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ARTICLE

Dietary patterns during adulthood and cognitive performance in midlife

The CARDIA study

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Abstract

Objective

To investigate whether dietary patterns (Mediterranean diet [MedDiet], Dietary Approaches to Stop Hypertension [DASH], and A Priori Diet Quality Score [APDQS]) during adulthood are associated with midlife cognitive performance.

Methods

We studied 2,621 Coronary Artery Risk Development in Young Adults (CARDIA) participants; 45% were black, 57% were female, and mean age was 25 ± 3.5 years at baseline (year 0). Mean diet scores were calculated from diet history at baseline, year 7, and year 20 (mean age 25, 32, and 45 years, respectively). Cognitive function was assessed at years 25 and 30 (mean age 50 and 55 years, respectively). Linear models were used to examine association between tertiles of diet score and change in composite cognitive function and cognitive *z* scores (verbal memory [Rey Auditory Verbal Learning Test], processing speed [Digit Symbol Substitution Test], and executive function [Stroop Interference test]) and the Montreal Cognitive Assessment (MoCA) at year 30.

Results

DASH was not associated with change in cognitive performance. Higher MedDiet and APDQS scores were associated with less decline in cognitive function (MedDiet: low −0.04, middle 0.03, high 0.03, $p = 0.03$; APDQS: low −0.04, middle −0.00, high 0.06, $p < 0.01$) and Stroop Interference (MedDiet: low 0.09, middle −0.06, high −0.03; APDQS: low 0.10, middle 0.01, high −0.09, both $p < 0.01$). Odds ratios (95% confidence interval) for poor global cognitive function (≥1 SD below mean MoCA score) comparing extreme tertiles of diet scores were 0.54 (0.39–0.74) for MedDiet, 0.48 (0.33–0.69) for APDQS, and 0.89 (0.68–1.17) for DASH.

Conclusion

Greater adherence to MedDiet and APDQS dietary patterns during adulthood was associated with better midlife cognitive performance. Additional studies are needed to define the combination of foods and nutrients for optimal brain health across the life course.

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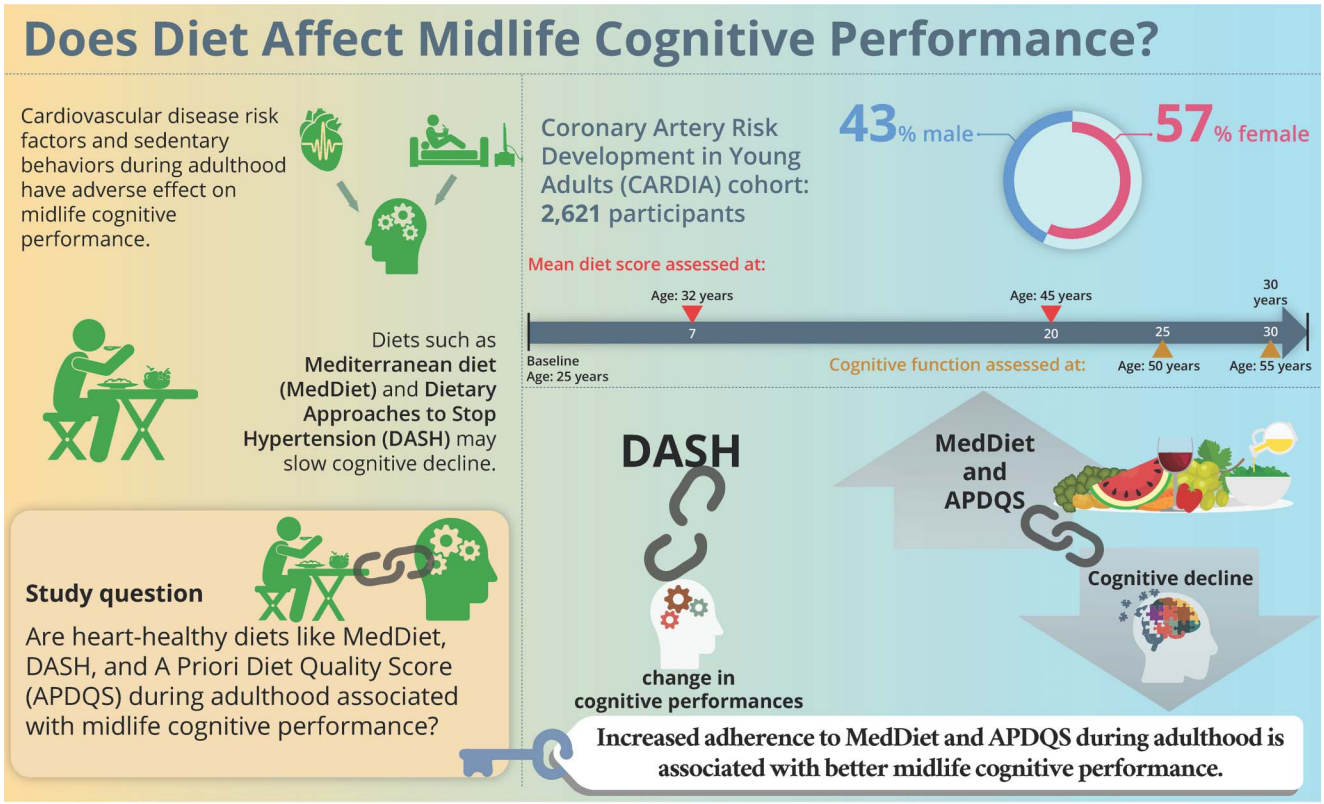
Glossary

APDQS = A Priori Diet Quality Score; **BMI** = body mass index; **CARDIA** = Coronary Artery Risk Development in Young Adults; **CES-D** = Center for Epidemiologic Studies Depression; **CI** = confidence interval; **DASH** = Dietary Approaches to Stop Hypertension; **DSST** = Digit Symbol Substitution Test; **MedDiet** = Mediterranean diet; **MoCA** = Montreal Cognitive Assessment; **OR** = odds ratio; **RAVLT** = Rey Auditory Verbal Learning Test.



