income, depressive symptoms, APOE4, cardiovascular disease, hypertension, diabetes, hypercholesterolemia, BMI, smoking status and dietary intake of fruits/vegetables, omega-3 oil, fish, coffee, and alcohol).

Table 2. Longitudinal association between olive oil consumption and cognitive decline

	Cognitive decline		Model 0		Model 1		Model 2	
	%	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Global cognitive functioning		0.37						
No use	14.9		1		1		1	
Moderate use	14.1		0.90 (0.74–1.08)	0.24	0.91 (0.76–1.10)	0.32	0.94 (0.78–1.13)	0.50
Intensive use	13.3		0.90 (0.74–1.09)	0.27	0.91 (0.75–1.10)	0.34	0.95 (0.78–1.15)	0.58
Verbal fluency		0.30						
No use	16.6		1		1		1	
Moderate use	15.7		0.93 (0.78–1.12)	0.47	0.95 (0.79–1.14)	0.55	0.96 (0.80–1.16)	0.69
Intensive use	14.8		0.83 (0.68–0.99)	0.04	0.83 (0.69–1.00)	0.05	0.85 (0.70–1.03)	0.10
Visual memory		0.01						
No use	21.4		1		1		1	
Moderate use	19.1		0.88 (0.75–1.05)	0.15	0.90 (0.76–1.07)	0.25	0.91 (0.77–1.09)	0.30
Intensive use	17.8		0.80 (0.68–0.96)	0.01	0.82 (0.69–0.97)	0.02	0.83 (0.69–0.99)	0.04

Model 0: Adjusted on age, sex, centre, education, income and baseline cognitive score.

Model 1: Model 0 plus depressive symptoms, APOE4, cardiovascular disease, hypertension, diabetes, hypercholesterolemia, BMI.

Model 2: Model 1 plus smoking status and dietary intake of fruits/vegetables, omega-3 oil, fish, coffee, and alcohol.

including omega-3 oil use (model 2), having an intensive olive oil use was associated with a nearly significant risk reduction of 15% in verbal fluency decline (OR = 0.85, 95% CI: 0.70–1.03) and with a significant risk reduction of 17% in visual memory decline (OR = 0.83, 95% CI: 0.69–0.99).

Sensitivity Analysis

To examine the possibility that the observed association may be due to dietary changes or inaccurate reporting among demented participants, we re-analysed the data after removing data for the 205 persons who developed incident dementia during the 4-year follow-up.

Odds of lower cognitive decline associated with intensive olive oil use remained similar to those presented for the whole sample (OR = 0.88, 95% CI: 0.72–1.08 for verbal fluency and OR = 0.82, 95% CI: 0.68–0.99 for visual memory).

Discussion

The present report shows in a large non-demented elderly population that olive oil consumption habits are significantly associated with selective cognitive deficit and cognitive decline, independently of other dietary intakes and after adjusting for potential confounders. Intensive use of olive oil in diet is associated with lower odds of cognitive deficit in visual memory and verbal fluency and decline in visual memory; however, the relationship is not significant when assessing global cognitive functioning with the MMSE.

Olive oil is a major component of the traditional Mediterranean diet. It has been suggested to have beneficial effect on coronary heart disease risk factors [29]. As cardiovascular risk factors have increasingly been shown to be important for dementia [30] and a greater adherence to the Mediterranean diet has been shown to reduce the incidence of Alzheimer's disease [2], it is of particular interest to investigate the association between olive oil consumption and cognitive decline in an elderly population. To our knowledge, this study is the first to investigate this relationship with olive oil in a follow-up study, thus making comparisons difficult.

Olive oil contains 70–80% of monounsaturated fatty acids (MUFA) [oleic acid (18:1 n-9)] and 8–10% of PUFA (6–7% linoleic acid and 1–2% α -linolenic acid) [31] with great variability depending on the production zone, latitude, climate, variety and stage of maturity of olives when collected [32]. Recent publications on diet in dementia have specifically focused on PUFA but few examine the association with MUFA intake. A Spanish cross-sectional study [33] showed that a lower intake of saturated fatty acids (SFA), MUFA and cholesterol was associated with a better cognitive performance. Cross-sectional analyses in the ILSA Italian cohort showed that MUFA intake was significantly associated with better global cognitive functions and selective attention [34]. More recently, a longitudinal analysis performed in the same cohort [18] showed that high MUFA and PUFA energy intakes were associated with a better cognitive performance in an 8.5-year follow-up. In the analyses of 732 participants of the EPIC Greek cohort [35], intake of olive oil, MUFA and SFA ex-

