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## Mediterranean Diet, Healthy Eating Index-2005, and Cognitive Function in Middle-Aged and Older Puerto Rican Adults

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## Abstract

Adherence to a Mediterranean diet (MeD) has recently been shown to protect against cognitive decline and dementia. It remains unclear, however, whether such protection extends to differing ethnic groups and middle-aged individuals, and how it may compare with adherence to the USDA *Dietary Guidelines for Americans 2005* (measured with Healthy Eating Index-2005, HEI-2005). This study examined associations between diet quality, as assessed by the MeD and HEI-2005, and cognitive performance in a sample of 1,269 Puerto Rican adults, aged 45–75 years, living in the Greater Boston area, Massachusetts. Dietary intake was assessed with a food-frequency questionnaire specifically designed for and validated with this population. Adherence to the MeD was assessed with a 0 to 9 point scale, and the HEI-2005 score was calculated with a maximum score of 100. Cognitive performance was measured with a battery of seven tests; the Mini Mental State Examination (MMSE) was used for global cognitive function. Greater adherence to the MeD

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was associated with higher MMSE score ( $P$  trend = 0.012) and lower likelihood (OR = 0.87 for each additional point, 95% CI, 0.80–0.94,  $P < 0.001$ ) of cognitive impairment, after adjustment for confounders. Similarly, individuals with higher HEI-2005 score had higher MMSE score ( $P$  trend = 0.011) and lower odds of cognitive impairment (OR = 0.86 for each 10 points, 95% CI, 0.74–0.99,  $P = 0.033$ ). In conclusion, high adherence to either the MeD or the diet recommended by the USDA dietary guidelines may protect cognitive function in middle-aged and older adults.

## Keywords

Mediterranean diet; Healthy Eating Index-2005; diet quality; Cognitive impairment

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## INTRODUCTION

The Mediterranean diet (MeD), characterized by high intake of vegetables, fruit, legumes, nuts, cereals and monounsaturated fat (olive oil); low intake of saturated fat; moderate intake of dairy foods, meat, poultry and fish; and regular moderate intake of alcohol, primarily from wine consumed with meals (1), has been associated with less cognitive decline (2) and lower risk for development of mild cognitive impairment (3) and Alzheimer disease (4, 5). However, available studies have focused mainly on older populations, with baseline age  $\geq 65$  years (2–6), and most have examined only the Mediterranean diet. One exception is a recent French study, where higher adherence to a healthy dietary pattern derived from an a posteriori statistical method in middle life was associated with better cognitive function 13 years later (7). To postpone cognitive decline, and, eventually, cognitive impairment and dementia, it is important to understand protective factors at an earlier age. It is also important to understand if there is something particular about the Mediterranean Diet itself in protecting cognitive function, or if other measures of a healthy diet are also protective.

The Healthy Eating Index-2005 (HEI-2005) is a measure of diet quality relative to adherence to the USDA *Dietary Guidelines for Americans 2005* (8). Higher HEI-2005 score indicates greater adherence to the dietary guidelines. Higher HEI-2005 scores have been associated with favorable lipid profile (9) and lower risk of obesity (10) but, in one study, they were not associated with cognitive decline in elderly adults (6). Additional investigation is needed to examine the role of dietary quality measured with the HEI-2005 in the preservation of cognitive function. To our knowledge, no study has shown associations between the HEI-2005 and cognitive function with participants aged  $< 65$  years.

Relative to non-Hispanic white adults, higher incidence of dementia has been shown in Latinos (11). Food insecurity has been found to be associated with increased risk for cognitive impairment in Puerto Rican adults (12). Puerto Rican adults consume foods in differing frequency and portion size compared with general US population (13). To identify a favorable dietary pattern for cognition could be particularly important for this population. We, therefore, aimed to investigate adherence to the Mediterranean diet and to the HEI-2005, and their associations with cognitive function in a sample of middle-aged and older Puerto Rican adults from the Greater Boston area, Massachusetts.

## METHODS

### Study sample

The Boston Puerto Rican Health Study is an ongoing study to investigate the sociological, environmental and genetic risk factors for chronic diseases, cognitive impairment and reduced quality of life. The design of the study has been described in detail previously (14).

