

**Associations between dietary fatty acid patterns and cognitive function in the Hispanic  
Community Health Study/Study of Latinos**

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**Shortened Title:** Dietary fat and cognitive function

**Abbreviations:**

SFA, saturated fatty acid

PUFA, polyunsaturated fatty acid

MUFA, monounsaturated fatty acid

TFA, trans fatty acid

L.A., Linolenic acid

DFA, dietary fatty acid

W.F., word fluency

B-SEVLT, Brief Spanish English verbal learning test

DSS, digit symbol substitution

DHA, docosahexaenoic acid

EPA, eicosapentaenoic acid

CVD, cardiovascular disease

HCHS/SOL, The Hispanic Community Health Study/ Study of Latinos

NCI, National Cancer Institute

SAS, statistical analysis software

GLA, Gamma linolenic acid

ALA, Alpha linolenic acid

**Abstract**

Our objective was to quantify the cross-sectional associations between dietary fatty acid (DFA) patterns and cognitive function among Hispanic/Latino adults. This study included data from 8,942 participants of the Hispanic Community Health Study/Study of Latinos, a population-based cohort study (weighted age 56.2 y and proportion female 55.2%). The NCI (National Cancer Institute) method was used to estimate dietary intake from two 24-hr recalls. We derived DFA patterns using principal components analysis with 26 fatty acid and total plant and animal monounsaturated fatty acid (MUFA) input variables. Global cognitive function was calculated as the average z-score of 4 neurocognitive tests. Survey linear regression models included multiple potential confounders such as age, sex, education, depressive symptoms, physical activity, energy intake, and cardiovascular disease. DFA patterns were characterized by consumption of long-chain saturated fatty acids (SFA), animal-based MUFA, and *trans* fatty acids (Factor 1); short to medium-chain SFA (Factor 2); very-long-chain omega-3 polyunsaturated fatty acids (PUFA) (Factor 3); very-long-chain SFA and plant-based MUFA and PUFA (Factor 4). Factor 2 was associated with greater scores for global cognitive function ( $\beta=0.037 \pm 0.012$ ) and the Digit Symbol Substitution (DSS) ( $\beta=0.56 \pm 0.17$ ), Brief Spanish English Verbal Learning-Sum (B-SEVLT) ( $\beta=0.23 \pm 0.11$ ), and B-SEVLT-Recall ( $\beta=0.11 \pm 0.05$ ) tests ( $P<0.05$  for all). Factors 1 ( $\beta=0.04 \pm 0.01$ ) and 4 ( $\beta=0.70 \pm 0.18$ ) were associated with the DSS test ( $P<0.05$  for all). Consumption of short to medium-chain SFA may be associated with higher cognitive function among U.S.-residing Hispanic/Latino adults. Prospective studies are necessary to confirm these findings.

**Keywords:** Fatty Acids, Hispanic/Latinos, Cognitive function, Dietary Patterns

## INTRODUCTION

Dementia and cognitive decline are of major public health concern worldwide <sup>(1)</sup>. The global cost of dementia increased by 35% between 2010 and 2015 to \$818 billion annually <sup>(2)</sup>. Approximately 50 million individuals are living with dementia, and this estimate is projected to triple by 2050 <sup>(1,3)</sup>. Based on limited data, it has been estimated that Hispanic/Latino adults in the U.S. have a 47% higher prevalence of dementia as compared to non-Hispanic whites <sup>(4)</sup>. The disproportionate burden of cognitive decline experienced by Hispanic/Latino adults is accompanied by lifestyle-related health conditions (i.e., cardiovascular disease and diabetes) <sup>(5-7)</sup>, that may further contribute to this observation.

