Diet Quality Is Associated with Better Cognitive Test Performance among Aging Men and Women[1,2]

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Abstract

Most studies of association between diet and cognition among the elderly focus on the role of single nutrients or foods and ignore the complexity of dietary patterns and total diet quality. We prospectively examined associations between an index of diet quality and cognitive function and decline among elderly men and women of the Cache County Study on Memory and Aging in Utah. In 1995, 3634 resident men and women $\geq$65 y of age completed a baseline survey that included a 142-item FFQ. Cognition was assessed using an adapted version of the Modified Mini-Mental State Examination (3MS) at baseline and 3 subsequent interviews spanning ~11 y. A recommended food score (RFS) and non-RFS were computed by summing the number of recommended foods ($n = 57$) and nonrecommended foods ($n = 23$) regularly consumed. Multivariable-mixed models were used to estimate associations between the RFS and non-RFS and average 3MS score over time. Those in the highest quartile of RFS scored 1.80 points higher on the baseline 3MS test than did those in the lowest quartile of RFS ($P < 0.001$). This effect was strengthened over 11 y of follow-up. Those with the highest RFS declined by 3.41 points over 11 y compared with the 5.2-point decline experienced by those with the lowest RFS ($P = 0.0013$). The non-RFS was not associated with cognitive scores. Consuming a diverse diet that includes a variety of recommended foods may help to attenuate age-related cognitive decline among the elderly.   J. Nutr. 139: 1944–1949, 2009.

Introduction

Cognitive decline is a risk factor for dementia and may be considered a marker of preclinical disease (1–3). Alzheimer's disease (AD),[5] the most common form of dementia, has emerged as the third most costly medical condition in the US, a burden expected to rise in coming years concurrent with the aging of the population. By one estimate, delaying the onset of AD by 5 y would reduce the number of cases by 50% (4). Effective strategies for early prevention or delayed onset of AD and other dementias are urgently needed.

Pathological hallmarks of AD include the aggregation and deposition of extracellular amyloid-β proteins and intracellular τ proteins that contribute to oxidative stress and inflammation and lead to neurodegeneration (5). Dietary factors that mediate these events likely affect risk for neurodegeneration. Evidence from observational studies, although not entirely consistent, support associations between higher intakes of several nutrients,

including antioxidants, B vitamins, and (n-3) fatty acids and reduced risk for AD or cognitive decline among aging populations (6–8). However, clinical supplementation trials have provided little evidence of cognitive benefits from supplements of vitamin E (9,10), a potent antioxidant and antiinflammatory agent, or B vitamins (11,12). The traditional reductionist approach of examining single nutrients or foods ignores the complexity of nutrients provided by foods in the context of diet and may miss important effects of diet when considered as a whole.

A few recent studies (13–15) have examined associations between indices of total diet and cognitive endpoints among the elderly. The recommended food score (RFS), developed by Kant et al. (16), is a simple measure of diet quality that takes into consideration the variety of foods consumed. Variety is an important component of diet quality and is mentioned in the current Dietary Guidelines for Americans (17). Michels and Wolk (18) later extended the method to include a non-RFS. The RFS has previously been associated with decreased risk of all-cause and cardiovascular disease mortality in large cohorts of both American and Swedish women (16,18) and Swedish men (19). Kaluza et al. (19) found higher non-RFS were associated with higher risk of all-cause and cardiovascular disease mortality.

No study to date has examined associations between a RFS/non-RFS and cognitive endpoints among elderly men and

women. Our objective in this study was to examine associations between a RFS and non-RFS, indices of overall diet quality and variety, and cognitive function and decline among elderly men and women of the Cache County Study on Memory and Aging (CCMS) in Utah.

Materials and Methods

The CCMS is a large population-based prospective study of the prevalence and incidence of dementia among elderly residents of Cache County, Utah. In 1995 all elderly residents of Cache County who were ≥65 y of age were invited to participate and 5092 (90%) completed the baseline interview (1995–1996). Reassessments of the cohort were completed in 1997–1998, 2002–2003, and 2006–2007. The average length of follow-up for those completing all 4 assessments was ~11 y. The study was approved by the institutional review boards of Utah State University, Johns Hopkins School of Public Health, and Duke University. All participants or their relatives in the case of impaired persons gave written, informed consent to participate.

