Nutritional status and cognitive functioning in a normally aging sample: a 6-y reassessment

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ABSTRACT
Associations between nutritional status and cognitive performance were examined in 137 elderly (aged 66–90 y) community residents. Participants were well-educated, adequately nourished, and free of significant cognitive impairment. Performance on cognitive tests in 1986 was related to both past (1980) and concurrent (1986) nutritional status. Several significant associations (P < 0.05) were observed between cognition and concurrent vitamin status, including better abstraction performance with higher biochemical status and dietary intake of thiamine, riboflavin, niacin, and folate (r = 0.19–0.29) and better visuospatial performance with higher plasma ascorbate (r = 0.22). Concurrent dietary protein in 1986 correlated significantly (r = 0.25–0.26) with memory scores, and serum albumin or transferrin with memory, visuospatial, or abstraction scores (r = 0.18–0.22). Higher past intake of vitamins E, A, B-6, and B-12 was related to better performance on visuospatial recall and/or abstraction tests (r = 0.19–0.28). Use of self-selected vitamin supplements was associated with better performance on a difficult visuospatial test and an abstraction test. Although associations were relatively weak in this well-nourished and cognitively intact sample, the pattern of outcomes suggests some directions for further research on cognition-nutrition associations in aging. Am J Clin Nutr 1997;65:20–9.

KEY WORDS Aging, nutrition, and cognition

INTRODUCTION
The possibility that nutritional deficiencies may play a role in cognitive deficits in old age has been recognized for several years (1, 2). However, among normally aging older adults, there is only scant information available about nutrition-cognition associations. The most widely cited study on this topic is that of Goodwin et al (3), who reported that healthy, community-residing older adults with comparatively low dietary intakes of protein and selected vitamins (vitamin C, thiamine, riboflavin, folate, niacin, and vitamin B-6) scored lower on average than their better-nourished peers on tests of verbal memory and nonverbal abstract reasoning. Significant associations were also noted between blood concentrations of certain nutrients (vitamin C, riboflavin, and vitamin B-12) and cognitive performance. More recently, on the basis of a small sample of healthy older adults, Tucker et al (4) reported several significant correlations between biochemical indexes of iron status, protein, vitamins A and C, and carotene, and laboratory tests of mental imagery, verbal fluency, and immediate memory. However, the direction of associations was variable, with negative correlations predominating. Other recent studies have reported associations between selected vitamins and single measures of cognitive performance in healthy aged samples (5, 6), and Riggs et al (7) found that plasma concentrations of vitamins B-12 and B-6, folate, and homocysteine were related to visuospatial copying and memory performance in normal older adults. Considered together, these investigations raise the possibility that differences in nutritional status too mild to meet criteria for clinical deficiency may have a subtle influence on cognitive performance among older nondemented adults. However, additional studies are clearly needed to establish the reliability of these relations and to explore brain-behavior mechanisms that might underlie the associations.

Data for the present analyses are from a longitudinal follow-up of the sample of healthy older adults studied by Goodwin et al (3). Changes in the cognitive test battery precluded a direct test-retest analysis. Instead, we focused on cognitive performance at retest and asked whether such performance was related to concurrent or past nutritional status. We had three aims in conducting these analyses: 1) to assess the stability of associations between cognition and nutrition over time, 2) to assess the generality of nutrition-cognition relations by looking at an expanded set of nutritional and cognitive measures, and 3) to examine associations between use of vitamins and other dietary supplements and cognitive performance.

SUBJECTS AND METHODS
Subjects
Participants were members of the New Mexico Aging Process Study, a longitudinal study of nutrition and aging that began in 1979 [see Garry et al (8) for a complete description of...
the sample]. Initially, 304 community-residing individuals (138 men and 166 women) > 60 y of age were enrolled. Participants were basically healthy for their age. For example, individuals with diabetes, coronary artery disease, and uncontrolled hypertension were not enrolled in the study. Entrance was not limited to any ethnic group, but all volunteers were white, with 3% being of Hispanic descent. More than 40% had college degrees and incomes were generally above average. In general, participants were well-educated, health-conscious, financially secure, and highly motivated, and as such, were not a random sample of older adults. At their entrance into the study, they were given physical examinations, dietary and biochemical tests to characterize their nutritional status, and a brief battery of cognitive tests. This study was approved by the Human Research Review Committee of the University of New Mexico School of Medicine. We obtained informed consent from each participant.

