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PROSPECTIVE STUDY OF READY-TO-EAT BREAKFAST CEREAL CONSUMPTION AND COGNITIVE DECLINE AMONG ELDERLY MEN AND WOMEN IN CACHE COUNTY, UTAH, STUDY ON MEMORY, HEALTH, AND AGING

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Abstract

Objective—To examine associations between frequency of ready-to-eat-cereal (RTEC) consumption and cognitive function among elderly men and women of the Cache County Study on Memory and Aging in Utah.

Design—A population-based prospective cohort study established in Cache County, Utah in 1995.

Setting and Participants—3831 men and women > 65 years of age who were living in Cache County, Utah in 1995.

Measurement—Diet was assessed using a 142-item food frequency questionnaire at baseline. Cognitive function was assessed using an adapted version of the Modified Mini-Mental State examination (3MS) at baseline and three subsequent interviews over 11 years. RTEC consumption was defined as daily, weekly, or infrequent use.

Results—In multivariable models, more frequent RTEC consumption was not associated with a cognitive benefit. Those consuming RTEC weekly but less than daily scored higher on their baseline 3MS than did those consuming RTEC more or less frequently (91.7, 90.6, 90.6, respectively; p-value <0.001). This association was maintained across 11 years of observation such that those consuming RTEC weekly but less than daily declined on average 3.96 points compared to an average 5.13 and 4.57 point decline for those consuming cereal more or less frequently (p-value = 0.0009).

Conclusion—Those consuming RTEC at least daily had poorer cognitive performance at baseline and over 11 years of follow-up compared to those who consumed cereal more or less frequently. RTEC is a nutrient dense food, but should not replace the consumption of other healthy foods in the diets' of elderly people. Associations between RTEC consumption, dietary patterns, and cognitive function deserve further study.

Introduction

Alzheimer's disease (AD), the most common form of dementia among the elderly, has emerged as a major public health threat and is now the third most costly medical condition in the U.S (1). Diagnosis of AD and other dementias are preceded by a progressive decline in cognitive function (2). Strategies aimed at preventing or slowing age-related decline in

cognitive function may have substantial importance for preventing or delaying the onset of dementia and thus curbing the enormous public health burden associated with this disease (3).

A growing body of evidence supports associations between dietary factors at the level of nutrients, foods, and dietary patterns and cognitive functioning among the elderly (4). Ready-to-eat cereal (RTEC) is an interesting target food to examine in association with cognitive outcomes because it is commonly eaten and is a dense source of several nutrients with proposed cognitive benefits including folate, other b-vitamins and vitamin E (4). RTEC is a common breakfast food in the U.S.; 21.7% of adult participants of The National Health and Nutrition Examination Survey (1999-2000) consumed RTEC on the day assessed (5). Regular consumption of RTEC has been associated with daily dietary intakes that are lower in fat and cholesterol and higher in fiber, B-vitamins including folate, vitamin E, iron, calcium, and magnesium (6-9).

RTEC consumption patterns among adults have been examined in regards to body mass index (BMI) (5), incident diabetes (10), weight loss (11), cardiovascular disease-specific mortality (12), and serum homocysteine concentration (13, 14), but there are no reports examining associations between RTEC consumption and cognitive outcomes among the elderly. The objective of this study was to examine prospective associations between patterns of RTEC consumption and cognitive decline over an 11-year period among a cohort of elderly men and women who are participants of the Cache County Study on Memory, Health and Aging (CCMS).

Methods

Participants and study design

The CCMS is a large population-based prospective study of the prevalence and incidence of dementia among elderly residence of Cache County Utah (15). In 1995 all residents of Cache County Utah who were 65-years of age or older were invited to participate and 5,092 (90%) completed the baseline interview (1995-1996) that included a cognitive assessment and detailed history of lifestyle factors and family history of disease. Three subsequent re-assessments of the cohort were completed in 1997-1998, 2002-2003, and 2006-2007. The average length of follow-up for those completing all four assessments was approximately 11 years. The study was approved by the Institutional Review Boards of participating institutions. All participants or their relatives (in cases of impaired persons) gave written, informed consent to participate.

