Monounsaturated, Trans, and Saturated Fatty Acids and Cognitive Decline in Women

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OBJECTIVES: To prospectively assess effects of select dietary fats on cognitive decline.

DESIGN: Prospective observational; 3-year follow-up.

SETTING: Northwestern University.

PARTICIPANTS: Four hundred eighty-two women aged 60 and older who participated in the Women’s Health Initiative (WHI) Observational Study or in the control group of the WHI Diet Modification arm.

MEASUREMENTS: 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 second FFQ) was averaged. Testing of memory, vision, executive function, language, and attention was performed twice, 3 years apart. A global Z-score was created for both time points by averaging all Z-scores for each participant, and global cognitive change was defined as the difference between follow-up and baseline Z-scores.

RESULTS: Median intake of saturated fat (SFA), trans-fat (TFA), dietary cholesterol (DC), and monounsaturated fat (MUFA) was 18.53, 3.45, 0.201, and 19.39 g/d, respectively. There were no associations between degree of cognitive decline and intake of SFA (P = .69), TFA (P = .54), or DC (P = .64) after adjusting for baseline cognition, total energy intake, age, education, reading ability, apolipoprotein E ε4 allele, body mass index, estrogen and beta-blocker use, and intake of caffeine and other fatty acids. In contrast, MUFA intake was associated with lower cognitive decline in fully adjusted linear regression models, with mean decline (standard error) of 0.21 (0.05) in the lowest and 0.05 (0.05) in the highest quartiles (P = .02). This effect of MUFA intake was primarily in the visual and memory domains (P = .03 for both).

CONCLUSION: Greater intake of SFA, TFA, and DC was not associated with cognitive decline, whereas greater MUFA intake was associated with less cognitive decline. J Am Geriatr Soc 59:837–843, 2011.

Key words: fatty acids; cognitive decline; monounsaturated fat intake; prospective

Cognitive impairment is a common disorder in elderly persons. Age-related cognitive decline (ACD) encompasses deterioration in several domains, including memory performance, executive function, 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 melitus3 and abnormal blood pressure.4 Few modifiable risk factors for ACD have been established, 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 acid (SFA),6–11 trans-unsaturated fatty acid (TFA),6,9 and mono-unsaturated fatty acid (MUFA)6–11 have had variable associations with cognitive decline, with most suggesting deleterious effects of SFA and TFA. Few studies of fatty acids and cognitive decline have measured individual components of cognitive function beyond the standard Mini-Mental State Examination,6,8,9 and only one had multiple assessments of diet.9 Thus, it remains unclear whether different fats have different effects on specific elements of cognitive function.

An association between higher dietary Ω3, but not Ω6, fatty acid intake and less cognitive decline in older women has been reported, but the corresponding associations with other fatty acids were not assessed.12 Given the established deleterious relationships between SFA and TFA and CVD and the beneficial relationship between MUFA and CVD, it was hypothesized that they would have similar relationships with cognitive decline. This study examined the prospective associations between these fatty acids and...
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), which was designed to examine associations between dietary and lifestyle factors and cognitive function in community-dwelling women aged 60 and older without dementia. The design and methods of the CCW study and the WHI are described in detail elsewhere.13,14 Briefly, women aged 60 and older with visual and hearing acuity sufficient for valid neuropsychological testing and previously enrolled in the WHI 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, or other neurological illness; alcohol or substance abuse; or regular use of medications known to affect cognitive function or that might preclude valid cognitive testing.

Of 1,201 women who were sent mailings, 679 (57%) responded positively, and 544 (80%) of those were eligible and were enrolled. Of those, 482 completed the baseline and follow-up CCW examinations, and 441 had complete data for the variables used in these analyses. Baseline CCW evaluations took place between January 1998 and November 2003, and follow-up assessments were between January 2001 and November 2006. Figure 1 shows the temporal relationship between WHI and CCW enrollment and follow-up and important variables collected at each time-point. The New England Research Institutes (Watertown, MA), Northwestern University Medical School (Chicago, IL), and Evanston-Northwestern Healthcare (Evanston, IL) institutional review boards reviewed and approved the WHI CCW study.

Cognitive Function Assessment

At CCW enrollment and again after 3 years, CCW participants received an extensive cognitive test battery, including the Consortium to Establish a Registry for Alzheimer’s Disease (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 (TMT) Part 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: memory (CERAD Word List, WMS-R Logical Memory and Visual Reproduction), executive function (TMT-B, Visual Verbal Test), language (Boston Naming Test, CERAD word fluency, F-A-S Word Fluency Test), attention (TMT-A, Digit Span), and visual (CERAD constructions, Judgment of Line Orientation Test, 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 Scale24 to measure depressive symptoms.

