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RESEARCH ARTICLE

Race/ethnicity and gender modify the association between diet and cognition in U.S. older adults: National Health and Nutrition Examination Survey 2011-2014

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Abstract

Introduction: It is unclear whether the association between Mediterranean-type Diet (MeDi) and cognition is similar across different racial/ethnic groups or between women and men.

Methods: The current study included 2435 participants (≥60 years of age) of the National Health and Nutrition Examination Survey (NHANES) 2011-2014. Linear regression models were applied to examine the association between diet and cognition, adjusted for multiple demographic variables. Interaction between MeDi and race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, other), and between MeDi and gender, were examined, followed by stratified analyses.

Results: One score increase in MeDi was associated with 0.039 (95%confidence interval [CI] = 0.016-0.062) higher global cognitive z-score. Significant associations between MeDi and global cognition and between MeDi and immediate recall were found in the non-Hispanic Whites only (*P*-interaction = 0.057 and 0.059, respectively). MeDi was associated with increased score of animal fluency score in men but not in women (*P*-interaction = 0.082).

Discussion: The positive association between MeDi and cognition might be dependent on race/ethnicity and gender.

KEYWORDS
aging, cognition, diet, epidemiology, NHANES

1 | INTRODUCTION

With an aging population, cognitive impairment and dementia have emerged as a public health challenge worldwide.[1] Currently there is no effective medical treatment for dementia; primary prevention through modifiable risk factors, such as healthy dietary habits, is thus an urgent priority to reduce the incidence of cognitive impairment and dementia.[2]

There is emerging evidence supporting protective roles of certain dietary patterns on cognitive aging and dementia prevention.[3–6] Mediterranean diet (MeDi) refers to a traditional diet in the Mediterranean countries, characterized by a high consumption of olive oil, leafy green vegetables, fruits, cereals, legumes, and fish; low intake of meat and dairy products; and moderate consumption of alcohol.[3] MeDi is the most commonly examined dietary pattern in the cognitive aging literature and shows a promising beneficial role on cognitive function in older adults,[7–20] although the findings are not always consistent.[21–25]

The inconsistency might be due to the discrepancies in study design, sample size, population, statistical methods, and assessments of diet and cognition.[3] In particular, cross-race variation in dietary habits and quality may have contributed to the inconsistency.[26] Non-Hispanic Blacks (NHBs) and Hispanics have lower consumption of fruits and vegetables than non-Hispanic Whites (NHWs).[26] Similarly, men and women also tend to have different dietary preference, appetite sensations, and overall dietary habits.[27,28] Meanwhile, there are sex/gender and racial/ethnic disparities in dementia risk and cognitive decline in late life, such that women have higher risk than men and NHBs and Hispanics have higher risk than NHWs, but the exact mechanism is unknown.[29,30] To reduce cognitive health disparities through healthier lifestyles, association between dietary pattern and cognitive health needs to be examined further in national representative samples with male and female participants of multiple racial/ethnic groups. Identifying the potential effect modifiers for the diet-cognition association may also help with developing subpopulation-specific preventive measures for cognitive aging.

However, there is a paucity of research examining the role of sex and race/ethnicity as modifiers of the diet-cognition association in later life, and the existing data have been inconsistent. Although the cognitive benefits of MeDi have been reported across regions and multiple races/ethnic groups,[6,8] most studies were based on predominantly White populations.[14,15,20,22,23,25] A few studies with multiple racial/ethnic groups did not examine[14] or did not find an interaction between race/ethnicity and MeDi on cognition.[7,9,11,31] In one study, stronger adherence to the MeDi reduced the rate of cognitive decline among African Americans, but not in White older adults.[13] Gender difference in the association between dietary factors and cognition has been rarely tested, and only one previous study found a stronger association of MeDi with cognition in men than in women.[16]

In the present study, we examined whether the associations of MeDi with cognition vary by race/ethnicity and gender, using data from the nationally representative sample, the National Health and Nutrition Examination Survey (NHANES) 2011-2014.

HIGHLIGHTS

- In the current cross-sectional study of elderly (age 60 and older) participants from the National Health and Nutrition Examination Survey (NHANES) 2011-2014, high adherence to Mediterranean-type Diet (MeDi) was associated with better cognition.
- Race/ethnicity and gender modified the positive association between MeDi and cognition.
- Higher adherence to MeDi was associated with higher cognitive scores in non-Hispanic Whites, but not in other racial/ethnic groups including non-Hispanic Blacks, Hispanics, and others.
- There was a significant association between MeDi and executive function in men but not in women.

RESEARCH IN CONTEXT

1. **Systematic review**: The author reviewed previously published findings on the Mediterranean-type Diet (MeDi) and cognition. Previous findings have suggested a positive association between MeDi and cognitive health, but it is unclear whether the association is similar across different racial/ethnic groups or between women and men.
2. **Interpretation**: Our study showed significant protective effects of MeDi on cognitive health in a nationally representative U.S. elderly population, and the positive association between MeDi and cognition seemed to be dependent on race/ethnicity and gender, with a stronger association in men than in women, and in non-Hispanic Whites than in other racial/ethnic groups.
3. **Future directions**: Future prospective studies with a large sample of minority older adults and with both men and women are warranted to confirm the findings.

