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Monounsaturated, trans & saturated fatty acids and cognitive decline in women

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Asghar Naqvi contributed to research design and data analysis, wrote the manuscript and had primary responsibility for final content. There are no other potential conflicts of interest to disclose.

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	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Employment/Affiliation	x		X		x		x		x		x	
Grants/Funds	x		X		x		x		x		x	
Honoraria	x		X		x		x		x		x	
Speaker Forum	x		X		x		x		x		x	
Consultant	x		X		x		x		x		x	
Stocks	x		X		x		x		x		x	
Royalties	x		X		x		x		x		x	
Expert Testimony	x		X		x		x		x		x	
Board Member	x		X		x		x		x		x	
Patents	x		X		x		x		x		x	
Personal Relationship	x		X		x		x		x		x	

Abstract

Objectives—Prospectively assess effects of select dietary fats on cognitive decline

Design—Prospective observational; 3-year follow-up

Setting—Subjects recruited at Northwestern University who participated in Women's Health Initiative Observational Study or control group of Diet Modification arm.

Participants—482 women ≥ 60 years

Measurements—We averaged dietary intake from a validated food frequency questionnaire (FFQ) administered twice (mean=2.7 years apart) before baseline cognitive assessment (mean=2.9 years after 2nd FFQ). Testing of memory, vision, executive function, language, and attention was performed at 2 time points, 3 years apart. We created a global Z-score for both time points by averaging all Z-scores for each participant and defined global cognitive change as the difference between follow-up and baseline Z-scores.

Results—Median intakes of saturated fats (SFA), trans-fats, (TFA), dietary cholesterol (DC) and monounsaturated fats (MUFA) were 18.53 g/d, 3.45 g/d, 0.201 g/d and 19.39 g/d, respectively. There were no associations between degree of cognitive decline and intakes of SFA ($p=0.69$), TFA ($p=0.54$) or DC ($p=0.64$) after adjusting for baseline cognition, total energy, age, education, reading ability, Apolipoprotein E ($\epsilon 4$) allele, BMI, estrogen and beta-blocker use, and intake of caffeine and other fatty acids. In contrast, compared with participants in the lowest quartile, MUFA intake was associated with lower cognitive decline in fully adjusted linear regression models, with decline of $0.21 + 0.05$ SE in the lowest versus $0.05 + 0.05$ SE in the highest quartiles ($p=0.02$). This effect of MUFA intake was primarily in the visual and memory domains ($p=0.03$ for both).

Conclusion—Higher intakes of SFA, TFA and DC in these women were not associated with cognitive decline, while MUFA intake was associated with less cognitive decline.

Keywords

Fatty acids; cognitive decline; monounsaturated fat intake and prospective

INTRODUCTION

Cognitive impairment is a common disorder among elderly persons. Age-related cognitive decline (ARCD) encompasses deterioration in several domains, including memory performance, executive functions, and speed of cognitive processing.¹ The causes of cognitive decline are unknown, but previous studies have linked it to cardiovascular disease (CVD)² and cardiovascular risk factors such as diabetes mellitus³ and abnormal blood pressure.⁴ Established modifiable risk factors for ARCD remain limited, but given its association with CVD, plausibly include dietary fatty acids, which have strong established roles in the etiology of CVD.⁵

Previous prospective studies of intake of dietary saturated fatty acids (SFA),⁶⁻¹¹ trans-unsaturated fatty acids (TFA),^{6, 9} and mono-unsaturated fatty acids (MUFA)⁶⁻¹¹ have had variable associations with cognitive decline with most suggesting deleterious effects of SFA and TFA. Of note, very few studies of fatty acids and cognitive decline have measured individual components of cognitive function beyond the standard Mini-Mental Status Exam^{6, 8, 9} and only one had multiple assessments of diet.⁹ Thus, it remains unclear if different fats have differential effects on specific elements of cognitive function.

We previously reported an association of higher dietary n-3, but not n-6, fatty acid intake with less cognitive decline in older women, but the corresponding associations with other fatty acids were not assessed.¹² Given the established deleterious relationships of SFA and TFA with CVD and beneficial relation of MUFA with CVD, we hypothesized that they would have similar relationships with cognitive decline. In this study, we examined the prospective associations of these fatty acids with cognitive decline in a population of older women using comprehensive neuropsychiatric testing for multiple domains of cognitive decline.

