Relation of DASH- and Mediterranean-like dietary patterns to cognitive decline in older persons

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ABSTRACT

Objectives: We examined whether accordance to the DASH (Dietary Approach to Stop Hypertension) and Mediterranean diets is associated with slower cognitive decline in a prospective Chicago cohort study of older persons, the Memory and Aging Project.

Methods: The sample comprised 826 Memory and Aging Project participants (aged 81.5 ± 7.1 years) who completed a 144-item food frequency questionnaire at baseline and 2 or more cognitive assessments over 4.1 years. Dietary scores were computed for accordance to the DASH diet (0–10) and the Mediterranean diet (MedDietScore) (0–55). For both, higher scores reflect greater accordance. Both patterns share at least 3 common food components. Cognitive function was assessed annually with 19 cognitive tests from which global cognitive scores and summary measures are computed.

Results: The mean global cognitive score at baseline was 0.12 (range, −3.23 to 1.60) with an overall mean annual change in score of −0.08 standardized units. Only 13 participants had possible dementia. The mean DASH score was 4.1 (range, 1.0–8.5) and the MedDietScore was 31.3 (range, 18–46). In mixed models adjusted for covariates, a 1-unit difference in DASH score was associated with a slower rate of global cognitive decline by 0.007 standardized units (standard error of estimate = 0.003, $p = 0.03$). Similarly, a 1-unit-higher MedDietScore was associated with a slower rate of global cognitive decline by 0.002 standardized units (standard error of estimate = 0.001, $p = 0.01$).

Conclusions: These findings support the hypothesis that both the DASH and Mediterranean diet patterns are associated with slower rates of cognitive decline in the same cohort of older persons. *Neurology*® 2014;83:1410–1416

GLOSSARY

CERAD = Consortium to Establish a Registry for Alzheimer's Disease; **DASH** = Dietary Approach to Stop Hypertension; **FFQ** = food frequency questionnaire; **MAP** = Memory and Aging Project; **MedDiet** = Mediterranean diet; **MedDietScore** = Mediterranean diet score; **SEE** = standard error of estimate.

Both the DASH (Dietary Approach to Stop Hypertension) diet and the Mediterranean-style diet have been shown to be protective against hypertension, obesity, cardiovascular disease, and diabetes.[1–4] Many of these conditions also increase cognitive decline.[5–7] We[8] and others[9,10] have observed that accordance to a Mediterranean diet (MedDiet) pattern is associated with slower cognitive decline, but others have not found such associations.[11–14] Limited information is available on the relation of the DASH diet to cognitive decline. In the Exercise and Intervention for Cardiovascular Health Trial,[15] 124 overweight, sedentary, prehypertensive or hypertensive adults assigned to the DASH diet and weight management treatment experienced improvements in executive function, memory, learning, and perceptual speed after 4 months.

The Mediterranean-style diet has many interpretations with several features distinct from the DASH diet: the almost exclusive use of olive oil as the primary fat, high consumption of fish, and moderate consumption of wines with meals. The DASH diet specifies low consumption of saturated fat and commercial pastries and sweets, and higher consumption of dairy than in the

Mediterranean pattern. In this study, we examined and compared the DASH and MedDiet pattern scores in relation to cognitive decline among older persons from a prospective cohort study with annual follow-up visits.

METHODS **Sample.** The sample largely comprised cognitively normal participants from the Memory and Aging Project (MAP), an ongoing cohort study of older persons living in Chicago retirement communities and subsidized housing that began in 1997.[16] At the beginning, volunteers must be dementia-free and agree to annual clinical neurologic evaluations. The ongoing nutrition component to the MAP study began in 2004. Of the 1,555 individuals who have participated in MAP since 1997, 1,360 were alive and still actively participating when the nutritional component was instituted (80 were deceased and 115 had withdrawn participation). Of these, 951 (70%) agreed to be in the nutrition study and 826 participants had undergone 2 or more cognitive assessments and completed a valid food frequency questionnaire (FFQ).

