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Association of Antioxidants with Memory in a Multiethnic Elderly Sample Using the Third National Health and Nutrition Examination Survey

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Oxidative stress has been implicated both in the aging process and in the pathological changes associated with Alzheimer's disease. Antioxidants, which have been shown to reduce oxidative stress in vitro, may represent a set of potentially modifiable protective factors for poor memory, which is a major component of the dementing disorders. The authors investigated the association between serum antioxidant (vitamins E, C, A, carotenoids, selenium) levels and poor memory performance in an elderly, multiethnic sample of the United States. The sample consisted of 4,809 non-Hispanic White, non-Hispanic Black, and Mexican-American elderly who visited the Mobile Examination Center during the Third National Health and Nutrition Examination Survey, a national cross-sectional survey conducted from 1988 to 1994. Memory is assessed using delayed recall (six points from a story and three words) with poor memory being defined as a combined score less than 4. Decreasing serum levels of vitamin E per unit of cholesterol were consistently associated with increasing levels of poor memory after adjustment for age, education, income, vascular risk factors, and other trace elements and minerals. Serum levels of vitamins A and C, β-carotene, and selenium were not associated with poor memory performance in this study. *Am J Epidemiol* 1999;150:37–44.

aged; antioxidants; memory; recall

The dementing disorders already represent a major burden for our society (1). Given the current demographic trends, the dimension of this public health problem is only likely to increase. A major component of the dementing disorders is memory loss, which is often associated with a loss of independent functioning. Identification of potentially modifiable protective factors for memory deficit or dementia is an increasingly important task. Antioxidants represent one such set of protective factors which have recently received a great deal of attention because of their ability to reduce oxidative stress (2–4). Oxidative stress (the imbalance between prooxidants and antioxidants in favor of the former) has been implicated both in the aging process and in the pathological changes associated with Alzheimer's disease (5–10). In addition, antioxidants have been shown to be beneficial in treating cardiovascular disease (11–13), and, because cardiovascular events are associated with cognitive impairment in some studies (14–16), it is therefore possible that they may protect against memory impairment through this mechanism. Antioxidant intake is easily modifiable by supplementation or dietary changes.

Prior studies that have examined the association between antioxidants and memory or cognition have primarily focused on vitamin C, vitamin E, vitamin A, and β-carotene (17–22). In the present study, in addition to these four antioxidants, we examined the association of selenium with poor memory. While not an antioxidant itself, selenium is associated with the antioxidant enzyme activity of glutathione peroxidase (GP-x) and has been shown to be beneficial in treatment of some forms of cancer (23, 24). Antioxidants work as a system and are affected by levels of other trace minerals and vitamins, and any assessments of antioxidants must include adjustments for those minerals and vitamins. The focus of this study was to determine if serum antioxidant (vitamins E, C, and A, carotenoids, selenium) levels are associated with memory deficit in an ethnically diverse elderly population in the United States.

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Abbreviations: MEC, Mobile Examination Center; NHANES III, Third National Health and Nutrition Examination Survey.

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MATERIALS AND METHODS

The data for this analysis come from the Third National Health and Nutrition Examination Survey (NHANES III). The NHANES III was a national cross-sectional survey of the noninstitutionalized population that oversampled the elderly, children under age 5 years, African-Americans, and Mexican-Americans in two phases, equal in time and sample size, from 1988 to 1994 (25, 26). There were two separate components of data collection for each sample person. The first component was collected at the sample person's home by interviewers using the Household Adult Questionnaire and the Family Questionnaire. The second component consisted of a health examination given at the Mobile Examination Center (MEC) or at the sample person's home. A total of 6,596 persons aged 60 years and over completed the Household Adult Questionnaire; however, only 5,302 people had a health examination at the MEC.