Whether dietary factors can inform lifestyle interventions to prevent or treat cognitive decline and dementia is of great interest. Past studies indicate that dietary fat, particularly saturated fat, is a modifiable risk factor for CVD <sup>(8)</sup>. Given that vascular diseases are the second leading cause of dementia <sup>(9)</sup>, the association of dietary fat with cognitive function merits investigation. Past studies on this topic, have been limited in scope because they do not consider the potentially unique effects of specific fatty acids on cardiometabolic pathways that may contribute to accelerated cognitive decline and dementia. These include pathways related to inflammation, insulin resistance, and dyslipidemia <sup>(10-12)</sup>. These shortcomings could partially explain why epidemiological investigations of dementia based on total saturated (SFA), monounsaturated (MUFA), polyunsaturated (PUFA), and *trans* fatty acid (TFA) intakes have resulted in inconsistent findings <sup>(13-16)</sup>.

Total SFA and TFA consumption are generally considered to adversely affect health. However, greater intakes or circulating concentrations of short [ $<6$  carbons (C)] to medium chain (6-12 C) <sup>(17)</sup> and very-long-chain SFA ( $\geq 20$  C) <sup>(18,19)</sup> have been related to lower risk of type 2 diabetes, a condition strongly linked to chronic insulin resistance. Moreover, greater circulating very-long-chain SFA have been associated with lower CVD risk <sup>(20)</sup>. Although the primary source of TFA in the U.S. diet is processed foods, they naturally occur in ruminant animal meats and milks <sup>(21)</sup>. In one meta-analysis, *trans*-palmitoleic acid, also known as *trans*-hexadecenoic acid, consumption and circulating concentration were inversely associated with type 2 diabetes, whereas industrial TFA elevated the risk for coronary heart disease and all-cause mortality <sup>(22)</sup>. MUFA and PUFA are recommended as replacements for SFA and TFA to improve

cardiovascular health<sup>(8)</sup>. MUFA can be derived from a variety of plant and animal food sources. Epidemiological evidence suggests that plant-based MUFA consumption benefits cardiovascular risk to a greater extent than animal-based MUFA<sup>(23,24)</sup>, though investigations with cognitive outcomes are not available. Very-long-chain omega-3 PUFA [e.g., docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)] consumption improves inflammatory profiles<sup>(25)</sup> and reduces cognitive decline in elderly individuals<sup>(26)</sup>. The endogenous elongation of the plant-based omega-3 ( $\alpha$ -linolenic acid) and omega-6 PUFA (linoleic acid) to their longer-chain products, EPA/DHA, and arachidonic acid (ARA), respectively, are dependent upon the same enzymes<sup>(27)</sup>. Considering that omega-3 metabolism is slowed in the presence of greater omega-6 PUFA consumption<sup>(28)</sup>, measuring the net impact of dietary omega-3 and omega-6 intakes have on cognitive function is essential to inform dietary fat recommendations for reduction in cognitive decline. Collectively, these data suggest that individual and subsets of fatty acids may differentially affect cardiometabolic pathways; however, the importance of these fatty acids to cognitive function is unknown.

Given the potentially unique effects of fatty acid subtypes and individual species on risk factors for cognitive decline, a more nuanced examination of dietary fat intake in relation to cognitive function is needed irrespective of the dietary fat class. To improve our understanding of the role of dietary fat intake and cognitive function, the overall aim of this study was to measure the associations of dietary fatty acid (DFA) patterns, informed by individual fatty acid species, with cognitive function in a large cohort of U.S. Hispanic/Latino adults. We hypothesized that DFA patterns high in short to medium and very-long-chain SFA, plant-based MUFA and very-long-chain omega-3 PUFA would be associated with greater global cognitive function; and, conversely, that DFA patterns characterized by industrially produced TFA and long-chain SFA would be associated with lower global cognitive function.

## METHODS

### *Participants*

We examined data from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) (n=16,415), a population-based US cohort that aims to identify risk factors associated with various health conditions and prevalence among Hispanic/Latinos 18-74 years of age<sup>(29)</sup>. Participants from diverse Hispanic/Latino backgrounds (Mexican, Cuban, Puerto Rican, Dominican, and Central/ South American) were recruited from four field sites (Bronx, NY, Chicago, IL, Miami, FL, and San Diego, CA)<sup>(30)</sup>. Target areas surrounding the site locations were determined via census blocks sampled from strata defined by the cross-classification of (i) high and low Hispanic/Latino concentration and (ii) high and low educational attainment from the 2000 US decennial census data. Baseline examinations (2008-2011) were conducted in the participant's preferred language (80% in Spanish).