hibited a weak but not significant positive association with cognitive function as assessed by the MMSE, 6–13 years after enrolment. In this cohort, intake of PUFA was inversely associated with performance in the MMSE. Furthermore, four other studies have investigated the association between intake of omega-3 PUFA and cognition or dementia, giving conflicting results [9, 15–17].

However, olive oil is more than a MUFA fat. Olive oil is a functional food which, besides having a high level of MUFA, contains other minor components with biological properties [36] such as natural antioxidants including phenolic compounds. Most antioxidant compounds have been hypothesized to have a protective effect against dementia and cognitive impairment [37]. Selective antioxidants, including E vitamins, and flavonoids, may reduce neuronal damage and death from oxidative reactions by inhibiting the generation of reactive oxygen species, lipid peroxidation, apoptosis, protein oxidation, damage to cell membranes and/or DNA and β -amyloid toxicity or deposition [38, 39]. Numerous epidemiological studies have supported these hypotheses in relation to antioxidant nutrients [40–45]. However, at this stage, it is difficult to be more precise as to the mechanism by which olive oil exerts its beneficial effect on cognitive outcomes, and further studies are needed.

Our study has the following limitations. First, tests proposed in the 3C study covered a limited number of cognitive functions but the battery was prepared in order to screen for dementia cases and these tests have different metrological properties [46]. Due to ceiling effects, the BVRT is less appropriate to assess cognitive changes in subjects with very high cognitive level functioning but is rather sensitive to cognitive change in the low cognitive levels. The multiple-choice forms used in the 3C study allow assessment of visuospatial working memory – a memory system particularly vulnerable to aging [47]. The selective association between this test and olive oil consumption could be explained by its metrological properties, different from those of IST, rather than by a direct biological explanation, which is more speculative. Furthermore, even if non-significant in the final model, we also observed an association between verbal fluency performance and olive oil. The absence of a significant association with MMSE score may also be related to its skewed distribution.

Secondly, our dietary questionnaire is relatively short. We did not collect any information on portion size, thus, excluding any quantitative approach or adjustment on caloric intake. Nevertheless, this FFQ allowed us to characterize olive oil consumers in this aged population and

to control for other dietary habits which have been previously associated with dementia and cognitive decline (fish or omega-3 oil, fruits and vegetables) [9–20]. Even in a more detailed FFQ, there is a large degree of reporting error in energy intake (generally underreporting) which is strongly correlated with BMI and low socio-economic status. The best we could do, according to the type of data collected, was to adjust for consumption of fish, consumption of vegetables, BMI and socio-economic status. Our analyses were also adjusted for other health behaviour factors such as smoking status and alcohol intake; however, the lack of data on physical activities in the whole population constitutes another limitation of this study. Moreover, we cannot exclude that the beneficial effect of olive oil on cognitive decline shown in our cohort could actually be explained by the healthy dietary habits and healthy life habit behaviours associated with the regular consumption of olive oil. However, the analyses adjusted for dietary intake and for socio-economic status showed that these factors had little impact on the observed associations between olive oil use and cognitive deficit or decline. Similarly, it could also be argued that the use of olive oil may reflect the physical and cognitive ability of the participants to prepare one's own meals. Our adjusted analyses for numerous health factors and the results obtained in our sensitivity analyses carried out after excluding incident cases of dementia make this less probable, as similar associations were observed while the rates of decline were lower.

Finally, the design of our study – an observational epidemiological study – does not permit us to conclude that there is a causal link between use of olive oil and prevention of cognitive decline. However, the longitudinal and multi-centric design, the large sample size including

more than 8,000 elderly subjects from the general population, the high quality of cognitive assessment, the low rate of attrition of our cohort, and the full adjustment for the potential confounders constitute the major strengths of this report.