Participants were not included if they had Mini Mental State Examination (MMSE) score  $\leq 10$ , an indicator of severe cognitive impairment (15) which may affect the quality of their response to questionnaires. A total of 1,500 Puerto Rican adults, aged 45–75 years, completed the baseline visit. Of those, individuals with implausible energy intake ( $<600$  kcal/d or  $>4800$  kcal/d) were excluded from the analysis, as were those with incomplete cognitive tests or blood analyses. Cleaned and complete data were available for 1,269 participants for this analysis. The Institutional Review Board at Tufts Medical Center approved the study protocol, and all participants provided written informed consent.

### Development of MeD score and HEI-2005 score

Dietary intake was assessed for the last 12 months with a validated semi-quantitative food frequency questionnaire (FFQ) during home interview (16). Ounce or cup equivalents of each food per day were calculated using the MyPyramid Equivalents Database, 2.0 for USDA Survey Foods, 2003-2004 (17). Food equivalents were then summed within each food group. Similar to the work of Scarmeas et al. (4) and Feart et al. (2), the MeD score was composed following the procedure described by Trichopoulos et al. (1). Food equivalents for each of nine food groups were adjusted for total energy intake using the regression residual method before further analysis (18). A score for adherence to the MeD was created by adding points from the nine food categories, resulting in a possible range of 0 to 9 (Supplemental text). The HEI-2005 score was calculated using an energy density approach according to procedures from the USDA Center for Nutrition Policy and Promotion (8). The HEI-2005 score is a sum of scores from 12 individual components, with maximum score 100 (Supplemental text).

### Assessment of cognitive function

A battery of seven neuropsychological tests, with the MMSE as a measure of global cognitive function, was conducted with each participant in their home by a qualified research assistant (supplemental text), before the FFQ was administered, on the same day (12). Higher scores on each of these exams reflect better cognitive function. To minimize the potential of redundancy in the neuropsychological tests and to reduce the possibility of type I error due to multiple testing (19), a factor analysis was performed with scores from the seven neuropsychological tests (12). Three factors were identified with Kaiser's criterion (eigenvalue  $>1$ ) (20). Orthogonal varimax rotation was then conducted to maximize interpretability. The three cognitive function factors were uncorrelated and were interpreted as executive function, memory, and attention, respectively (Supplemental Table 1).

Cognitive impairment was defined as MMSE score  $<21$  for those with less than high school education,  $<23$  for those with high school completion, and  $<24$  for those with at least some college education (14).

### Statistical analyses

Participants were placed in quintile categories by scores of MeD and HEI-2005, respectively. Cognitive performance scores for each category of the MeD adherence score were calculated after multivariable adjustment using general linear models. Model 1 was adjusted for age (years), sex, and educational attainment (primary school, secondary school, high school, or some college). Model 2 was further adjusted for household income below the poverty threshold (yes/no), acculturation score, smoking status (never, past or current smoker), physical activity score, supplement use (yes/no), taking more than 5 types of medications within the past 12 months (yes/no), body mass index ( $\text{kg}/\text{m}^2$ ), hypertension (yes/no), diabetes (yes/no), total cholesterol (mg/dL), high-density lipoprotein cholesterol (mg/dL) and triglycerides (mg/dL). Original continuous dietary scores were used for trend tests. Finally, possible interactions between age (in three categories: 45-54, 55-64, 65-75

years) and adherence to the MeD were tested by additionally including the product of age and diet score in the models for cognitive function outcomes. In the current study, MMSE scores were treated as the primary outcome, because the MMSE measures global cognitive function. Secondary analyses examined associations between the diet quality scores and the three derived cognitive function factors. Logistic regression models were used to calculate odds ratios for cognitive impairment per point change of continuous MeD scores and for the upper four quintiles of MeD scores, when compared with first quintile.

All analyses were repeated to estimate associations between HEI-2005 score and cognitive performance. All statistical analyses were conducted with SAS version 9.2 (SAS Institute Inc, Cary, NC). A value of  $P < 0.05$  (two-sided) was considered statistically significant.

## RESULTS AND DISCUSSION

### The MeD score and cognitive function

In this population-based cross-sectional sample of middle-aged and older Puerto Rican adults, the mean age was 57.3 years (SD 7.6), and the mean MeD score was 4.37 (SD 1.61) with a range of 0 to 9; 45.0% had a score of 4 or 5, and 0.2%, 3.0%, 2.7% and 0.2% had scores of 0, 1, 8, and 9, respectively. The average MeD score in our study was similar to the mean MeD score (4.36, SD: 1.67) in two cohorts of the Washington-Heights-Inwood Columbia Aging Project in New York, NY (3).