2 | METHODS

2.1 | Participants and setting

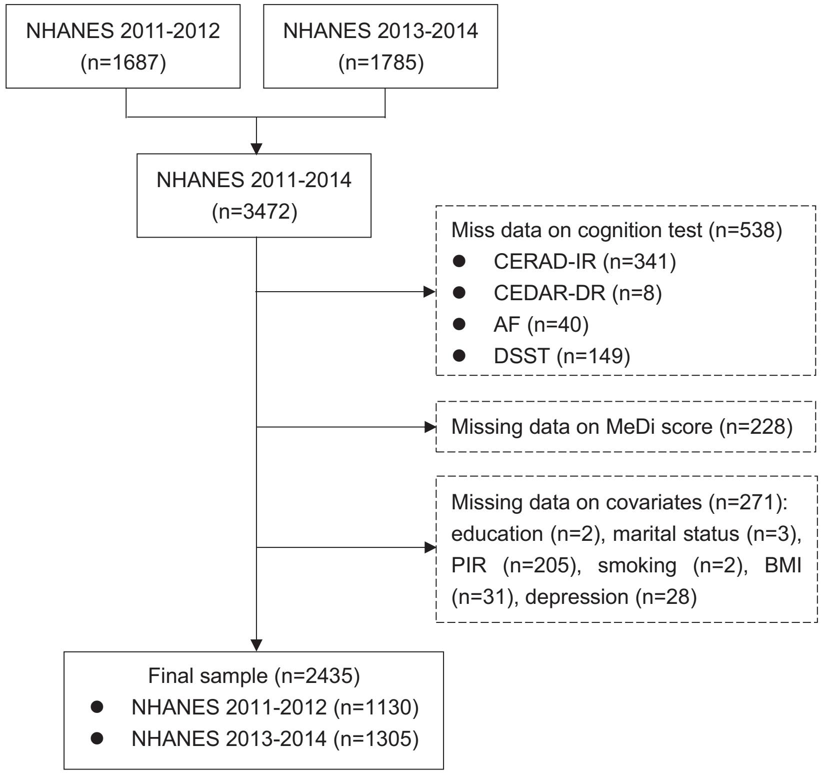
The NHANES study, an ongoing cross-sectional survey, is conducted biennially to assess the health and nutritional status of the noninstitutionalized U.S. population. Details of the study design and data collection were reported elsewhere.[32] Briefly, individuals who completed the in-home interview were then invited to participate in the physical examination. The interview survey included demographic, dietary, lifestyle, and health-related factors; the examination component consisted of medical and physical measurements and laboratory tests administered by highly trained medical personnel. The protocol of NHANES was approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board. Written informed consent was obtained from each participant.

The present study analyzed cognitive data from NHANES 2011-2014 in which a series of tests were conducted to assess the cognitive function (n = 3472) (Figure 1). Participates were excluded for the missing data on cognition assessment (n = 538), MeDi score (n = 228), and covariates (n = 271). Finally, a total of 2435 subjects were included in the primary data analyses (Table S1).

2.2 | Assessment of MeDi

Dietary information was obtained through validated computer-assisted 24-hour dietary recall interviews using the U.S. Department of Agriculture's Automated Multiple-Pass Method; the interviews

FIGURE 1 Flow chart of subject selection



were conducted by trained dietary interviewers.[33] The degree of adherence to MeDi was assessed by the MeDi scale constructed with nine components.[7] The sex-specific median of energy-adjusted intake was used as the cut-off value for each of the nine MeDi components. One point was given for intake equal or greater than the cut-off value for the beneficial components (vegetables, fruits, legumes, cereals, fish, and mono-unsaturated fatty acids: saturated fatty acids ratio), or for intake less than the cut-off value for the detrimental components (dairy products, and meat and poultry), or for a mild-to-moderate consumption of alcohol (> 0 to ≤1 drink/day for women, and > 0 and ≤2 drink/day for men). The total MeDi ranged from 0 to 9, with higher score indicating a better adherence to MeDi.

2.3 | Assessment of cognition

There were three tests administered to assess the cognitive function among the subjects age 60 and older: the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Word Learning subset to evaluate immediate and delayed recall of new verbal information (memory sub-domain); the Animal Fluency (AF) test to examine verbal semantic fluency (component of executive function); and the Digit Symbol Substitution Test (DSST) to assess attention, processing speed, and working memory.[32]

The module from CERAD consisted of 10-item word list learning trials. The participants were asked to recall as many words as possible immediately after 10 unrelated words were read. Three consecutive immediate learning trials and one delayed trial were conducted in CERAD. The immediate recall (CERAD-IR) score, calculated as the sum of the three immediate recalls, ranged from 0 to 30, and the delayed recall (CERAD-DR) score ranged from 0 to 10.

Participants taking the AF test were asked to name as many animals as possible in 1 minute, with 1 point given for each correct answer. The score corresponds to the total number of correct answers.

The DSST was a module from the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III). Participants were asked to copy in 2 minutes as many number-corresponding symbols as possible in 133 boxes on paper with keys at the top containing nine numbers paired with symbols. The total score was summarized as the number of the correct matches (ranging from 0 to 133).

To assess the global cognitive function, which was more consistently associated with MeDi compared to other individual cognitive tests,[5] we calculated a composite cognitive z-score by averaging the standardized scores of each cognitive test (CERAD-IR, DERAD-DR, AF, and DSST).

2.4 | Covariates

The information on demographics including age, self-reported gender (male, female), race/ethnicity (NHW, NHB, Hispanic, (Mexican-American, and other Hispanics), Others (including Asians, others, and mixed race/ethnicities), education attainment (under high school, high school, above high school), marital status (married/cohabiting, divorced/widowed/separated, never married), and ratio of family income to poverty (PIR; ≤1, > 1) were collected via questionnaires. Smokers were the subjects who reported at least 100 lifetime cigarettes, and smoking status was categorized into three groups of never, current, and past. Dietary caloric (kcal) intake was obtained from the 24-hour dietary recall. Recreational physical activity was classified into four levels: sedentary (no regular physical activity), insufficient (regular activity, <500 metabolic equivalent [MET] minutes/week), moderate (500 to 1000 MET minutes/week), and high (>1000 MET-minutes/week). The body mass index (BMI) was divided into normal weight of <25, overweight of 25 to <30, and obesity of ≥30 kg/m^2. Depression was measured by the brief Patient Health Questionnaire (PHQ-9), and a cut-off score of 10 was applied to identify clinically relevant depression. Co-morbidity burden was calculated as the total number (ranging 0-4) of self-reported comorbidities including hypertension, hyperlipidemia, diabetes, and cardiovascular disease (any history of heart failure, coronary heart disease, angina pectoris, heart attack).