In the report by Goodwin et al (3), nutrition-cognition relations were examined in 260 of the original study participants (119 men and 141 women with mean ages of 71.9 and 71.6 y, respectively) who had complete nutritional and cognitive data from the first round of testing and who were free of disorders that might directly affect metabolism. The present analyses are based on data for 137 persons (67 men and 70 women) who completed cognitive testing ~6 y after the initial test round and who had nutritional findings available from both 1986 and 1980. Their mean age at reassessment was 76.9 y (range: 66–90 y); 94% had completed high school and 80% had attended some college. Consistent with attrition trends in other longitudinal studies (9), these 137 subjects were younger and had better memory test performance initially than the subjects who were not reassessed.

**Procedures**

**Nutrition evaluation**

Three-day dietary records were collected annually, together with clinical, anthropometric, and biochemical measures of nutritional status. Subjects received instructions on keeping accurate diet records, such as inclusion of all foods and beverages consumed, detailed descriptions of items recorded, recording of home-prepared recipes, and correct estimation of portion sizes. Food models and standard utensils were used to demonstrate portion sizes, and each subject received a diet scale and instruction booklet. After subjects recorded their dietary intake for three successive weekdays, project staff visited their homes to collect the completed records and review them for completeness and clarity. If vitamin or mineral supplements were used by the subject, the brand name, contents, and amounts of each nutrient were recorded to determine total intakes. Records for this analysis were coded and analyzed by using the Highland View Hospital–Case Western Reserve University (CWRU) Nutrient Database, release 5, 1980, for 1980 data and release 6, 1982, for 1986 data (10). The dietary intake of 270 participants in 1980, the initial study year, was reported in detail (10).

After an overnight fast, ~50 mL blood was obtained with heparin from each participant for biochemical measurements. Serum albumin was measured by the New Mexico Medical Reference Laboratory as part of a routine battery of clinical chemistry measures (11). Serum transferrin and vitamin status were measured in the Clinical Nutrition Laboratory. Plasma ascorbic acid was measured by an automated colorimetric procedure (12). Riboflavin status was determined as the erythrocyte glutathione reductase activity coefficient (EGRAC) by using an automated method (13). The normal range for the EGRAC by this method is 1.00–1.35, with a higher activity coefficient indicating poorer riboflavin status. Thiamine status was determined as the erythrocyte transketolase activity coefficient (ETKAC), also with an automated method, and with a higher activity coefficient indicating poorer vitamin status. Plasma and erythrocyte folate and plasma vitamin B-12 concentrations were measured simultaneously by using a radioassay kit from Becton Dickinson Immunodiagnostics, Orangeburg, NY (14). Serum transferrin was measured as total iron-binding capacity simultaneously with measurement of serum iron by an automated colorimetric method that used sulfonated bathophenathroline as the chromogen (15). The biochemical vitamin status of this study population was reported in detail (12–16).

**Cognitive assessment**

All cognitive tests were administered individually by trained research technicians in a single session of ~2 h. The test battery included the following standardized measures that evaluate cognitive processes commonly affected by aging or age-related disorders.

The Abstraction Scale from the Shipley-Hartford Intelligence Test (17) asks the subject to specify missing items in several logically determined series (eg, AB BC CD D?). It provides a measure of abstract reasoning.

The Logical Memory and Visual Reproduction subtests from the Wechsler Memory Scale (WMS; 18) assess verbal and nonverbal memory, respectively. For the Logical Memory test, the subject listens to two short stories and then attempts to recall them immediately after presentation and after a delay of 30 min. For the Visual Reproduction test, the subject studies each of four geometric designs and then attempts to draw the designs from memory, immediately and after a 30-min delay.

In the Rey-Osterrieth Complex Figure test (19, 20), the subject is first asked to copy a complex geometric design and is then asked to draw it from memory, immediately after copying it and again after a 30-min delay. The copying task provides a measure of visuospatial skills whereas the recall tasks measure nonverbal learning and memory. The Rey-Osterrieth test provides a more difficult test of visuospatial skill and nonverbal memory than does the WMS Visual Reproduction test.