Of the 5092 participants who completed a 3MS at the baseline interview, 355 were considered cognitively impaired according to the cognitive assessment (3MS score < 87) and were not asked to complete a dietary assessment. Of the 4737 who were asked to complete the dietary assessment, 3831 (81%) completed and returned the questionnaire. An additional 197 participants were later excluded because of implausible caloric intake (<= 500 or >= 5,000 kcals per day). Thus, 3634 participants who were not demented and provided plausible and complete dietary data at the baseline interview are included in the analyses presented here.

Dietary Data

Usual dietary intake was assessed at the baseline interview using a 142-item food semi-quantitative frequency questionnaire patterned after the methods developed for use in the Nurses' Health Study (16). Similar semi-quantitative food frequency questionnaires have been shown to provide reasonable estimates of usual dietary intake of micronutrients and foods among populations of varied ages and demographic characteristics including the elderly (17-20). In validation studies comparing FFQs with dietary records, RTEC was among the foods with the highest correlation between methods (r = 0.79)(21), an indication that participants can accurately report the consumption of frequently eaten foods, especially those with little seasonal variability, such as RTEC (21, 22).

Participants were asked to report their frequency of consumption of a standard serving size of each food item from a list of nine frequency categories. In addition, participants provided information on the brand and type of RTEC consumed, and could report up to two choices. Time-specific (1995-1996) information on the nutrient composition of each brand and type of RTEC (n=62), in addition to other food items was obtained using a time-stamped 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 each 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 (17).

Information on the whole-grain and total grain content of the RTEC was obtained from a database created by Newby et al.(23) using information from the Pyramid Servings Database (2001-2002). Following the methods presented by Liu et al. (12), a RTEC was categorized as being a whole-grain containing RTEC if > 25 percent of the total grains were whole grains. Following the methods of Kant et al.(24) a recommended food score (RFS; range: 2-56), a measure of diet quality and variety, was previously calculated among participants of the Cache cohort (25).

Cognitive assessment

The Modified Mini-mental State Examination (3MS) for epidemiological studies (26) was used to assess cognitive function at the baseline and subsequent assessments. The 3MS is a 100-point, expanded version of the Mini-Mental State Examination (27) that has been used in many epidemiological studies and found useful as a global measure of cognitive function and decline among non-institutionalized elderly men and women (28). Participants who were diagnosed with dementia using a multi-stage clinical assessment protocol, described in detail elsewhere (29), did not complete a 3MS at subsequent assessments.

Other variables

Sociodemographic information collected from participants at the baseline interview included age, gender, marital status, and education level. Body mass index was computed from self-reported height and weight. Medical and health history was recorded, including past myocardial infarct, stroke, or diabetes. Current and past histories smoking, physical activity,

and multivitamin supplement use were also recorded. Information on the degree of help needed for intermediate activities of daily living (IADL) that included shopping and preparing meals was collected and used to create a IADL score (range: 0-9) (30). Higher IADL scores indicate less functional ability. In addition, participants provided a cheek swab DNA sample that was used to genotype the APOE gene for the presence or absence of an e-4 allele (0, 1 or 2 copies).

Statistical Methods

The cohort specific distribution of the frequency of RTEC consumption was examined and participants were categorized into groups that represented those who consumed cereal daily (28%; at least 1 serving per day), weekly (53%; 1-6 times per week), and infrequently (19%; less than 1 serving per week).

Mixed effects linear regression models were used to examine associations between frequency of RTEC consumption and average 3MS score over time. Because the analysis revealed significant non-linear effects of change in 3MS scores over time, both linear and quadratic terms for time (time, time2) were included in the models. Thus, the association between frequency of RTEC consumption and 3MS scores over time was examined by including the three level variable indicating frequency of RTEC (daily, weekly, infrequently) and its interaction with time and time2. The average change in 3MS score was summarized by providing means and standard errors of the cumulative estimated change across each RTEC category for each time point (3, 7, and 11 years of follow-up).