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Cognitive impairment is associated with increased risk of mortality, disability, and late-life dementia, as well as high health care costs.[1,2] Cognitive decline has been demonstrated in midlife,[3] and accumulating data indicate that longitudinal exposure to cardiovascular disease risk factors and sedentary behaviors during adulthood has an adverse effect on midlife cognitive performance.[4–6]

Diet is a modifiable lifelong exposure, yet few studies have examined whether dietary factors in adulthood influence the risk of cognitive impairment. Dietary patterns such as the Mediterranean diet (MedDiet) and Dietary Approaches to Stop Hypertension (DASH) have shown promise as strategies to slow cognitive decline[7–9] and to reduce dementia risk in later life.[10,11] However, only a few studies have been conducted, mainly in older populations >60 years of age, and evidence has not been consistent,[12,13] in part because of variation between studies in measures of both diet and cognition. Furthermore, most observational studies are limited by a single time point measurement of diet and unlikely to reflect longitudinal variation in habitual dietary intake.[14]

The Coronary Artery Risk Development in Young Adults (CARDIA) study provides a unique opportunity to investigate diet during early to middle adulthood and change in midlife cognitive function in black and white adults. We aimed to examine associations between 3 heart-healthy diet patterns characterized by the MedDiet,[15] the DASH,[16] and the CARDIA A Priori Diet Quality Score (APDQS)[17] scores and cognitive performance at midlife. We hypothesized that greater long-term adherence to these diet patterns would be associated with preservation of cognitive function.

Methods

Study design

We studied participants enrolled in the CARDIA study, a multicenter longitudinal study of the development of cardiovascular risk factors and disease in 5,115 randomly selected

black and white healthy adults 18 to 30 years of age at baseline in 1985 to 1986. The study design and procedures have been previously described.[18] Eight follow-up examinations were completed over 30 years: 1987 to 1988 (year 2), 1990 to 1991 (year 5), 1992 to 1993 (year 7), 1995 to 1996 (year 10), 2000 to 2001 (year 15), 2005 to 2006 (year 20), 2010 to 2011 (year 25), and 2015 to 2016 (year 30). Dietary intake was assessed at 3 examinations (baseline and years 7 and 20), and cognitive function was assessed at years 25 and 30 with standard protocols. This study focused on 2,693 participants who completed both cognitive examinations and at least 2 of the 3 dietary assessments. The final analytical cohort comprised 2,621 participants after exclusion of persons with implausible energy intake (<600 or >8,000 kcal/d) (n = 34) and those with missing baseline covariate data (n = 38). Excluded participants were more likely to be female and black and to have lower educational attainment and worse cognitive performance at the year 25 visit (all $p < 0.01$, data not shown).

Standard protocol approvals, registrations, and patient consents

The study was approved by institutional review boards for the protection of human participants for the CARDIA study sites, and written informed consent was obtained from all participants at each examination.

Diet measure and dietary pattern scores

At the baseline, year 7, and year 20 visits (mean age 25, 32, and 45 years, respectively), dietary intake over the previous month was assessed by a trained interviewer-administered CARDIA diet history.[19] Food and beverages consumed were assigned to 1 of 166 created food groups devised by the Nutrition Coordinating Center at the University of Minnesota and based on a modified US Department of Agriculture food grouping system.[17,20,21] Reported servings for each food/beverage item were converted to standard serving according to US Department of Agriculture recommendations. Individual food-group intake was calculated as the total number of standard servings reported per day of each food within a given food group.

For each time point, individual dietary pattern scores were determined with the MedDiet,[15] DASH,[16] and APDQS[17] scoring systems. Diet scores were computed from predefined food group and nutrient (diet components) criteria for the dietary patterns as decribed.[15–17] The main foods and nutrients contributing to each diet score are shown in table 1 available from Dryad (doi.org/10.5061/dryad.443gv60). For each of the 3 diet patterns, individual components contributed equally to the summed score, and the highest possible score indicated higher diet quality or greatest concordance to the dietary pattern.

The MedDiet score[15] was calculated from 11 individual diet components scored between 0 and 5 points and then summed for a total score between 0 and 55. Points were assigned monotonically for increasing intake of nonrefined grains, fruits, vegetables, potatoes, legumes, fish, and olive oil and decreasing intake of red meat, poultry, and full-fat dairy. Because information was not available for olive oil, we calculated a ratio of monounsaturated to saturated fatty acid intake and divided this component into sextiles as described previously in a US population.[22] We scored the ratio of monounsaturated to saturated fatty acid monotonically from 0 to 5 points, with a ratio ≥2 assigned the highest score in accordance with a Greek MedDiet. Alcohol was scored 0 for nonconsumption or a high intake (>4.5 drinks per day) to a maximum score of 5 for moderate consumption (up to 2 drinks per day).

The DASH diet score[16] was calculated from 10 diet components scored 0, 0.5, or 1, depending on frequency of intake. Points were assigned monotonically for increasing intake of total grains, vegetables, fruit, low-fat dairy, legumes, and nuts and decreasing intake of meat, fish and poultry, total fat, saturated fat, sweets, and sodium. Diet component scores were summed for a total score ranging from 0 to 10. In a secondary analysis, we used an alternate version of DASH in which intake of total grains was replaced with whole grains.