2.5 | Statistical analysis

Weighted analyses were applied to account for the complex sampling design of NHANES. The 2-year weights (WTMEC2YR) were selected for the cognitive testing subsamples in NHANES 2011-2012 and 2013-2014. The final weight (WTMEC2YR/2) for NHANES 2011-2014 was recalculated when the two survey cycles were combined. Taylor linearization[34] was used for the variance estimation.

The characteristics of participants were presented as means and proportions for continuous and categorical variables, respectively. Subjects were categorized into three groups according to the tertiles of MeDi. Differences of characteristics across the tertiles of MeDi, race/ethnicity, and gender, were tested with the chi-square test for categorical variables and a linear regression model for continuous variable.

The association between adherence to MeDi and cognitive performance was examined by linear regression models with global cognitive z-score as dependent variables and tertiles of MeDi as predictors (with the lowest tertile as the reference), first unadjusted and then adjusted for age, gender, race/ethnicity, education, marital status, PIR, smoking status, BMI category, physical activity, depression, and dietary calories. The linear trend of associations across tertiles of MeDi was tested by assigning the median values to each tertile and treating as a continuous variable in the adjusted models. The MeDi was also treated as a continuous variable to fit the models.

To examine the potential effect modification, a product term between MeDi (continuous score) and race/ethnicity (categorical, NHW as the reference group) or gender (men as the reference group) was added separately in the adjusted models, in which the product term was tested by the adjusted Wald test, with P values ≤0.10 considered as significant for the interaction. Stratification analyses were subsequently performed. Marginal effects of MeDi (continuous score) on cognition function were separately calculated by race/ethnicity and by gender.

Post hoc analyses were performed for each individual cognitive score, and for nine MeDi components (simultaneously in the model), similar to the main analysis for global cognitive score. Sensitivity analyses were performed: (1) Subjects who had difficulties in thinking and remembering, based on the question "During the past 12 months, have you (or has she/has he) experienced confusion or memory loss that is happening more often or is getting worse?", were excluded from the data analyses; (2) co-morbidity burden was additionally adjusted; and (3) using an alternative dietary pattern score, Healthy Eating Index-2015 (HEI-2015).

3 | RESULTS

3.1 | Characteristics of the study participants

Participant characteristics are presented in Table 1. The study sample included a total of 46,488,866 U.S. older subjects. Among all the subjects, the mean age was 68.99 years, and male subjects accounted for 46.25%. The proportions of NHW, NHB, Hispanic, and Others were 81.16%, 7.83%, 6.50%, and 4.51%, respectively. Participants with higher adherence to MeDi were more likely to be older, to be women, to have higher education levels, to be married/cohabiting, to have better economic conditions, to be never smokers, to have normal BMI, and to have higher levels of physical activity ($P < 0.05$, Table 1). Mean scores of all the cognitive tests, except for CERAD-IR and CERAD-DR, increased with increasing MeDi ($P < 0.05$).

The mean MeDi score in NHWs was similar to that in NHBs or Hispanics, but lower than in Others (Table S2). NHWs had higher global cognitive score than other racial/ethnic groups (Table S2). NHWs were more likely to have above high school education, be above poverty level, and be past smokers; were less likely to have depression compared to NHBs and Hispanics; and were more likely to have normal BMI and be married and cohabiting than NHBs (data not shown). NHWs consumed more fish, vegetables, cereal, and dairy but less legumes compared to Hispanics, consumed more vegetables, cereal, alcohol, and dairy but less meat compared to NHBs, and consumed more dairy and alcohol but less legumes compared to Others (data not shown).

Men had similar MeDi scores but had lower global cognitive score than women (Table S3). Compared to men, women had a lower percentage of being married or cohabiting with partners, and were less likely to be smokers but more likely to be below poverty level or to have depression (data not shown). Men consumed less fruits but more legumes, meat, and alcohol than women (data not shown).

3.2 | Associations between MeDi and cognitive function

Compared with subjects in the first tertile (low adherence) of MeDi, those in the third tertiles (high adherence) ($\beta = 0.162$, 95% CIs = 0.050 to 0.275) had significantly higher global cognitive score ($P_{trend} = 0.006$) in the adjusted model. An increase of 1 point in MeDi was significantly associated with an average increase of 0.039 in global cognitive score. Significantly positive associations were also observed for all individual cognitive test scores except for DSST (Table 2).