**Statistical analyses**

Because scores on the immediate and delayed versions of the memory tasks were highly intercorrelated, only immediate recall scores were included in statistical analyses. Associations between nutritional variables and cognitive performance were tested by Spearman rank-order correlations; all pairings of cognitive scores obtained in 1986 with nutritional values from 1986 and 1980 were examined. Analyses of variance were used to compare mean scores on cognitive measures for participants who took vitamin supplements with those who did not take supplements. Wilcoxin nonparametric analyses were used to compare supplement user and nonuser groups if cognitive test scores were not normally distributed.
Before conducting these analyses, we examined associations between cognitive and nutritional measures and several variables (age, education, sex) that might confound nutrition-cognition associations. Sex was related to several nutritional variables, but there were no significant effects of sex on cognitive performance; by contrast, education was related to cognitive performance, but generally not to nutritional variables; therefore, we did not adjust for sex or education in the correlational analyses. Age consistently influenced cognitive performance, and was also inversely correlated with three biochemical variables (albumin in 1980, vitamin B-12 in 1980, and vitamin C in 1986); accordingly, age was covaried in the correlational analyses for these nutrients. Age and education did not differ for users and nonusers of vitamin supplements, except for an age differential between users and nonusers of supplemental vitamin C in 1986 and a difference in education for folate supplement users and nonusers in 1986; these factors were covaried in pertinent comparisons of cognitive test scores. The SAS program (version 6, release 6.04; Cary, NC) was used for statistical analyses.

**RESULTS**

The mean scores on cognitive tests in 1986 are given in Table 1, biochemical measures in 1980 and 1986 are given in Table 2, and the median, 25th percentile, and 75th percentile scores for dietary intake measures in 1980 and 1986 are presented in Table 3. Also shown for comparison in Table 3 is the 1989 recommended dietary allowance (RDA) for each nutrient for men and women aged > 50 y (21). In general, cognitive performance was at or above normative levels expected for age, and average dietary intake of nutrients clearly exceeded RDA values (eg, the 25th percentile of dietary intake is at or above the RDA for all nutrients except vitamin B-6, vitamin E, and protein).

The results of correlational analyses relating cognitive and nutritional measures are presented in Table 4. For simplicity, the pairs of correlations shown are those with a significant ($P < 0.05$) or nearly significant ($P < 0.10$) result for either past (1980) or concurrent (1986) nutritional status or both. Because the aim of the analyses was to identify patterns of potentially important associations in a sample with above-average nutrition and cognition, these levels of significance were considered appropriate, in contrast with a conservative (eg, Bonferroni) approach of adjusting alpha levels for multiple correlations. Of 90 possible intercorrelations with concurrent nutritional status, 15 were significant, compared with $\leq 5$ expected by chance.

This was a greater proportion than for past nutritional status, for which there were 10 significant correlations of 90 possible.

**Concurrent nutrition-cognition correlations**

There were several significant associations between concurrent biochemical or dietary vitamin status and cognitive performance. Plasma concentrations of vitamin C were positively correlated with Rey-Osterrieth Copy test performance and nearly significant for the Visual Reproduction test. Dietary vitamin C was nearly significantly correlated with the same cognitive scores. For both thiamine and riboflavin, concurrent dietary intake was positively correlated with Abstraction test performance, and biochemical activity coefficients were negatively correlated with Abstraction test results (with higher coefficients indicating poorer nutrient status). Concurrent dietary niacin intake correlated significantly with Rey-Osterrieth Recall and Abstraction test performance. All three measures of concurrent folate status correlated significantly with Abstraction test results.

There were also several associations between concurrent dietary and biochemical measures of protein and cognitive scores. Serum albumin correlated significantly with Logical Memory scores, serum transferrin with Rey-Osterrieth Copy scores and Abstraction test scores, and dietary protein with Rey-Osterrieth Recall and Logical Memory scores. When total dietary protein was adjusted for body weight (g protein/kg body wt), the correlations with Rey-Osterrieth Recall and Logical Memory scores remained significant ($r = 0.19$ and 0.20, respectively, $P < 0.05$). Rey-Osterrieth Recall scores, but not other cognitive scores, were significantly correlated with past total energy intake ($r = 0.23$, $P < 0.05$) and nearly significant for concurrent energy intake ($r = 0.16$, $P < 0.09$). This association was no longer present when energy intake was corrected for body weight (MJ/kg body wt).