The association between RTEC category and change in cognitive function over 11 years was examined in models that adjusted for age and gender, and then in more complex models that controlled for the effects of other factors associated with both 3MS scores and frequency of RTEC consumption. Covariates were added one at a time and were retained in the model if the individual term was significant (Wald statistic $p < 0.05$) or if the fit of the model was improved by including the covariate. The difference in the fit of a model was determined by the chi square distribution of the likelihood ratio test statistics between models with and without the new covariate. Reported p-values are two-sided, and type I error rate for statistical significance was 0.05. Analyses were performed using SAS software (9.1 release, 2002-2003; SAS Institute, Cary NC).

Results

Characteristics of the participants by gender are provided in Table 1. Women were slightly older and a larger percentage of them had a high school or greater education compared to men. In addition, fewer women than men ever regularly drank or smoked during their lifetime. Women also scored higher on the 3MS scores at all periods of assessment. The frequency of RTEC consumption (servings/day) was not different for men and women although women were more likely to consume whole grain RTECs than were men (65.9 vs, 59.9 percent). Sixty-two different brands and types of RTECs were reported, 55 percent of which were classified as containing at least 25 percent whole-grain. The most frequently consumed types of RTECs included corn flakes (14%), shredded wheat (11%), and raisin bran (6%).

Characteristics of the participants by frequency of RTEC consumption categories are provided in Table 2. Daily RTEC consumers were older, had lower BMIs and higher IADL scores (indicating a lower degree of self-reliance in activities of daily living) than those consuming RTEC infrequently or weekly. Daily consumers of RTEC, compared to infrequent and weekly consumers, had greater intakes of total kilocalories, yet lower intakes of protein and fat and higher intakes of carbohydrate, fiber and most vitamins and minerals. Daily consumers of RTEC consumed more low-fat dairy products and whole grains and less meat and vegetables than infrequent and weekly RTEC consumers. The mean RFS, indicating the intake of the number of recommended healthy foods, was greatest in the weekly RTEC group (30.4) and lower in the daily (28.0) and infrequent (28.0) RTEC groups ($p < 0.001$).

The associations between frequency of RTEC consumption and 3MS scores across 11 years of follow-up were assessed in mixed linear effect regression models. The reference group was those who consumed RTEC infrequently. In a model that controlled for the effects of age and gender, the mean baseline 3MS score was 0.73 points greater (95 percent confidence interval (CI), 0.51-0.95) among those in the weekly RTEC group compared to those in the infrequent RTEC group; there was no significant difference between 3MS scores among those in the daily and infrequent RTEC groups. In the multivariable model that controlled for lifestyle and health factors including education level, BMI, IADL, level of physical activity, smoking and drinking status, history of heart attack, stroke, and diabetes, total calorie intake, and marital status the mean baseline 3MS score was 0.66 points greater (95 percent CI 0.45-0.87) among those in the weekly RTEC group compared to those in the infrequent RTEC group and 0.35 point greater (95 percent CI = 0.08-0.62) among those in the daily RTEC group compared to those in the infrequent RTEC group (figure 1).

The rate of decline in cognitive function across 11 years of follow-up differed by frequency of RTEC use (multivariate adjusted p-value for time2 by RTEC intake interaction = 0.0009, Table 3 and Figure 1) and this association was non-linear. By the 11th year of follow-up weekly consumers of RTEC declined by an average 3.96 points compared to the average 5.13 point decline observed among daily RTEC consumers and 4.57 point decline observed among infrequent RTEC consumers. The magnitude of the difference observed for the baseline difference in cognitive function and the rate of decline in cognitive function across 11 years of follow-up was similar to that observed for those having one copy of the e-4 allele of the APOE genotype when a variable indicating the number of e-4 alleles was included in the multivariable model described above. The e-4 variant of the APOE genotype is a genetic risk marker for Alzheimer's Disease (15). Participants with one copy of the e-4 allele scored 0.68 points higher on the baseline 3MS compared to those with no copies of the e-4 allele (p-value <0.001) and declined by an average of 5.09 points over 11 years compared to the 3.77 point decline observed for those with no copies of the e-4 allele.