The APDQS was derived from classification of 46 foods groups hypothesized to have beneficial, neutral, or adverse health effects.[17] The APDQS score, ranging from 0 to 132, was calculated from increasing intake of 20 beneficial components (including fruit, vegetables, legumes, low-fat dairy, fish, and moderate alcohol intake) and decreasing intake of 13 adverse components (including fried foods, salty snacks, desserts, high-fat dairy, and sugar-sweetened soft drinks). Scores for beneficial components increased monotonically from 0 to 4 with higher consumption of reported servings, and scores were reversed for the 13 adverse components.

Our primary predictor was diet during adulthood characterized by the 3 dietary pattern scores. To represent diet patterns over the long term and to reduce within-person variation, we calculated an average score for each of the 3 dietary patterns by taking the mean of the baseline, year 7, and year 20 diet scores.

Cognitive measures

At the year 25 visit, trained interviewers assessed cognitive function using 3 standardized tests: (1) Rey Auditory Verbal Learning Test (RAVLT) to assess verbal learning and memory; the number of words correctly recalled after a 10-minute delay was used in the current analyses (range 0–15), with higher scores indicating better performance; (2) Digit Symbol Substitution Test (DSST) to assess processing speed and executive function (range 0–133), with higher scores for digits correctly substituted indicating better performance; and (3) Stroop test to assess executive function. The Stroop Interference score was obtained by subtracting the score on subtest 2 from the score on subtest 3, with lower scores indicating better performance. A composite cognitive function score was computed by transforming each of the 3 tests to standardized z scores and averaging the summed total.

The cognitive test battery was repeated at the year 30 visit and expanded to include the Montreal Cognitive Assessment (MoCA) to assess global cognitive function with components of attention, executive function, memory, language, visuospatial skills, calculations, and orientation. Scores range from 0 to 30, with higher scores indicating better global cognitive function.

We examined 5-year change in the repeated cognitive z scores (delayed RAVLT, DSST, and Stroop Interference) and in composite cognitive function z score that was computed by averaging change in cognitive z scores (change delayed RAVLT z score − change Stroop Interference z score + change DSST z score/3). Negative z score change values indicated a decline from the initial examination except for the Stroop test, for which a positive z score change reflected a decline in performance.

Covariates

Covariates were determined at baseline. Demographics, including age, race, sex, education attainment (maximum number of education years), and smoking, were obtained by self- and interviewer-administered questionnaires. Physical activity was calculated as a total exercise score derived from the self-reported frequency and intensity of 13 activities during the past year.[23] Body weight and height were measured with standard clinic techniques, and body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Diabetes diagnosis at baseline was defined as fasting glucose level ≥126 mg/dL or taking antidiabetic medication. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or taking antihypertensive medication.

For sensitivity analyses, *APOE4* genotype was measured in year 7 blood samples by the method previously described.[24] The Center for Epidemiologic Studies Depression (CES-D) questionnaire (score range 0–60) was used to assess midlife depressive symptoms.

Statistical analysis

Participant characteristics by tertile of each dietary score were compared by use of analysis of variance for continuous variables and the χ^2 test for dichotomous variables, with corresponding tests for linear trend. Skewed variables were log transformed before analysis.

We used general linear models to examine independent associations between the 3 dietary scores and the cognitive outcomes. Dietary scores were modeled continuously per 1-SD increase and in tertile categories of low, middle, and high score.

We found little evidence of race or sex interaction in relations between dietary scores and change in cognitive measures ($p > 0.05$); therefore, analyses were performed with data from the full sample. To account for interindividual differences in baseline cognitive performance influencing the rate of cognitive change, the 5-year change in cognitive z scores was adjusted for the initial year 25 z score. Multivariable linear models were further adjusted for the effects of baseline sex, age, race, education attainment (years), BMI, smoking, physical activity, diabetes mellitus, and energy intake that differed according to tertile of diet score.

We also performed logistic regression analyses to examine associations between the 3 dietary patterns and risk of clinically relevant poor cognitive function (defined as 1 SD below the mean MoCA score), adjusting for potential confounders described above.

In sensitivity analyses, we further controlled for *APOE4* genotype and CES-D score. All analyses were carried out with SPSS version 22 (IBM Corp, Armonk, NY), and a value of $p < 0.05$ was considered significant.

Data availability

Anonymized data are available from the CARDIA Coordinating Center (cardia.dopm.uab.edu/contact-cardia). A description of the National Heart, Lung, and Blood Institute policies governing the data and describing access to the data can be found online (cardia.dopm.uab.edu/study-information/nhlbi-data-repository-data).

Results

The mean age of the 2,621 participants at baseline was 25.2 ± 3.5 years; 57% were female; 45% were black; and most (94%) had >12 years of education. Mean MedDiet and DASH scores increased while APDQS score slightly decreased over the 20 years (table 2 available from Dryad, doi.org/10.5061/dryad.443gv60).

The average long-term score for MedDiet was 28.4 ± 4.5 points (range 14.7–44.5), for DASH was 3.0 ± 0.90 points (range 0.8–7.8), and for APDQS was 63.2 ± 11.4 points (range 30.0–98.5). Long-term MedDiet scores positively correlated with both APDQS ($r = 0.69$, $p < 0.01$) and DASH ($r = 0.60$, $p < 0.01$) long-term scores.

As table 1 shows, participants with highest long-term dietary scores were more likely to be older, white, more highly educated, and physically active; had lower BMIs; and were less likely to smoke compared with those with the lowest scores. Those with higher DASH or APDQS scores were also more likely to be female. Total serum carotenoids (an objective marker of fruit and vegetable consumption) and self-reported fruit and vegetable intake during adulthood increased linearly across tertiles of each diet pattern score (all $p_{Trend} < 0.001$); fruit and vegetable servings almost doubled between the extreme tertiles for all 3 diet patterns examined.