Interviewers and technicians who had undergone standardized training at the Northwestern Alzheimer’s Disease Center Clinical Core and underwent recalibration training approximately twice per year administered and scored the tests. Interrater reliability for scoring was assessed by randomly selecting 20 participant records that a different interviewer rescored. Intraclass correlation (r) for continuous test scores exceeded 0.8 for all test scores and exceeded 0.9 for all but one, demonstrating excellent interrater reliability. For tests that were scored categorically or that had a limited range of possible scores, scorers showed 100% agreement (Cohen 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%) participants exhibited mixed-domain impairment. The mixed cognitive impairment variable could not classify 65 women (13%) 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.

Figure 1. Data collection. WHI = Women’s Health Initiative; CCW = Cognitive Change in Women.
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 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. Others have previously employed this method of generating a composite score from multiple cognitive test scores.25

Dietary Assessment
Dietary intake data were assessed twice before baseline cognitive testing using 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, and to 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 with 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, the values from the two administrations of the WHI FFQ, collected 3 years apart (WHI baseline and 3-year visits), were averaged if they were both present. If the 3-year FFQ was missing (n = 134), the baseline measure was carried forward. As seen in Figure 1, the first WHI FFQ was collected an average of 5.6 years before CCW baseline cognitive testing and the second an average of 2.9 years before. Vitamin supplement use was assessed at the baseline and 3-year follow-up WHI and CCW visits, neither of which included MUFA supplementation.

Individual dietary fats, including total SFA (g), TFA (g), dietary cholesterol (DC; mg), Ω-3 polyunsaturated fatty acid (PUFA, g), Ω-6 PUFA (g), MUFA (g), and dietary carbohydrate (g) intake data were computed from the WHI baseline and 3-year FFQs. These dietary macronutrients were averaged, and their percentage of total energy was calculated by dividing intake (g) by energy intake (kcal) per day and multiplying by the energy content of that macro-nutrient. Individual SFA, 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
Age, ANART score at CCW baseline, dietary and supplemental vitamin D (µg), dietary and supplemental betacarotene (µg), dietary and supplementary copper (mg), caffeine intake (mg), alcohol (g), and the dietary antioxidants genistein (mg) and daidzein (mg) were treated as continuous variables. Educational attainment was categorized as high school or less, some college, and college degree or beyond. Smoking status was categorized as never, past smoker (≥100 cigarettes), and current smoker. Race and ethnicity was categorized as non-Hispanic white, non-Hispanic black, and all others. Nonsteroidal anti-inflammatory drug use was categorized as nonuser, irregular user, and regular user. Physical activity was dichotomized into none to some activity of limited duration versus moderate to strenuous physical activity (equivalent to 2–4 episodes/week of walking fast for ≥20 minutes). Body mass index (BMI) was calculated by dividing weight (kg) by height (m²) and was categorized less than 25.0, 25.0 to 29.9, and 30 kg/m² or more. The following self-reported physician-diagnosed cardiovascular-related diseases were assessed at the baseline WHI or CCW visit: diabetes mellitus at CCW, hyperlipidemia at WHI, cardiovascular disease at WHI, hypertension at CCW, and unipolar depression at CCW. Use of cardiovascular-related medications, including cholesterol-lowering medications, beta-blockers, diuretics, aspirin, and estrogen hormone replacement therapy, was ascertained. Dietary and supplemental vitamin E intake collected at WHI baseline and 3-year visits and at CCW baseline and 3-year visits were averaged (Figure 1). Average intake was then categorized based on the estimated requirement for vitamin E for women aged 51 and older (12 mg/d)27 as consistently less than 12 mg/d, fluctuating, or consistently greater than 12 mg/d. Apolipoprotein E (ApoE) was dichotomized to reflect presence or absence of an ε4 allele.28 Covariates were included in final models if they reached statistical significance in bivariate analysis, which was determined a priori as P < 0.10.