Discussion

In a large prospective study of community-dwelling elders in the Cache County, Utah, Study on Memory, Health, and Aging, the association between frequency of RTEC consumption

and cognitive function was non-linear. Moderate (weekly) consumers of RTEC ate a greater diversity of recommended foods and performed better on a global test of cognitive function at each of four assessments spanning 11 years than did either daily or infrequent consumers of RTEC. The magnitude of this effect was similar to that observed for those with one copy of the APOE e-4 allele, a genetic risk factor for AD and cognitive decline (15, 31). The combination of moderate RTEC use, defined as consuming 1-6 servings of RTEC per week, and greater dietary diversity of recommended foods may provide greater cognitive benefits among the elderly than either daily or infrequent RTEC use with less dietary diversity.

Cognitive decline is a risk factor for dementia, may be considered a marker of neurodegenerative disease (32, 33), and is a statistically powerful study outcome in cohort studies with repeated measures. A growing body of biologically plausible evidence from animal and human studies supports the role of several micronutrients in the pathogenesis of neurodegeneration (4). For example, reactive oxygen species cause oxidative stress and are associated with neuronal damage in AD (34); antioxidants found in foods such as vitamin C, vitamin E, and carotene may offer neuroprotection. Deficiencies of folate, vitamin B12, and vitamin B6 result in high concentrations of homocysteine through defects in 1-carbon metabolism (35). Homocysteine may contribute to neurodegeneration through vascular mechanisms that include inflammation and oxidation, or as a direct or indirect neurotoxin (36) (37).

Daily consumers of RTEC had higher estimated intakes of most micronutrients than did those consuming RTEC less frequently. This finding is not surprising and is consistent with previous reports of nutrient contributions by RTEC. Due largely to current trends of high levels of RTEC fortification, RTEC was among the top ten single food contributors to the dietary intakes of over 15 nutrients (including folate, vitamin B-6, vitamin E, and iron) among adults 19 years or older in the 1994-1996 Continuing Survey of Food Intakes by Individuals (38). This is consistent with other reports that elderly individuals who ate RTEC at breakfast 4-7 times per week consumed more vitamins, minerals, fiber, carbohydrate, and total sugar than did those who did not eat RTEC at breakfast (6).

The observed non-linear association between frequency of RTEC consumption and cognitive function is biologically plausible. Many RTEC are now fortified with high levels of nutrients such that a single serving provides 100% or greater of the Dietary Reference Intakes, making a single serving of some RTECs similar to a multivitamin tablet. A number of studies have shown that dietary supplements even at modest doses have adverse health consequences in some situations (39-41). Studies demonstrating harmful effects from supplementing with large-doses of beneficial nutrients provide evidence that more is not necessarily better, even when some amount offers clear benefit (41). For example, in the nationally representative U.S. NHANES survey, elderly persons with low vitamin B-12 status and high serum folate levels had an elevated risk of cognitive impairment (42), suggesting that high levels of folate provided by supplementation and fortification may in fact be harmful in the elderly who often have difficulty consuming and absorbing adequate amounts of vitamin B12. Thus it seems plausible that while RTECs provide a good source of many nutrients that offer cognitive benefits, a more modest consumption of RTEC at a

frequency of less than one time per day may provide quantities of nutrients more optimal for health than that provided by more frequent consumption.

Second, weekly consumption of RTEC was associated with a greater degree of diet diversity as measured by the recommended food score (RFS) than was either daily or rare consumption of RTEC. Although use of highly fortified RTECs offers a simple means of consuming many micronutrients, too frequent use may displace the regular consumption of other important foods and nutrients. In the present analysis, participants who consumed RTEC daily ate fewer servings of eggs, cheese, added fat (butter, margarine, cream), meat, vegetables, and other grains than those who consumed RTECs less frequently (table 2, though some data not shown). The RFS is an index of diet diversity and quality and was previously found to be associated with cognitive benefits among elderly participants of the Cache County Study (25). The total intake of most nutrients differed by frequency of RTEC use (see Table 2). Daily RTEC consumers had higher intakes of all micronutrients but lower intakes of protein and fat and lower diet quality as indicated by mean RFS compared to those eating RTEC weekly. RFS was associated with both frequency of RTEC consumption and cognitive function, yet including RFS in the multivariable model did not change the observed associations.