Table 1 Baseline characteristics of CARDIA participants by tertile of long-term diet scores in adulthood (n = 2,621)

	MedDiet (score range 0–55)[a]				DASH (score range 0–10)[a]				APDQS (score range 0–132)[a]			
	Low (≤26) (n = 805)	Mid (>26–30) (n = 946)	High (>30) (n = 870)	*p* Value[b]	Low (≤2.5) (n = 996)	Mid (>2.5–3.3) (n = 788)	High (>3.3) (n = 837)	*p* Value[b]	Low (≤56.7) (n = 812)	Mid (>56.7–67.0) (n = 869)	HIGH (>67.0) (n = 940)	*p* Value[b]
Age, y	24.3 (3.7)	25.1 (3.6)	26.0 (3.1)	<0.001	24.8 (3.6)	25.0 (3.5)	25.7 (3.4)	<0.001	23.8 (3.7)	25.4 (3.5)	26.2 (3.1)	<0.001
Female, n (%)	463 (58)	519 (55)	511 (59)	0.59	489 (49)	448 (57)	556 (66)	<0.001	412 (51)	483 (56)	598 (64)	<0.001
White, n (%)	287 (36)	523 (55)	645 (74)	<0.001	442 (44)	427 (54)	586 (70)	<0.001	204 (25)	465 (54)	786 (84)	<0.001
Education <12 y, n (%)	90 (11)	40 (4)	24 (3)	<0.001	86 (9)	39 (5)	29 (4)	<0.001	100 (12)	41 (5)	13 (1)	<0.001
Current smoker, n (%)	212 (26)	228 (24)	189 (22)	0.03	263 (26)	204 (26)	162 (19)	0.001	229 (28)	207 (24)	193 (21)	<0.001
BMI, kg/m^2	25.2 (5.4)	24.5 (4.8)	23.5 (4.0)	<0.001	24.8 (5.1)	24.3 (4.4)	23.9 (4.7)	<0.001	25.1 (5.5)	24.6 (4.7)	23.6 (4.0)	<0.001
Hypertension, n (%)	76 (10)	78 (8)	65 (8)	0.14	95 (10)	64 (8)	60 (7)	0.06	70 (9)	78 (9)	71 (8)	0.39
Diabetes mellitus, n (%)	7 (1)	6 (1)	1 (0.1)	0.03	7 (1)	5 (1)	2 (0.2)	0.18	8 (1)	5 (1)	1 (0.1)	0.01
Physical activity, units/d	342 (269)	418 (290)	490 (297)	<0.001	377 (280)	406 (290)	480 (299)	<0.001	363 (289)	400 (292)	484 (282)	<0.001
Total calories, kcal/d	2,660 (1,323)	2,757 (1,293)	2,788 (1,251)	0.04	2,818 (1,253)	2,782 (1,347)	2,599 (1,265)	<0.001	3,065 (1,492)	2,740 (1,256)	2,453 (1,040)	<0.001
Fruit, servings/d	2.3 (2.8)	3.1 (2.8)	4.2 (3.1)	<0.001	2.3 (2.2)	3.2 (2.8)	4.4 (3.5)	<0.001	2.7 (2.9)	3.2 (2.9)	3.7 (3.0)	<0.001
Vegetables, servings/d	2.8 (1.9)	3.7 (2.5)	5.1 (3.3)	<0.001	3.1 (2.0)	3.9 (2.5)	4.8 (3.5)	<0.001	3.1 (2.2)	3.6 (2.4)	4.9 (3.3)	<0.001
Log serum carotenoids[c]	4.2 (0.41)	4.3 (0.39)	4.4 (0.39)	<0.001	4.2 (0.40)	4.3 (0.41)	4.4 (0.40)	<0.001	4.1 (0.40)	4.3 (0.39)	4.4 (0.39)	<0.001

Abbreviations: APDQS = CARDIA A Priori Diet Quality Score; BMI = body mass index; CARDIA = Coronary Artery Risk Development in Young Adults; DASH = Dietary Approaches to Stop Hypertension; MedDiet = Mediterranean Diet score.
Values are mean (SD) when appropriate.
[a] Long-term diet scores in adulthood were computed as average diet score at years 0, 7, and 20 (mean age 25, 32, and 45 years, respectively).
[b] Indicates *p* value for linear trend across tertiles of diet score.
[c] Summed concentrations of 5 carotenoids (zeaxanthin/lutein, β-cryptoxanthin, lycopene, α- and β-carotene) in 2,465 participants at baseline. Data were skewed and therefore log transformed for analysis.

Table 2 Association (β [95% CI]) of 1-SD increase in long-term diet score with cognitive performance at mean age 50 years

	Cognitive score at the initial year 25 examination, β (95% CI)			
	Overall cognitive function[a] (n = 2,591)	Delayed RAVLT (n = 2,621)	DSST (n = 2,608)	Stroop Interference (n = 2,597)
MedDiet[b]				
Basic	0.20 (0.17 to 0.23)	0.18 (0.15 to 0.22)	0.23 (0.19 to 0.27)	−0.20 (−0.24 to −0.16)
Adjusted[c]	0.08 (0.05 to 0.10)	0.06 (0.02 to 0.10)	0.10 (0.06 to 0.13)	−0.07 (−0.11 to −0.03)
DASH[b]				
Basic	0.15 (0.12 to 0.18)	0.16 (0.12 to 0.19)	0.19 (0.15 to 0.22)	−0.12 (−0.16 to −0.08)
Adjusted[c]	0.02 (−0.01 to 0.05)	0.02 (−0.02 to 0.05)	0.03 (−0.00 to 0.07)	−0.01 (−0.05 to 0.03)
APDQS[b]				
Basic	0.27 (0.25 to 0.30)	0.27 (0.23 to 0.31)	0.31 (0.27 to 0.35)	−0.25 (−0.29 to −0.22)
Adjusted[c]	0.09 (0.06 to 0.12)	0.06 (0.02 to 0.11)	0.11 (0.07 to 0.16)	−0.08 (−0.13 to −0.04)