Standard protocol approvals, registrations, and patient consents. The institutional review board of Rush University Medical Center approved the study. All participants gave written informed consent.

Dietary assessment. The self-administered MAP FFQ is a modified 144-item version of the Chicago Health and Aging Project semiquantitative FFQ in which participants record the usual frequency of consumption of specified portions of various food items. The FFQ was completed at the first cognitive assessment and, once reviewed for completeness, the questionnaires are sent for optical scanning at Harvard University. Daily nutrient or dietary intakes were calculated as the product of frequency of the food consumed and nutrient amount of selected item, and summing these for all food items. Validation and reliability of the Chicago Health and Aging Project FFQ have been previously reported.[17,18]

Food items on the MAP FFQ were assigned to 7 DASH food groups, and 3 components, the proportion of energy from total fat, from saturated fat, and milligrams sodium per day, were computed using the Harvard nutrient database. The composite DASH diet accordance score (0–10) was calculated[19] with further modifications[20] (table e-1 on the *Neurology*® Web site at Neurology.org). The MedDiet score (MedDietScore)[21] is based on intakes of alcohol and 10 food groups. The maximum number of points for MedDietScore is 55, where higher scores connote greater accordance. MedDiet component values (from 0 to 5) are assigned on the basis of a predefined number of servings for each point value based on the traditional Greek Mediterranean diet.[21] In contrast, for the more popular Mediterranean score, the MeDi,[22] point values (0 or 1) for each of the 9 components are assigned on the basis of meeting and/or exceeding the sex-specific population median of food component distribution.

Cognitive assessments. In annual neurologic examinations, MAP participants' cognitive function was assessed with a battery of 19 cognitive tests summarized as a global measure of cognition and 5 separate summary measures including: (1) episodic memory (a composite score of the following 7 tests: logical memory [immediate], logical memory [delayed], Consortium to Establish a Registry for Alzheimer's Disease [CERAD] immediate word list recall, CERAD delayed word list recall, CERAD word list recognition, East Boston Story immediate, and East Boston Story delayed); (2) semantic memory (a composite score of 3 tests: verbal fluency from CERAD, 15-item version of the Boston Naming Test, and 15-item reading test); (3) working memory (a composite score of 3 tests: Digit Span subset Forward, Digit Span subset Backward, and Digit Ordering); (4) perceptual speed (4 tests: oral version of the Symbol Digit Modalities Test, Number Comparison, and 2 indices from the modified Stroop Neuropsychological Screening); and (5) visuospatial ability (2 tests, which include 15-item Judgment of Line Orientation, and 16-item of Standard Progressive Matrices).[23] We computed composite scores of all 19 tests (global) and for each cognitive domain to minimize floor and ceiling effects and other sources of measurement error of the individual tests. Raw scores on each test were converted to z scores by using the baseline mean and SD, and then scores were averaged to form the composite measures.[24]

Other nondietary variables. Other nondietary variables were acquired at the participants' baseline interviews. Age was computed from self-reported birth date and date of baseline cognitive assessment. Education was computed from self-reported years of education. An evaluation of depressive symptoms was made using the 10-item version of the Center for Epidemiologic Studies–Depression Scale and was derived from the original 30-item version with acceptable reliability and similar factor structure to the original version.[25] Presence or absence of diabetes was based on self-reported history or diabetic medication use (including insulin injections). Hypertension was defined by measured systolic/diastolic blood pressures exceeding 160/90 mm Hg or current use of antihypertensive medications at the time of FFQ completion. Presence or absence of stroke was defined on the basis of medical history and neurologic examination. A composite score ranging from 0 to 7 reflecting the frequency of participation in cognitive activities (e.g., reading newspapers) was constructed as described previously; higher scores indicate participation in more activities.[26] A physical activity score reflects the sum of hours per week in 5 exercises (walking for exercise, yard work or gardening, calisthenics or general exercises, bicycling, and swimming), as adapted from the National Health Interview Survey. *APOE* genotyping (Agencourt Bioscience Corporation, Beverly, MA) was based on high-throughput sequencing assay.[27]