TABLE 1 Characteristics of study subjects from NHANES 2011-2014

		Tertiles of MeDi			*P* values			
Characteristics	**Total**	**T1 (0 to 3)**	**T2 (4 to 5)**	**T3 (6 to 9)**	**Overall**	**T1 *vs* T2[a]**	**T1 *vs* T3[a]**	**T2 *vs* T3[a]**
Sample size, n (%)	2435	841	1129	465				
Representative population size	46,488,866	15,620,163	21,740,153	9,128,550				
MeDi, mean (SD)	4.15 (1.55)	2.43 (0.76)	4.44 (0.50)	6.39 (0.63)	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**
Age (years), mean (SD)	68.99 (6.58)	68.02 (6.45)	69.45 (6.60)	69.57 (6.62)	**0.001**	**0.003**	**0.003**	0.803
Gender, n (%)								
Male	1190 (46.25)	399 (43.97)	543 (44.66)	248 (53.94)	0.049	0.850	**0.027**	**0.044**
Female	1245 (53.75)	442 (56.03)	586 (55.34)	217 (46.06)				
Race/ethnicity, n (%)								
Non-Hispanic White	1224 (81.16)	415 (81.27)	574 (81.21)	235 (80.86)	**0.004**	**0.047**	**0.002**	0.178
Non-Hispanic Black	566 (7.83)	214 (8.56)	252 (7.67)	100 (6.97)				
Hispanic	445 (6.50)	179 (7.75)	201 (6.22)	65 (5.03)				
Others	200 (4.51)	33 (2.42)	102 (4.90)	65 (7.15)				
Education, n (%)								
Less than high school	574 (14.84)	240 (18.66)	263 (14.59)	71 (8.87)	**< 0.001**	0.142	**< 0.001**	**0.002**
High school or equivalent	567 (21.40)	226 (23.65)	263 (22.23)	78 (15.56)				
Above high school	1294 (63.76)	375 (57.68)	603 (63.17)	316 (75.57)				
Marital status, n (%)								
Married/cohabiting	1415 (65.69)	459 (62.76)	658 (64.66)	298 (73.17)	**0.018**	0.738	**0.010**	**0.035**
Devoiced/widowed/separated	885 (30.18)	330 (33.26)	419 (31.48)	136 (21.82)				
Never married	135 (4.13)	52 (3.98)	52 (3.87)	31 (5.00)				
PIR, n (%)								
≤1	398 (8.70)	169 (10.91)	180 (8.82)	49 (4.63)	**< 0.001**	0.088	**< 0.001**	**0.001**
>1	2037 (91.3)	672 (89.09)	949 (91.18)	416 (95.37)				
Smoking, n (%)								
Never	1189 (49.26)	376 (46.3)	572 (49.97)	241 (52.61)	**0.001**	**0.025**	**0.001**	**0.025**
Current	298 (10.69)	149 (15.88)	116 (9.46)	33 (4.73)				
Past	948 (40.05)	316 (37.81)	441 (40.57)	191 (42.66)				
BMI category, n (%)								
Normal	637 (25.82)	200 (23.05)	287 (24.22)	150 (34.38)	**0.008**	0.735	**0.002**	**0.011**
Overweight	854 (36.04)	288 (35.50)	399 (36.68)	167 (35.45)				
Obese	944 (38.13)	353 (41.45)	443 (39.09)	148 (30.17)				
Physical activity, n (%)								
Sedentary	1381 (53.49)	569 (64.78)	617 (52.82)	195 (35.78)	**< 0.001**	**0.016**	**< 0.001**	**< 0.001**
Insufficient	353 (14.16)	103 (11.76)	185 (15.98)	65 (13.94)				
Moderate	275 (12.01)	70 (9.25)	131 (12.08)	74 (16.57)				
High	426 (20.34)	99 (14.21)	196 (19.12)	131 (33.71)				
Depression, n (%)								
No	2218 (92.89)	747 (91.37)	1036 (92.79)	435 (95.7)	0.077	0.358	0.075	0.162
Yes	217 (7.11)	94 (8.63)	93 (7.21)	30 (4.30)				

(Continues)

TABLE 1 (Continued)

Characteristics	Total	Tertiles of MeDi			P values			
		T1 (0 to 3)	T2 (4 to 5)	T3 (6 to 9)	Overall	T1 vs T2[a]	T1 vs T3[a]	T2 vs T3[a]
Dietary calories (kcal), mean (SD)	1905.61 (794.54)	2011.84 (797.26)	1846.56 (749.70)	1864.49 (873.09)	**0.001**	**0.001**	0.120	0.799
Co-morbidities, mean (SD)[b]	1.67 (1.21)	1.65 (1.20)	1.72 (1.20)	1.56 (1.23)	0.391	0.434	0.434	0.434
NHANES wave, n (%)								
2011-2012	1130 (47.46)	417 (49.35)	541 (49.84)	172 (38.53)	**0.030**	0.883	0.066	**0.031**
2013-2014	1305 (52.54)	424 (50.65)	588 (50.16)	293 (61.47)				
Global cognitive score, mean (SD)	0.00 (0.79)	−0.05 (0.81)	−0.02 (0.77)	0.14 (0.80)	**0.006**	0.641	**0.022**	**0.005**
CERAD-IR, mean (SD)	19.84 (4.42)	19.76 (4.42)	19.60 (4.40)	20.55 (4.41)	**0.003**	0.553	**0.026**	**0.002**
CERAD-DR, mean (SD)	6.30 (2.27)	6.31 (2.30)	6.19 (2.20)	6.53 (2.33)	**0.040**	0.445	0.344	**0.037**
Animal Fluency, mean (SD)	18.38 (5.67)	17.77 (5.68)	18.40 (5.56)	19.34 (5.78)	**0.017**	0.114	**0.014**	**0.041**
DSST, mean (SD)	52.78 (16.43)	51.47 (16.77)	52.76 (16.05)	55.05 (16.50)	0.119	0.254	0.124	0.140

Abbreviations: %, weighted proportion.; BMI, body mass index (kg/m^2); CERAD, Consortium to Establish a Registry for Alzheimer's disease; CERAD-DR, delayed recall in CERAD trial; CERAD-IR, immediate recall in CERAD trial; DSST, Digit Symbol substitution test; MeDi, Mediterranean Diet score; PIR, ratio of family income to poverty; SD, standard deviation; T1-T3, the 1st to the 3rd tertiles.

[a] *P* values of multiple comparisons were corrected by the False Discovery Rate method.