In conclusion, to the best of our knowledge, this is the first study to show that self-reported use of olive oil is associated with lower odds of visual memory decline in a large general elderly population independently of other dietary intakes and after taking into account potential confounders. Even if further research is needed to confirm our finding, our results highlight the importance of olive oil in the Mediterranean diet and in its beneficial effects on health outcome.

Acknowledgments

The 3C Study is conducted under a partnership agreement between the Institut National de la Santé et de la Recherche Médicale (INSERM), the Institut de Santé Publique et Développement of the Victor Segalen Bordeaux 2 University, and Sanofi-Aventis. The Fondation pour la Recherche Médicale funded the preparation and initiation of the study. The 3C Study is also supported by the Caisse Nationale Maladie des Travailleurs Salariés, Direction Générale de la Santé, Mutuelle Générale de l'Éducation Nationale, Institut de la Longévité, Regional Councils of Aquitaine and Bourgogne, Fondation de France, and Ministry of Research – INSERM Programme 'Cohortes et collections de données biologiques'. The Lille Genopole was supported by an unconditional grant from Eisai.

This work was carried out with the financial support of the 'ANR – Agence Nationale de la Recherche – The French National Research Agency' under the 'Programme National de Recherche en Alimentation et nutrition humaine', project COGINUT 'ANR-06-PNRA-005'.

References

- 1 Sofi F, Cesari F, Abbate R, Gensini GF, Casini A: Adherence to Mediterranean diet and health status: meta-analysis. *BMJ* 2008;337:a1344.
- 2 Scarmeas N, Stern Y, Tang MX, Mayeux R, Luchsinger JA: Mediterranean diet and risk for Alzheimer's disease. *Ann Neurol* 2006;59:912–921.
- 3 Scarmeas N, Luchsinger JA, Mayeux R, Stern Y: Mediterranean diet and Alzheimer disease mortality. *Neurology* 2007;69:1084–1093.
- 4 Scarmeas N, Stern Y, Mayeux R, Manly JJ, Schupf N, Luchsinger JA: Mediterranean diet and mild cognitive impairment. *Arch Neurol* 2009;66:216–225.
- 5 Scarmeas N, Luchsinger JA, Schupf N, Brickman AM, Cosentino S, Tang MX, Stern Y: Physical activity, diet, and risk of Alzheimer disease. *JAMA* 2009;302:627–637.
- 6 Feart C, Samieri C, Rondeau V, Amieva H, Portet F, Dartigues JF, Scarmeas N, Barberger-Gateau P: Adherence to a Mediterranean diet, cognitive decline, and risk of dementia. *JAMA* 2009;302:638–648.
- 7 Knopman DS: Mediterranean diet and late-life cognitive impairment: a taste of benefit. *JAMA* 2009;302:686–687.
- 8 Trichopoulou A, Kouris-Blazos A, Wahlqvist ML, Gnardellis C, Lagiou P, Polychronopoulos E, Vassilakou T, Lipworth L, Trichopoulos D: Diet and overall survival in elderly people. *BMJ* 1995;311:1457–1460.
- 9 Morris MC, Evans DA, Bienias JL, Tangney CC, Bennett DA, Wilson RS, Aggarwal N, Schneider J: Consumption of fish and n-3 fatty acids and risk of incident Alzheimer disease. *Arch Neurol* 2003;60:940–946.
- 10 Kalmijn S, Launer LJ, Ott A, Witteman JC, Hofman A, Breteler MM: Dietary fat intake and the risk of incident dementia in the Rotterdam study. *Ann Neurol* 1997;42:776–782.