The baseline survey included information on demographic characteristics; health history; family history of dementia; use of medications, alcohol, and tobacco; usual intake of dietary supplements, and other lifestyle factors. Participants also provided a cheek-swab DNA sample that was used for *APOE* genotyping. The 100-point Modified Mini-mental State Examination (3MS) was used to assess cognitive function and to screen for dementia at the baseline and subsequent assessments. The 3MS has been found to provide a useful estimate of global cognitive function and decline among noninstitutionalized elderly men and women (20). Participants who were diagnosed with dementia using a multi-stage clinical assessment protocol, described in detail elsewhere (21), did not complete a 3MS at subsequent assessments.

Usual dietary intake was assessed using a 142-item modified version of the FFQ used in the Nurses' Health Study. The Nurses' Health Study FFQ has been extensively validated among populations of varied ages (22) and demographic characteristics, including a population of elderly women (23). Participants were given instructions on how to complete and return the FFQ near the conclusion of their baseline survey. Using standard FFQ methodology, participants were asked to report their frequency of consumption of the listed food items or groups. Nutrient composition of food items was obtained using a time-specific version of the Food Processor Program (ESHA Research, Portland, Oregon), a nutrient composition database with information from both the USDA Nutrient Composition Table and manufacturer information. Daily intakes of nutrients were computed by multiplying the nutrient content of the food item by the reported frequency of intake and summing over all food items. Nutrients were adjusted for total energy intake using the regression-residual method described by Willett (22).

A RFS was computed following the methods of Kant et al. (16) and modified by Kaluza et al. (19) by summing the number of foods recommended by current dietary guidelines. Current Dietary Guidelines for Americans emphasize consumption of fruits, vegetables, lean meats, fish, low-fat dairy products, and whole grains (17). The following 57 food items consumed were included in the RFS: low-fat milk and low-fat dairy products ($n = 2$); fruit and fruit juice ($n = 15$); vegetables and vegetable juice, not including potatoes ($n = 29$ vegetables); whole grains ($n = 7$); nonfried fatty fish ($n = 2$); and nuts ($n = 2$). Consumption of any of the recommended foods in a frequency of at least 1–3 times/mo was assigned 1 point, and if consumed less often, 0 points. The RFS was calculated as the sum of points. The frequency of 1–3 times/mo is consistent with the frequency used by Kaluza et al. (19), who created a RFS from a FFQ that included 97 food items. In addition, following the methods of Kaluza et al. (19), a nonrecommended food score (non-RFS) was computed by summing the number of nonrecommended highly processed, energy-dense foods consumed at a frequency of at least 3 times/wk. The following foods were included in the non-RFS: processed meats ($n = 2$), refined bread and grains ($n = 6$), French fries and chips ($n = 2$), and sweets ($n = 13$). The other 62 FFQ items did not meet the criteria for inclusion in the RFS or non-RFS.

Of the 5092 participants who completed a 3MS at the baseline interview, 355 were considered cognitively impaired (scores ≤ 87 points on the 3MS at the baseline interview, a cut-off previously determined) (24) and did not receive a FFQ. Of the 4737 who were asked to complete the FFQ, 3829 (81%) completed and returned the questionnaire. An additional 197 participants were later excluded because of implausible energy intake (≤2100 or ≥21,000 kJ/d). Thus, 3634 participants who were cognitively healthy and provided plausible and complete dietary data at the baseline interview were included in the analyses presented here. Participants who did not provide dietary data at the baseline interview were older and had higher prevalence of dementia and other comorbidities compared with participants who were cognitively healthy and provided dietary data.

Statistical methods. The distributions of the diet diversity scores were used to categorize individuals into quartiles of RFS/non-RFS. Each quartile was weighted with the value for the median score within that quartile. Associations between quartile of RFS/non-RFS and continuous variables were tested using ANOVA. Associations between quartile of RFS/non-RFS and categorical variables were analyzed using unadjusted cross-tabulation with chi-square tests.