All participants provided informed consent which was witnessed and formally recorded. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all HCHS/SOL study procedures were approved by the Institutional Review Boards at each study site.

### *Assessment of Dietary Intake*

Estimated intake from foods was measured using two bilingual-interviewer administered 24-hr dietary recalls according to the multiple-pass method established by the Nutrition Coordinating Center, University of Minnesota<sup>(31)</sup>. An initial recall was administered in person during the baseline examination, and the second about 5 to 30 days later by telephone<sup>(32)</sup>. Nutrients were analyzed using the Nutrition Data System (NDS-R) for Research version 11 software<sup>(31)</sup>. As previously described<sup>(32,33)</sup>, nutrient intake was estimated by the NCI (National Cancer Institute) method<sup>(34)</sup>, with data from individuals with one or two valid 24-hr recalls. The NCI method includes a weighting factor to account for the sampling probabilities. A one-part model was fit with the following covariates: age, sex, field site, Hispanic/Latino background (Central American, Cuban, Dominican, Mexican, Puerto Rican, South American, and more than one/other), 1st or 2nd 24-hr recall, recall day of the week, and self-reported intake being greater, same, or less than usual.

Total animal- and plant-based MUFA consumption was derived using methods similar to others<sup>(35)</sup>. Plant-based MUFA included those from fruit, vegetables and grains products while animal-based MUFA included meats, animal fats (e.g., lard), and dairy products. For mixed foods/dishes with both animal- and plant-based components (e.g., desserts, soups), food labels from manufactures or recipes were used to identify plant and animal ingredients. Total animal- and plant-based MUFA were calculated by summing the gram intake for each food/dish reported.

### *Dietary Fatty Acid Patterns*

Consistent with methods used previously<sup>(36, 37)</sup>, DFA patterns were identified using principal components analysis (PCA) with varimax rotation (proc factor in SAS). PCA is a statistical method widely-employed in nutritional epidemiology to identify latent underlying diet and nutrient patterns from a set of foods and nutrients<sup>(38, 39)</sup>. Input variables were expressed as a proportion of total energy, and included 26 individual fatty acids, as well as total animal and plant based MUFA (**Table 1**). To decide on the number of DFA patterns (factors) to retain, we initially selected 3 to 8 factor solutions. The choice to use a 4-factor solution was based on the scree plot, eigenvalues, and interpretability of identified factors. For each of these 4 DFA patterns, a factor score was calculated by summing the fatty acid inputs weighted by loadings of each fatty acid input.

### *Neurocognitive Testing*

At baseline, neurocognitive testing was conducted with participants  $\geq 45$  y, as previously described<sup>(40)</sup>. The battery of tests included the Spanish English Verbal Learning Test (B-SEVLT) to evaluate episodic memory, the Word Fluency Test (WF) to evaluate executive function, and the digit symbol substitution test (DSS) to evaluate psychomotor speed. Tests were conducted by trained examiners and in the language preferred by the participant. The B-SEVLT asked participants to reiterate a list of 15 words that were read to them over three trials. Two scores were derived, including: (1) the sum total of correctly learned words (B-SEVLT-Sum) and (2) the number of correctly recalled words after an interference trial (B-SVELT-Recall). For the WF, participants were asked to list as many words as they could that began with the letter A or F in 60 seconds. The DSS test required participants to decipher a code by translating numbers to symbols from a key on the test form within a 90 second window. Our primary outcome was global cognitive function, which was calculated as the average score of each of the four cognitive

tests scores, following a z-score transformation<sup>(41)</sup>. The secondary outcomes were individual scores on the B-SEVLT-Sum, B-SEVLT-Recall, WF, and DSS.