Higher adherence to the MeD was associated with better global cognitive function, as measured by higher MMSE score, after adjusting for age, sex and educational attainment (Table 1). These associations remained significant after further adjustment for confounders. Each MeD score point was associated with a 0.14 point higher MMSE score ( $\beta = 0.14$ , SE = 0.05,  $P = 0.012$ ). This was inversely comparable to a difference in MMSE score associated with 3-years of age ( $\beta = -0.14$ , SE = 0.04,  $P < 0.001$ ) in model 2. MeD adherence was also significantly associated with the attention factor (model 1), but significance was attenuated with full adjustment. MeD score was not associated with executive function or memory factors.

Higher adherence to the MeD was also associated with lower likelihood of cognitive impairment, defined by MMSE cutoff points, after adjustment for potential confounders (Figure 1a). Those in the highest (vs. lowest) quintile of MeD score had about 50% lower odds (odds ratio [OR]: 0.51, 95% confidence interval [CI]: 0.33-0.79) of cognitive impairment. Using continuous MeD score as the independent variable, each additional point of MeD score was associated with 13% lower odds of cognitive impairment after multivariable adjustment (OR: 0.87, 95% CI: 0.80 - 0.94,  $P_{trend} < 0.001$ ).

Analyses were repeated in three subgroups, stratified by age (45–54, 55–64, and >64 years), to explore whether associations were limited to groups within specific age ranges. In general, similar positive associations between MeD scores and MMSE were observed across each of the three age groups ( $P$  for interaction  $> 0.35$ ) after multivariable adjustment (Supplemental Table 2).

The positive association between adherence to the MeD and MMSE score seen in the current study is consistent with findings from previous reports in diverse populations (2, 3, 5, 6). In the Three-city cohort from France, with a total of 1,410 adults aged  $\geq 65$  years, higher adherence to the MeD score was associated with less MMSE decline over time (2). Greater adherence to the MeD score was also associated with lower risk of developing mild cognitive impairment (3), and with reduced risk of mild cognitive impairment conversion to Alzheimer's disease (5) in the Washington-Heights-Inwood Columbia Aging Project, with

recruited participants aged  $\geq 65$  years at baseline (11). Higher MeD score, measured in a different way, was also associated with slower rates of cognitive decline in the Chicago Health and Aging Project (CHAP) (6). Importantly, the association between adherence to MeD and MMSE score was also observed among individuals aged  $<65$  years in the current study.

In agreement with previous studies (2, 3), the association between MeD adherence and cognitive function remained unchanged after adjustment for several vascular risk factors, suggesting that the benefits of MeD may be, in part, through non-vascular mechanisms. The MeD usually captures a composition of high intakes of monounsaturated fatty acids, B vitamins, and antioxidants such as complex phenols, vitamins C and E, and carotenoids (2). Higher intake of monounsaturated fatty acids has been associated with better cognitive function or lower risk for cognitive decline (21). B vitamins including folate, vitamins B-6 and B-12 have also been related to cognitive performance (22). In addition, cumulative evidence suggests that oxidative damage contributes to the pathogenesis of mild cognitive impairment and Alzheimer disease (23, 24), and that antioxidants in fruit, vegetables and wine may improve the antioxidative defense system (25). Further, greater adherence to the MeD has been associated with lower concentrations of several inflammatory factors including C-reactive protein, interleukin 6 and white blood cell counts (26-28). Available data suggest that inflammation is involved in the pathogenesis of cognitive impairment and Alzheimer's disease (24). Therefore, the MeD may protect cognitive function through effects on inflammation and oxidative stress.

### The HEI-2005 score and cognitive function

The question remains as to whether it is the Mediterranean diet per se or a healthy diet in general that is protective. Importantly, in the present study, adherence to the USDA *Dietary Guidelines for Americans 2005* (measured by the HEI-2005) was also associated with MMSE score (Table 2), and these associations remained after multivariable adjustment. Each 10 points of HEI-2005 score ( $\beta = 0.25$ , SE = 0.10,  $P = 0.011$ ) was inversely similar to 5 years of age ( $\beta = -0.25$ , SE = 0.07,  $P < 0.001$ ) on MMSE scores, after multivariable adjustment. As with the MeD, the HEI-2005 was not significantly associated with executive function. In contrast, however, the HEI-2005 was associated with memory (rather than attention) in the initial model, but this was attenuated after further adjustment for covariates.