The memory performance variable is constructed from two items, delayed word recall and delayed story recall. One section of the Household Adult Questionnaire had the interviewer tell the sample persons the following three items: "apple," "table," and "penny." The sample person was to repeat the three items and then to repeat the items until they learned all three. After performing another task, sample persons were asked to recall the three items. One point is awarded for the delayed recall of each item with a total score ranging from zero to three. During the health examination, sample persons age 60 years and over were read the following story:

> Three children were alone at home and the house caught on fire. A brave fireman managed to climb in a back window and carry them to safety. Aside from minor cuts and bruises, all were well.

The sample persons were asked to repeat the story immediately after it was read to them. After a few minutes of answering unrelated questions, sample persons were asked to recall the story. The story is scored such that a point is awarded for each recall of the following ideas: three children, house on fire, fireman climbed in the house, children rescued, minor injuries, and everyone was well. This scoring algorithm results in a score ranging from 0 to 6. Combining the two scores results in a possible score of 0 to 9. For the purpose of our analysis, we defined poor memory as a combined score of 3 or less.

During the health examination, blood samples were drawn from each sample person. Procedures for collection and storage of the blood as well as the assay methods and the list of laboratories performing the assays can be found in the *Plan and Operation of the Third National Health and Nutrition Examination Survey* (26). Serum antioxidant levels collected include selenium, vitamin C, vitamin E, vitamin A, and the carotenoids (α-carotene, β-carotene, β-cryptoxanthin, lutein/zeaxanthin, lycopene). Other serum levels of interest that were collected include folate, calcium, several iron measures (iron, ferritin, total iron binding capacity, transferrin saturation percentage), total cholesterol, triglycerides, and high density lipoprotein (HDL) cholesterol. Low folate levels have been correlated with poor memory or cognition (20, 21, 27), while calcium regulation may be associated with oxidative stress (28). The iron measures allow us to have measures of possible prooxidant activity while cholesterol has been shown to be associated with other vascular risk factors. In addition, vitamin E, vitamin A, and β-carotene are fat-soluble vitamins and correlated with total cholesterol; therefore, all results reported for these variables will be per unit of cholesterol. We categorized serum levels into quartiles, assuming the effect of trace minerals and vitamins on memory would not be linear.

Other independent variables of interest are those that have been shown to be associated with poor memory or cognitive impairment. These include age (60–69, 70–79, ≥80 years), education (0–8, 9–11, 12, ≥13 years), income (<$20,000 annually), lifetime abstention from alcohol, smoking history (never, former, current), and cardiovascular conditions (previous stroke, hypertension). Hypertension is defined using two different definitions. The first is uncontrolled hypertension defined as systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥95 mmHg. The second variable is defined as taking medication for hypertension. In addition, we used two different definitions for surrogate markers of malnutrition. The first is a serum albumin level below 3.5 g/dL, and the second is skipping meals for financial reasons or not having enough food to eat. Finally, variables for interview language (English or Spanish) and whether interview language differed from language normally spoken at home were included to adjust for the possibility of translation/language bias in these recall items.

A total of 1,787 people were excluded from the analysis for the following reasons: not receiving a health examination (n = 872), receiving a home examination (n = 422), other race-ethnicity (n = 159), and people with missing memory data (n = 334). Demographic characteristics of the excluded group and the remaining sample are presented in table 1. Sample persons excluded from the analysis are more likely to be female, older, less educated, and have lower incomes than the people who remained in the analysis. In addition, sample persons who received a

TABLE 1. Distribution (%) of demographic characteristics and risk factors for people excluded from the analysis and those included in the analysis: sample of 6,596 US elderly studied to examine the association between antioxidants and poor memory performance, NHANES III,* 1988–1994