Statistical analyses. Analyses were performed using SAS version 9.1 (SAS Institute Inc., Cary, NC). We used mixed-effects models to estimate the effect of accordance to the DASH and MedDiet patterns on the rates of within-person change in cognitive scores over time. The basic-adjusted model included terms for the diet pattern, age, sex, education, participation in cognitive activities, total energy intake (kcal), time, and the interaction between time and each covariate. Secondary models were also run that included the basic covariates as well as physical activity, *APOE* ε4 alleles, depression, and stroke. The interaction terms with time represent the effects of the variables on the rate of change in cognitive scores. The β coefficients for the diet scores represent the associations between diet scores and either baseline cognitive scores or rates of change in cognitive scores (interaction terms with time and dietary scores). A positive β coefficient for interaction terms with time and diet score reflects a decrease in the rate of decline with higher diet scores. Effect modification was examined by modeling 2- and 3-factor interaction terms among the covariates (presence or absence of *APOE* ε4 alleles, depression, stroke, hypertension, diabetes, as well as age and sex), diet score, and time. DASH and MedDiet scores were also modeled in tertiles with the lowest as the referent category to assess whether the influence on cognitive changes was driven by the highest scores. To

determine whether DASH and MedDiet scores were related to some cognitive abilities but not others, an examination was made of their associations with separate summary measures of 5 different cognitive abilities. In an effort to ascertain whether these relations were attributable to participants who had the lowest global cognitive scores in the sample, we excluded those with the lowest scores (lowest 10% of global scores) and reran these models.

RESULTS The average age of MAP participants was 81.5 ± 7.1 years with no remarkable differences in age among those categorized into DASH score or MedDietScore tertiles (table 1). Participants were mostly female with 14.9 years of education; approximately one-fifth had at least one *APOE* ε4 allele. Average daily energy was 1,733 ± 547 kcal with 30% ± 6% energy from total fat, 10% ± 2% from saturated fat, and 2,335 ± 822 mg sodium per day. Because annual cognitive assessments are performed, 17.4% of the sample had 2 cognitive assessments, nearly a quarter (21.5%) had 5 assessments, and 12.4% had 8. The average follow-up of MAP participants in this analysis was 4.1 years, with a range of 1 to 10 years.

No one received a perfect DASH or MedDiet score. The average DASH score of participants was 4.1 ± 1.4 with a range of 1.0 to 8.5, and for

MedDietScore, 31.3 ± 5.1, range, 18 to 46. DASH and MedDiet scores were correlated ($r = 0.51$, $p < 0.0001$). An assessment of food group servings and dietary estimates that constitute the basis for DASH and MedDiet scoring are shown in table e-1. For the DASH scoring, the number of grain servings was exceptionally low with only 1.3% achieving the target frequency amount of 7 servings per day. Only 35% reported consuming 4 or more servings of vegetables per day and even less. Although a large proportion of MAP participants consumed 2 or fewer daily servings of meat, fish, or poultry, relatively few met targets (limits) for intakes of saturated fat or sweets. More than half reported consuming less than 2,400 mg sodium per day. For MedDietScores, only 5.8% received a perfect score for the MedDiet vegetable component, meaning those participants had consumed more than 33 vegetable servings per week. Few met targets for potatoes (0.1%), olive oil (4.3%), or fish (0.2), although 46.4% did meet the optimal intakes of alcohol in this group.