**Past nutrition-cognition associations**

There was a single significant correlation between past biochemical nutrition status and cognitive performance. This was between serum transferrin and Rey-Osterrieth Copy score, an association also seen for concurrent nutrition status. Of the nine significant correlations between past dietary intake and cognitive status, four were for dietary vitamin E, two each were for vitamin A and vitamin B-12, and one was for vitamin B-6. None of these associations for past dietary intake matched significant associations for concurrent intake, although there were nearly significant associations for concurrent dietary vitamin B-6 and B-12 intakes and Abstraction performance.

**Vitamin supplements**

At both study times, several subjects reported taking self-selected supplements of various vitamins. In 1980, 31% of subjects took folate supplements, 59% took vitamin C supplements, and 46–49% took supplements of the remaining seven vitamins listed in Table 1. Supplement use was fairly stable over time, increasing just slightly in 1986, when 43% took folate supplements, 62% took vitamin C supplements, and 49–55% took supplements of the remaining vitamins. For each of the six B vitamins (thiamine, riboflavin, niacin, vitamin B-6, folate, and vitamin B-12), there were no differences between supplement users and nonusers in performance on the Logical
TABLE 2
Average values for biochemical measures in 1980 and 1986¹

<table>
<thead>
<tr>
<th>Biochemical measure</th>
<th>n</th>
<th>1980</th>
<th>1986</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma ascorbate (μmol/L)</td>
<td>133</td>
<td>69.3 ± 19.7 (9.1-134.6)</td>
<td>70.9 ± 20.3 (14.8-154.4)</td>
</tr>
<tr>
<td>Thiamine (activity coefficient)</td>
<td>135</td>
<td>1.6 ± 0.23 (0.95-2.15)</td>
<td>1.1 ± 0.03 (1.04-1.18)</td>
</tr>
<tr>
<td>Riboflavin (activity coefficient)</td>
<td>135</td>
<td>1.1 ± 0.07 (0.97-1.35)</td>
<td>1.1 ± 0.09 (1.00-1.49)</td>
</tr>
<tr>
<td>Plasma folate (nmol/L)</td>
<td>133</td>
<td>14.3 ± 6.0 (3.4-33.5)</td>
<td>27.4 ± 14.3 (8.8-94.7)</td>
</tr>
<tr>
<td>Erythrocyte folate (nmol/L)</td>
<td>134</td>
<td>759 ± 347 (249-2184)</td>
<td>1007 ± 408 (435-3172)</td>
</tr>
<tr>
<td>Plasma vitamin B-12 (pmol/L)</td>
<td>133</td>
<td>437 ± 186 (111-1033)</td>
<td>343 ± 174 (108-1204)</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>132</td>
<td>41.6 ± 2.3 (36-47)</td>
<td>43.5 ± 2.2 (37-49)</td>
</tr>
<tr>
<td>Serum transferrin (g/L)</td>
<td>134</td>
<td>2.3 ± 0.4 (1.6-3.6)</td>
<td>2.1 ± 0.3 (1.4-3.1)</td>
</tr>
</tbody>
</table>

¹ x ± SD; range in parentheses.

Memory or Visual Reproduction tests. However, as shown in Figures 1–3, B vitamin supplement users in 1986 had significantly higher mean scores than nonusers on the Rey-Osterrieth Copy (P < 0.05), Rey-Osterrieth Recall (P < 0.05), and Abstraction (P < 0.01) tests, except for folate and the Rey-Osterrieth Copy and Recall tests. No comparable associations were seen between cognitive performance and past vitamin use.

Vitamin C and A supplement use in 1986 had a few associations with higher cognitive scores: vitamin C with Visual Reproduction (P < 0.05) (not shown) and Rey-Osterrieth Copy scores (Figures 1–2) and vitamin A with Abstraction scores (P < 0.01) (Figure 3). Past users of vitamin C supplements also had higher scores than nonusers on the Rey-Osterrieth Copy test (P < 0.05) (not shown). Past users of vitamin E supplements had higher scores than nonusers on four of the cognitive measures, as shown in Figure 4: Rey-Osterrieth Copy, Rey-Osterrieth Recall, Visual Reproduction (all P < 0.01), and Abstraction tests (P < 0.05). For the Rey-Osterrieth Recall and Abstraction tests, mean scores were also higher for concurrent (1986) vitamin E supplement users (P < 0.05 and 0.01, respectively).