Abbreviations: APDQS = CARDIA A Priori Diet Quality Score; CI = confidence interval; DASH = Dietary Approaches to Stop Hypertension; DSST = Digit Symbol Substitution Test; MedDiet = Mediterranean Diet score; RAVLT = Rey Auditory Verbal Learning Test.
[a] Composite cognitive function score = year 25 (delayed RAVLT *z* score − Stroop Interference *z* score + DSST *z* score)/3.
[b] 1-SD MedDiet = 4.48; 1-SD DASH = 0.90; 1-SD APDQS = 11.43.
[c] Adjusted for sex, age, race (white, black), education (years), smoking, body mass index, diabetes mellitus, physical activity, and total energy intake (kcal/d).

Diet patterns during adulthood and cognitive performance in midlife

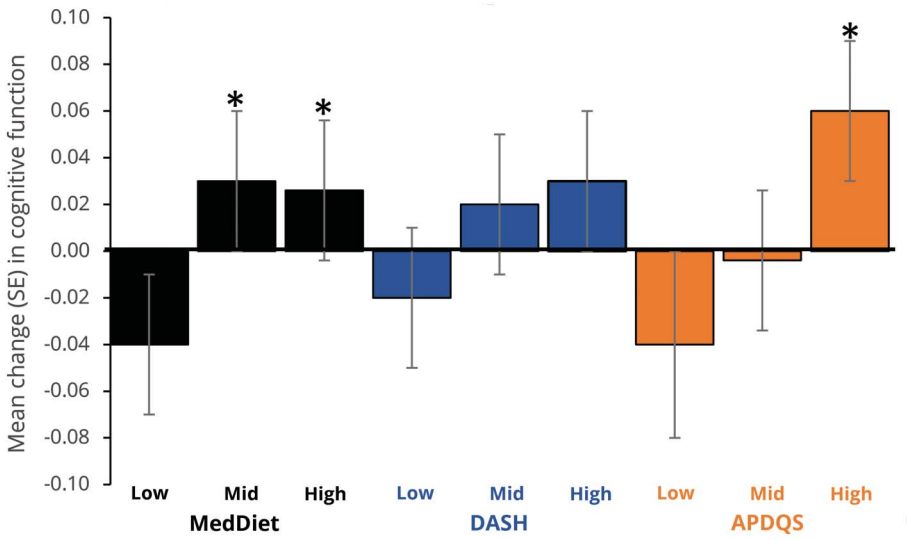
The mean age at the initial cognitive examination was 50.2 years (range 42–59 years). As table 2 shows, long-term scores in each diet pattern were positively associated with better cognitive performance at the initial examination. After adjustment for demographic, lifestyle, health factors, and energy intake, DASH score was no longer associated with initial cognitive performance. However, a 1-SD increase in the MedDiet score (4.5 points) and APDQS score (11.4 points) was associated with better performance in composite cognitive function and all 3 cognitive tests (all $p < 0.01$).

Diet patterns during adulthood and change in midlife cognitive function

After 5 years of follow-up, small changes were observed in cognitive test scores: RAVLT scores improved on average 0.2 ± 2.6 points, while DSST and Stroop performance declined by 2.5 ± 9.3 and 0.1 ± 9.1 points, respectively. The 5-year change in cognitive function by tertile of long-term diet scores adjusted for demographic, lifestyle, and health factors is shown in figures 1 through 4 and table 3 available from Dryad (doi.org/10.5061/dryad.443gv60).

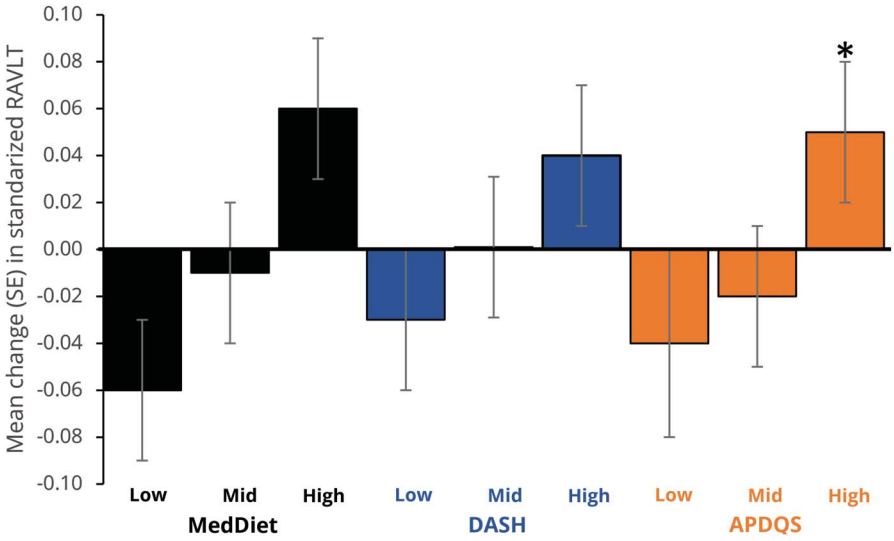
As figure 1 shows, compared to individuals with low diet scores, those with middle and high MedDiet or APDQS

Figure 1 Adjusted mean (SE) 5-year change in midlife cognitive function (50–55 years) by tertile of diet score in adulthood



APDQS = A Priori Diet Quality Score; DASH = Dietary Approaches to Stop Hypertension; MedDiet = Mediterranean diet; SE = standard error. *Differs ($p \leq 0.05$) from low tertile aftercorrection for multiple comparisons (Bonferroni).