- 11 Barberger-Gateau P, Letenneur L, Deschamps V, Peres K, Dartigues JF, Renaud S: Fish, meat, and risk of dementia: cohort study. *BMJ* 2002;325:932–933.
- 12 Huang TL, Zandi PP, Tucker KL, Fitzpatrick AL, Kuller LH, Fried LP, Burke GL, Carlson MC: Benefits of fatty fish on dementia risk are stronger for those without APOE epsilon4. *Neurology* 2005;65:1409–1414.
- 13 Barberger-Gateau P, Raffaitin C, Letenneur L, Berr C, Tzourio C, Dartigues JF, Alperovitch A: Dietary patterns and risk of dementia: the Three-City cohort study. *Neurology* 2007;69:1921–1930.
- 14 Barberger-Gateau P, Commenges D, Gagnon M, Letenneur L, Sauvel C, Dartigues JF: Instrumental activities of daily living as a screening tool for cognitive impairment and dementia in elderly community dwellers. *J Am Geriatr Soc* 1992;40:1129–1134.
- 15 Kalmijn S, Feskens EJ, Launer LJ, Kromhout D: Polyunsaturated fatty acids, antioxidants, and cognitive function in very old men. *Am J Epidemiol* 1997;145:33–41.
- 16 van Gelder BM, Tijhuis M, Kalmijn S, Kromhout D: Fish consumption, n-3 fatty acids, and subsequent 5-y cognitive decline in elderly men: the Zutphen Elderly Study. *Am J Clin Nutr* 2007;85:1142–1147.
- 17 Engelhart MJ, Geerlings MI, Ruitenberg A, Van Swieten JC, Hofman A, Witteman JC, Breteler MM: Diet and risk of dementia: does fat matter? The Rotterdam Study. *Neurology* 2002;59:1915–1921.
- 18 Solfrizzi V, Colacicco AM, D'Introno A, Capurso C, Torres F, Rizzo C, Capurso A, Panza F: Dietary intake of unsaturated fatty acids and age-related cognitive decline: a 8.5-year follow-up of the Italian longitudinal study on aging. *Neurobiol Aging* 2006;27:1694–1704.
- 19 Dai Q, Borenstein AR, Wu Y, Jackson JC, Larson EB: Fruit and vegetable juices and Alzheimer's disease: the Kame project. *The Am J Med* 2006;119:751–759.
- 20 Morris MC, Evans DA, Tangney CC, Bienias JL, Wilson RS: Associations of vegetable and fruit consumption with age-related cognitive change. *Neurology* 2006;67:1370–1376.
- 21 Three-City Study Group: Vascular factors and risk of dementia: design of the Three-City Study and baseline characteristics of the study population. *Neuroepidemiology* 2003;22:316–325.
- 22 Larrieu S, Letenneur L, Berr C, Dartigues JF, Ritchie K, Alperovitch A, Tavernier B, Barberger-Gateau P: Sociodemographic differences in dietary habits in a population-based sample of elderly subjects: the 3C Study. *J Nutr Health Aging* 2004;8:497–502.
- 23 Folstein MF, Folstein SE, McHugh PR: 'Minimal state'. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–198.
- 24 Amieva H, Gaestel Y, Dartigues JF: The multiple-choice formats (forms F and G) of the Benton Visual Retention Test as a tool to detect age-related memory changes in population-based studies and clinical settings. *Nat Protoc* 2006;1:1936–1938.
- 25 Isaacs B, Kennie AT: The Set test as an aid to the detection of dementia in old people. *Br J Psychiatry* 1973;123:467–470.
- 26 American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, ed 4. Washington DC, APA Press, 1994.
- 27 Brindel P, Hanon O, Dartigues JF, Ritchie K, Lacombe JM, Ducimetiere P, Alperovitch A, Tzourio C: Prevalence, awareness, treatment, and control of hypertension in the elderly. The Three-City Study. *J Hypertens* 2006;24:51–58.
- 28 Radloff LS: The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1977;1:385–401.
- 29 Psaltopoulou T, Naska A, Orfanos P, Trichopoulos D, Mountokalakis T, Trichopoulou A: Olive oil, the Mediterranean diet, and arterial blood pressure: the Greek European prospective investigation into cancer and nutrition (EPIC) study. *Am J Clin Nutr* 2004;80:1012–1018.