METHODS

Study Sample

The Cognitive Change in Women (CCW) study is an ancillary study to the Observational study (OS) of the Women's Health Initiative (WHI) that was designed to examine associations of dietary and lifestyle factors with cognitive function in non-demented, community-dwelling women aged 60 years and older. Design and methods for CCW and WHI studies are described in detail elsewhere.^{13, 14} Briefly, women age 60 and over with visual and hearing acuity sufficient for valid neuropsychological testing and previously enrolled in the WHI Observational Study (OS) cohort or in the control ("usual diet") group of the WHI Diet Modification arm at the Northwestern University and Evanston-Northwestern Healthcare WHI clinical centers were recruited, screened and excluded for history of dementia, stroke, and other neurologic illness, alcohol or substance abuse, or regular use of medications, known to affect cognitive function or that might preclude valid cognitive testing.

Of 1201 women who were sent mailings, 679 (57%) responded positively and 544 (80%) of these screened eligible and were enrolled. Of those, 482 completed both baseline and follow-up CCW exams, and 441 had complete data for the variables used in these analyses. Baseline CCW evaluations took place between Jan 1998 and Nov 2003 and follow-up assessments were between Jan 2001 and Nov 2006. Figure 1 shows the temporal relationship between WHI enrollment and CCW enrollment and follow-up, and key variables collected at each time-point. The WHI CCW study was reviewed and approved by the Institutional Review Boards at New England Research Institutes, Watertown, MA; Northwestern University Medical School, Chicago, IL; and Evanston-Northwestern Healthcare, Evanston, IL.

Cognitive Function Assessment

At CCW enrollment and again after 3 years, CCW participants received an extensive cognitive test battery, including the CERAD word list learning, constructions, and word fluency tests,^{15, 16} Wechsler Memory Scale-Revised (WMS-R) Logical Memory, Visual Reproduction, and Digit Span tests,¹⁷ Boston Naming Test,¹⁸ F-A-S Word Fluency and Judgment of Line Orientation tests,¹⁹ Visual Target Cancellation Test,²⁰ Trail Making Test parts A and B,²¹ and a modification of the Visual-Verbal Test.²² These 10 tests yielded 17 separate scores. The tests were grouped into four domains, including memory: CERAD Word List, WMS-R Logical Memory, WMS-R Visual Reproduction; executive function: Trail Making Part B, Visual Verbal Test; language: Boston Naming Test, CERAD word fluency, F-A-S Word Fluency Test; attention: Trail Making Part A, Digit Span; and visual: CERAD Constructions, Judgment of Line Orientation, and Visual Target Cancellation Test. In addition, the American National Adult Reading Test (ANART)²³ was administered to measure reading ability and the 30-item Geriatric Depression Scale (GDS)²⁴ to measure depressive symptoms.

Testing and scoring were performed by interviewer / technicians who had undergone standardized training at the Northwestern Alzheimer's Disease Center Clinical Core, and who underwent recalibration training approximately twice per year. Inter-rater reliability for scoring was assessed by randomly selecting 20 participant records which were re-scored by a different interviewer. Intra-class correlation (r) for continuous test scores exceeded 0.8 for all test scores and exceeded 0.9 for all but one, demonstrating excellent inter-rater reliability. For tests that were scored categorically or that had a limited range of possible scores, scorers showed 100% agreement (Cohen's kappa=1).

One hundred four participants (22%) exhibited at least one impaired score on memory tests at baseline, 68 (14%) on tests of visual spatial perception, 29 (6%) on tests of executive function, 22 (5%) on tests of language, and 10 (2%) on tests of attention. When the domain-specific impairments were considered together, 51 (11%) of participants exhibited mixed-domain impairment. A total of 65 women (13%) could not be classified by our mixed cognitive impairment variable because of missing values on one or more tests. Of the 51 women with impairment in two or more domains, 39 (76%) had memory impairment and 12 had impairment in two or more domains, not including memory.