Statistical Analysis
Least squares linear modeling methods were used to explore the associations between dietary fats and dietary cholesterol and change in cognitive function. Two sequential linear regression models for 3-year change in global cognitive Z-score were computed. The first model was adjusted for age, education, ApoE ε4 allele, reading ability according to the ANART, dietary total energy, and baseline global cognitive Z-score. A second model was then computed, controlling for factors that were associated with cognitive change in bivariate analysis with P < 0.10, including BMI, estrogen use, beta-blocker use, and dietary caffeine intake, and dietary intake in quartiles of MUFA, PUFA, SFA, TFA, and DC was forced into the model. Results are reported as increase or decrease in cognitive function in standard deviation units per specified increment of dietary intake. The interaction between the effects of dietary copper29 and ApoE ε428 and those of dietary fats on cognitive decline was tested. All analyses were performed using SAS statistical software (SAS Institute, Inc., Cary, NC).

RESULTS
This cohort consisted 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 Median (interquartile range) dietary MUFA intakes were slightly lower than those found in this same comparison group (11.5 (3.6) vs 14.4 (2.3)).30 The proportions of calories from various dietary fats were moderately correlated (Table 2).

This study found that higher intake of dietary MUFA was associated with less cognitive decline in partially and fully adjusted linear regression models. Greater MUFA intake was associated with less cognitive decline (decline of
0.21 ± 0.05 in the lowest quartile of intake vs 0.05 ± 0.05 SD in the highest; $P = .02$) 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 (decline of 0.18 ± 0.03 in the lowest quartile vs 0.03 ± 0.03 in the highest; $P = .01$). This association with cognitive decline was null in fully adjusted models ($P = .69$), primarily because of confounding by MUFA intake. There was no association between TFA and cognitive decline in partial ($P = .07$) or fully adjusted models ($P = .54$).

In sensitivity analyses, all of the above associations were minimally changed in models without baseline cognitive $z$-score included. All of the above associations were also minimally changed in an energy substitution model for dietary protein intake that included carbohydrates, alcohol, other fats, and other variables in the fully adjusted models. 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 between MUFA intake and global cognitive decline, its associations with individual cognitive domains, including memory, executive function, language, and visual, were tested (Table 4). Greater MUFA intake was associated with less decline in the visual domain and memory domains ($P = .03$ for both). There was no evidence of effect modification between ApoE ε4 ($P > .55$) or dietary copper ($P > .29$) and intakes of SFA, TFA, DC, and MUFA. There was also no evidence of effect modification between MUFA intake and SFA ($P = .90$), TFA ($P = .98$), or PUFA ($P = .37$) intakes.