### *Covariates*

Sociodemographic covariates reported at baseline included sex (male/female), age (y), education (< high school, high school or equivalent, >high school), household income (< \$30,000 or  $\geq$  \$30,000), field center (Miami, Bronx, San Diego, Chicago), Hispanic/Latino background (Central American, Cuban, Dominican, Mexican, Puerto Rican, South American, or more than one/other), and smoking status (current smoker vs. not). Clinical covariates included: type 2 diabetes (yes/no), cardiovascular disease (yes/no), hypertension (yes/no), depressive symptoms score, and physical activity level (MET-mins/day), ascertained using the WHO Global Physical Activity Questionnaire (GPAQ)<sup>(42)</sup>. Participants were categorized as having type 2 diabetes if they (1) self-reported, (2) were using anti-hyperglycemic medication, (3) had fasting blood glucose  $>126$  mg/dL, or  $\geq 200$  mg/dL on an oral glucose tolerance test, or (4) HbA1c  $\geq 6.5\%$ . Cardiovascular disease was determined based on self-reported history of myocardial infarction, transient ischemic attack, or stroke. Hypertension was defined by (1) self-report, (2) anti-hypertension medication use, or (3) systolic blood pressure  $>140$  mmHg or diastolic blood pressure  $>90$  mmHg. Depressive symptoms were assessed using the 10-item Center for Epidemiologic Studies Depression Scale (CES-D)<sup>(43)</sup>.

We also considered dietary factors that may confound associations between fat intakes and cognitive function, including added sugar<sup>(44)</sup>, fruits and vegetables<sup>(45)</sup>, and alcohol<sup>(46)</sup>. Animal products, including red meat, are sources of saturated fat, but are also rich in certain B vitamins, including B6, B12, and niacin. Intake of these nutrients has been associated with better cognitive functioning<sup>(47-52)</sup>. Therefore, models were also adjusted for these micronutrients. Dietary factors were expressed relative to total energy intake, either as a percent of total energy or as servings or g/2000 kcals.

### *Statistical Analyses*

Of the 16,415 participants 9,714 individuals were eligible to participate in neurocognitive testing ( $\geq 45$  y). From these, 9,170 had complete neurocognitive data available, 9,553 had one or two valid 24-hr dietary recalls, and 9,141 had complete covariate information. The final analytic



sample size was 8,942. Analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC). Significance was set at  $P < 0.05$  for all analyses. Survey linear regression was utilized for descriptive purposes and primary and secondary analyses, as this process accounts for the non-random sampling methods conducted in HCHS/SOL, and the over sampling of individuals older than 45 y<sup>(29)</sup>. Differences in baseline characteristics by quintile of DFA pattern scores were adjusted for age and sex, as appropriate.

Spearman correlations were used to identify food categories most closely associated with each DFA pattern. Correlations were adjusted for age, sex, and total energy intake. Food categories were informed by the Nutrition Coordinating Center (NCC) predefined food groupings available in the NDSR software package. The 135 food groups were subsequently collapsed to 32 broader food categories. Consumption of each food category was estimated using the mean value from two valid 24-hr recalls. Correlations were only conducted for individuals with two valid 24-hr recalls (n=8,435).

In primary analyses, survey linear regression was used to examine the linear association between each continuous DFA pattern and the global cognitive function continuous score. As a complementary analysis, we also examined DFA pattern scores expressed in quintiles. Tukey's post hoc tests were used to conduct pairwise DFA pattern comparisons across quintiles. Model covariates included age, sex, total energy intake, physical activity, education, income, Hispanic/Latino background, field site, CES-D score, smoking status, diabetes, CVD, and hypertension, as well as intakes of added sugar, alcohol, vitamin B6, vitamin B12, niacin, fruit, and vegetables. In secondary analyses, we examined relationships between continuous DFA patterns and the continuous score of each neurocognitive test. For all models, total energy was adjusted for using the nutrient density approach.