Third, though our analysis controls for several factors associated with both frequency of RTEC consumption and cognitive decline, the observed association may be due in part to residual confounding. Frequency of consumption of RTEC is associated with many diet and lifestyle factors. It is not possible to determine if the observed associations are causal or due to other factors that co-occur with the pattern of RTEC consumption. For example, differences in physical activity level may explain why RTEC consumers report higher total energy intake yet have lower BMIs than do those with less frequent RTEC consumption. It is also possible that cognitive decline results in more frequent consumption of RTEC although the classification of RTEC consumption at the baseline interview is restricted to non-demented participants who were able to complete the FFQ, a non-trivial cognitive task.

Few prospective studies have examined associations between RTEC consumption and chronic disease risk. Among male participants of the Physicians Health Studies (PHS) (12), (10),(43) a beneficial effect of daily consumption of RTEC on mortality and lower risk of type 2 diabetes, and heart failure was limited to whole grain RTEC. Further, the PHS analyses did not examine associations between frequency of RTEC consumption and indicators of diet variety or micronutrient intakes. There are no prior reports of associations between RTEC consumption and cognitive outcomes among elderly individuals.

Several strengths and limitations of the present study are important. Cache County is a long-lived population and the Cache County Study has high rates of participation and follow-up, factors known to reduce bias in observational studies of the elderly. The Cognitive function decline is a risk factor for dementia, may be considered a marker of neurodegenerative disease (32, 33), and is a statistically powerful study outcome in cohort studies with repeated measures. However, cognitive status is a broad concept and one test of global cognitive function, such as the 3MS used in the present study, may not provide a complete measure of cognitive function in the non-demented elderly. The Cache County Study population is

primarily Caucasian and of northern European decent. Thus, the results obtained here may not generalize to other population with different ethnic representations. In addition, the dietary assessment did not include meal-specific information, so it is not possible to assess if daily consumers of RTEC consumed RTEC as a replacement for meals other than breakfast or as snacks in addition to other meals.

Conclusion

Ready-to-eat cereal (RTECs) is a commonly eaten food with a high density of added nutrients and should be considered an important contributor of micronutrient intakes, including folate and other b-vitamins with proposed cognitive benefits, among elderly men and women. However, in a large prospective study of elderly men and women in Utah, daily consumers of RTECs had a pattern of cognitive decline over 11 years similar to infrequent consumers and both groups performed more poorly than did weekly consumers.

Over-dependence on RTEC as a quick, easy, and cost efficient meal may be an indicator of an individual's deteriorating ability to procure and or prepare more varied foods. Dietary recommendations to promote cognitive health among the elderly may include RTEC but should not ignore the importance of consuming a wide variety of whole and healthy foods. Future studies should examine how patterns of RTEC consumption contribute to broader dietary patterns and eating behaviors in populations of aging men and women, and how such patterns may be associated with cognitive outcomes. Analyzing food consumption as a dietary pattern may provide a clearer link to food-based recommendations aimed at disease prevention.

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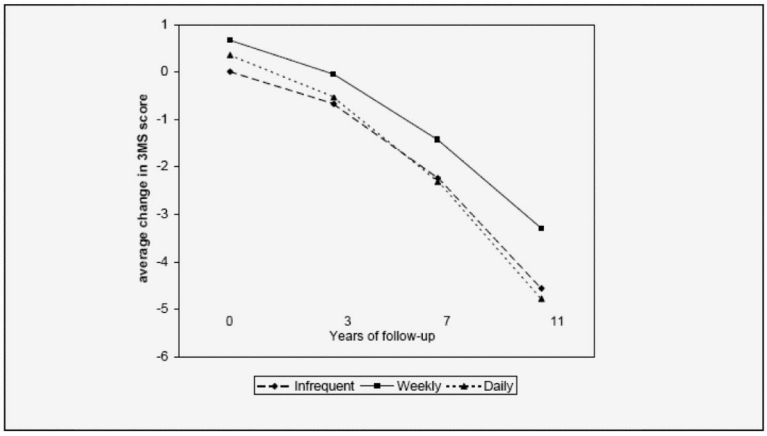

Figure 1.