Characteristic or risk factor	Excluded from analysis (n = 1,787)	Remaining sample (n = 4,809)
Female	62.3	55.4
Race/ethnicity		
Non-Hispanic Whites	89.1	88.8
Non-Hispanic Blacks	9.2	8.6
Mexican-Americans	1.7	2.6
Age (years)		
60–69	41.4	53.1
70–79	34.3	34.8
≥80	24.3	12.2
Education (years)		
0–8	34.1	22.4
9–11	17.9	17.2
12	27.7	31.5
≥13	20.2	29.0
Annual income <$20,000	62.0	47.0
Previous stroke	10.0	6.0
Lifetime alcohol abstention	29.5	18.9
Ever smoked	55.3	56.2
Serum albumin <3.5 g/dL	7.5	3.8
Not enough food or skipped meals in past month	3.3	2.0

* NHANES III, Third National Health and Nutrition Examination Survey.

health examination with missing memory scores were more likely to be non-Hispanic Blacks while sample persons who received an examination at home had the highest prevalence of poor memory (data not shown).

Statistical analysis

Due to the arbitrary nature of the poor memory definition defined above ("original definition"), we performed a sensitivity analysis to determine if our results were sensitive to the definition used. Our second definition (or first alternate definition) was to define those that recalled two or less points from the story and one or no words as having poor memory. This definition requires poor memory from both tests and therefore contains the fewest number of cases. We refer to this definition as the "specific definition," because it should contain the fewest number of incorrectly identified cases (false positives) and, therefore, be the definition with the highest specificity. The third (or second alternative) definition comprises subjects who recall four or less points on both tests combined. This definition contains the most cases of poor memory and will be able to identify more true cases. Therefore, this definition should have the highest sensitivity. We refer to it as the "sensitive definition." If antioxidants are related to memory impairment, we would expect the relation between memory impairment and the antioxidant of interest to be consistent across all three definitions of poor memory. In addition, we tried to validate the definitions of poor memory by comparing them to other surrogate markers of cognition.

Because the data were collected using complex sampling designs, all analyses conducted were weighted using appropriate sampling weights provided with the data to account for the unequal probability of selection of the study subjects. Weighted percents were calculated to yield prevalence estimates of poor memory across different demographic groups. Weighted means and percentages were used to summarize demographic information for the three race-ethnic groups and to describe the distributions of vitamin and mineral levels. Weighted logistic regression models were used to derive odds ratios of decreasing antioxidant levels for the three definitions of poor memory adjusting for demographic factors and other vitamin and mineral levels. Wald F tests were used to test for the significance of the association between each vitamin/mineral and poor memory. All analyses were conducted using the software SUDAAN (29).

RESULTS

All results reported refer to analyses using the original definition of poor memory. The prevalence of poor memory for non-Hispanic Whites, non-Hispanic Blacks, and Mexican-Americans 60 years of age and older was 7.0 percent. This value is consistent with the reported 5.3 percent prevalence of memory loss for the Canadian elderly population (age 65 years and older) and recent reports of dementia among subjects aged 65 years and older in North America, where the prevalence of memory loss ranged from 6 to 10 percent (30, 31). After adjustment for other demographic factors such as age and education, subjects who were defined as having poor memory were at least twice as likely to report that they had at least some difficulty managing their money or preparing meals.

Weighted prevalence estimates of poor memory across several demographic factors are presented in table 2. Non-Hispanic Blacks had the highest prevalence of poor memory, and non-Hispanic Whites had the lowest prevalence of poor memory. Increasing age, decreasing education, annual family income less than

TABLE 2. Weighted prevalence (%) of poor memory across demographic variables and risk factors: sample of 4,809 US elderly studied to examine the association between antioxidants and poor memory performance, NHANES III,* 1988–1994

Variable or risk factor	% with memory loss
Overall	7.0
Sex	
Male	8.4
Female	6.0
Race/ethnicity	
Non-Hispanic Whites	5.5
Non-Hispanic Blacks	20.6
Mexican-Americans	15.8
Age (years)	
60–69	3.2
70–79	7.1
≥80	19.8
Education (years)	
0–8	17.1
9–11	7.0
12	3.7
≥13	2.6
Annual income	
<$20,000	11.2
≥$20,000	3.0
Stroke history	
Previous stroke	14.0
No previous stroke	6.6
Alcohol consumption	
Lifetime alcohol abstention	13.7
Did not abstain	5.4
Smoking	
Ever smoked	5.9
Never smoked	8.4
Serum albumin (g/dL)	
<3.5	11.1
≥3.5	6.6
Eating habits in past month	
Not enough food or skipped meals	19.5
Enough food and did not skip meals	6.8

* NHANES III, Third National Health and Nutrition Examination Survey.