Several additional analyses were considered. We examined the associations between fatty acid subgroups and global cognitive function using survey linear regression. Fatty acids were grouped as follows: short and medium chain SFA (butyric, caproic, caprylic, capric, and lauric acids), long-chain SFA (myristic, palmitic, margaric, and stearic acids), very-long-chain SFA (arachidic and behenic acids), plant-based MUFA, animal-based MUFA, omega-6 PUFA (linoleic, parinaric, and arachidonic), very-long-chain omega-3 PUFA (EPA, DPA, and DHA), and linolenic acid. Due to limitations of the dietary analysis software version, linolenic acid

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could not be distinguished between alpha-linolenic and gamma-linolenic isomers, which are omega-3 and omega-6 class fatty acids, respectively. The nutrient density approach was used to model the associations with the proportions of energy from fatty acid subgroups as independent variables modeled simultaneously along with total energy and the proportions of energy from protein and alcohol. Regression coefficients represent the predicted change in global cognitive function (z-score) when the fatty acid subgroup increases by 1% of energy at the expense of an equal amount of energy from carbohydrates. Models were adjusted for age, sex, total energy intake, physical activity, education, Hispanic/Latino background, field site, CES-D score, smoking status, diabetes, CVD, hypertension, and dietary B6, B12, niacin, fruits, and vegetables.

Cardiovascular disease predicts the onset of dementia<sup>(53, 54)</sup>. Due to concerns that individuals with CVD may have altered dietary fat intake as part of disease management, we also conducted sensitivity analyses, where models were repeated excluding individuals with prevalent CVD (n=549). Further, as greater educational attainment may lower the risk of dementia<sup>(55)</sup>, we also conducted sensitivity analyses excluding individuals attaining less than a high school education (n=3,738).

## RESULTS

### *Dietary Fatty Acid Patterns*

Four DFA patterns were identified using PCA (Table 1). Factor 1 was characterized by long chain (13 to 20 C) SFA and MUFA, as well as animal based MUFA and TFA. Short (<6 C) and medium-chain SFA (6-12 C) loaded onto Factor 2. The animal-based omega-3 PUFA (EPA, DPA, and DHA), and the omega-6 PUFA arachidonic acid (ARA) loaded onto Factor 3. Factor 4 was distinguished by long-chain plant-based MUFA and PUFA (linoleic and linolenic acid). Factors 1 through 4 explained 8.1%, 4.8%, 4.1%, and 2.3% of the variability in fatty acid intake, respectively.

Factor 1 was most strongly and positively correlated with consumption of red, processed, and organ meats, and eggs, and negatively correlated with pasta and rice dishes, fruit, vegetables, and cold and cooked cereals (**Supplementary Table 1**). Factor 2 was positively correlated with milk, cheese, and related products, as well as animal fats (e.g., butter) and other grain-based recipes (e.g., tacos), and negatively with red, processed, and organ meats and meat, poultry, and fish recipes. Factor 3 was most strongly associated with seafood, poultry, and egg consumption.

Factor 4 was positively correlated with the consumption of plant-based fats and oils specifically margarine and shortening, oil, salad dressing, and nuts and nut butters and negatively correlated with breads and related products.

### *Descriptive Characteristics by Dietary Fatty Acid Patterns*

Age was positively associated with Factors 2 and 4, but inversely with Factor 1 (**Table 2**). Participants with high DFA intake most reflective of Factor 1 tended to be women, whereas men had DFA patterns more consistent with Factors 2 and 3. Total energy intake was inversely associated with Factors 1 to 3 (Table 2). Hispanic/Latino background and field site location, and intakes of fruit and vegetables, added sugar, alcohol, and B-vitamins (B6, B12, and niacin) varied significantly across DFA patterns.