Mixed effect linear regression models using the SAS statistical software package (SAS Institute) were used to examine associations across increasing quartiles of the RFS/non-RFS and average 3MS score at up to 4 periods of assessment spanning 11 y (1995–2006). This technique, using the repeated statement in the proc mixed command, takes into consideration the correlation between repeated 3MS scores on the same individual at different time periods while including information provided by participants at all available assessments. All participants were assessed over the same time intervals. Both linear and quadratic terms for time were included in the mixed models to account for the nonlinear trajectories of 3MS performance over time. The significance of the quadratic term for time was formally tested by comparing the difference in the likelihood ratio statistics between a model with and without the quadratic term for time ($P = <0.001$). Because this term was significant, indicating that it improved the fit of the model to the data, it was included in all subsequent models. Interactions between the RFS/non-RFS and time were tested by comparing the likelihood ratio test statistics between models with and without the interaction terms. Variables associated with both 3MS scores and RFS/non-RFS, as well as other potential confounders as identified in the literature, were included in multi-variable models (7,25,26). Covariates included in the multi-variable model included education (less than or at least a high school education), age at baseline (y), gender, *APOE* genotype (0 or at least 1 copy of the e4 allele), physical activity (frequency of moderate physical activity per week), use of multivitamin/mineral supplements (yes or no regular use), total energy intake, activity of daily living (score indicating the degree of help needed for activities of daily living; higher scores indicate less functional ability), BMI (weight in kg/height in m^2), history of usual alcohol intake (ever or never), smoking (ever or never), and history of diabetes, stroke, and heart attack at the baseline interview. The quintile scores of the RFS/non-RFS were added into the model as a single continuous variable to test for the linear trend (P-trend) across increasing quintiles.

Because of evidence from previous observational studies that *APOE* genotype may modify associations between diet and cognitive outcomes (13,27–29), we examined the effect modification by the presence of the e4 allele of the *APOE* gene by comparing the likelihood ratio statistics between models that included and did not include the interaction between RFS and *APOE* e4 status and RFS and non-RFS. Reported P-values are 2-sided and type I error rate for significance was 0.05.

Results

Several characteristics of the population differed across increasing quartile of RFS (**Table 1**). Participants with a diet that provided a greater variety of recommended foods (higher RFS scores) were younger, had lower BMI, were more educated, and more likely to have at least 1 copy of the *APOE* e4 allele than were those with less varied diets. In addition, those with more varied diets were more likely to exercise and take a multivitamin

TABLE 1 Characteristics of participants by quartile of RFS[1,2]

	Q1	Q2	Q3	Q4	P-value[3]
n	910	941	901	882	
RFS[1]	7.7 ± 2.7	14.1 ± 1.4	19.3 ± 1.7	27.7 ± 4.3	
Demographics					
Female, %	57	59	58	55	0.284
Age, y	75.6 ± 7.1	74.7 ± 6.8	74.6 ± 6.7	73.8 ± 5.9	<0.001
BMI, kg/m^{2}	25.9 ± 4.5	26.5 ± 4.5	26.1 ± 4.3	26.2 ± 4.3	0.025
Education (≥high school), %	77	84	87	90	<0.001
Smoke (ever), %	23.4	19.8	16.6	15.7	<0.001
Drink alcohol (ever), %	18.6	16.6	14.4	14.2	0.066
History of heart attack, %	13.5	13.8	10.5	12.7	0.122
History of stroke, %	3.6	3.3	2.8	3.5	0.744
History of diabetes, %	12.5	12.9	11.4	14.8	0.210
Presence of *APOE* e4 allele,[4] %	30.2	29.9	29.4	36.4	0.004
Multivitamin use, %	39.9	41.8	41.9	47.4	0.011
Daily moderate activity, %	33	37.8	40.4	45.5	<0.001
Baseline 3MS score	90.4 ± 7.1	91.1 ± 6.4	91.7 ± 6.2	91.6 ± 6.1	<0.001
Diet characteristics					
Total energy, kJ/d	6858 ± 3224	7666 ± 2809	8503 ± 2985	9755 ± 3278	<0.001
Protein, % energy	17.0 ± 4.1	17.6 ± 3.6	17.7 ± 3.2	18.0 ± 3.1	<0.001
Carbohydrate, % energy	52.9 ± 8.6	53.8 ± 7.6	54.2 ± 7.3	54.2 ± 7.1	<0.001
Fat, % energy	32.2 ± 7.1	30.9 ± 6.1	30.5 ± 5.9	30.3 ± 5.7	<0.001
Cholesterol,[5] mg/d	315 ± 172	291 ± 144	288 ± 135	284 ± 167	<0.001
Fiber,[5] g/d	16.7 ± 5.6	18.9 ± 6.4	20.4 ± 6.4	23.0 ± 8.2	<0.001
Vitamin C,[5] mg/d	110 ± 59	130.8 ± 67	152.1 ± 68	175.6 ± 82	<0.001
Vitamin E,[5] mg/d	7.8 ± 3.9	8.1 ± 4.5	8.7 ± 7.5	8.9 ± 6.2	<0.001
Folate,[5] μg/d	275 ± 93	305 ± 146	331 ± 116	372 ± 130	<0.001
Vitamin B-12,[5] μg/d	6.11 ± 4.9	5.99 ± 3.6	6.11 ± 3.8	6.39 ± 5.2	0.266
Calcium,[5] mg/d	938 ± 412	956 ± 384	978 ± 353	1000 ± 367	0.004
Zinc,[5] mg/d	11.3 ± 3.3	11.6 ± 3.5	11.7 ± 4.3	11.7 ± 3.9	0.044
Non-RFS[6]	4.0 ± 2.8	4.4 ± 3.0	4.9 ± 3.0	5.6 ± 3.5	<0.001