Figure 2 Adjusted mean (SE) 5-year change in midlife delayed RAVLT (50–55 years) by tertile of diet score in adulthood



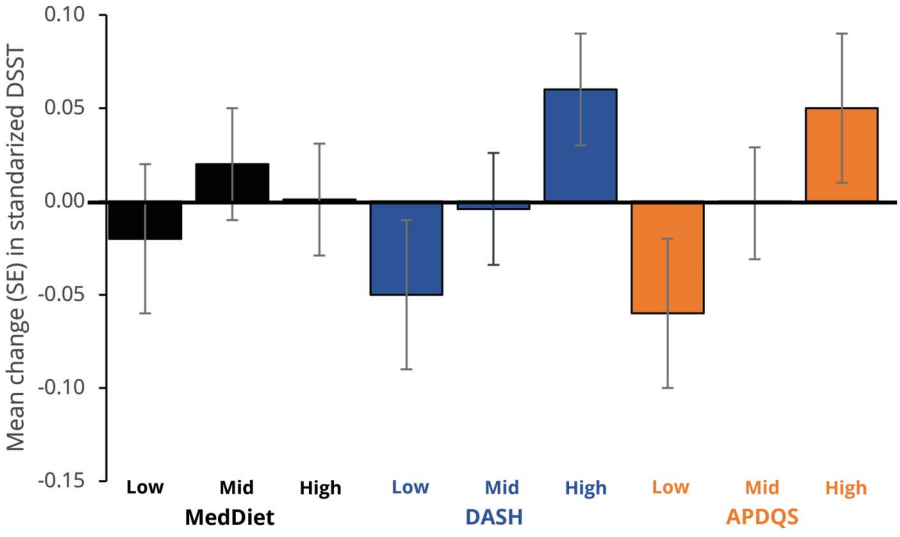
APDQS = A Priori Diet Quality Score; DASH = Dietary Approaches to Stop Hypertension; MedDiet = Mediterranean diet; RAVLT = Rey Auditory Verbal Learning Test; SE = standard error. *Differs ($p \leq 0.05$) from low tertile aftercorrection for multiple comparisons (Bonferroni).

scores had less decline in midlife global cognitive function ($p < 0.05$ in all multivariable-adjusted models), with a linear relationship observed for both MedDiet ($p_{Trend} = 0.03$) and APDQS ($p_{Trend} = 0.003$) dietary patterns. DASH score was not associated with 5-year change in global cognitive function in the adjusted model.

Figures 2 through 4 show the multivariate-adjusted 5-year change in cognitive *z* scores by tertile of diet score. DASH and APDQS scores were not associated with change in delayed RAVLT, but participants with high MedDiet scores showed improvement in word recall compared to those with low scores ($p = 0.05$) (figure 2). Change in DSST score did not differ by adherence to the 3 dietary patterns examined (figure 3). Change in Stroop Interference score did not differ by DASH, but participants with higher MedDiet or APDQS scores had faster performance on the Stroop Interference at follow-up (p_{Trend} <0.01 for both) (figure 4).

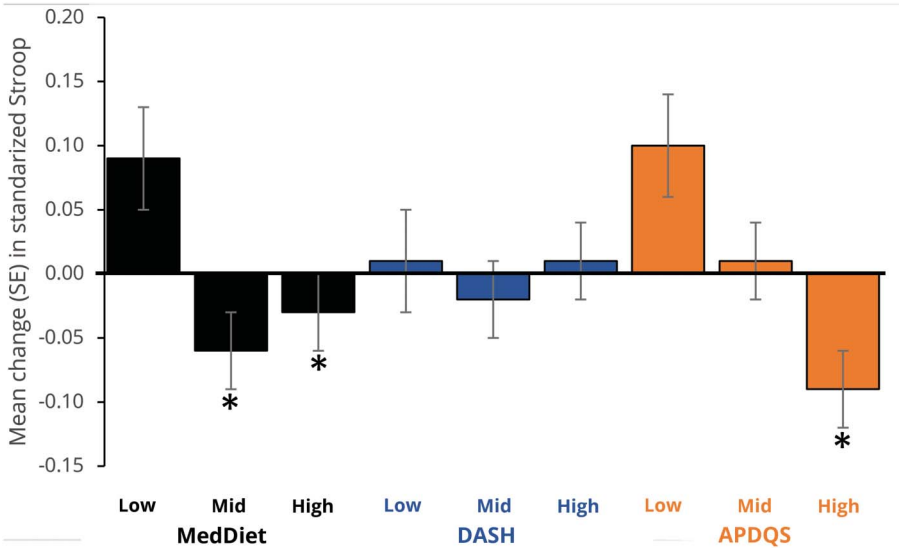
Further adjustment for *APOE4* status or CES-D score slightly attenuated the associations, but the overall findings were unchanged. Associations between alternate long-term DASH score and midlife cognitive performance were similar to those reported for the long-term DASH score (data not shown). When we repeated the analyses by replacing the long-term diet scores with the baseline or year 20 diet scores as predictor variables (table 4 available from Dryad, doi.org/10.5061/dryad.443gv60), the baseline scores were not associated with

Figure 3 Adjusted mean (SE) 5-year change in midlife DSST (50–55 years) by tertile of diet score in adulthood



APDQS = A Priori Diet Quality Score; DASH = Dietary Approaches to Stop Hypertension; DSST = Digit Symbol Substitution Test; MedDiet = Mediterranean diet; SE = standard error.