$20,000, self-report of previous stroke, not having enough food to eat or skipping meals because of no food or money, and lifetime abstention from alcohol were associated with a higher prevalence of memory impairment. These results are consistent with our expectations with the exception of lifetime abstention from alcohol. However, previous studies on the effects of alcohol consumption on cognition, mortality, and heart disease have shown a J-shaped relation (32–34). Light to moderate drinking was associated with the lowest rates, heavy drinking with the highest rates, and abstention with rates between the two.

Comparisons of demographic characteristics and risk factors across race-ethnicity (data not shown) indicated that Mexican-Americans had the youngest population and the lowest education levels, while non-Hispanic Whites had the oldest population and highest education levels. Non-Hispanic Blacks had a higher prevalence of self-reported stroke, while non-Hispanic Whites had a lower prevalence of lifetime alcohol abstention and a higher level of income. Finally, Mexican-Americans were more likely to skip meals or not have enough food to eat than were non-Hispanic Blacks or non-Hispanic Whites.

The distributions of demographic factors, socioeconomic factors, and poor memory are presented in table 3 by vitamin and mineral levels. Increasing levels of vitamin E (per unit of total cholesterol), selenium, and vitamin C were associated with higher education levels, a higher proportion of people taking vitamin supplements, higher levels of income, and an increasing proportion of people being non-Hispanic White. Memory impairment decreased with increasing levels of vitamin E per unit of cholesterol while low levels of vitamin C and selenium were associated with a higher prevalence of memory impairment. No association was found between poor memory and β-carotene and vitamin A.

Results from the logistic regression analysis, presented in table 4, showed that decreasing education, lifetime abstention from alcohol, annual income less than $20,000 per year, and being male were associated with increased odds of having poor memory. In addition, there was a marginally significant interaction between race-ethnicity and age on the association with poor memory. The association was such that the odds of poor memory increased with increasing age for all race-ethnicity groups, but had the greatest increase for non-Hispanic Whites. The odds of people aged 80 years and older having poor memory compared with those aged 60–69 years were 8.0, 3.4, and 4.1 for non-Hispanic Whites, non-Hispanic Blacks, and Mexican-Americans, respectively. The results also showed that decreasing levels of vitamin E per unit of total cholesterol were associated with higher odds of having poor memory, while selenium, vitamin C, β-carotene per unit of cholesterol, and vitamin A per unit of cholesterol were not associated with poor memory. No consistent associations were found between poor memory and folate, calcium, cholesterol (total or HDL), lead,

TABLE 3. Distribution of demographic factors and poor memory within antioxidant quartiles: sample of 4,809 US elderly studied to examine the association between antioxidants and poor memory performance, NHANES III,* 1988–1994