The mean global cognitive score at baseline was 0.12 (range, −3.23 to 1.60), and the overall mean change in score per year was a decline of −0.08 standardized units. As shown in table 2, there was a positive association between global cognitive scores over

Table 1	Demographic characteristics of 826 MAP participants and stratified by tertiles of DASH and MedDiet scores						
		DASH tertiles			MedDiet tertiles		
Characteristic	Total (n = 826)	Lowest (n = 364); 2.9[a]	Middle (n = 233); 4.3	Highest (n = 229); 5.8	Lowest (n = 288); 26[a]	Middle (n = 268); 31	Highest (n = 270); 37
Age, y	81.5 ± 7.1	81.1 ± 7.6	81.8 ± 6.8	81.7 ± 6.8	81.6 ± 7.5	81.8 ± 7.2	81.0 ± 6.6
Male, %	26	25	25	28	19	28	30
Education, y	14.9 ± 2.9	14.6 ± 2.9	14.9 ± 3.2	15.4 ± 2.7	13.9 ± 2.9	15.1 ± 2.8	15.8 ± 2.8
Body mass index,[b] kg/m²	27.1 ± 5.2	27.5 ± 5.1	27.4 ± 5.5	26.3 ± 5.0	27.4 ± 5.0	27.4 ± 5.2	26.7 ± 5.5
Cognitive activities[c]	4.8 ± 1.3	4.6 ± 1.4	4.8 ± 1.3	5.0 ± 1.2	4.4 ± 1.8	4.8 ± 1.4	5.1 ± 1.1
Physical activities	3.2 ± 3.6	2.7 ± 2.9	3.2 ± 4.4	4.2 ± 4.3	2.4 ± 2.7	3.4 ± 3.8	4.0 ± 3.8
Energy intake, kcal/d	1,733 ± 547	1,661 ± 557	1,808 ± 529	1,789 ± 524	1,501 ± 513	1,795 ± 545	1,926 ± 485
Depression[d]	1.1 ± 1.6	1.2 ± 1.6	1.2 ± 1.7	0.9 ± 1.4	1.5 ± 1.8	1.1 ± 1.6	0.8 ± 1.3
Hypertension,[e] %	64.6	65.4	66.5	61.6	68.1	66.4	59.3
Diabetes,[f] %	13.9	14.6	15.7	11.0	19.2	13.5	8.6
Stroke,[g] %	15.1	12.3	18.0	16.8	17.1	14.5	13.6

Abbreviations: DASH = Dietary Approach to Stop Hypertension; MAP = Memory and Aging Project; MedDiet = Mediterranean diet.
Data are mean ± SD unless otherwise indicated.
[a] Mean score for each tertile.
[b] Measured weight and height to calculate body mass index; n = 796.
[c] Sum of 7 cognitive activities across each year of study participation, including reading, visiting a library, reading newspapers, reading magazines, reading books, writing letter, and playing games. Higher scores signify greater activities.
[d] Depression scores, range 0-10, based on a modification of the Center for Epidemiologic Studies-Depression Scale. Higher scores signify more depression.
[e] Hypertension defined as measured systolic/diastolic blood pressures exceeding 160/90 mm Hg or current use of antihypertensive medications.
[f] Diabetes defined on the basis of self-reported history or diabetic medication use, including insulin.
[g] Stroke defined on the basis of medical history and neurologic examination.

Table 2 The β coefficients of rates of change in global cognitive scores and individual cognitive domains associated with total DASH scores and MedDietScores based on adjusted linear mixed models in 826 Memory and Aging Project participants, 2004–2013[a]

Global/cognitive domain outcome	Baseline cognitive score[b]	DASH scores			MedDietScores		
		Linear			Linear		
		β (SEE), p value[c]	Standardized β	Nonlinear; tertile 3[c]	β (SEE), p value[c]	Standardized β	Nonlinear; tertile 3[c]
Global cognitive score	0.12 (0.61)	0.007 (0.003), 0.03	2.33	0.022 (0.011), 0.04	0.002 (0.001), 0.01	2.0	0.034 (0.012), 0.003
Episodic memory	0.16 (0.77)	0.008 (0.004), 0.04	2.0	0.024 (0.013), 0.07	0.003 (0.001), 0.02	3.0	0.040 (0.015), 0.007
Visuospatial memory	0.11 (0.80)	0.007 (0.004), 0.07	1.75	0.018 (0.013), 0.17	0.002 (0.001), 0.08	2.0	0.022 (0.014), 0.12
Perceptual speed	0.07 (0.78)	0.007 (0.004), 0.06	1.75	0.021 (0.012), 0.08	0.002 (0.001), 0.07	2.0	0.024 (0.013), 0.07
Semantic memory	0.14 (0.68)	0.009 (0.004), 0.02	2.25	0.023 (0.012), 0.05	0.003 (0.001), 0.02	2.0	0.033 (0.013), 0.01
Working memory	0.10 (0.77)	0.005 (0.004), 0.15	1.25	0.016 (0.012), 0.20	0.002 (0.001), 0.14	2.0	0.033 (0.013), 0.01