[1] Data are presented as means ± SD or percent, n = 3634.
[2] Foods included in the RFS included the following 57 food items consumed at a frequency of at least 1–3 times/mo: low-fat milk and low-fat dairy products (n = 2); fruit and fruit juice (n = 15); vegetables and vegetable juice, not including potatoes (n = 29 vegetables); whole grains (n = 7); nonfried fatty fish (n = 2); and nuts (n = 2).
[3] P-values are from ANOVA for continuous variables and chi-squared distribution for categorical variables.
[4] One or 2 copies of the *APOE* e4 allele.
[5] Energy-adjusted amount provided by food.
[6] Non-RFS was computed by summing the number of nonrecommended foods [processed meats (n = 2), refined bread and grains (n = 6), French fries and chips (n = 2), sweets (n = 13)] consumed at a frequency of at least 3 times/wk.

mineral supplement and less likely to have ever regularly smoked.

Although those with the highest RFS consumed more total energy than did those with lower RFS, they also had healthier diet profiles that included a lower percent of total energy from fat, lower cholesterol, higher fiber, and higher amounts of most vitamins and minerals (Table 1). Interestingly, those with higher RFS also had higher non-RFS (r = 0.213; P = <0.001).

Using mixed effects linear regression models that controlled for the effects of age, gender, and education, increasing quartile of the RFS was associated with higher mean 3MS scores at the baseline interview (Q1, reference; Q2, 1.11; Q3, 1.78; Q4, 2.19; P-trend = <0.001). The magnitude of the differences in mean 3MS score was greater than the effect observed for *APOE* e4 allele status, a known genetic risk factor for cognitive decline among the aged. In the multivariable model that included age, gender, and education, and RFS, those without an e4 allele scored 0.75 points higher on the 3MS than did those with 1 copy of the e4 allele and 1.51 points higher on the 3MS than did those with 2 copies of the e4 allele. This information is provided as a reference for the magnitude of difference associated with increasing RFS.

The association between diet variety and 3MS score remained significant in models that included the effects of age, gender, education level, *APOE* genotype, BMI, activity of daily living, level of physical activity, smoking and drinking status, multivitamin mineral supplement use, history of heart attack, stroke, and diabetes, and total energy intake (Table 2). In the multivariable model, mean baseline 3MS scores increased across increasing quartiles of RFS (Q1, reference; Q2, 0.94; Q3, 1.48; Q4, 1.8; P-trend < 0.001). These differences were strengthened over time such that by y 11 of follow-up, those with the most varied healthy diets (Q4 RFS) declined by an average of 3.41 points compared with the 5.15-point decline for those with the least varied diets (Q1) (Table 2; **Fig. 1**).