Each baseline score was standardized to zero mean and unit standard deviation (Z-score). The follow-up scores were similarly standardized using the baseline means and standard deviations. A global Z-score was created for both CCW baseline and 3-year time points by averaging individual test Z-scores for each study participant, at each time point. Cognitive change was defined as the difference between follow-up and baseline global Z-score. This method of generating a composite score from multiple cognitive test scores has been employed previously by others.²⁵

Dietary Assessment

Dietary intake data was assessed twice prior to baseline cognitive testing by a food frequency questionnaire (FFQ) that was developed for the WHI. This WHI FFQ has been found to have precision similar to other FFQs in terms of correlation of nutrient estimates, including fatty acids, with those obtained from four 24-hour dietary recalls and a 4-day food record.²⁶ Briefly, the WHI FFQ includes 122 foods or food groups with questions on usual frequency of intake and portion size (compared to pictures of a medium portion size) over the "last 3 months". Adjustment questions permitted more refined analyses of fat intake by asking about food preparation practices and types of added fats. For each dietary intake measure, we averaged the values from the 2 administrations of the WHI FFQ, collected 3 years apart (WHI baseline and 3-year visits) if they were both present. If the 3 year FFQ was missing (N=134), we carried the baseline measure forward. As seen in Figure 1, the first WHI FFQ was collected an average of 5.6 years prior to CCW baseline cognitive testing, and the second, an average of 2.9 years prior. Vitamin supplement use was assessed at both the baseline and 3-year follow-up WHI and CCW visits, neither of which included MUFA supplementation.

Individual dietary fats, including total SFA (gm), TFA (gm), dietary cholesterol (DC) (mg), n-3 polyunsaturated fatty acids (PUFAs, gm), n-6 PUFAs (gm), MUFAs (gm) and dietary carbohydrate (gm) intake data were computed from the WHI baseline and 3-year FFQs. We averaged these dietary macronutrients and calculated their percentage of total energy by dividing intake (gm/day) by energy intake (kcal) per day and multiplying by the energy content of that macronutrient. Individual saturated fatty acids, including palmitic (16:0), stearic (18:0) and myristic acid (14:0), were all strongly correlated ($r=0.90-0.98$), even when expressed as a proportion of total energy ($r=0.73-0.93$), which precluded their analysis separately.

Covariates

We treated age, American National Adult Reading Test (ANART) score at CCW baseline, dietary and supplemental vitamin D (mcg), dietary and supplemental beta-carotene (mcg), dietary and supplementary copper (mg), caffeine intake (mg), alcohol intake (gm) and dietary antioxidants, genistein (mg) and daidzein (mg), as continuous variables. We categorized educational attainment as high-school or less, some college and college degree or beyond. We assigned smoking status as never, past smoker (at least 100 cigarettes), and current smoker. We categorized race/ethnicity as non-Hispanic white, non-Hispanic black and all others. We assigned non-steroidal anti-inflammatory drug use as non-user, irregular user and regular user. We dichotomized physical activity into none/some activity of limited duration and moderate/strenuous physical activity (equivalent to 2-4 episodes/week of walking fast for ≥ 20 minutes or more). We calculated Body Mass Index (BMI) by dividing weight (kg) by height (m^2) and categorized BMI into $<25 \text{ kg}/m^2$, $25\text{-}30 \text{ kg}/m^2$ and $>30 \text{ kg}/m^2$. The following self-reported physician-diagnosed cardiovascular-related diseases were assessed either at the baseline WHI or CCW visit: diabetes at CCW, hyperlipidemia at WHI, cardiovascular disease at WHI, hypertension at CCW, and unipolar depression at CCW. None were included in final models due to not reaching statistical significance in bivariate analysis, which was determined a priori as <0.10 . We ascertained use of cardiovascular-related medications, including cholesterol lowering medications, beta-blockers, diuretics, aspirin and estrogen hormone replacement therapy. We averaged dietary and supplemental vitamin E intake collected at WHI baseline and 3-year visits, as well as CCW baseline and 3-year visits (see Figure 1). We then categorized average intake based on the estimated requirement for Vitamin E for women 51 years of age and over ($12 \text{ mg}/\text{day}$)²⁷ as 1) consistently less than $12 \text{ mg}/\text{day}$; 2) fluctuating; 3) consistently greater than $12 \text{ mg}/\text{day}$. We dichotomized apolipoprotein E (ApoE) to reflect presence or absence of an $\epsilon 4$ allele.²⁸