### *Dietary Fatty Acid Patterns and Cognitive Function*

The distribution of the cognitive scores is reported in **Supplementary Table 2**. Factor 2 was linearly and positively associated with the global cognitive function score ( $P=0.002$ ) and there was a trend towards a positive association with Factor 4 ( $P=0.053$ ) (**Table 3**). However, significant associations were not observed for Factors 1 or 3. In complementary analyses, global cognitive function scores were significantly higher among individuals in Factor 2 quintile 5, compared with quintiles 1 and 2 (Table 3,  $P_{F\text{-test}}=0.008$ ). There was a suggestion of differences in global cognitive function score between Factor 3 quintiles 1 and 2 ( $P_{F\text{-test}}=0.04$ ;  $P_{Q1\text{ vs. }Q2}=0.08$ ). Conversely, the global cognitive function score did not vary significantly by Factor 1 or Factor 4 score quintile. In secondary analyses, we evaluated associations between the DFA patterns and individual cognitive function tests (**Table 4**). Factor 2 was associated with greater scores on the DSS, B-SEVLT-Sum, and B-SEVLT-Recall ( $P=0.03$  to  $0.007$ ) and approached significance with WF ( $P=0.06$ ). Both Factors 1 and 4 were positively and significantly associated with the DSS test, but not with other tests. Null associations were observed with Factor 3.

### *Additional analyses*

The exclusion of individuals with CVD did not change the observed associations between the DFA patterns and global cognitive function (**Supplementary Table 3**). In general, the result with global cognitive function remained similar after excluding individuals with less than a high

school education, though we observed a significant and positive association between Factor 4 and global cognitive function (**Supplementary Table 4**). Factor 2 remained significantly and positively associated with DSS and B-SEVLT-Sum neurocognitive tests in sensitivity analyses excluding individuals with CVD (**Supplementary Table 5**) or less than a high school education (**Supplementary Table 6**). In contrast, effect estimates strengthened between Factor 2 and WF, but associations with B-SEVLT-Recall were not statistically significant (Supplementary Tables 5 and 6).

Global cognitive function was regressed on to fatty acid subgroups: short and medium chain SFA, long-chain SFA, very-long chain SFA, plant-based MUFA, animal-based MUFA, linolenic acid, omega-3 PUFA, omega-6 PUFA, *trans*-hexadecenoic acid (ruminant TFA), and industrial TFA (**Supplementary Table 7**). Using survey linear regression, most fatty acid subgroups were not significantly associated with global cognitive function. However, we observed that the predicted change in global cognitive score was  $0.13 \pm 0.06$  units for a 1% of energy increase in short and medium chain SFA consumption in exchange for an equivalent amount of energy from carbohydrates ( $P=0.04$ , Supplementary Table 7).

Considering the observed significant and positive associations of Factor 2 (short and medium chain length saturated fatty acids) with global cognitive function and multiple individual neurocognitive tests examined, we conducted food rankings (**Supplementary Table 8**) to identify foods contributing to food categories that were most correlated with Factor 2 (Supplementary Table 1). Both reduced and regular fat milk, as well as regular fat cheese, ice cream, and yogurt were the main contributors to the 'Milk, cheese, and related products' food category. Butter was the main contributor to animal fat. Lastly, masa-based mixed dishes (e.g., enchiladas and tamales); pizzas/calzones; quesadillas; burritos; and dumplings, turnovers, and fritters were the main contributors to the 'Miscellaneous Grain Recipes without Meat, Poultry, and Fish' food category.

## DISCUSSION

Using data from HCHS/SOL, we identified four DFA patterns that varied in their associations with cognitive function. Most consistently, the DFA pattern distinguished by greater short to medium chain SFA (Factor 2), was associated with greater global cognitive function, as well as better scores on each neurocognitive test. The DFA pattern consistent with consumption of plant-based fatty acids (Factor 4) tended to be associated with better global cognitive function, and significantly so with the DSS test. There was a lack of evidence for the very-long-chain omega-3 DFA pattern (Factor 3) or the DFA pattern characterized by greater long-chain SFA, animal-based MUFA, and TFA (Factor 1) in relation to global cognitive function, though the latter was positively associated with the DSS test.