Those in the highest (vs. lowest) quartile of the HEI-2005 score had about 40% lower odds (OR: 0.58, 95% CI: 0.38 - 0.89) of cognitive impairment (Figure 1b). Similarly, each 10 HEI-2005 point increase in score was associated with 14% lower odds of cognitive impairment (OR: 0.86, 95% CI: 0.74 - 0.99,  $P_{trend} = 0.033$ ). In general, positive associations between the HEI-2005 and MMSE scores were observed across the three age groups (45–54, 55–64, and  $>64$  years;  $P$  for interaction  $>0.35$ ) after multivariable adjustment (Supplemental Table 2).

In contrast to these findings, the HEI-2005 score was not associated with cognitive function in the CHAP study (6). There are several plausible explanations for this inconsistency. The FFQ used here has many more food items compared with the one used in the CHAP (246 vs. 139 food items). Greater detail on the FFQ may improve the calculation of the HEI-2005 score, which was originally designed from 24-hour dietary recalls. Further, the participants in the present study were much younger than those in the CHAP (mean age, 75.4 years), and the HEI-2005 score was higher in our study (72.8 for women and 68.9 for men) than in the CHAP (61.6 for women and 60.5 for men). All these features in our study may increase power to detect potential associations between HEI-2005 scores and cognitive function. Indeed, Wengreen et al. reported that adherence to a diet with higher quality, reflected by higher recommended food score, was associated with lower 11 year cognitive decline among

elderly men and women aged ≥ 65 years at baseline (29). More studies with prospective designs are warranted to examine associations between adherence to the USDA *Dietary Guidelines for Americans 2005* and cognitive function.

### Strengths and limitations

Because of the cross-sectional nature of this analysis, a causal direction between MeD score or HEI-2005 score and cognitive function cannot be assumed. However, significant dose-response associations were observed between these diet quality scores with cognitive measures, which are unlikely to be due to reverse causation, as it is unlikely that those with more cognitive impairment would choose lower quality of overall diet in a dose-response manner. Strengths of our study include a population-based design, a high proportion of middle-aged, as well as older, participants, and careful control for confounders, although residual confounding may still exist.

### CONCLUSIONS

Diets with higher quality, measured either by the MeD score or HEI-2005 score, were associated with greater cognitive function and lower likelihood of cognitive impairment in middle-aged and older Puerto Rican adults. Further studies, including intervention trials, will be useful to determine whether the whole-diet approach is effective in slowing the progress of cognitive impairment and delaying onset of dementia in this and other ethnic groups.

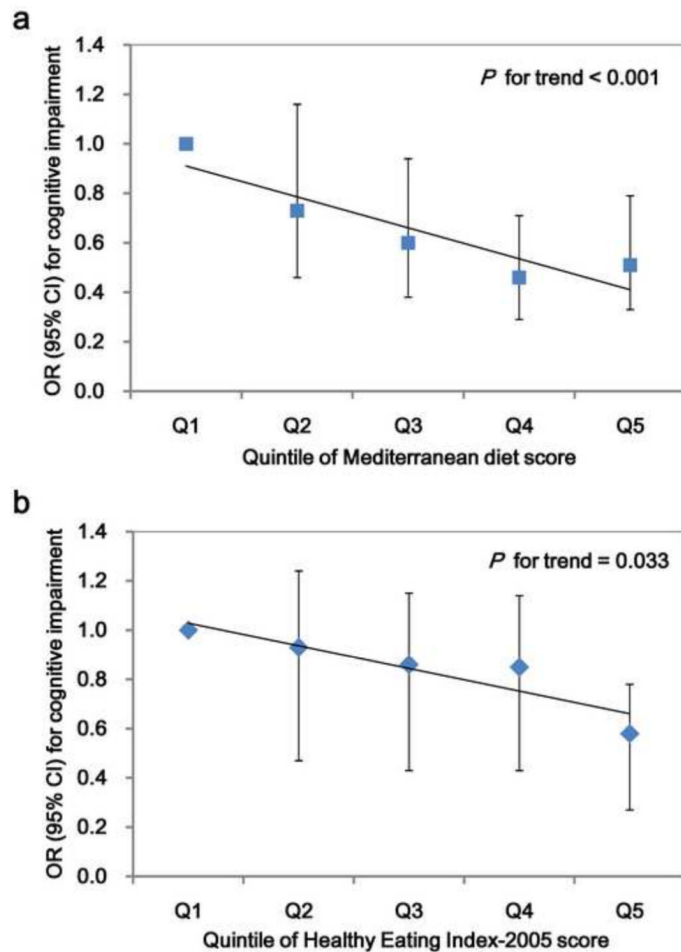
### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Figure 1. Odds of cognitive impairment by quintile category of diet score**