Table 1. Baseline Characteristics in the Cognitive Change in Women (CCW) Study According to Monounsaturated Fatty Acid Intake Quartile (% of Energy Intake)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Quartile 1 (0–9.75)</th>
<th>Quartile 2 (9.76–11.50)</th>
<th>Quartile 3 (11.51–13.26)</th>
<th>Quartile 4 ($&gt;13.27$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated fatty acid intake, % of energy, mean (SE)</td>
<td>7.9 (2.1)</td>
<td>11.0 (1.9)</td>
<td>12.2 (2.1)</td>
<td>13.3 (2.7)</td>
</tr>
<tr>
<td>Trans-fatty acid intake, % of energy, mean (SE)</td>
<td>1.34 (0.54)</td>
<td>1.98 (0.57)</td>
<td>2.28 (0.72)</td>
<td>2.92 (1.22)</td>
</tr>
<tr>
<td>Dietary cholesterol intake, mg/d, mean (SE)</td>
<td>152.0 (70.5)</td>
<td>209.5 (86.8)</td>
<td>249.9 (111.9)</td>
<td>261.4 (129.0)</td>
</tr>
<tr>
<td>Baseline global $z$-score mean (SE)</td>
<td>0.02 (0.61)</td>
<td>0.04 (0.49)</td>
<td>0.05 (0.50)</td>
<td>−0.02 (0.58)</td>
</tr>
<tr>
<td>Follow-up global $z$-score, mean (SE)</td>
<td>−0.13 (0.34)</td>
<td>−0.14 (0.39)</td>
<td>−0.06 (0.30)</td>
<td>0.00 (0.28)</td>
</tr>
<tr>
<td>Age, mean (SE)</td>
<td>70.9 (6.7)</td>
<td>71.4 (6.5)</td>
<td>69.9 (6.7)</td>
<td>70.2 (6.0)</td>
</tr>
<tr>
<td>Polyunsaturated fatty acid intake, % of energy, mean (SE)</td>
<td>5.1 (1.5)</td>
<td>6.2 (1.8)</td>
<td>7.0 (1.4)</td>
<td>8.6 (2.2)</td>
</tr>
<tr>
<td>Caffeine use, mg/d, mean (SE)</td>
<td>151.0 (107.3)</td>
<td>160.5 (131.2)</td>
<td>184.0 (120.7)</td>
<td>160.5 (132.5)</td>
</tr>
<tr>
<td>American National Adult Reading Test (reading ability), mean (SE)</td>
<td>9.0 (6.8)</td>
<td>7.9 (6.1)</td>
<td>8.5 (6.0)</td>
<td>11.0 (8.3)</td>
</tr>
<tr>
<td>Mini-Mental State Examination score, mean (SE)</td>
<td>29.0 (1.4)</td>
<td>28.9 (1.3)</td>
<td>29.0 (1.2)</td>
<td>28.9 (1.3)</td>
</tr>
<tr>
<td>Body mass index, kg/m$^2$ (SE)</td>
<td>26.0 (5.4)</td>
<td>26.6 (4.9)</td>
<td>26.8 (5.4)</td>
<td>27.2 (5.1)</td>
</tr>
<tr>
<td>$&lt;25$, n (%)</td>
<td>59 (49)</td>
<td>46 (38)</td>
<td>49 (41)</td>
<td>45 (37)</td>
</tr>
<tr>
<td>25–30, n (%)</td>
<td>43 (36)</td>
<td>47 (39)</td>
<td>44 (37)</td>
<td>44 (36)</td>
</tr>
<tr>
<td>$&gt;30$, n (%)</td>
<td>18 (15)</td>
<td>27 (23)</td>
<td>27 (23)</td>
<td>32 (26)</td>
</tr>
<tr>
<td>Education, n (%)</td>
<td>22 (18)</td>
<td>24 (20)</td>
<td>20 (17)</td>
<td>30 (25)</td>
</tr>
<tr>
<td>$&lt;$High school</td>
<td>27 (23)</td>
<td>26 (21)</td>
<td>32 (27)</td>
<td>30 (25)</td>
</tr>
<tr>
<td>Some college</td>
<td>71 (59)</td>
<td>71 (59)</td>
<td>68 (57)</td>
<td>61 (50)</td>
</tr>
<tr>
<td>Apolipoprotein E ε4, n (%)</td>
<td>34 (31)</td>
<td>25 (23)</td>
<td>28 (24)</td>
<td>23 (20)</td>
</tr>
<tr>
<td>Yes</td>
<td>76 (69)</td>
<td>86 (77)</td>
<td>89 (76)</td>
<td>93 (80)</td>
</tr>
<tr>
<td>No</td>
<td>34 (28)</td>
<td>31 (26)</td>
<td>42 (35)</td>
<td>37 (31)</td>
</tr>
<tr>
<td>Estrogen use, n (%)</td>
<td>86 (72)</td>
<td>89 (74)</td>
<td>78 (65)</td>
<td>84 (69)</td>
</tr>
<tr>
<td>Yes</td>
<td>10 (8)</td>
<td>22 (18)</td>
<td>14 (12)</td>
<td>14 (12)</td>
</tr>
<tr>
<td>No</td>
<td>110 (92)</td>
<td>99 (82)</td>
<td>106 (88)</td>
<td>107 (88)</td>
</tr>
</tbody>
</table>

SE = standard error.

Table 2. Pearson Correlations of Dietary Exposures

<table>
<thead>
<tr>
<th>Variable</th>
<th>MUFA</th>
<th>SFA</th>
<th>TFA</th>
<th>DC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (Interquartile Range)</td>
<td>11.5 (3.6)</td>
<td>11.1 (4.0)</td>
<td>1.9 (1.2)</td>
<td>200.8 (149.7)</td>
</tr>
<tr>
<td>MUFA</td>
<td>1.00</td>
<td>0.67</td>
<td>0.85</td>
<td>0.37</td>
</tr>
<tr>
<td>SFA</td>
<td></td>
<td>0.67</td>
<td>0.45</td>
<td>0.49</td>
</tr>
<tr>
<td>TFA</td>
<td></td>
<td></td>
<td>1.00</td>
<td>0.23</td>
</tr>
<tr>
<td>DC</td>
<td></td>
<td></td>
<td></td>
<td>1.00</td>
</tr>
</tbody>
</table>