In similar multivariable models, there was no association between increasing quintile of the non-RFS and 3MS scores at baseline (Q1, reference; Q2, 0.37; Q3, 0.31; Q4, 0.52; P = 0.51) or over time (P for the interaction of time and non-RFS = 0.3452). In addition, there were no significant interactions between RFS and non-RFS or RFS and *APOE* e4 allele status and baseline 3MS or change in 3MS over time (P for the interaction of RFS and non-RFS = 0.34, P for the interaction of RFS and *APOE* e4 status = 0.21).

TABLE 2 Mean difference in 3MS scores at the baseline interview and mean cumulative decline (95% CI) in 3MS scores across 11 y of follow-up across quartiles of a RFS[1,2]

	Time since baseline interview (1995–1997), y (n)			
RFS	0 (3634)	3 (2743)	7 (1907)	11 (1256)
Q1	0 (reference)	−1.14 ± 0.39	−2.96 ± 0.64	−5.15 ± 0.69
Q2	0.94 ± 0.26	−0.64 ± 0.60	−2.02 ± 0.66	−3.98 ± 1.08
Q3	1.48 ± 0.28	−0.81 ± 0.38	−2.51 ± 0.66	−4.91 ± 1.08
Q4	1.80 ± 0.28	−0.41 ± 0.36	−1.56 ± 0.65	−3.41 ± 0.79

[1] Values are coefficient ± SE, n = 3634.

[2] Multivariable model included age, gender, education level, BMI, APOE e4 status, ever smoker, ever drinker, frequency of moderate physical activity per week, history of myocardial infarct, stroke, and diabetes, index of help needed with daily activities, multivitamin/mineral use, total energy intake, time, time × time, and interactions between time and increasing quintile of RFS.

Discussion

In this large prospective study of elderly men and women in Cache County, Utah, a dietary pattern that provided a variety of foods recommended in the current Dietary Guidelines for Americans, including fruits, vegetables, whole grains, nuts, fatty fish, and low-fat milk and low-fat dairy products, was associated with better cognitive test scores than were diets that contained few of these foods. The difference between these groups widened over 11 y of follow-up. This effect is more than double the effect for those with at least 1 copy of the *APOE* e-4 allele, a genetic risk factor for AD and cognitive decline (24,30). Our results provide evidence that diet variety is an important aspect of diet quality among aging adults and that a varied diet of recommended foods may provide benefits to cognitive function in late life.

Few studies have examined associations between global measures of diet quality and cognitive function and risk for

FIGURE 1 Mean change in 3MS scores by increasing quartile of RFS across 11 y of follow-up [reference (0) = quartile 1, time 0] using multivariable mixed effects linear regression; *P*-value for the significance of the difference in trajectories across increasing quintile of the RFS = 0.0013.

dementia among the elderly. In the Three-Cities cohort in France, participants consuming diets high in fruits, vegetables, fish, and (n-3) fatty acids had decreased incidence of all-cause dementia and AD compared with those with diets low in these foods and nutrients (13). This association was strongest among those without an *APOE* e-4 allele. In a smaller U.S. cohort (*n* = 2258 New Yorkers), Scarmeas (14,15) reported that those adhering to a Mediterranean dietary pattern (a diet high in fruits, vegetables, legumes, whole grains, fish, and healthy fats) had a decreased incidence of and mortality from AD.

A key component of dietary quality is nutrient adequacy, an issue of particular importance among the elderly who are more vulnerable to inadequate nutrition compared with younger adults (31,32). Simple measures of diet variety predicted the mean probability of nutrient adequacy among participants of the CSFII study (33). Others have observed positive associations between greater diet diversity and adequate nutrient intakes among the elderly specifically (34–36).

The RFS accounts for diet variety and was patterned after the methods developed by Kant et al. (16) and used by others (18,19,37,38). The RFS is a simple way to define dietary patterns based on the count of the number of foods consumed over a defined period of time identified as being recommended by current dietary guidelines. A RFS was inversely associated with all-cause mortality in large cohorts of adult women (16,18) and men (37), including a nationally representative U.S. cohort (39). The RFS has been compared with dietary patterns derived from alternative data-driven approaches, including cluster and factor analyses, as well as to the Healthy Eating Index, an index of diet quality developed by the USDA to monitor the diet of the U.S. population (39,40). Results from analyses examining associations between quartiles of the RFS and mortality for men and women in a nationally representative U.S. cohort (National Health Interview Surveys; 1987, 1992) were similar to associations observed using dietary patterns derived by factor and cluster analyses (40). The RFS performed as well or better than the Healthy Eating Index for predicting serum concentrations of nutrients and biomarkers of disease risk, including serum concentrations of vitamin C and E, folate, C-reactive protein, plasma glucose, hemoglobin A1c, blood pressure, and serum cholesterol (39).