Cognitive impairment was defined as: Mini Mental State Examination score <21 for those with less than high school education, <23 for those with high school completion, or <24 for those with at least some college education (14). Logistic regression was used to calculate odds ratios (OR) and 95% confidence interval (CI) for cognitive impairment with PROC LOGISTIC in SAS 9.2, adjusting for age (years), sex, educational attainment (primary school, secondary school, high school, or some college), household income below threshold (yes/no), acculturation score (continuous), smoking status (never, past smoker or current smoker), physical activity score (continuous), supplement use (yes/no), taking more than 5 types of medications within the last 12 months (yes/no), body mass index ( $\text{kg}/\text{m}^2$ ), hypertension (yes/no), diabetes (yes/no), total cholesterol (mg/dL), high-density lipoprotein cholesterol (mg/dL), and triglycerides (mg/dL). *P* for trend was the *P* value for continuous dietary scores.



Table 1

Cognitive performance by quintile of Mediterranean diet score

	Mediterranean diet score					Continuous	$\beta$ (SE) <sup>c</sup>	P for trend <sup>d</sup>
	Quintile 1 (0–2)	Quintile 2 (3)	Quintile 3 (4)	Quintile 4 (5)	Quintile 5 (6–9)			
n	159	232	278	287	313			
Score	1.74 (0.47) <sup>a</sup>	3 (0) <sup>a</sup>	4 (0) <sup>a</sup>	5 (0) <sup>a</sup>	6.48 (0.73) <sup>a</sup>			
Age (years) <sup>b</sup>	56.1 (7.5) <sup>a</sup>	57.3 (7.5) <sup>a</sup>	57.5 (7.5) <sup>a</sup>	57.4 (7.8) <sup>a</sup>	57.7 (7.6) <sup>a</sup>			
	Mean (SE) <sup>c</sup>							
MMSE <sup>e</sup>								
Model 1 <sup>f</sup>	23.1 (0.2)	23.3 (0.2)	23.6 (0.2)	23.8 (0.2)	23.9 (0.2)	0.19 (0.05)	<0.001	
Model 2 <sup>g</sup>	23.0 (0.3)	23.3 (0.2)	23.5 (0.2)	23.7 (0.2)	23.7 (0.2)	0.14 (0.05)	0.012	
Executive function								
Model 1 <sup>f</sup>	-0.06 (0.07)	-0.004 (0.06)	0.002 (0.06)	-0.08 (0.06)	0.05 (0.05)	0.02 (0.02)	0.34	
Model 2 <sup>g</sup>	-0.14 (0.08)	-0.03 (0.07)	-0.08 (0.06)	-0.11 (0.06)	-0.02 (0.06)	0.01 (0.02)	0.52	
Memory								
Model 1 <sup>f</sup>	-0.15 (0.08)	-0.16 (0.07)	0.08 (0.07)	-0.08 (0.07)	-0.06 (0.06)	0.02 (0.02)	0.23	
Model 2 <sup>g</sup>	-0.13 (0.09)	-0.17 (0.07)	0.12 (0.07)	-0.07 (0.07)	-0.07 (0.07)	0.02 (0.02)	0.39	
Attention								
Model 1 <sup>f</sup>	-0.03 (0.08)	0.03 (0.07)	0.17 (0.06)	0.09 (0.06)	0.19 (0.06)	0.04 (0.02)	0.017	
Model 2 <sup>g</sup>	-0.08 (0.09)	0.02 (0.07)	0.15 (0.07)	0.06 (0.07)	0.13 (0.07)	0.03 (0.02)	0.067	

<sup>a</sup>Mean (SD).<sup>b</sup>P = 0.30 for age differences across quintiles of Mediterranean diet score (PROC GLM in SAS 9.2).<sup>c</sup>Adjusted means (standard error, SE) by quintile category, and  $\beta$  coefficients (SE) for linear scores were calculated using general linear models (PROC GLM in SAS 9.2) after adjustment for covariates.<sup>d</sup>P values for trend were calculated using the continuous diet score in general linear models (PROC GLM in SAS 9.2).<sup>e</sup>Mini Mental State Examination (MMSE) score.<sup>f</sup>Model 1, adjusted for age (years), sex, and educational attainment (primary school, secondary school, high school, or some college).<sup>g</sup>Model 2, further adjusted for household income below threshold (yes/no), acculturation score (continuous), smoking status (never, past smoker or current smoker), physical activity score (continuous), supplement use (yes/no), taking more than 5 types of medications within the last 12 months (yes/no), body mass index (kg/m<sup>2</sup>), hypertension (yes/no), diabetes (yes/no), total cholesterol (mg/dL), high-density lipoprotein cholesterol (mg/dL) and triglycerides (mg/dL).