Antioxidant	Average age (years)	Average education (years)	Non-Hispanic White (%)	Non-Hispanic Black (%)	Mexican-American (%)	Take vitamin supplements (%)	Annual family income <$20,000 (%)	Poor memory (%)
Vitamin E/cholesterol								
<4.8	69.7	10.1	83.2	14.2	2.6	14.4	57.4	11.3
4.8–5.8	70.2	11.3	88.9	8.1	3.1	26.2	46.2	6.9
5.8–7.2	70.9	11.7	91.9	5.6	2.5	47.2	46.4	5.0
>7.2	71.6	12.0	95.8	2.8	1.4	78.4	41.6	4.1
Selenium (ng/mL)								
<113.4	71.1	10.7	85.8	12.2	2.0	36.4	55.8	9.8
113.4–124.1	70.2	11.4	90.0	7.5	2.4	43.7	45.9	6.2
124.1–135.4	70.3	11.3	90.9	6.5	2.6	42.1	46.7	6.0
>135.4	70.7	11.7	93.2	4.5	2.4	43.8	43.0	5.3
Vitamin C (mg/dL)								
<0.53	70.1	10.1	82.7	13.9	3.5	18.1	59.0	10.4
0.53–0.88	70.3	11.4	88.1	9.5	2.4	34.3	47.7	7.0
0.87–1.15	70.7	11.8	93.5	4.5	2.0	46.1	42.2	4.2
>1.15	71.1	11.9	95.8	2.7	1.4	66.9	42.8	5.2
β-Carotene/cholesterol								
<0.06	69.1	10.7	89.5	7.3	3.2	28.6	54.7	6.6
0.06–0.09	70.4	11.3	90.5	6.8	2.7	34.6	48.5	6.6
0.09–0.15	71.1	11.6	90.7	7.4	1.9	44.7	44.6	6.7
>0.15	72.0	11.7	89.1	9.4	1.5	59.9	43.2	7.4
Vitamin A/cholesterol								
<0.24	70.3	10.8	86.5	9.9	3.6	34.4	54.2	7.3
0.24–0.28	70.1	11.3	90.2	7.2	2.6	41.2	47.4	6.2
0.28–0.34	70.2	11.4	91.7	6.5	1.9	41.9	44.6	7.1
>0.34	71.8	11.7	91.8	7.0	1.3	49.7	44.9	6.4

* NHANES III, Third National Health and Nutrition Examination Survey.

triglycerides, iron measures, or vitamin supplementation with poor memory (data not shown). No significant interactions based on the literature such as vitamin C with vitamin E or selenium with vitamin E were found.

Associations of vitamin E per unit of cholesterol and poor memory in separate logistic regression models by race-ethnicity are presented in table 5. Decreasing levels of vitamin E per unit of cholesterol were significantly associated with increasing odds of poor memory for Mexican-Americans and non-Hispanic Whites. While there was no significant association between vitamin E per unit of cholesterol and poor memory for non-Hispanic Blacks, lower levels of vitamin E per unit of cholesterol tended to have increased odds of having poor memory. One explanation for the lack of significance is that people with missing memory scores are more likely to be non-Hispanic Black and to have lower levels of vitamin E, which could lead to a lack of power for this subgroup.

The univariate trends presented in tables 2 and 3 were also evident using the specific and sensitive definitions of poor memory. The logistic regression analyses using the specific and sensitive definition showed similar trends of low levels of vitamin E having higher odds of poor memory. The association was not significant for the specific definition, which may be due to the smaller number of positive outcomes.

DISCUSSION

Increasing levels of vitamin E were associated with better memory performance for this ethnically diverse elderly population. This association was consistent across all three definitions of memory and significant for the original and sensitive definition. Using the specific definition, vitamin E was not significantly associated with memory; however, low levels of vitamin E tended to be associated with poor memory. In addition, low levels of vitamin E per unit of cholesterol were associated with poor memory within all three race-ethnicities. However, no associations of vitamin A, β-carotene, selenium, vitamin C, or any of the other vitamins or essential trace elements with poor memory were found.