Figure 4 Adjusted mean (SE) 5-year change in midlife Stroop Interference (50–55 years) by tertile of diet score in adulthood



APDQS = A Priori Diet Quality Score; DASH = Dietary Approaches to Stop Hypertension; MedDiet = Mediterranean diet; SE = standard error. *Differs ($p \leq 0.05$) from low tertile after correction for multiple comparisons (Bonferroni).

5-year change in either midlife global cognitive function or individual cognitive domains. There was no association between year 20 DASH score and change in midlife global cognitive function. However, MedDiet and APDQS scores at year 20 showed slightly stronger inverse associations with 5-year global cognitive decline than the long-term diet scores ($p < 0.01$ in all multivariable-adjusted models). Higher MedDiet score at year 20 was associated with faster performance on Stroop Interference and less decline in word recall and DSST scores (all $p = 0.02$); higher DASH score at year 20 was associated with less decline in DSST score ($p = 0.007$); and higher APDQS score at year 20 was associated with faster performance on Stroop Interference ($p = 0.001$).

Diet patterns during adulthood and risk of clinically poor cognitive global function in midlife

Clinically relevant poor global cognitive function, defined as >1 SD (3.9 points) below the population mean MoCA score, was documented in almost 18% of the sample. Table 3 shows that individuals in the high and middle tertiles of long-term MedDiet, DASH, or APDQS scores were less likely to have poor global cognitive function compared to those with low

Table 3 OR (95% CI) of poor global cognitive function at mean age 55 years by tertile of long-term diet score in adulthood

	OR (95% CI) poor global cognitive function[a]		
N = 2,607 (n poor cognition[a] = 467, 17.8%)	**Low tertile**	**Mid tertile**	**High tertile**
MedDiet, n (%) poor cognition	798 (29)	941 (16)	868 (9)
Basic	Referent	0.48 (0.38–0.60)	0.25 (0.19–0.33)
Adjusted[b]	Referent	0.66 (0.51–0.85)	0.54 (0.39–0.74)
DASH, n (%) poor cognition	764 (23)	996 (18)	847 (13)
Basic	Referent	0.72 (0.57–0.91)	0.49 (0.38–0.63)
Adjusted[b]	Referent	0.96 (0.72–1.29)	0.89 (0.69–1.17)
APDQS, n (%) poor cognition	805 (32)	864 (17)	938 (6)
Basic	Referent	0.44 (0.35–0.55)	0.14 (0.10–0.19)
Adjusted[b]	Referent	0.68 (0.52–0.88)	0.48 (0.33–0.69)

Abbreviations: APDQS = CARDIA A Priori Diet Quality Score; CI = confidence interval; DASH = Dietary Approaches to Stop Hypertension; MedDiet = Mediterranean Diet score; OR = odds ratio.
[a] Defined as ≥1 SD (3.9) below the population mean Montreal Cognitive Assessment score (24.0) (range 0–30) at year 30 and mean age of 55 years; long-term diet scores adulthood were computed as average diet score at years 0, 7, and 20 examinations (mean age 25, 32 and 45 years, respectively).
[b] Adjusted for sex, age, race (white, black), education (years), smoking, body mass index, diabetes mellitus, physical activity, and total energy intake (kcal/d).

diet scores (odds ratios [ORs] for the high vs low MedDiet, DASH, and APDQS tertiles 0.25 [95% confidence interval (CI) 0.19–0.33], 0.49 [95% CI 0.38–0.63], 0.14 [95% CI 0.10–0.19], respectively). After adjustment for demographic, lifestyle, and health factors, only the MedDiet and APDQS scores were independently and linearly associated with a lower risk of poor global cognitive performance. Individuals in the middle and high APDQS tertiles had a respective 32% (OR 0.68 [95% CI 0.52–0.88]) and 52% (OR 0.48 [95% CI 0.33–0.69]) lower risk of poor cognitive function relative to those in the low APDQS tertile (p_{Trend} <0.001). The associations were similar for participants scoring in the middle and high vs low tertile of MedDiet (OR 0.66 [95% CI 0.51–0.85] and OR 0.54 [95% CI–0.39, 0.74], respectively). Similar to the DASH score, the alternate DASH score was not related to risk of poor global cognitive function. In adjusted models, the OR was 0.95 (95% CI 0.70–1.23) and 0.90 (95% CI 0.70–1.17) for middle and high tertiles, respectively, compared to low tertile of alternate DASH score.

In sensitivity analyses, we adjusted the models for the presence of the *APOE4* allele. Associations were slightly attenuated, but there was little notable difference to the overall pattern of findings. Results were not appreciably altered when we removed 102 participants who scored <17 points on the MoCA from the analyses (data not shown), nor when we adjusted the models further for midlife depression score, midlife obesity, or midlife hypertension. Furthermore, when we repeated the analysis with the baseline and year 20 diet scores (table 5 available from Dryad doi.org/10.5061/dryad.443gv60), observed risk estimates were attenuated for baseline diet scores but similar for year 20 diet scores in the fully adjusted models.

Discussion

In this study, we examined longitudinal associations between 3 dietary patterns during adulthood and cognitive performance in midlife. Our findings in a large sample of biracial adults indicate that greater long-term adherence to MedDiet or APDQS, but not DASH, was associated with less decline in global cognitive function at midlife. Higher long-term MedDiet and APQDS scores were particularly associated with less decline in midlife executive function. Mean verbal memory scores increased at follow-up in this population. This could be explained by a performance gain or a "practice effect" carried over from the initial test, which is especially likely with memory tests.[25] Even so, higher MedDiet scores were associated with small improvement in verbal memory score. Furthermore, individuals with the highest adherence to MedDiet or APDQS had a 46% to 52% lower risk of poor global cognitive function after adjustment for demographic, health, and lifestyle covariates. Overall, our findings indicate that long-term adherence to a dietary pattern consistent with the MedDiet and APDQS and general dietary recommendations for heart health[26] is associated with better midlife cognitive function.