Statistical Analysis

To explore the associations of dietary fats and dietary cholesterol on change in cognitive function, we used least squares linear modeling methods. We computed two sequential linear regression models for 3-year change in global cognitive Z-score. We adjusted the first model for age, education, ApoE $\epsilon 4$ allele, reading ability in the American National Adult Reading Test (ANART), dietary total energy and baseline global cognitive Z-score. We then computed a second model controlling for factors that were associated with cognitive change in bivariate analysis with $p < 0.10$, including BMI, estrogen use, beta blocker use, dietary caffeine intake, and forced dietary intake in quartiles of MUFA, PUFA, SFA, TFA and DC into the model. Results are reported as the increase or decrease in cognitive function in standard deviation units per specified increment of dietary intake. We tested the interaction effects of dietary copper²⁹ and ApoE $\epsilon 4$ ²⁸ with dietary fats on cognitive decline. All analyses were carried out using SAS statistical software (SAS Institute, Inc. Cary NC)

RESULTS

This cohort is comprised primarily of older, Caucasian (87%) women. Median intakes of SFA, TFA and DC were similar to levels found in the larger WHI cohort of older women (Table 1).³⁰ Dietary MUFA intakes were slightly lower than levels found in this same comparison group, $11.5 (3.6)$ versus $14.4 (2.3)$.³⁰ The proportions of calories from various dietary fats were moderately correlated (Table 2).

We found that higher intake of dietary MUFA was associated with less cognitive decline in both partially and fully adjusted models. Compared with participants in the lowest quartile, MUFA intake was associated with lower cognitive decline in fully adjusted linear regression models, with decline of $0.21 \pm 0.05 \text{ SD}$ in the lowest versus $0.05 \pm 0.05 \text{ SD}$ in the highest

quartiles ($p=0.02$) after adjustment for total energy, age, education, ANART (reading ability) score, cognitive z-score at baseline, ApoE status, SFA, TFA and DC. (Table 3). In partially adjusted models, SFA intake was associated with less cognitive decline ($p=0.01$), with decline of 0.18 ± 0.03 in the lowest quartile versus 0.03 ± 0.03 in the highest. However, this association with cognitive decline was null in fully adjusted models ($p=0.69$), primarily due to confounding by MUFA intake. There was no association between TFA and cognitive decline in partial ($p=0.07$) or fully adjusted models ($p=0.54$).

In sensitivity analyses, all of the above associations were minimally changed in models without baseline cognitive z-score included or in an energy substitution model for dietary protein intake. The energy substitution model included carbohydrates, alcohol and other variables in the fully adjusted models and can be interpreted as follows, compared with participants in the lowest quartiles, dietary MUFA intake in exchange for an equivalent amount of energy from dietary protein, was minimally changed from the associations with cognitive decline in our primary analysis. There was no change in the associations when an indicator variable for the number of FFQs completed was added to fully adjusted models.

Given the association of MUFA intake with less global cognitive decline, we tested its associations with individual cognitive domains, including memory, executive function, language and visual (Table 4). MUFA intake was associated with less decline in the visual domain and memory domains ($p=0.03$ for both). There was no evidence of effect modification by ApoE e4 ($p>0.55$) or dietary copper ($p>0.29$) with intakes of SFA, TFA, DC and MUFA. Additionally, there was no evidence of effect modification by SFA ($p=0.90$), TFA ($p=0.98$) or PUFA ($p=0.37$) with MUFA intake.

DISCUSSION

In this cohort of older women, we found that MUFA intake was associated with less cognitive decline over a three year period. Previous studies generally but not invariably support this association. One previous prospective study found increased dietary MUFA intake to be associated with less cognitive decline,¹⁰ a second found a trend in the same direction,⁹ a third found a trend in the same direction in restricted analyses,⁶ and three others were null.^{7, 8, 11} Among the null studies, none of them had multiple measures of diet, although one assessed diet through a measure of fatty acid composition of erythrocyte membranes.⁷ However, that study assessed cognitive decline exclusively with the Mini-Mental State Examination, which is likely not as sensitive as the neuropsychological test battery used in this study.