Previous studies have presented mixed results with regard to associations of antioxidants with memory and cognition. Some studies have found associations between poor memory and lower levels (serum values

TABLE 4. Odds of having poor memory for selected demographic factors and antioxidants from logistic regression: sample of 4,809 US elderly studied to examine the association between antioxidants and poor memory performance, NHANES III,* 1988–1994

Demographic factor or antioxidant	Odds ratio	95% CI*	p value
Sex			
Male	1.95	1.30–2.94	0.002
Female	1.00†		
Alcohol consumption			
Lifetime abstention	1.98	1.42–2.77	<0.0001
No lifetime abstention	1.00†		
Education (years)			
0–8	3.29	2.04–5.31	<0.0001
9–11	1.96	1.10–3.48	
12	1.47	0.85–2.54	
13	1.00†		
Annual income			
<$20,000	1.74	1.24–2.44	0.002
≥$20,000	1.00†		
Vitamin E/cholesterol			
<4.8	2.09	1.02–4.26	0.025
4.8–5.8	1.42	0.79–2.55	
5.8–7.2	1.03	0.62–1.71	
>7.2	1.00†		
Selenium (ng/dL)			
<113.4	1.15	0.72–1.82	0.505
113.4–121.4	1.04	0.64–1.69	
124.1–135.4	1.08	0.59–1.98	
>135.4	1.00†		
Vitamin C (mg/dL)			
<0.53	1.07	0.69–1.66	0.650
0.53–0.88	0.89	0.59–1.32	
0.87–1.15	0.79	0.51–1.22	
>1.15	1.00†		
β-Carotene/cholesterol			
<0.06	0.79	0.45–1.38	0.552
0.06–0.09	0.99	0.60–1.63	
0.09–0.15	0.91	0.62–1.33	
>0.15	1.00†		
Vitamin A/cholesterol			
<0.24	0.83	0.52–1.33	0.317
0.24–0.28	1.00	0.64–1.58	
0.28–0.34	1.14	0.68–1.91	
>0.34	1.00†		

* NHANES III, Third National Health and Nutrition Examination Survey; CI, confidence interval.
† Reference category.

TABLE 5. Adjusted odds ratios of having poor memory for vitamin E per unit of cholesterol from separate logistic regressions using the original and sensitive definition of poor memory, by race-ethnicity: sample of 4,809 US elderly studied to examine the association between antioxidants and poor memory performance, NHANES III,* 1988–1994

Race/ethnicity	Vitamin E/ cholesterol	Adjusted odds ratio	95% CI*	p value
Non-Hispanic Whites	<4.8	2.32	1.00–5.40	0.043
	4.8–5.8	1.39	0.73–2.65	
	5.8–7.2	0.95	0.53–1.72	
	>7.2	1.00†		
Non-Hispanic Blacks	<4.8	1.55	0.49–4.94	0.191
	4.8–5.8	1.44	0.39–5.33	
	5.8–7.2	1.13	0.31–4.12	
	>7.2	1.00†		
Mexican-Americans	<4.8	4.09	1.39–11.99	0.014
	4.8–5.8	1.95	0.71–5.41	
	5.8–7.2	3.22	1.00–10.33	
	>7.2	1.00†		

* NHANES III, Third National Health and Nutrition Examination Survey; CI, confidence interval.
† Reference category.

or dietary intake) of β-carotene (17, 18) and vitamin C (17, 20, 21). To our knowledge, only one of the previous studies showed a relation between vitamin E and cognitive functioning (21), and several additional studies have reported no association between antioxidant vitamin deficiency and cognition (19, 22). One controlled trial showed that treatment with α-tocopherol slows the progression of Alzheimer's disease in patients with moderately severe impairment by delaying time to death, institutionalization, severe dementia, or loss in the ability to perform basic activities of living, but that treatment did not affect cognition (35). One community-based study showed a protective effect of vitamin E and Parkinson's disease (36), but a randomized control trial showed that treatment with α-tocopherol did not affect cognition in patients with Parkinson's disease (37).

There are several factors that may explain why our results differ from previous studies. The first factor is the composition of each population. This is a large multiethnic sample from the United States in which the subjects span all levels of income and education. The study population for the two previous US studies (20, 21) is the same (i.e., population for La Rue et al. (21) is a subset of that of Goodwin et al. (20)), with subjects being highly educated (80 percent some college and 94 percent high school graduate) and mainly non-Hispanic White. This is quite different from the population presented in this analysis, where over 20 percent of the population had less than an eighth grade education. Several of the populations studied are European populations (17–19), and factors which affect both memory and antioxidant levels and which differ across populations could lead to different results. For instance, in this analysis, socioeconomic factors such as education and income are highly correlated with both serum antioxidant levels and with memory, and the distribution of these factors may differ across populations.