DISCUSSION

In light of the growing population of older people and the prevalence of cognitive impairment in old age, understanding of any and all factors that contribute to maintenance of cognitive ability is a high priority. Our findings, combined with those of an earlier report from this sample (3), suggest some associations between cognitive performance and dietary intake and/or plasma concentrations of specific nutrients among normally aging older adults. Generally, participants with the best cognitive performance also had higher nutrient concentrations; however, the magnitude of correlations is modest at best, accounting for small percentages of the total variation in cognitive scores. This is consistent with the outcomes of other recent studies of healthy elderly samples (4–7). The possibility that findings are due to chance cannot be excluded given the weakness of the intercorrelations; however, the number of significant associations exceeds that expected by chance, and the consistency of relations with certain cognitive measures argues against an entirely spurious set of outcomes.

Cognitive performance was not affected in a uniform way by any nutrient. Dietary protein was more closely related to memory than to visuospatial or abstraction test performance, whereas the opposite pattern was found for associations with certain vitamins. However, given the modest size of the significant correlations, and the fact that cognitive as well as nutritional measures tend to be intercorrelated, it seems most plausible that our findings suggest a general relation between nutritional status and cognition, rather than any more specific link between a particular nutrient and a given mode of cognitive performance.

Among the cognitive tests, the Abstraction test was most often associated with nutrition measures. This test is one of the most age-sensitive in the current battery, and although normative data are limited for very old cohorts, subjects in the present

TABLE 3
Average values for dietary intake measures in 1980 and 1986

<table>
<thead>
<tr>
<th>Dietary intake measure</th>
<th>1980</th>
<th></th>
<th>1986</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Median</td>
<td>25th percentile</td>
<td>75th percentile</td>
</tr>
<tr>
<td>Vitamin C (mg/d)</td>
<td>122</td>
<td>270</td>
<td>145</td>
<td>649</td>
</tr>
<tr>
<td>Vitamin A (IU/d)</td>
<td>122</td>
<td>10 496</td>
<td>6519</td>
<td>16 248</td>
</tr>
<tr>
<td>Vitamin E (mg/d)</td>
<td>122</td>
<td>16.6</td>
<td>8.2</td>
<td>110.0</td>
</tr>
<tr>
<td>Thiamine (mg/d)</td>
<td>122</td>
<td>1.93</td>
<td>1.18</td>
<td>9.34</td>
</tr>
<tr>
<td>Riboflavin (mg/d)</td>
<td>122</td>
<td>2.78</td>
<td>1.50</td>
<td>6.61</td>
</tr>
<tr>
<td>Niacin (mg/d)</td>
<td>122</td>
<td>27.5</td>
<td>18.3</td>
<td>57.7</td>
</tr>
<tr>
<td>Vitamin B-6 (mg/d)</td>
<td>122</td>
<td>1.73</td>
<td>0.88</td>
<td>5.30</td>
</tr>
<tr>
<td>Folate (μg/d)</td>
<td>122</td>
<td>255</td>
<td>190</td>
<td>470</td>
</tr>
<tr>
<td>Vitamin B-12 (μg/d)</td>
<td>122</td>
<td>5.4</td>
<td>2.9</td>
<td>11.7</td>
</tr>
<tr>
<td>Protein (g/d)</td>
<td>122</td>
<td>75</td>
<td>64</td>
<td>85</td>
</tr>
</tbody>
</table>