Mean Change in 3MS Scores by Frequency of Ready-to-Eat Cereal Consumption Across 11 Years of Follow-up (reference (0) = daily consumers at time 0) Using the Multivariable Model[a]

a. Adjusted for age, gender, education level, BMI, 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, marital status, time, time*time and interactions between time and RTEC frequency category.

Table 1

Characteristics (mean (SD) or percent) of Participants; Cache County Study on Memory, Health and Aging; 1995

	Male (n=1564)	Female (n=2070)	P[a]
Age (yrs)	74.19 ± 6.5	75.00 ± 6.75	<0.001
BMI (weight in kg/height in m^2)	26.40 ± 3.87	26.05 ± 4.82	0.019
Education (% high school or greater)	81.5	86.6	<0.001
Marital status (% married)	89.6	56.4	<0.001
Ever regularly drink alcohol (%)	27.3	7.4	<0.001
Ever regularly smoked (%)	34.8	6.9	<0.001
History of diabetes (%)	14.0	12.0	0.077
History of heart attack (%)	17.5	8.8	<0.001
History of stroke (%)	4.5	3.5	0.390
Moderate physical activity (%)[b]	76	66.1	<0.001
Multivitamin use (%)	38.6	45.8	<0.001
3MSE[c] scores	90.55 ± 6.9	91.67 ± 6.11	<0.001
Ready-to-eat cereal (RTEC) (servings/day)	0.46 ± 0.56	0.45 ± 0.48	0.592
Recommended food score (RFS)	29.3 ± 8.9	29.2 ± 8.5	0.748
Whole-grain containing RTEC (%)[d]	59.9%	65.9%	<0.001

[a] p-value for analysis of variance, or Chi-square distribution

[b] Participates in moderate physical activity at least two times per week

[c] Modified mini-mental state examination scores

[d] Whole-grain containing RTEC is defined as RTEC with > 25% of total grains as whole grains; the percent of participants who reported eating whole-grain containing RTEC.

Table 2

Baseline characteristics of participants by frequency of Ready-to-eat Cereal Consumption (RTEC); the Cache County Study on Memory, Health and Aging

	Infrequent (<1 s/wk) (n=1067)	Weekly (1-6 s/wk) (n=1900)	Daily (>=1 s/d) (n=667)	P[a]
RTEC (s/d)	0.03 ± 0.34	0.45 ± 0.23	1.15 ± 0.73	<0.001
Age (yrs)	74.99 ± 6.8	74.14 ± 6.5	75.57 ± 6.8	<0.001
Female (%)	57.6	56.5	57.3	0.815
BMI (wt in kg/ht in m^2)	26.04 ± 4.4	26.41 ± 4.5	25.88 ± 4.2	0.012
Marital status (% married)	66.9	73.0	68.6	0.003
Ever regularly drink alcohol (%)	18.8	15.0	14.2	0.003
Ever regularly smoked (%)	21.9	18.2	16.1	0.001
Moderate physical activity[b] (%)	68.1	71.2	70.1	<0.001
IADL[c]	0.76 ± 1.4	0.67 ± 1.3	0.87 1± .5	0.004
3MS scores (1995)	90.62 6± .6	91.73 ± 6.3	90.55 ± 6.7	<0.001
Dietary intake (units/d) and other diet characteristics				
Energy (kcals/d)	1815 7± 86	1967 7 ± 29	2138 ± 852	<0.001
Fat (% energy)	32.0 ± 6.9	31.0 5 ± .8	29.4 6 ± .3	<0.001
Protein (% energy)	17.6 3 ± .9	17.7 ± 3.3	17.2 ± 3.4	0.004
Carbohydrate (% energy)	52.3 ± 8.6	53.7 ± 7.0	56.4 7± .4	<0.001
Saturated fat (gm/d)	24.41 ± 6.6 2	23.31 ± 5.6	21.99 ± 6.5	<0.001
Fiber (gm/d)	17.5 ± 10.0	19.2 ± 9.2	22.5 ± 10.3	<0.001
Folate (ug/d)	253 ± 129	320 ± 135	420 ± 215	<0.001
Thiamin (mg/d)	1.4 ± 0.29	1.6 ± 0.6	2.02 ± 0.9	<0.001
Riboflavin (mg/d)	1.88 ± .89	2.2 ± 0.83	2.67 ± 1.22	<0.001
Vitamin B6 (mg/d)	1.8 ± 0.88	2.2 ± 0.86	2.8 ± 1.2	<0.001
Vitamin B12 (ug/d)	5.1 ± 4.2	6.2 ± 4.8	7.4 ± 5.9	<0.001
Vitamin C (mg/d)	139 ± 74	142 ± 71	146 ± 79	0.167
Iron (mg/d)	13.3 ± 7.0	16.4 ± 7.2	22.7 ± 15.5	<0.001
Calcium (mg/d)	935 ± 396	975 ± 363	999 ± 400	0.001
Whole grains (serv/d)	1.5 ± 1.4	1.6 ± 1.3	2.0 ± 1.7	<0.001
Low fat dairy (serv/d)	1.2 ± 1.3	1.5 ± 1.2	1.6 ± 1.3	<0.001
Sweetened dessert and beverages (serv/d)	2.7 ± 1.6	2.6 ± 1.4	2.6 ± 1.6	0.683
Nuts and legumes (serv/d)	0.43 ± 0.40	0.41 ± 0.39	0.40 ± 0.43	0.292
Fruit and 100% juice (serv/d)	2.7 ± 2.0	2.7 ± 1.6	2.7 ± 1.6	0.676
Vegetables (serv/d)	3.7 ± 2.5	3.5 ± 2.1	3.3 ± 2.3	0.003
Fish (serv/d)	0.23 ± 0.21	0.24 ± 0.21	0.22 ± 0.22	0.460
Meat (serv/d)	1.26 ± 0.67	1.25 ± 0.58	1.14 ± 0.66	<0.001
Whole-grain RTEC	32.8%	73.9%	81.9%	<0.001