Abbreviations: DASH = Dietary Approach to Stop Hypertension; MedDietScore = Mediterranean diet score; SEE = standard error of estimate.
[a] Linear mixed models for change in global and individual cognitive domains over time associated with total DASH scores or MedDietScores with adjustment for energy (kcal), age, sex, education, and cognitive activities.
[b] Values reflect mean (SD).
[c] Values reflect β or rate of change (SEE), and p value.

time and total DASH score reflecting a reduction in the rate of decline in cognitive scores. Per 1-unit-higher DASH score, the decline rate was slower by 0.007 standardized units (standard error of estimate [SEE] = 0.003, p = 0.03). Models were repeated using tertiles of the diet scores in place of the total DASH or MedDiet score. As shown in the figure, only the top tertile (DASH scores with a mean of 5.8) reduced the rates of cognitive decline (β = 0.022, SEE = 0.011, p = 0.04). Results were not changed with additional adjustment for depressive symptoms, the presence of *APOE* ε4 alleles, stroke, hypertension, or diabetes (table e-2). In addition, there was no evidence of effect modification by age, sex, presence of *APOE* ε4 alleles, stroke, hypertension, or diabetes (p values for interaction were each >0.10). Similar associations were also noted for global cognitive changes over time and the total MedDietScores; for 1-unit-higher MedDietScore, the rate of cognitive decline was slower by 0.002 standardized units (SEE = 0.001, p = 0.01). Only the upper tertile of MedDietScores was associated with rates of global cognitive change (β = 0.034, SEE = 0.012, p = 0.003). When we examined whether the associations with MedDietScores and cognitive decline differed by age, sex, presence of *APOE* ε4 alleles, stroke, hypertension, or diabetes, no significant interactions were found (p values for interaction were each >0.10). When total DASH scores were regressed on rates of changes in each of the cognitive domains, the scores were associated with

2 of the 5 domains (episodic memory and semantic memory) (table 2). For MedDietScores, the rates of change in episodic memory and in semantic memory were also slower. Standardized regression coefficients are also provided in table 2. Based on a comparison of standardized β coefficients from the basic-adjusted models, DASH scores (2.33) were as predictive of cognitive decline as those of MedDietScores (2.00) in this cohort. DASH scores in the top tertile were significantly associated with reduced rates of change for not only global scores but also semantic memory. MedDietScores in the upper tertile were associated with slower decline rates in episodic, semantic, and working memory domains.

When we repeated analyses excluding participants whose baseline global cognitive scores were in the bottom 10% of the distribution, the multiple adjusted estimates for total DASH score changed very little (β = 0.01, SEE = 0.003, p = 0.01, n = 741). When such analyses were run for MedDietScores, the estimates also were minimally affected (β = 0.002, SEE = 0.001, p = 0.01). Additional sensitivity analyses were run excluding those persons with possible dementia at baseline; there were minimal changes in the cognitive rates of change.