¹ Recommended dietary allowances for women and men.
study appear to have had greater difficulty with this test than with some other measures. For example, whereas the mean Abstraction score for the highest-performing quartile in our sample was at the 30th percentile of normative data for 40–49-y olds (22), the mean Logical Memory score in the highest-performing quartile was above the 60th percentile of norms for 40–49-y olds (18). That is, although many of our subjects scored as well or better than younger adults on verbal memory, they scored below what is expected for younger people on the Abstraction test. In the present sample, therefore, Abstraction may have been the test most likely to detect any mild, subclinical cognitive impairments.
The present results concur in a general way with those reported by Goodwin et al (3). Both analyses found modest associations between cognitive performance and nutritional measures, and in both, significant associations were noted with several different nutrients, including protein, folate, niacin, ascorbate, vitamins B-6 and B-12, thiamine, and riboflavin. We found fewer significant relations between nutrition and verbal memory than did Goodwin et al, perhaps because of selective attrition effects. As noted above, a majority of subjects in the current analyses had good verbal memory performance, which resulted in a more restricted range of scores. By contrast, we found more frequent associations between nutrients and abstraction performance than had been reported by Goodwin et al; different measures of abstraction were used in the 1980 and 1986 testings, which may account for the discrepancy in findings. Alternatively, the increased age of the sample in 1986 may have lowered abstraction performance overall, thereby increasing the sensitivity of this measure to nutrition effects.

There is a clear trend in the present analyses toward higher cognitive performance among participants taking vitamin supplements compared with those not taking supplements. This was not attributable to higher education or younger age among supplement users. Our original reason for testing the association of cognition with supplement use was the puzzling result for dietary vitamin E (Table 2). Past, but not concurrent, vitamin E intake was associated with four of the five cognitive measures, a pattern different from that for any of the other nutrients. We had no biochemical measure of vitamin E status, and we knew that the nutrient database for vitamin E was incomplete. Wondering if the result for past vitamin E intake

**FIGURE 2.** Mean scores on the Rey-Osterrieth Recall test for participants with and without vitamin supplementation. Higher scores indicate better nonverbal memory performance.

**FIGURE 3.** Mean scores on the Abstraction test for participants with and without vitamin supplementation.
was spurious, we used supplementation as a marker for vitamin E intake, obtaining results consistent generally with those in Table 2. Additionally, the analysis of supplement intake showed two cognitive measures associated with concurrent vitamin E intake, associations that were not significant in correlational analyses (Table 2).

Concurrent, but not past, supplementation with B vitamins was associated with better performance on the abstraction measure and the more difficult of the two visuospatial tests (Rey-Osterrieth Complex Figure as opposed to WMS Visual Reproduction). The B vitamin supplement association was mirrored by significant or near-significant association of abstraction with all of the concurrent biochemical and dietary B vitamin measures (Table 2) and of Rey-Osterrieth Recall with several concurrent dietary B vitamin measures (Table 2). This similarity of findings for the six B vitamins is reasonable because most were consumed as part of a multivitamin preparation. Supplement use was associated both with better biochemical and dietary vitamin status and with better performance on some cognitive tests. However, whether the association is specific to one or to several B vitamins or involves all six cannot be distinguished because of the use of multivitamin preparations. The few associations of vitamin A and C supplement use with cognition involved the same cognitive measures correlated with those vitamins in Table 2, but the association with either past or concurrent nutrition was not consistent.

Prevalence of supplement intake may have provided a crude indication of vitamin status, identifying individuals with optimal status for the nine vitamins included in the analysis. Thus, supplement intake may have contributed in a positive way to the observed associations between cognition and nutrition. Alternatively, persons with higher cognitive function may be more apt to take vitamin supplements than those with lower cognitive performance. In the present sample, participants were generally average or above average in educational and occupational attainment and in their performance on cognitive tests; therefore, these findings do not appear attributable to poor nutritional habits resulting from dementia. Whether excessive supplementation might have adverse effects on cognition could not be addressed in these data because of the small number of participants with unusually high supplement intakes.

The strength of associations in these analyses is likely to have been attenuated by the fact that our participants were generally well nourished and cognitively intact, and interpretation of outcomes must be made bearing this in mind. Nonetheless, our findings provide an opportunity to examine some of the hypotheses that have been raised about brain mechanisms that might underlie cognition-nutrition relations. Possible models are nonspecific regarding the time line for interaction between nutrition and cognition. One possibility is that past nutritional status would influence brain processes over time and be demonstrated in concurrent cognitive function, as discussed below for vitamins A and E. Alternatively, concurrent nutritional status might influence immediate brain processes and be reflected concurrently in cognitive function, as suggested by the data for some of the other nutrients. These possibilities are not mutually exclusive and both might coexist. For most nutrient variables, there were significant correlations in the relative rankings of participants from 1980 to 1986 (data not shown), suggesting moderate intraindividual continuity in nutritional status.