The MedDiet and DASH diets have been linked to lower risk of cognitive decline[7,8] and dementia,[10,11] but findings from epidemiologic studies have been conflicting.[12,13] Prior studies have tended to examine relations between diet and cognition in older, predominately white populations without considering earlier life dietary exposures. Our findings build on an earlier CARDIA study[27] that reported positive associations between APDQS score and midlife cognitive performance measured at 1 time point. Given that progression from normal cognition to cognitive impairment can take years to manifest, maintaining a healthy diet over the life course may offer accruing cognitive protection. Longitudinal investigations of midlife dietary patterns and cognition later in life are limited but generally support this assertion; for example, a healthy dietary pattern in midlife has been associated with better global cognition and verbal memory scores[28] and reduced risk of dementia[29] in older adults, and long-term adherence to the MedDiet was associated with better overall cognitive function but not with cognitive decline in educated women.[30] In the current study, baseline diet scores at an average age of 25 years were not related to change in midlife cognitive function, while the more recent diet scores, particularly the MedDiet score, at an average age of 45 years tended to be more strongly associated with cognitive performance in middle-age. Few dietary intervention studies have been conducted; however, modest improvement in cognitive function with MedDiet[31] and calorie-restricted DASH[32] interventions has been reported in middle-aged to older adults at increased vascular risk. It is not yet known whether dietary modification in early to midlife can affect the rate of cognitive decline during aging.

The mechanisms by which diet can influence midlife cognitive function are not clear but likely to involve oxidative stress, inflammatory, and vascular disease pathways that contribute to accelerated cognitive decline and dementia.[33] Antioxidants from foods (e.g., fruit, vegetables, legumes, and nuts) and beverages (tea, red wine) protect against oxidative damage and can alter inflammatory processes.[34] Antioxidant-rich diets, particularly the MedDiet and DASH diet, are shown to reduce markers of oxidative stress,[35,36] and in CARDIA, the APDQS score has been inversely related to oxidative stress.[37] Furthermore, dietary components (polyphenols and omega-3 fatty acids, fruits, and vegetables) have anti-inflammatory properties with likely synergistic or additive effects in vivo[38] that can decrease markers of systemic inflammation.[39] It is well established that diet can modify several vascular risk factors, including hypertension, dyslipidemia, obesity, and insulin resistance,[40] as well as endothelial function[41] and risk of developing cardiovascular disease.[26,40] The MedDiet has demonstrated reduced cardiovascular events, particularly rates of stroke, in adults at high cardiovascular risk.[42]

In contrast to MedDiet and APDQS scores, higher DASH diet scores were not associated with global cognitive function or executive function. Dietary patterns characterized by MedDiet, DASH, and APDQS scores share similar profiles but also have unique components that may account for different

strengths of association observed across the cognitive domains. DASH uniquely limits sodium intake; however, APDQS also accounts for foods considered high in sodium, including salty snacks and processed foods. Moderate alcohol is recommended in both MedDiet and APDQS but is not considered in the DASH score system, suggesting that moderate alcohol intake as part of a healthy diet could be relevant for brain health in midlife. The role of alcohol in brain health is not clear, but moderate alcohol may exert protective effects on cognitive function either directly by enhancing acetylcholine release in the hippocampus[43] or indirectly by mediating vascular risk reduction via decreased platelet aggregation or modification of serum lipids.[44]

This study had several strengths, including 30 years of follow-up data and 5-year change in 3 aspects of cognitive testing in a relatively large sample with adequate representation of both men and women and blacks and whites. Other strengths were the detailed and repeated measures of diet to capture long-term dietary exposure and the repeated cognitive measures using validated neuropsychological tests to determine change in cognition across several domains. A further advantage was that dietary exposure was determined early in adulthood and before the assessment of cognitive function, thus minimizing the possibility of reverse causation.

There were some limitations to consider in this study. We were unable to incorporate olive oil as a beneficial component in the derived MedDiet score,[15] which may have underestimated the association of this dietary pattern on cognitive decline. The observed effect sizes between diet scores and change in cognitive function were small but of a magnitude similar to that of effects observed for relations between vascular and genetic risk factors and cognitive function in midlife.[5,45] Despite being able to adjust our analysis for important confounders measured during adulthood, residual confounding by unidentified confounders cannot be excluded. Furthermore, our findings may not be generalizable beyond black and white US adults in midlife.

This study shows that the MedDiet and APDQS dietary patterns are associated with better overall cognitive performance in midlife. Additional investigations are needed to define the combination of foods and nutrients for optimal brain health, but our findings lend support to heart-healthy dietary patterns high in fruit, vegetables, and legumes; moderate in nuts, fish, and alcohol; and low in meat for neuroprotection in midlife. Further prospective studies are required to understand how the duration of dietary exposure influences risk of cognitive impairment across the life course in different populations to help inform the nature and timing of dietary interventions targeted for brain health.

Author contributions

C.T. McEvoy: conception, design, data acquisition, analysis and interpretation, statistical analysis, drafting and editing the manuscript. T. Hoang: design, interpretation of data, editing the manuscript and revising it critically for intellectual content. S. Sidney and L.M. Steffen: editing the manuscript and revising it critically for intellectual content. D.R. Jacobs, Jr.: data acquisition (diet) and design, editing the manuscript and revising it critically for intellectual content. J.M. Shikany and J.T. Wilkins: editing the manuscript and revising it critically for intellectual content. K. Yaffe: study supervision, conception, design, data interpretation and analysis, editing the manuscript and revising it critically for intellectual content, final manuscript approval.

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Disclosure

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