MUFAs are thought to be one of the major protective components of the traditional Mediterranean diet, where they are consumed primarily from olive oil (46 g/d or 4 tbs/d).¹⁰ Two recent prospective studies of Mediterranean diet have found greater adherence to be associated with less cognitive decline or Alzheimer Disease (AD) incidence.^{31, 32} One of these studies found an effect of Mediterranean diet on an individual cognitive domain, namely memory.³¹ This finding is consistent with the observed protective effect of MUFAs on memory in the WHI CCW. In addition, we found an association of MUFAs with less decline in visual-spatial abilities (copying and matching), a finding not previously made to our knowledge. Decline in visuospatial function has been associated with driving errors in older adults³³ and has also been suggested as a potential predictor (along with amnesic impairment) of transition from mild cognitive impairment to Alzheimer's disease.³⁴

Several pathways may explain the apparent relationship of MUFA intake with cognitive function. MUFAs and MUFA derivatives have anti-inflammatory effects *in vivo*.^{35, 36} This may be important since chronic inflammation appears as a precursor of symptomatic AD.

³⁷⁻³⁹ Oxidative stress has also been demonstrated in patients with mild cognitive impairment and AD,⁴⁰ and derivatives from MUFAs, including low molecular weight phenols, have been found to have anti-oxidant effects.⁴¹ MUFAs may also exert their potentially beneficial effects on cognition indirectly by decreasing cardiovascular risk through reducing macrophage uptake of plasma oxidized low-density lipoprotein, reduction of apolipoprotein B and reduction of triglycerides.⁴²⁻⁴⁴

Intakes of SFA, TFA and DC were not associated with cognitive decline in this cohort of relatively healthy elderly women. SFA had a protective effect on cognitive decline in the partial model, which is likely due to confounding by MUFA, which was moderately correlated with SFA. However, there was no association between SFA and cognitive decline in the fully adjusted model. Previous prospective studies found dietary SFA intake to be either deleterious(5-8) or null^{10, 11} in associations with cognitive decline. Similarly, previous prospective studies found TFA intake to be either deleterious⁹ or trending towards deleterious effects⁶. Of note, these studies had substantially higher absolute and relative SFA and TFA intakes than did the women in this study, and hence the deleterious effects of these fatty acids may be limited to individuals with higher levels of intake.

Strengths of this study include the use of a battery of sensitive cognitive tests, rather than a global cognitive instrument in order to better detect the fairly small changes that were anticipated over 3 years in this group of generally healthy, well-educated women who were cognitively intact at baseline. Assessment of multiple domains of cognition allowed for a more detailed characterization of cognitive effects. Another strength of this study is the administration of a validated FFQ at two time-points rather than a single measurement, as was done in most prospective studies of MUFAs and cognitive decline.⁶⁻¹¹ Finally, the WHI and CCW measured a wide variety of characteristics of subjects, allowing for the ability to control for various potential confounders and interactions in a systematic fashion.

Limitations of this study include the modest sample size and follow-up time of 3 years, which may preclude detection of modest long-term effects on cognition. This limits the ability to adjust for potential confounding among dietary fatty acids and to detect non-linear associations. This may contribute to why associations between SFA and TFA intake and cognitive decline were null. Limitations of using FFQs for dietary assessment include restrictions imposed by a fixed list of foods, reliance on memory, perception of portion sizes, and interpretation of questions. Also, blood fatty acid measurements, which are objective but can also have limitations of measurement error, were not available for our analyses. However, the FFQ used in this study was validated against a 4-day food record, which does not share these limitations. As with any observational study, we can not rule out the possibility of residual confounding by unknown risk factors, such as a generally healthier lifestyle of individuals with a higher MUFA intake. Finally, our study population consisted of primarily healthy, highly educated, older, Caucasian women, which limits the generalizability of these findings to other populations.