**An antioxidant model**

In the normal aging brain, there is a sharp increase in monoamine oxidase B, important for breakdown of catecholamines, and a corresponding decrease in dopamine in the striatum and of norepinephrine in the locus ceruleus, septum, and substantia nigra (23). Behaviorally, there are a variety of changes consistent with mild impairment of frontal/subcortical brain systems, including psychomotor slowing, decreased performance on effortful memory tasks, and reduced flexibility in thought and action (24, 25).

According to Wolters and Calne (26) and others, the nigrostriatal system may be particularly vulnerable to lifelong wear and tear resulting from accumulation of free radicals, neuromelanin, or other products of dopamineoxidation. Research with Parkinson disease patients suggests that sustained use of
medications with antioxidant properties (e.g., monoamine oxidase inhibitors) may slow the course of nigrostriatal brain dysfunction (27). A diet rich in nutrients with antioxidant properties (e.g., vitamins A, E, and C, and carotenes) might yield similar beneficial effects, and if so, frontal/subcortical behavioral functions might also be facilitated.

Our findings provide some limited support for an antioxidant model. Plasma concentrations of vitamin C and use of vitamin C supplements were related to scores on a visuospatial task (Rey-Osterrieth Copy) that places demands on frontoparietal brain function. Other potentially relevant performances (e.g., on tests of abstract reasoning or learning and memory) were either unrelated or only marginally related to vitamin C, although cognitive tests that are more specifically sensitive to frontal/subcortical functioning would provide a better test of this theory.

For the other antioxidant vitamins, our results include dietary and supplemental intake, but not biochemical measures. We lacked biochemical results for vitamin E and carotene, and did not include serum concentrations of vitamin A in these analyses, because they are known to be insensitive to vitamin A nutritional status except in cases of frank deficiency or toxicity. Associations of cognition with dietary and supplemental intake of vitamins A and E were stronger for past than for concurrent intake, a pattern different from that seen for the other nutrients. These vitamins function as fat-soluble antioxidants, and as such may exhibit a different time course of interaction with brain function and cognition than do the water-soluble vitamins. Vitamin stores accumulated in the past, such as vitamin A in liver and vitamin E in adipose tissue, might be available for antioxidant function at a later time, yielding an association between cognition and past intake. Alternatively, the antioxidant protection provided by these vitamins, localized in lipid-soluble environments in the brain (e.g., myelin or cell membranes), may prevent slow oxidative changes that would be manifest by poorer cognition at a later time.

At best, our study provides an incomplete test of antioxidant effects, due to the specific measurement problems noted, and because the relatively high intakes of these vitamins for the sample as a whole would be expected to attenuate any possible relations. The possibility that prior intake of fat-soluble antioxidants might convey some protection against subsequent age-related neurobiological changes cannot be dismissed, but more definitive study is clearly needed.

**Homocysteine**

Based on their review of the nutritional literature, Rosenberg and Miller (28) suggested that vitamin B-6, vitamin B-12, and folate may be particularly important for maintenance of cognitive ability in old age. Each of these nutrients is involved in the metabolism of the sulfur amino acid homocysteine, and high homocysteine blood concentrations have been associated with increased risk for cardiovascular disease in some populations (29–32). Moreover, relations between homocysteine concentrations and folate, vitamin B-6, and vitamin B-12 nutrient have been observed in both middle-aged and older adults (33–36). It was suggested, therefore, that neurocognitive changes in old age may be mediated by cerebrovascular changes, which in turn, may be linked to chronically elevated homocysteine concentrations. Other mechanisms for associations between these nutrients and brain function include inhibited methylation of methyl acceptors such as myelin, neurotransmitters, and membrane phospholipids (28). Regland et al (37) reported an association between vitamin B-12 supplementation and a lowering of monoamine oxidase activity in older adults with Alzheimer’s disease, suggesting another possible means by which vitamin B-12 concentrations might influence cognition function, as discussed above.