[b] Total number of self-reported co-morbidities including hypertension, hyperlipidemia, diabetes, and cardiovascular disease (heart failure, coronary heart disease, angina pectoris, heart attack). There were 149 subjects with missing data on comorbidities.

TABLE 2 Associations between MeDi and cognitive scores

Cognition test	MeDi levels				
	Low (0 to 3) (n = 841)	Middle (4 to 5) (n = 1129)	High (6 to 9) (n = 465)	P_{trend} [b]	Continuous MeDi
Global cognition					
Crude model	Reference	0.027 (−0.088, 0.141)	**0.193 (0.041, 0.344)**	**0.012**	**0.043 (0.011, 0.074)**
Adjusted model [a]	Reference	0.058 (−0.015, 0.131)	**0.162 (0.050, 0.275)**	**0.006**	**0.039 (0.016, 0.062)**
CERAD-IR					
Crude model	Reference	−0.151 (−0.666, 0.363)	**0.795 (0.152, 1.439)**	**0.013**	**0.178 (0.032, 0.324)**
Adjusted model [a]	Reference	0.062 (−0.292, 0.415)	**0.922 (0.386, 1.458)**	**0.001**	**0.219 (0.102, 0.336)**
CERAD-DR					
Crude model	Reference	−0.113 (−0.410, 0.184)	0.219 (−0.145, 0.582)	0.200	0.051 (−0.033, 0.135)
Adjusted model [a]	Reference	−0.002 (−0.237, 0.233)	**0.296 (0.015, 0.577)**	**0.031**	**0.075 (0.004, 0.146)**
Animal fluency					
Crude model	Reference	0.632 (−0.160, 1.423)	**1.569 (0.519, 2.619)**	**0.004**	**0.361 (0.155, 0.566)**
Adjusted model [a]	Reference	**0.750 (0.149, 1.351)**	**1.078 (0.123, 2.033)**	**0.035**	**0.276 (0.084, 0.468)**
DSST					
Crude model	Reference	1.294 (−0.974, 3.562)	**3.578 (0.151, 7.004)**	**0.040**	0.729 (−0.012, 1.470)
Adjusted model [a]	Reference	1.433 (−0.058, 2.923)	1.982 (−0.233, 4.198)	0.090	0.389 (−0.136, 0.914)

Abbreviations: CERAD, consortium to establish a registry for Alzheimer's disease; CERAD-DR, delayed recall in CERAD trial; CERAD-IR, immediate recall in CERAD trial; DSST, the Digit Symbol Substitution test; MeDi, Mediterranean Diet score; T1-T3, the 1st to the 3rd tertiles.

[a] The models were adjusted for age, gender, race, education, marital status, PIR, smoking, BMI category, physical activity, depression, dietary calories.

[b] *P* values for the medians of each tertile of MeDi included in the linear regression models.

Values in bold text mean statistically significant ($P < 0.05$).

3.3 | Effect modification analyses

The marginal effects of MeDi on the cognitive function varied across race/ethnicity and gender (Figure 2). Potential interaction effects were found between MeDi and race/ethnicity on global cognitive function ($p_{interaction} = 0.057$), and in CERAD-IR test ($P_{interaction} = 0.059$). For both global cognitive function and CERAD-IR, significant results were found only in NHWs—not in other racial/ethnic groups (Table 3)—and the difference in the MeDi-cognition association was mainly between NHWs and NHBs ($P_{interaction\ n} = 0.055$ for global score, and 0.085 for