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/d).
One of these studies found an effect of the Mediterranean diet on an individual cognitive domain, namely memory. This finding is consistent with the observed protective effect of MUFA on memory in the WHI CCW. In addition, the current study found an association between MUFA and less decline in visual–spatial abilities (copying and matching), a finding not previously made to the knowledge of the authors of the current study. Decline in visual–spatial function has been associated with driving errors in older adults and has also been suggested as a potential predictor (along with amnestic impairment) of transition from mild cognitive impairment to AD. Several pathways may explain the apparent relationship between MUFA intake and cognitive function. MUFA and MUFA derivatives have antiinflammatory effects in vivo, which may be important because chronic inflammation appears to be a precursor of symptomatic AD. Oxidative stress has also been demonstrated in patients with mild cognitive impairment and AD. and derivatives from MUFA, including low-molecular-weight phenols, have been found to have antioxidant effects. MUFA may also exert their potentially beneficial effects on cognition indirectly by decreasing cardiovascular risk by reducing macrophage uptake of plasma oxidized low-density lipoprotein, apolipoprotein B, and f triglycerides.

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>1 (0–9.75)</th>
<th>2 (9.76–11.50)</th>
<th>3 (11.51–13.26)</th>
<th>4 (&gt;13.27)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MUFA, % of energy intake</td>
<td>-0.16 (0.03)</td>
<td>-0.16 (0.03)</td>
<td>-0.10 (0.03)</td>
<td>0.00 (0.03)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Partial, regression coefficient (SE)</td>
<td>-0.18 (0.03)</td>
<td>-0.11 (0.03)</td>
<td>-0.10 (0.03)</td>
<td>-0.03 (0.03)</td>
<td>.01</td>
</tr>
<tr>
<td>Full, regression coefficient (SE)</td>
<td>-0.20 (0.05)</td>
<td>-0.16 (0.04)</td>
<td>-0.16 (0.04)</td>
<td>-0.13 (0.04)</td>
<td>.69</td>
</tr>
<tr>
<td>SFA, % of energy intake</td>
<td>0–9.12</td>
<td>9.13–11.11</td>
<td>11.12–13.00</td>
<td>≥13.01</td>
<td></td>
</tr>
<tr>
<td>Partial, regression coefficient (SE)</td>
<td>-0.18 (0.03)</td>
<td>-0.11 (0.03)</td>
<td>-0.10 (0.03)</td>
<td>-0.03 (0.03)</td>
<td>.01</td>
</tr>
<tr>
<td>Full, regression coefficient (SE)</td>
<td>-0.20 (0.05)</td>
<td>-0.16 (0.04)</td>
<td>-0.16 (0.04)</td>
<td>-0.13 (0.04)</td>
<td>.69</td>
</tr>
<tr>
<td>TFA, % of energy intake</td>
<td>0–1.45</td>
<td>1.46–1.92</td>
<td>1.93–2.64</td>
<td>≥2.65</td>
<td></td>
</tr>
<tr>
<td>Partial, regression coefficient (SE)</td>
<td>-0.13 (0.03)</td>
<td>-0.16 (0.03)</td>
<td>-0.07 (0.03)</td>
<td>-0.06 (0.03)</td>
<td>.07</td>
</tr>
<tr>
<td>Full, regression coefficient (SE)</td>
<td>-0.17 (0.04)</td>
<td>-0.19 (0.04)</td>
<td>-0.13 (0.04)</td>
<td>-0.17 (0.04)</td>
<td>.54</td>
</tr>
<tr>
<td>DC intake, mg</td>
<td>0–136.17</td>
<td>136.18–203.53</td>
<td>203.54–281.58</td>
<td>≥281.59</td>
<td></td>
</tr>
<tr>
<td>Partial, regression coefficient (SE)</td>
<td>-0.11 (0.04)</td>
<td>-0.10 (0.03)</td>
<td>-0.11 (0.03)</td>
<td>-0.10 (0.04)</td>
<td>.97</td>
</tr>
<tr>
<td>Full, regression coefficient (SE)</td>
<td>-0.14 (0.04)</td>
<td>-0.14 (0.04)</td>
<td>-0.18 (0.04)</td>
<td>-0.19 (0.04)</td>
<td>.64</td>
</tr>
</tbody>
</table>

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

**Further adjusted for body mass index, estrogen use, caffeine use, beta-blocker use, and other fatty acid (monounsaturated fatty acid (MUFA), polyunsaturated fatty acid (PUFA), saturated fatty acid (SFA), trans-unsaturated fatty acid (TFA) % energy; dietary cholesterol (DC) mg/d) intake.

SE = standard error.