Table 2

Cognitive performance by quintile of Healthy Eating Index-2005 score

	Healthy Eating Index-2005 score					Continuous	
	Quintile 1 (<64.5)	Quintile 2 (64.5–70.5)	Quintile 3 (70.6–75.5)	Quintile 4 (75.6–80.0)	Quintile 5 (>80.0)		
n	253	254	254	254	254		
Score	57.4 (5.1) <sup>a</sup>	67.2 (1.8) <sup>a</sup>	72.6 (1.4) <sup>a</sup>	77.3 (1.3) <sup>a</sup>	83.9 (3.3) <sup>a</sup>		
Age (year) <sup>b</sup>	55.1 (7.0) <sup>a</sup>	56.4 (7.5) <sup>a</sup>	56.5 (7.6) <sup>a</sup>	59.1 (7.6) <sup>*** a</sup>	59.3 (7.4) <sup>*** a</sup>		
	Mean (SE) <sup>c</sup>					$\beta$ (SE) <sup>c d</sup>	P for trend <sup>e</sup>
MMSE <sup>f</sup>							
Model 1 <sup>g</sup>	23.4 (0.2)	23.3 (0.2)	23.6 (0.2)	23.7 (0.2)	24.2 (0.2)	0.27 (0.09)	0.004
Model 2 <sup>h</sup>	23.4 (0.2)	23.2 (0.2)	23.4 (0.2)	23.6 (0.2)	24.1 (0.3)	0.25 (0.10)	0.011
Executive function							
Model 1 <sup>g</sup>	-0.04 (0.06)	-0.05 (0.06)	-0.03 (0.06)	0.02 (0.06)	0.04 (0.06)	0.03 (0.03)	0.27
Model 2 <sup>h</sup>	-0.09 (0.06)	-0.14 (0.06)	-0.08 (0.06)	-0.04 (0.06)	0.001 (0.07)	0.04 (0.03)	0.23
Memory							
Model 1 <sup>g</sup>	-0.15 (0.07)	-0.08 (0.07)	-0.04 (0.07)	-0.05 (0.07)	0.01 (0.07)	0.07 (0.03)	0.025
Model 2 <sup>h</sup>	-0.11 (0.07)	-0.13 (0.07)	-0.03 (0.07)	-0.02 (0.07)	-0.002 (0.08)	0.06 (0.03)	0.059
Attention							
Model 1 <sup>g</sup>	0.13 (0.06)	-0.01 (0.06)	0.08 (0.07)	0.13 (0.07)	0.22 (0.07)	0.03 (0.03)	0.32
Model 2 <sup>h</sup>	0.05 (0.07)	-0.04 (0.07)	0.03 (0.07)	0.12 (0.07)	0.18 (0.08)	0.05 (0.03)	0.10

<sup>a</sup>Mean (SD).<sup>b</sup> $P < 0.001$  for age differences across quintiles of Healthy Eating Index-2005 score (PROC GLM in SAS 9.2).<sup>c</sup>Adjusted means (standard error, SE) by quintile category, and  $\beta$  coefficients (SE) for linear scores were calculated using general linear models (PROC GLM in SAS 9.2) after adjustment for covariates.<sup>d</sup> $\beta$  coefficients per 10 points of Healthy Eating Index-2005.<sup>e</sup> $P$  values for trend were calculated using continuous Healthy Eating Index-2005 score (PROC GLM in SAS 9.2).<sup>f</sup>Mini Mental State Examination (MMSE) score.<sup>g</sup>Model 1, adjusted for age (years), sex, and educational attainment (primary school, secondary school, high school, or some college).<sup>h</sup>Model 2, further adjusted for household income below threshold (yes/no), acculturation score (continuous), smoking status (never, past smoker or current smoker), physical activity score (continuous), supplement use (yes/no), taking more than 5 types of medications within the last 12 months (yes/no), body mass index ( $\text{kg}/\text{m}^2$ ), hypertension (yes/no), diabetes (yes/no), total cholesterol (mg/dL), high-density lipoprotein cholesterol (mg/dL) and triglycerides (mg/dL).\*  $P < 0.05$ \*\*\*  $P < 0.001$  compared with the lowest category with Tukey's adjustment for multiple comparisons.