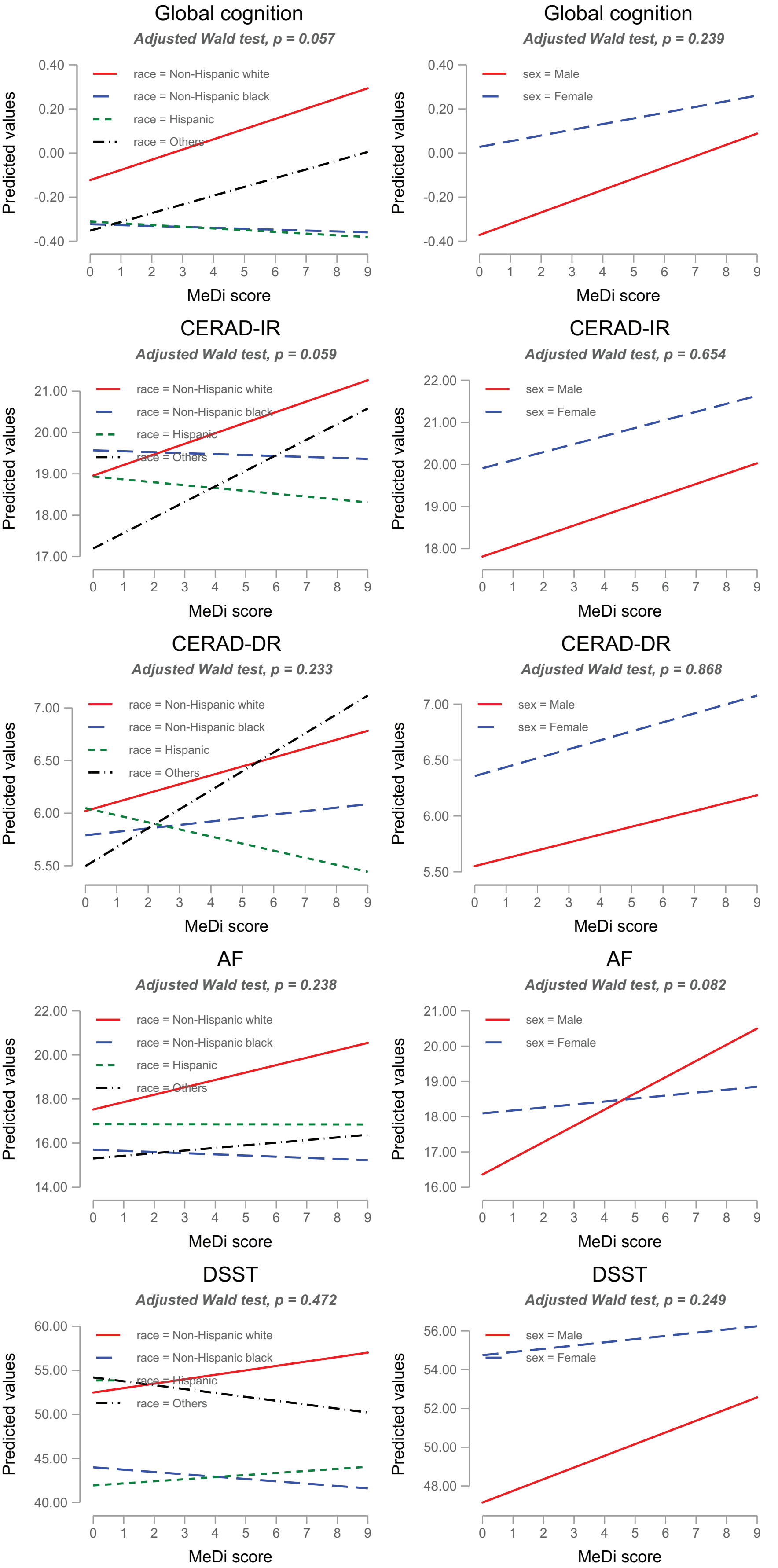


FIGURE 2 Marginal effects of MeDi on cognitive function by race/ethnicity and by gender. Predicted values of the scores of cognitive tests (y-axis) were plotted against the MeDi (x-axis) by race/ethnicity or gender based on the adjusted models. The product term between MeDi and race/ethnicity or between MeDi and gender was tested by the method of adjusted Wald test

CERAD-IR), and between NHWs and Hispanics ($P_{\text{interaction}} = 0.020$ for global score, and 0.033 for CERAD-IR).

Potential interaction effects were identified between MeDi and gender in the AF test ($P_{\text{interaction}} = 0.082$). MeDi was significantly associated with increased score of the AF test in men, but not in women (Table 3).

3.4 | Sensitivity analyses

When excluding subjects with difficulties in thinking or remembering (Table S4), the associations were attenuated slightly, but remained significant for global score, CERAD-IR, and AF in the adjusted models. The results remained almost unchanged when additionally adjusting for the self-reported co-morbidities (Table S5). We found similar results using alternative healthy dietary pattern HEI-2015, with each 1 unit increase in HEI-2015 associated with global cognition (β [95% CI] = 0.003 [0.000-0.006]) and AF (0.025 [0.004-0.046]). We found potential interactions between HEI-2015 and sex for CERAD-DR (*P interaction* = 0.080), between HEI-2015 and race/ethnicity for AF (*P interaction* = 0.025) and global cognition (*P interaction* = 0.041). Among the food components of MeDi, higher consumption of fish ($\beta = 0.20$, 95% CI = 0.12-0.29, $P < 0.0001$) and vegetables ($\beta = 0.10$, 95% CI = 0.02-0.17, $P = 0.015$), and moderate consumption of alcohol ($\beta = 0.09$, 95% CI = 0.006-0.18, $P = 0.036$) were associated with higher global cognition. The stratified results in sensitivity analyses were similar to the main analyses (data not shown).

4 | DISCUSSION

In the current cross-sectional study based on data from NHANES 2011-2014, we found that high adherence to MeDi was associated with better cognition in older adults, age 60 years and older. Furthermore, the positive association between MeDi and cognition seemed to be dependent on race/ethnicity and gender, with a stronger association in men than in women, and in NHWs than in other racial/ethnic groups. Our results confirmed a previous report on adherence to a Mediterranean-type diet and cognition in NHANES study population,[35] despite different ways in constructing MeDi score.[4] Our findings are also in line with previous reports on beneficial role of MeDi on cognition in population-based studies,[3–6] but with a nationally representative U.S. population, are more generalizable.

We found a protective role of MeDi on cognition in NHWs but not in other race/ethnic groups, consistent with previous studies[31,36] on diet and cognition. It has been well documented that minorities are disproportionately burdened by cognitive impairment and risk of AD compared to NHWs.[30] Although the exact mechanisms are unclear, potential factors leading to such racial/ethnic disparities in cognition may include differences in socioeconomic status, early life adversities, educational attainment and quality of education, stress levels, perceived discrimination, and other psychosocial factors.[37] In addition to these distal factors, NHBs and Hispanics also have a higher prevalence of more proximal risk factors for AD, including cardiovascular risk factors,[38] heightened oxidative stress,[39] and higher inflammatory status.[39] Finally, dietary habit and quality can be affected by many of the distal factors and are also associated with downstream cardiovascular factors, and thus may play an important role in modifying or mediating the pathway from the contextual factors to cognition.[30] Our results suggest that following a healthy dietary pattern may have limited the effect to mitigate the overall heightened risk burden for cognitive impairment in minorities. Alternatively, as NHWs consumed more fish and vegetables (two key beneficial components), but less legumes than NHBs and Hispanics, the differences in the MeDi-cognition association across racial/ethnic groups might be due to the subtle difference in how a high MeDi score was comprised. Improving neighborhood food environment, eliminating food deserts, and promoting nutritional education may provide a unique venue for reducing racial/ethnic disparities in diet quality and subsequent health status.[40]Nevertheless, some studies have found MeDi[13] or other dietary factors[41] were associated with slower cognitive decline for NHB but not for NHW participants, and others did not find a significant difference across racial/ethnic groups in terms of MeDi-cognition/AD association.[7,9,11,31] Previous prospective studies investigating the association between the MeDi and cognition have been in predominately white populations[14,15,20,22,23,25] and rarely in minorities.[8] Therefore, current evidence is insufficient to conclude whether MeDi offer benefits for cognitive performance or AD prevention differently across racial/ethnic groups. With the growing and aging Black and Hispanic population in the United States, further studies are urgently needed to improve our understanding of preventive/risk factors in minorities that may inform interventions.[42]