We found that plasma, erythrocyte, and dietary folate were all positively correlated with Abstraction scores, when folate status and cognition were measured at the same time. Dietary intakes of vitamins B-6 and B-12 were also related to Abstraction performance. Analyses of data obtained subsequently from this sample show that serum homocysteine was negatively correlated with serum and erythrocyte folate in 100 elderly volunteers in 1993, and mean homocysteine concentrations were significantly lower in those consuming self-selected supplements of folate and vitamins B-6 and B-12 than in the nonsupplemented participants (38). These results suggest that further study of cognitive status is warranted in relation to vitamin status, supplement use, serum homocysteine, and vascular disease.

Riggs et al (7) recently reported poorer visuospatial performance among older adults with lower plasma concentrations of vitamin B-12 and folate and higher concentrations of homocysteine; higher concentrations of vitamin B-6 were associated with better performance on tests of working memory and incidental memory, but not with visuospatial performance. These associations were not explained by clinical diagnoses of cerebrovascular disease. Our study showed associations between performance on a difficult spatial copying and memory task (the Rey-Osterrieth Complex Figure test) and dietary intake or supplemental use of B vitamins, and in contrast with Riggs et al, showed relatively consistent associations between B vitamin intakes and Abstraction scores. We found a single association between supplemental use of vitamin B-6 and memory performance, out of several such possible comparisons. Differences in correlated skills may reflect differences in specific cognitive tests used in the two studies. For example, the test of reasoning included by Riggs et al was a paper-folding task, which differs substantially from the verbal and conceptual measure of abstraction included in the present research.

**A possible role for protein**

An intriguing finding in the present analyses was the association between protein intake and cognitive performance. Concurrent dietary protein correlated significantly with two tests of learning and memory (Rey-Osterrieth Recall and Logical Memory tests), serum albumin concentration also correlated with verbal memory performance (Logical Memory test), and serum transferrin concentration was related to visuospatial (Rey-Osterrieth Copy test) and abstraction performance.

Why might protein concentrations be important for cognition? Tyrosine, the precursor for the catecholamine neurotransmitters dopamine, norepinephrine, and epinephrine, is a common constituent of protein foods. In normal aging, as noted above, there is a reduction in brain dopamine that may be linked to the mild impairments commonly observed in the cognitive test profiles of older adults (39). Dietary intake of
protein may have an effect on catecholamine production and release, which in turn, can influence cognitive performance. Animals studies have reported facilitation of motor activity and moderation of the deleterious effects of stress in old mice as a result of dietary supplementation with tyrosine; however, to our knowledge, there are no parallel studies in humans. Because cognitive testing is often considered mildly stressful, tyrosine concentrations may be of particular importance with respect to behavior during such testing or during everyday situations that make demands for high performance. Studies that manipulate tyrosine through acute administration in the laboratory or through long-term dietary supplementation, using cognitive, motor, and mood outcome measures, would be valuable in addressing these issues.

There are several reasons to suspect that older individuals may be particularly vulnerable to reductions in protein intake. Because of body composition changes in aging, particularly decreased skeletal mass, there is a shift in the overall pattern of whole-body protein synthesis and breakdown (39). Thus, muscle contributes ~30% to whole-body protein turnover in young adults, but only ~20% in elderly individuals. Young (39) speculated that these changes may reduce the efficiency of dietary protein use in old age. Additionally, the reduced skeletal muscle protein reservoir may decrease the capacity to adapt successfully to decreased dietary intake or to physiological stress requiring protein synthesis. For example, the release of the amino acid glutamine from skeletal muscle is important for immune function and also provides a labile store of nitrogen for protein synthesis by other tissues during stress such as infection, surgery, or trauma (37). One might further speculate that changes in the pattern of whole-body protein synthesis and breakdown might affect the availability in neural tissue of neurotransmitter precursors, such as tyrosine, or might have some other unforeseen effect on function of neural tissue.

Conclusions

Because our results are correlational, they cannot be used to support any causal associations among nutritional and cognitive variables, nor can we exclude the possibility that the associations observed were due to unidentified factors (e.g., exercise patterns) affecting both nutrition and cognition. However, considered together with the earlier findings from this study and other recent reports, the present outcomes support the potential value of further research on cognitive effects of nutritional status in normally aging adults. It will be important to study larger samples at multiple points in time to assess the time course of associations between specific nutrients and age-sensitive aspects of cognitive performance.

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