### DISCUSSION

In this cohort of older women, greater MUFA intake was associated with less cognitive decline over a 3-year period. Previous studies generally but not invariably support this association. One previous prospective study found greater dietary MUFA intake to be associated with less cognitive decline, a second found a trend in the same direction, a third found a trend in the same direction in restricted analyses, and three others were null. None of the null studies had multiple measures of diet; one assessed diet using a measure of fatty acid composition of erythrocyte membranes, but that study assessed cognitive decline exclusively using the Mini-Mental State Examination, which is probably not as sensitive as the neuropsychological test battery used in this study.

MUFA is thought to be one of the major protective components of the traditional Mediterranean diet, in which it is derived primarily from olive oil (median 46 g/d). Two recent prospective studies of the Mediterranean diet have found greater adherence to be associated with less cognitive decline and lower incidence of Alzheimer’s disease (AD). One of these studies found an effect of the Mediterranean diet on an individual cognitive domain, namely memory. This finding is consistent with the observed protective effect of MUFA on memory in the WHI CCW. In addition, the current study found an association between MUFA and less decline in visual–spatial abilities (copying and matching), a finding not previously made to the knowledge of the authors of the current study. Decline in visual–spatial function has been associated with driving errors in older adults and has also been suggested as a potential predictor (along with amnestic impairment) of transition from mild cognitive impairment to AD.

Several pathways may explain the apparent relationship between MUFA intake and cognitive function. MUFA and MUFA derivatives have antiinflammatory effects in vivo, which may be important because chronic inflammation appears to be a precursor of symptomatic AD. Oxidative stress has also been demonstrated in patients with mild cognitive impairment and AD. and derivatives from MUFA, including low-molecular-weight phenols, have been found to have antioxidant effects. MUFA may also exert their potentially beneficial effects on cognition indirectly by decreasing cardiovascular risk by reducing macrophage uptake of plasma oxidized low-density lipoprotein, apolipoprotein B, and f triglycerides.
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, probably because of confounding by MUFA, which was moderately correlated with SFA, although there was no association between SFA and cognitive decline in the fully adjusted model. Previous prospective studies found dietary SFA intake to be deleterious\(^6\)–\(^8\) or null\(^10,11\) in associations with cognitive decline. Similarly, previous prospective studies found TFA intake to be deleterious\(^3\) or trending toward deleterious.\(^6\) Participants in these studies had substantially higher absolute and relative SFA and TFA intakes than did the women in the current 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, to better detect the 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 MUFA and cognitive decline.\(^6\)–\(^11\) Finally, the WHI and CCW measured a wide variety of characteristics of participants, 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 of dietary fatty acids and to detect nonlinear 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 that analyses. Nevertheless, 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, the possibility of residual confounding by unknown risk factors, such as a generally healthier lifestyle of individuals with a higher MUFA intake, cannot be excluded. Finally, the study population consisted of primarily healthy, highly educated, older Caucasian women, which limits the generalizability of these findings to other populations.

In conclusion, greater dietary MUFA intake was found 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 are needed to confirm the possible protective effects of MUFA on cognitive decline.

ACKNOWLEDGMENTS

Conflict of Interest: Dr. Mukamal is the principal investigator on an ongoing study funded by Harvard Medical School for which Beth Israel Deaconess Medical Center (BIDMC) received a donation of docosahexaenoic acid and placebo capsules from Martek Corporation. Dr. Naqvi is a co-investigator on that trial. Martek provided no other resources or funds and has no role in the conduct or analysis of that study. Martek had no role whatsoever in the current manuscript. There are no other financial or personal interests to disclose.

All authors have no other potential conflicts of interest to disclose.

This work was exclusively funded by the National Institutes of Health (T32 AT000051 and R01 AG018695-01A1). The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services through Contracts N01WH22110, 24152, 32100-2, 32105-6, 32108-9, 32111-13, 32115, 32118-32119, 32122, 42107-26, 42129-32, and 44221.

Author Contributions: Asghar Naqvi contributed to research design and data analysis, wrote the manuscript, and had primary responsibility for final content. Brian Harty performed statistical analyses and contributed to manuscript writing and revision. Kenneth J. Mukamal contributed to research design, data analysis, and manuscript writing and revision. Anne Stoddard supervised statistical analyses and contributed to manuscript writing and revision. Mara Vitolins contributed to research design and manuscript revision. Julie E. Dunn supervised research design and data analysis and contributed to manuscript writing and revision.

Sponsor’s Role: None.

REFERENCES

FATTY ACIDS AND COGNITIVE DECLINE


SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Short List of WHI Investigators

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