- 30 Kivipelto M, Helkala EL, Laakso MP, Hanninen T, Hallikainen M, Alhainen K, Soininen H, Tuomilehto J, Nissinen A: Midlife vascular risk factors and Alzheimer's disease in later life: longitudinal, population based study. *BMJ* 2001;322:1447–1451.
- 31 Solfrizzi V, D'Introno A, Colacicco AM, Capurso C, Del Parigi A, Capurso S, Gadaleta A, Capurso A, Panza F: Dietary fatty acids intake: possible role in cognitive decline and dementia. *Exp Gerontol* 2005;40:257–270.
- 32 Boskou D: Olive oil; in Simopoulos A, Visioli F (eds): *Mediterranean Diets*. Basel, Karger, 2000, vol 87, pp 56–77.
- 33 Ortega RM, Requejo AM, Andres P, Lopez-Sobaler AM, Quintas ME, Redondo MR, Navia B, Rivas T: Dietary intake and cognitive function in a group of elderly people. *Am J Clin Nutr* 1997;66:803–809.
- 34 Solfrizzi V, Panza F, Torres F, Mastroianni F, DelParigi A, Venezia A, Capurso A: High monounsaturated fatty acids intake protects against age-related cognitive decline. *Neurology* 1999;52:1563–1569.
- 35 Psaltopoulou T, Kyrozis A, Stathopoulos P, Trichopoulos D, Vassilopoulos D, Trichopoulou A: Diet, physical activity and cognitive impairment among elders: the EPIC-Greece cohort (European Prospective Investigation into Cancer and Nutrition). *Public Health Nutr* 2008;11:1054–1062.
- 36 Covas MI: Olive oil and the cardiovascular system. *Pharmacol Res* 2007;55:175–186.
- 37 Gillette Guyonnet S, Abellan Van Kan G, Andrieu S, Barberger Gateau P, Berr C, Bonnefoy M, Dartigues JF, de Groot L, Ferry M, Galan P, Hercberg S, Jeandel C, Morris MC, Nourhashemi F, Payette H, Poulain JP, Portet F, Roussel AM, Ritz P, Rolland Y, Vellas B: IANA task force on nutrition and cognitive decline with aging. *J Nutr Health Aging* 2007;11:132–152.
- 38 Floyd RA, Hensley K: Oxidative stress in brain aging. Implications for therapeutics of neurodegenerative diseases. *Neurobiol Aging* 2002;23:795–807.
- 39 Akwa Y, Allain H, Bentue-Ferrer D, Berr C, Bordet R, Geerts H, Nieoullon A, Onteniente B, Vercelletto M: Neuroprotection and neurodegenerative diseases: from biology to clinical practice. *Alzheimer Dis Assoc Disord* 2005;19:226–239.
- 40 Engelhart MJ, Geerlings MI, Ruitenberg A, van Swieten JC, Holman A, Witteman JCM, Breteler MMB: Dietary intake of antioxidants and risk of Alzheimer disease. *JAMA* 2002;287:3223–3229.
- 41 Morris MC, Evans DA, Bienias JL, Tangney CC, Bennett DA, Aggarwal N, Wilson RS, Scherr PA: Dietary intake of antioxidant nutrients and the risk of incident Alzheimer disease on a biracial community study. *JAMA* 2002;287:3230–3237.
- 42 Zandi PP, Anthony JC, Khachaturian AS, Stone SV, Gustafson D, Tschanz JT, Norton MC, Welsh Bohmer KA, Breitner JCS: Reduced risk of Alzheimer disease in users of antioxidant vitamin supplements: the Cache County Study. *Arch Neurol* 2004;61:82–88.
- 43 Akbaraly NT, Hininger-Favier I, Carrière I, Arnaud J, Gourlet V, Roussel AM, Berr C: Plasma selenium over time and cognitive decline in the elderly. *Epidemiology* 2007;18:52–58.
- 44 Akbaraly NT, Faure H, Gourlet V, Favier A, Berr C: Plasma carotenoid levels and cognitive performance in an elderly population: results of the EVA study. *J Gerontol A Biol Sci Med Sci* 2007;62:308–316.
- 45 Letenneur L, Proust-Lima C, Le Gouge A, Dartigues J, Barberger-Gateau P: Flavonoid intake and cognitive decline over a 10-year period. *Am J Epidemiol* 2007;165:1364–1371.
- 46 Proust-Lima C, Amieva H, Dartigues JF, Jacqmin-Gadda H: Sensitivity of four psychometric tests to measure cognitive changes in brain aging-population-based studies. *Am J Epidemiol* 2007;165:344–350.
- 47 Amieva H, Jacqmin-Gadda H, Orgogozo JM, Le Carret N, Helmer C, Letenneur L, Barberger-Gateau P, Fabrigoule C, Dartigues JF: The 9 year cognitive decline before dementia of the Alzheimer type: a prospective population-based study. *Brain* 2005;128:1093–1101.