In conclusion, we found dietary MUFA intake to be associated with less cognitive decline in older women. Dietary intakes of SFA, TFA and DC were not associated with cognitive decline. Further larger, prospective studies with longer follow-up time are needed to confirm the possible protective effects of MUFAs for cognitive decline

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APPENDIX

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For a list of all the investigators who have contributed to WHI science, please visit: http://www.whiscience.org/publications/WHI_investigators_longlist.pdf

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Figure 1.
Data Collection

Table 1

Baseline characteristics at CCW

Characteristic	MUFA Quartiles			
	1 [0-9.75]	2 [9.76-11.50]	3 [11.51-13.26]	4 [≥13.27]
SFA (SE)	7.90 (2.15)	10.99 (1.93)	12.20 (2.06)	13.26 (2.73)
TFA (SE)	1.34 (0.54)	1.98 (0.57)	2.28 (0.72)	2.92 (1.22)
DC (SE)	152.0 (70.5)	209.5 (86.8)	249.9 (111.9)	261.4 (129.0)
Baseline global z-score (SE)	0.02 (0.61)	0.04 (.49)	0.05 (0.50)	-0.02 (0.58)
Follow-up global z-score (SE)	-0.13 (0.34)	-0.14 (0.39)	-0.06 (0.30)	0.00 (0.28)
Age (years, SE)	70.89 (6.70)	71.36 (6.55)	69.95 (6.67)	70.17 (5.99)
PUFA (SE)	5.12 (1.48)	6.25 (1.78)	6.99 (1.38)	8.62 (2.16)
Caffeine Use (mg/day, SE)	151.0 (107.3)	160.5 (131.2)	184.0 (120.7)	160.5 (132.5)
ANART (reading ability, SE)	9.04 (6.80)	7.95 (6.06)	8.48 (6.00)	10.99 (8.29)
MMSE (SE)	28.96 (1.44)	28.87 (1.32)	29.00 (1.16)	28.87 (1.28)
BMI (kg/m ² , SE)	26.01 (5.42)	26.64 (4.86)	26.76 (5.36)	27.18 (5.10)
<25 kg/m ² (N, %)	59 (49%)	46 (38%)	49 (41%)	45 (37%)
25-30 kg/m ² (N, %)	43 (36%)	47 (39%)	44 (37%)	44 (36%)
>30 kg/m ² (N, %)	18 (15%)	27 (23%)	27 (23%)	32 (26%)
Education				
≥High school (N, %)	22 (18%)	24 (20%)	20 (17%)	30 (25%)
Some college (N, %)	27 (23%)	26 (21%)	32 (27%)	30 (25%)
≥College degree (N, %)	71 (59%)	71 (59%)	68 (57%)	61 (50%)
ApoE ε4				
Yes (N, %)	34 (31%)	25 (23%)	28 (24%)	23 (20%)
No (N, %)	76 (69%)	86 (77%)	89 (76%)	93 (80%)
Estrogen Use				
Yes (N, %)	34 (28%)	31 (26%)	42 (35%)	37 (31%)
No (N, %)	86 (72%)	89 (74%)	78 (65%)	84 (69%)
Beta-Blocker Use				
Yes (N, %)	10 (8%)	22 (18%)	14 (12%)	14 (12%)
No (N, %)	110 (92%)	99 (82%)	106 (88%)	107 (88%)

Abbreviations:

N: Number of subjects

SE: Standard error

MUFA: Monounsaturated fatty acid intake (% of Energy)

SFA: Saturated fatty acid intake (% of Energy)

TFA: Trans-fatty acid intake (% of Energy)

DC: Dietary Cholesterol intake (mg/day)

PUFA: Polyunsaturated fatty acid intake (% of Energy)

BMI: Body mass index

ApoEε4: Apolipoprotein E epsilon 4

ANART: American National Adult Reading Test

CCW: Cognitive Change in Women

MMSE: Mini Mental Status Exam

Table 2

Pearson correlations of dietary exposures

Variable	Median (IQR)	MUFA	SFA	TFA	DC
MUFA	11.5 (3.6)	1.00			
SFA	11.1 (4.0)	0.67	1.00		
TFA	1.9 (1.2)	0.65	0.45	1.00	
DC	200.8 (149.7)	0.37	0.49	0.23	1.00