We found a significant association between MeDi and AF, a measure of executive function, in men but not in women. Gender differences in eating habits, taste perception, and preference have been well documented.[27,28] It is possible that the differences in the MeDi-cognition association between men and women in the current study might be due to the different ways of reaching a high MeDi score, that is, by high intake of fruits and low intake of meat in women and by high intake of legumes in men. Furthermore, multiple lines of evidence suggest that women had a higher risk of AD than men.[29] Our findings are in line with a Greek study, which found that adherence to MeDi was associated with a lower risk of cognitive impairment in men but an increased risk in women.[16] Of interest, among existing studies reporting null associations between MeDi and cognition, several of them are large-scale studies including women participants only.[21–24] Animal studies also support that males tend to be more susceptible to dietary stimuli for physiological changes such as weight gain, insulin resistance, hyperglycemia, metabolic alterations, deficits of learning, and hippocampal synaptic plasticity.[43] Sex differences in multiple physiobiological parameters, such as vascular dysfunction, inflammation, hypertension, circulating triglycerides and homocysteine, and microbiome responses, in response to special diets have also been reported in humans,[44–46] and may be the mechanisms underlying the observed sexual dimorphism in MeDi-cognition association. Along this line, a recent study found genetic polymorphisms (*rs34331204*), associated with neurofibrillary tangles only among males, was positively

TABLE 3 Stratification analyses on the associations between MeDi and cognitive scores

Cognitive score and stratification [a]	Tertiles of MeDi					
	T1 (0 to 3)	T2 (4 to 5)	T3 (6 to 9)	P_{trend} [b]	Continuous MeDi	*P-interaction* [c]
	(n = 841)	(n = 1129)	(n = 465)			
Global cognition						
By sex						–
Male	Reference	0.088 (−0.026, 0.202)	**0.240 (0.079, 0.402)**	**0.004**	**0.049 (0.017, 0.080)**	–
Female	Reference	0.030 (−0.060, 0.120)	0.091 (−0.034, 0.216)	0.148	0.028 (−0.004, 0.060)	0.239
By Race/ethnicity						**0.057**
Non-Hispanic White	Reference	0.072 (−0.015, 0.160)	**0.201 (0.065, 0.337)**	**0.005**	**0.047 (0.020, 0.074)**	–
Non-Hispanic Black	Reference	−0.027 (−0.151, 0.097)	−0.051 (−0.222, 0.121)	0.554	−0.005 (−0.046, 0.036)	**0.055**
Hispanic	Reference	−0.004 (−0.107, 0.099)	−0.133 (−0.301, 0.036)	0.131	−0.016 (−0.058, 0.026)	**0.020**
Others	Reference	0.112 (−0.082, 0.307)	0.162 (−0.106, 0.430)	0.223	0.040 (−0.027, 0.106)	0.882
CERAD-IR						
By sex						
Male	Reference	0.121 (−0.454, 0.696)	**1.191 (0.299, 2.082)**	**0.006**	**0.258 (0.086, 0.429)**	–
Female	Reference	−0.029 (−0.604, 0.546)	**0.649 (0.054, 1.244)**	**0.033**	**0.173 (0.008, 0.339)**	0.654
By Race/ethnicity						**0.059**
Non-Hispanic White	Reference	0.153 (−0.267, 0.574)	**1.117 (0.482, 1.752)**	**< 0.001**	**0.264 (0.124, 0.404)**	–
Non-Hispanic Black	Reference	−0.604 (−1.517, 0.308)	−0.349 (−1.679, 0.981)	0.620	−0.053 (−0.334, 0.228)	**0.085**
Hispanic	Reference	−0.385 (−1.077, 0.306)	−0.912 (−2.303, 0.480)	0.176	−0.137 (−0.422, 0.148)	**0.033**
Others	Reference	0.776 (−0.665, 2.217)	1.455 (−0.097, 3.006)	0.068	0.312 (−0.060, 0.684)	0.613
CERAD-DR						
By sex						
Male	Reference	−0.032 (−0.374, 0.311)	0.330 (−0.130, 0.790)	0.124	0.068 (−0.029, 0.164)	–
Female	Reference	0.000 (−0.341, 0.341)	0.244 (−0.079, 0.567)	0.134	0.078 (−0.014, 0.171)	0.868
By Race/ethnicity						0.233
Non-Hispanic White	Reference	0.023 (−0.249, 0.295)	**0.385 (0.051, 0.719)**	**0.021**	**0.095 (0.014, 0.177)**	–
Non-Hispanic Black	Reference	−0.060 (−0.436, 0.316)	−0.112 (−0.598, 0.375)	0.646	−0.018 (−0.124, 0.087)	0.439
Hispanic	Reference	−0.120 (−0.525, 0.285)	**−0.625 (−1.156, −0.093)**	**0.026**	−0.114 (−0.249, 0.021)	**0.053**
Others	Reference	0.143 (−0.322, 0.609)	0.551 (−0.388, 1.489)	0.249	0.156 (−0.110, 0.423)	0.461
Animal Fluency						
By sex						
Male	Reference	**1.285 (0.335, 2.234)**	**2.009 (0.594, 3.425)**	**0.013**	**0.436 (0.132, 0.741)**	–
Female	Reference	0.299 (−0.602, 1.200)	0.259 (−0.893, 1.410)	0.651	0.107 (−0.151, 0.365)	**0.082**
By Race/ethnicity						0.238
Non-Hispanic White	Reference	**0.790 (0.016, 1.564)**	**1.285 (0.118, 2.453)**	**0.037**	**0.318 (0.086, 0.549)**	–
Non-Hispanic Black	Reference	0.273 (−0.939, 1.486)	−0.421 (−2.009, 1.167)	0.578	−0.002 (−0.384, 0.380)	0.104
Hispanic	Reference	0.409 (−0.616, 1.435)	−0.167 (−1.644, 1.310)	0.885	0.065 (−0.331, 0.461)	**0.089**
Others	Reference	1.831 (−0.630, 4.292)	1.393 (−1.167, 3.954)	0.267	0.227 (−0.353, 0.808)	0.527
DSST						
By Sex						
Male	Reference	1.825 (−0.794, 4.444)	**3.161 (0.155, 6.167)**	**0.045**	0.476 (−0.197, 1.149)	–
Female	Reference	1.227 (−0.621, 3.075)	1.053 (−1.429, 3.535)	0.395	0.315 (−0.338, 0.968)	0.249