DISCUSSION In the MAP community cohort of older persons, accordance to both the DASH and MedDiet dietary patterns was associated with slower rates of cognitive decline. For a 1-unit-higher DASH score, rates of cognitive decline were 0.007
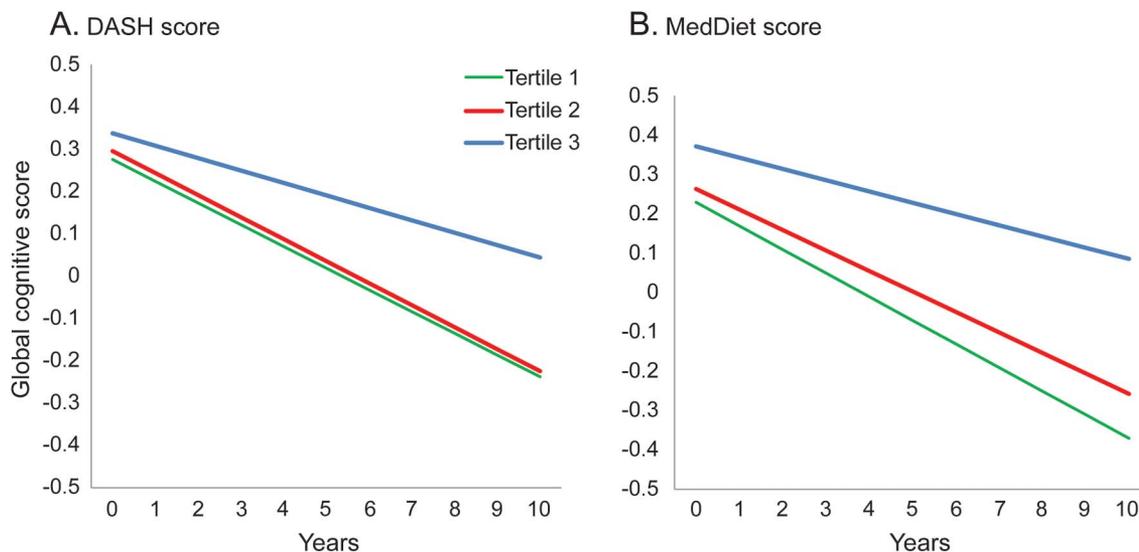
Changes in global cognitive scores over time as a function of (A) DASH score tertiles (left) and (B) MedDietScore tertiles (right). All mixed models included covariable adjustments by age, sex, education, energy, and late-life cognitive activities. Change rates in global cognitive scores of Memory and Aging Project participants were significantly associated in the highest tertiles of either score—DASH ($\beta = 0.022$, SEE = 0.011, $p = 0.04$) or MedDiet ($\beta = 0.034$, SEE = 0.012, $p = 0.003$)—but not for those whose DASH scores ($\beta = -0.001$, SEE = 0.010, $p = 0.95$) or MedDietScores ($\beta = 0.01$, SEE = 0.011, $p = 0.37$) were in the second tertiles. DASH = Dietary Approach to Stop Hypertension; MedDiet = Mediterranean diet; MedDietScore = Mediterranean diet score; SEE = standard error of estimate.

standardized units slower or equivalent to at least 4.4 years younger age. These findings were not wholly unexpected because many of the food components that constitute the selected diet scores are those we have previously observed to be related to cognitive change,[8,28–30] as have other groups.[31] Similar components of DASH and Mediterranean-style diet scores among Cache County cohort participants were also associated with cognitive decline over an 11-year period; these included 3 DASH components (whole grains, vegetables, and nuts plus legumes) and 2 Mediterranean components (legumes and vegetables).[9] In the Women's Health Study participants, investigators[14] observed that higher monounsaturated-to-saturated ratios were related to more favorable cognitive trajectories, although total scores (the alternate MeDi) were not associated with cognitive change. The present study findings also confirm those of the 4-month randomized trial of a DASH diet intervention with or without a weight management program vs usual care in middle-aged, hypertensive adults; executive memory and learning functions improved in the DASH plus weight group while psychomotor function improved in both DASH interventions regardless of weight strategies.[15] It is intriguing to note that in this older, largely hypertensive MAP population, accordance to either diet pattern—not an active dietary intervention—was associated with improvements in cognitive domains over a period of 4 years. Similar findings from studies with different research designs and duration suggest that

the cognitive effects from this dietary pattern may be rapid. There are 2 other reports from observational cohorts of older persons in the United States that support the associations of Mediterranean-style diet scores with cognitive decline.[8,9]