	Infrequent (<1 s/wk) (n=1067)	Weekly (1-6 s/wk) (n=1900)	Daily (>=1 s/d) (n=667)	P[a]
(% of RTEC)[d]				
Multivitamin user (% yes)	43	42.7	42.3	0.971
Recommended food score (RFS)	28.0 ± 8.9	30.4 ± 8.5	28.0 ± 8.4	<0.001

[a] statistical significance of an analysis of variance or χ^2 test

[b] Participates in moderate physical activity at least two times per week

[c] Index of instrumental activities of daily living – a higher index score indicates more help needed with activities of daily living

[d] Whole-grain containing RTEC is defined as RTEC with > 25% of total grains as whole grains; the percent of participants who reported eating whole-grain containing RTEC.

Table 3

Mean (95% confidence interval) Cumulative Decline in 3MS Scores Across 11 Years of Follow-up by Categories of RTEC Consumption; Cache County Study on Memory Health and Aging

	Years of follow-up			
	3 (n=2743)	**7 (n=1907)**	**11 (n=1256)**	**p[a]**
Age-gender adjusted			0.004	
Infrequent	−0.72 (−1.06, −0.37)	−2.38 (−2.94, −1.82)	−4.84 (−5.65, −4.04)	
Weekly	−0.74 (−1.19, −0.30)	−2.20 (−2.61, −1.79)	−4.21 (−4.78, −3.64)	
Daily	−0.88 (−1.32, −0.44)	−2.70 (−3.36, −2.05)	−5.27 (−6.03, −4.50)	
Multivariable adjusted[b]			0.0009	
Rarely	−0.68 (−1.03, −0.33)	−2.25 (−2.82, −1.67)	−4.57 (−5.39, −3.74)	
Weekly	−0.72 (−1.17, −0.26)	−2.10 (−2.47, −1.72)	−3.96 (−4.18, −3.57)	
Daily	−0.89 (−1.33, −0.44)	−2.67 (−3.37, −1.96)	−5.13 (−6.09, −4.35)	

[a] p-value for the interaction terms for time and RTEC; this value is an indicator of the statistical significance of whether cognitive trajectories by RTEC consumption category differ by period of observation

[b] Adjusted for age, gender, education level, BMI, 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, marital status, time, time*time and interactions between time and RTEC frequency category.