(Continues)

TABLE 3 (Continued)

Cognitive score and stratification [a]	Tertiles of MeDi T1 (0 to 3)	T2 (4 to 5)	T3 (6 to 9)	P_{trend} [b]	Continuous MeDi	*P-interaction* [c]
By Race/ethnicity						0.472
Non-Hispanic White	Reference	1.738 (−0.013, 3.488)	2.561 (−0.137, 5.260)	0.070	0.491 (−0.140, 1.122)	–
Non-Hispanic Black	Reference	0.124 (−1.513, 1.761)	−0.005 (−3.287, 3.276)	0.995	−0.003 (−0.751, 0.745)	0.107
Hispanic	Reference	0.852 (−1.330, 3.033)	−0.332 (−4.543, 3.879)	0.919	0.089 (−0.742, 0.921)	0.600
Others	Reference	−1.851 (−7.093, 3.391)	−2.804 (−9.853, 4.246)	0.421	−0.343 (−1.896, 1.210)	0.333

Abbreviations: MeDi, Mediterranean Diet score; T1-T3, the 1st to the 3rd tertiles.
[a]Stratification analyses were conducted when the *P* values of product term between Medi (continuous score) and each cognitive function were <0.10. The models were adjusted for age, gender, race/ethnicity, education, marital status, PIR, smoking, BMI category, physical activity, depression, and dietary calories, except for gender or race/ethnicity when it was under stratification.
[b]*P* values for the medians of each tertile of MeDi included in the linear regression models.
[c]A product term between tertiles of MeDi and race/sex were included in the adjusted models.
Values in bold text mean statistically significant ($P < 0.05$ for MeDi, $P < 0.10$ for interaction between MeDi and race/sex).

associated with hippocampal volume, executive function, and delayed onset in males to a larger extent than in females.[47] Nevertheless, contrasting results, with diet-cognition stronger in women than in men, have also been reported in a few studies.[48–50] Moreover, several studies observed no evidence for effect modification by gender on the association between diet and cognition.[11] To date, the gender-diet interaction on cognition has not been routinely tested in previous epidemiological studies.[9,10,12,14,17–19] In the current era of precision medicine, further understanding of gender differences in the potential dietary intervention on cognitive aging should be prioritized to develop individualized prevention and treatment for cognitive aging and dementia.

The outstanding advantage of the current study lies in the study population, a large nationally representative sample of multiethnic older adults in the United States. It serves as an ideal population to explore the racial/ethnic differences and gender differences in diet-cognition association. Furthermore, standard and detailed information on many potential confounders such as socioeconomic factors and physical activity were available from the survey and were controlled for in our study, and the results remained significant. Dietary consumption was estimated using USDA's Dietary Intake Data System 24-hour dietary recall, which by nature was able to capture a wide range of foods and dietary habits including race and culturally specific foods, and thus was particularly appropriate for this multiethnic population with diverse cultural backgrounds. Multiple sensitivity analyses were performed, and the results were robust.

Our study has some limitations. Due to the nature of cross-sectional study design, the temporal relationship between diet and cognition cannot be confirmed. There could be selection bias, as only slightly over half of older adults responded to the cognitive survey invitation, and some subjects were excluded due to missing data. However, a non-response bias analysis showed similar cognitive scores with and without weighting adjustments.[32] The 24-hour dietary recall might not be the best measure of long-term dietary exposures and might be subject to recall bias. Genetic information such as apolipoprotein E (*APOE*) ε4 status was not available in NHANES 2011-2014 cycles. Cognitive measures in NHANES were chosen for ease of administration, availability, and use in other surveys, so it may not be comprehensive enough to capture the entire cognitive profile of a subject and not sufficient for diagnosing cognitive impairment or dementia.

5 | CONCLUSIONS

Higher adherence to MeDi is associated with better cognitive function in the U.S. elderly population. The positive association between MeDi and cognition is stronger in NHWs and men, compared to other racial/ethnic groups and women, respectively. Prospective studies with a large sample of minority older adults and with both men and women are warranted to confirm the findings.

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CONFLICT OF INTEREST

All authors have nothing to disclose.

AUTHOR CONTRIBUTIONS

J. Guo conducted the statistical analyses, and contributed to data interpretation and critical revision of the manuscript; A. J. Moshfegh contributed to data interpretation and the critical review of the manuscript; Y. Gu designed the study, contributed to data interpretation, supervised the study process, and drafted the manuscript; and all authors read and approved the final manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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