The CCMS, a large prospective study of elderly men and women from a geographically defined area where the median life expectancy exceeds that of the U.S. population by 10–12 y (41), has high rates of participation, factors known to reduce bias in observational studies of the aged. An additional unique feature of the Cache cohort is that 90% of the participants are members of the Church of Jesus Christ of Latter-Day Saints (or Mormon) religion. This religion discourages its members from drinking alcohol or smoking and low smoking and drinking rates are observed among Cache Study participants. This lifestyle likely contributes to the increased longevity and low burden of chronic disease (42,43), especially among the oldest-old, an advantage for studying conditions or diseases of the aged.

Cognitive function was assessed over 11 y of follow-up using the 3MS, a widely used screening tool for dementia that provides a global measure of cognitive function (20). Andrew and Rockwood (44) reported from the Canadian Study of Health and Aging that a ≥1-point change in 3MS scores was clinically detectable for individuals and a change of ≥5 points likely represents a clinical meaningful difference for groups. In these analyses, the magnitude of the change in 3MS scores across the 11 y of follow-up is on the order of a 5-point change; those consuming the least diverse diets declined by 5.13 points.
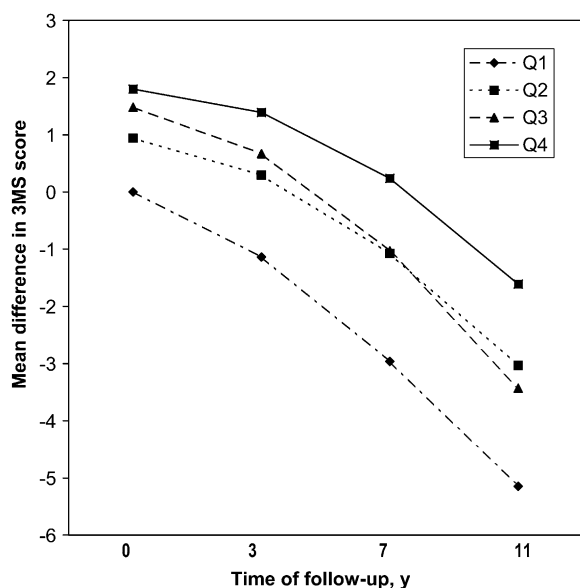
Usually dietary intake was estimated using a 142-item FFQ and like all dietary assessment methods is subject to measurement error. However, in the present study, an index of diet diversity was determined by counting the number of foods reported in a frequency of at least once per month over the past year, independent of the amount consumed or absolute nutrient composition of the diet, 2 often-cited limitations of using FFQ (45–47). Although it is difficult to recount the exact foods consumed at any 1 occasion, it is likely easier to report a typical dietary pattern that usually includes or excludes certain foods (48). In addition, despite our attempt to control for many potential confounders in statistical models, the observed protective effect of the RFS may be due to uncontrolled confounding. The RFS was associated with many diet and lifestyle factors and thus it is not possible to determine whether the observed effect is from the nutrients provided by diet or from other behaviors that may be associated with diet quality and variety among the elderly.

A RFS that takes into consideration diet variety is associated with favorable nutrient intakes and other lifestyle factors, including physical activity, supplement use, and level of independence, among the elderly men and women of the CCMS. A decline in the variety of food choices and consumption of a nutritionally inadequate diet is likely to be the result of a combination of medical, social, physical, environmental, and economic factors that affect eating habits and nutrition status among elderly persons (49). In this large prospective study of elderly men and women, those with the most varied diets of foods recommended by the current Dietary Guidelines for Americans had higher 3MS scores, an indicator of cognitive function, across 11 y of follow-up than did those with the least varied diets. A RFS appears to be a simple indicator of overall diet quality among the elderly and its association with cognitive outcomes in late life deserves further study.

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