In addition, several studies examined the relation of memory or cognition with dietary antioxidant intake and not serum values (18, 19). Previous studies have shown that the associations between memory and

antioxidants sometimes differ when measuring dietary intake instead of serum values. For instance, Goodwin et al. (20) showed a correlation between plasma ascorbate and the Wechsler Memory Test, but not a correlation between dietary intake of vitamin C and the Wechsler Memory Test. Furthermore, antioxidants work as a system and are affected by levels of other trace minerals and vitamins. Reports from several studies did not adjust for other trace elements and vitamins in their analysis (20, 21). While the remaining studies adjusted for cholesterol or fat intake (17–19) and ferritin (19), we were able to adjust for these and additional minerals and vitamins such as folate, calcium, and lead.

Finally, not all studies were looking at the same components of memory or cognition. We used a relatively simple measure of memory, delayed recall. Goodwin et al. (20) and La Rue et al. (21) both used the Halstead-Reitan Categories Test (a test of abstract thinking ability) and the Wechsler Memory Test, which measures immediate and delayed recall. Jama et al. (18) and Kalmijn et al. (19) both use the Mini-Mental State Examination (MMSE) to measure cognitive impairment or cognitive decline. Perrig et al. (17) examine associations of antioxidants with several definitions of memory including free recall of items pictured, recognition, and vocabulary.

Several design and methodological issues need to be taken into account when interpreting these results. First, because we used an arbitrary definition of poor memory, we can not be sure if these subjects had poor memory or were cognitively impaired. The rates of poor memory are similar to the rates of memory loss in the Canadian elderly population and to rates of dementia in North America. Sample persons with poor memory were at least twice as likely to report at least some difficulty managing their money or preparing meals after adjustment for other demographic factors such as age and education. In addition, we varied the definition slightly to determine if our results were consistent across these definitions. Because the results of vitamin E were consistent across definition for the overall sample and within each race-ethnicity, we can be reasonably sure that the results are not the artifact of using an arbitrary definition of poor memory.

The data collected for this analysis are cross-sectional. Therefore, we do not know if low serum levels of vitamin E preceded the onset of poor memory or that low levels of vitamin E are a result of having poor memory. In addition, the relation may be due to the effect of poor memory on factors related to vitamin E such as supplementation. The percent of people taking vitamin supplements was lower for people with poor memory, however, vitamin supplementation was not significantly associated with poor memory in the logistic regression. This indicates for this sample that the association between antioxidants and poor memory was specific to vitamin E and not vitamin supplementation. Serum measurements are dependent on recent intake and are not indicative of long-term history. In addition, we may not have adequately adjusted for all confounding factors. While we have adjusted for factors associated with vitamin levels and memory such as education, income, and supplementation, we may not have controlled for all socioeconomic factors.

Finally, there is the possibility of selection bias. Only 81 percent of those interviewed with the Household Adult Questionnaire received a full examination at the MEC. People who were not examined at the MEC or who had missing memory scores were older, less educated, more likely to have abstained from alcohol, more likely to be non-Hispanic Black, to have lower levels of income, and to have lower serum levels of vitamin E per unit of cholesterol. Sample persons with missing laboratory values were more likely to have poor memory and be non-Hispanic Black.

In summary, we found a consistent association between vitamin E and poor memory overall and within each race-ethnicity group even after adjusting for socioeconomic factors and other trace elements and vitamins. No such associations were found for vitamin A, vitamin C, β-carotene, and selenium. The observed association between vitamin E and memory loss deserves further investigation.

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