Abbreviations:
IQR: Inter-quartile range
MUFA: Monounsaturated fatty acid intake (% of Energy)
SFA: Saturated fatty acid intake (% of Energy)
TFA: Trans-fatty acid intake (% of Energy)
DC: Dietary Cholesterol intake (mg/day)

Table 3

Regression coefficients (and SEs) for multivariable linear regression analysis of fatty acid intake in quartiles on prospective cognitive function z-score; N=482

	Quartile of Fatty Acid Intake				p-value
	1	2	3	4	
MUFA	[0-9.75]	[9.76-11.50]	[11.51-13.26]	[≥13.27]	
Partial *	-0.16 (0.03)	-0.16 (0.03)	-0.10 (0.03)	0.00 (0.03)	<0.01
Full **	-0.21 (0.05)	-0.23 (0.04)	-0.16 (0.04)	-0.05 (0.05)	0.02
SFA	[0-9.12]	[9.13-11.11]	[11.12-13.00]	[≥13.01]	
Partial *	-0.18 (0.03)	-0.11 (0.03)	-0.10 (0.03)	-0.03 (0.03)	0.01
Full **	-0.20 (0.05)	-0.16 (0.04)	-0.16 (0.04)	-0.13 (0.04)	0.69
TFA	[0-1.45]	[1.46-1.92]	[1.93-2.64]	[≥2.65]	
Partial *	-0.13 (0.03)	-0.16 (0.03)	-0.07 (0.03)	-0.06 (0.03)	0.07
Full **	-0.17 (0.04)	-0.19 (0.04)	-0.13 (0.04)	-0.17 (0.04)	0.54
DC	[0-136.17]	[136.18-203.53]	[203.54-281.58]	[≥281.59]	
Partial *	-0.11 (0.04)	-0.10 (0.03)	-0.11 (0.03)	-0.10 (0.04)	0.97
Full **	-0.14 (0.04)	-0.14 (0.04)	-0.18 (0.04)	-0.19 (0.04)	0.64

Abbreviations:

SE: Standard error

MUFA: Monounsaturated fatty acid intake (% energy)

SFA: Saturated fatty acid intake (% energy)

TFA: Trans-unsaturated fatty acid intake (% energy)

DC: Dietary cholesterol (mg/day)

* Partial: Adjusted for global z-score at baseline, dietary total energy (kcal), age, education, American National Adult Reading Test score and apolipoprotein E (ε4) allele

** Full: Further adjusted for BMI, estrogen use, caffeine use, beta-blocker use and other fatty acid (MUFA, PUFA, SFA, TFA, % energy; DC, mg/day) intake

Multivariable linear regression analysis of MUFA intake (% of energy) in quartiles on prospective change in mean (SE) cognitive function domains z-score; N=482

Table 4

Cognitive Function Domain	MUFA Quartiles				p-value
	1 [0-9.75]	2 [9.76-11.50]	3 [11.51-13.26]	4 [≥13.27]	
Memory	-0.23 (0.08)	-0.30 (0.06)	-0.17 (0.06)	-0.05 (0.07)	0.03
Executive Function	-0.14 (0.10)	-0.18 (0.08)	-0.22 (0.08)	-0.04 (0.10)	0.25
Language	-0.08 (0.07)	-0.20 (0.05)	-0.13 (0.05)	-0.06 (0.06)	0.16
Attention	-0.19 (0.10)	-0.16 (0.07)	-0.16 (0.07)	-0.18 (0.09)	0.99
Visual	-0.26 (0.08)	-0.20 (0.06)	-0.18 (0.06)	0.02 (0.08)	0.03

Adjusted for baseline cognitive test z-score, dietary total energy (kcal), age, education, American National Adult Reading Test score and apolipoprotein E (ε4) allele, BMI, estrogen use, caffeine use and beta-blocker use, PUFA (% energy), SFA (% energy), TFA (% energy) and DC (mg/day)

Abbreviations:

SE: Standard Error

MUFA: Monounsaturated fatty acid intake (% of Energy)

SFA: Saturated fatty acid intake (% energy)

TFA: Trans-unsaturated fatty acid intake (% energy)

DC: Dietary cholesterol (mg/day)