DASH scores (mean of 4.1) observed in the present study are similar to those of other American adult population samples. Others reported DASH scores ranging from 3.6 to 3.9 among Exercise and Intervention for Cardiovascular Health Trial participants[20]; this group used a DASH scoring system similar to that used in the present study. In a much larger cohort—more than 20,993 Iowa Women's Health Study participants in 1986—DASH scores averaged 4.2 with a considerable range from 0.5 to 10; no one had a perfect accordance score of 11.[19] Examination of reported MedDietScores of participants in several US cohorts is more tenuous, because of different scoring paradigms and different analytic approaches.

The mechanism(s) underlying the associations between these 2 dietary patterns on cognition or cognitive decline is mostly unknown but may involve inflammatory processes. Inflammation is generally believed to be the key process contributing to cerebrovascular pathology, stroke, and heart disease. In a 24-year follow-up of participants in the Nurses' Health Study, DASH scores were associated with reduced risk of stroke ($p < 0.002$ for trend), and reduced levels of inflammatory markers.[32] Similarly, based on the findings from a recent clinical trial of 2 MedDiet interventions against a control low-fat

treatment, the MedDiets over a 5-year period reduced cardiovascular events—in particular, incident stroke.[3] Reduced levels of circulating inflammatory markers and improved endothelial function have been shown when participants adopt this dietary pattern.[33] Alternatively, antioxidant protection afforded by many of the DASH and Mediterranean food components (vegetables, nuts, legumes) that are enriched in tocopherols, omega-3 fatty acids, thiamin, lutein, other carotenoids, vitamin K, folate, and certain polyphenols may be responsible for the relations to cognitive decline.[34–36] Perhaps the presence of such foods in the gut may favor certain bacteria that, in turn, facilitate maintenance of factors that are neuroprotective.[37] It is possible that these foods may influence β-amyloid or tau metabolism; evidence for these mechanisms are largely from animal studies[38,39] and require further assessment and confirmation. Moreover, the literature is even more limited for the influence of these dietary patterns on individual cognitive domains. Many groups use different series of cognitive tests to examine cognitive domains. There is considerable overlap in tests selected and how these domains are described as discussed recently.[40]

Strengths of the present study include the prospective design, a community sample, use of a well-validated dietary questionnaire, use of DASH and Med-Diet scoring tools that have been applied to other population samples, and use of multiple tests to measure cognitive function longitudinally. Moreover, the present analyses included adjustment for many confounders. Some of the limitations include relatively few items reflecting nonrefined grains (only 3 items), few fish items (particularly regarding preparation), and less specific information on type of olive oils on the MAP FFQ. Because of the observational study design, we must caution against a causal interpretation of findings. Furthermore, this cohort may not be representative of the diverse older population in the United States.

These findings attest to the need for more research to determine whether a food-based approach can attenuate neurocognitive decline in older populations at risk of Alzheimer disease or vascular cognitive impairment. A food-based clinical trial for primary prevention of cardiovascular disease has been fruitful (i.e., PREDIMED[3]). The need for similar efforts is critical in the face of the growing number of aging adults who are at risk of dementias.

AUTHOR CONTRIBUTIONS

Dr. Tangney: study concept and design, acquisition of data, analysis and interpretation of data, and critical revision of the manuscript for important intellectual content. Ms. Li and Dr. Wang: analysis and interpretation of data. Dr. Barnes: study concept and design, interpretation of data, and critical revision of the manuscript for important intellectual content; other contribution: study supervising or coordination. Dr. Schneider: study concept and design, interpretation of data, and critical revision of the manuscript for important intellectual content; other contribution:

acquisition of data. Dr. Bennett: study concept and design, interpretation of data, and critical revision of the manuscript for important intellectual content; other contribution: study supervising or coordination. Dr. Morris: study concept and design, interpretation of data, and critical revision of the manuscript for important intellectual content.

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