Observational studies examining associations between total SFA intake and dementia, mild cognitive impairment and cognitive decline have reported null and adverse associations<sup>(13-15)</sup>. This inconclusive evidence could be because SFA chain lengths may differentially impact cognitive function and metabolic risk factors that contribute to cognitive decline (e.g., inflammation and insulin resistance). We observed that the short to medium chain SFA pattern was associated with better scores on all cognitive measures examined. In animal models, the short chain SFA, butyric acid, has been shown to improve learning and memory performance, as well as restore cognitive function post neurodegeneration<sup>(56)</sup>, though human trials are lacking. Conversely, medium chain SFA supplementation has been shown to benefit cognitive performance in individuals with mild cognitive impairment or Alzheimer disease<sup>(57)</sup>. Murine studies demonstrated that short and medium chain SFA exhibit insulin sensitizing<sup>(58,59)</sup> and anti-inflammatory properties<sup>(58,60)</sup>. This is supported by data from a large prospective cohort study, where intake of these SFA was associated with lower risk of type 2 diabetes<sup>(17)</sup>. The anti-inflammatory and insulin sensitizing effects of SCFA may be through activation of G-Protein Coupled Receptors and inhibition of histone deacetylase<sup>(61,62)</sup>.

It is also thought that medium-chain SFAs may serve as an alternative fuel source in the impaired glucose metabolism<sup>(63)</sup> observed in mild cognitive impairment and dementia<sup>(64,65)</sup>. Although the brain primarily uses glucose for energy metabolism, it has the capacity to utilize ketone bodies. Medium-chain SFA are unique compared to longer chain fatty acids in that they bypass the general circulation post-absorption and are directed to the liver where ketogenesis

occurs. Indeed, experimental studies demonstrate that consumption of medium-chain SFAs increases circulating ketone bodies as compared to longer chain fatty acids<sup>(57)</sup> and upregulates brain ketone metabolism<sup>(66)</sup>. In the current study we observed that the short and medium chain SFA pattern was distinctly correlated with milk and milk product consumption. Systematic reviews of primarily observational studies suggest that the impact of dairy consumption on cognitive function is inconclusive, and that randomized controlled trials are needed to clarify these associations<sup>(67, 68)</sup>.

We observed that a DFA pattern correlated with very-long-chain SFA (arachidic and behenic acid) and plant-based MUFA and PUFA (linolenic and linoleic acids), tended to be associated with better global cognitive function score, and was significantly and positively associated with processing speed (DSS score). Greater adherence to this DFA pattern correlated with intakes of vegetable fats and oils and nuts and nut butters. There is a lack of evidence examining very-long-chain SFA intake with cognitive function. However, these fatty acids may positively impact cognitive performance through improvement in cardiometabolic risk profiles. Greater intake or circulating concentrations of very-long-chain SFAs, have been related to lower risk of the metabolic syndrome<sup>(69)</sup>, type 2 diabetes<sup>(18, 19)</sup>, and CVD<sup>(20)</sup>. We know of no previous epidemiological studies that have examined plant based MUFA in relation to cognitive outcomes. Our results are consistent with findings from the PREDIMED (Prevención con Dieta Mediterránea) trial conducted among older Spaniards with high CVD risk. Compared to the low-fat diet control arm, the Mediterranean diet with olive oil or mixed nuts arms, improved cognitive function after 4.1 years of follow-up<sup>(70)</sup>. Olive oil is mainly composed of MUFA, whereas nuts are a source of PUFA and very-long-chain SFA.

Due to limitations of the nutrient database, we could not examine undifferentiated linolenic acid (LA), which is composed of the omega-3  $\alpha$ -linolenic acid (ALA) and the omega-6 gamma-linolenic acid (GLA). A paucity of evidence is available on the impacts of ALA, GLA, and LA consumption on cognitive function or dementia. Circulating ALA concentration has been shown to be lower among individuals with dementia<sup>(71)</sup> and, inversely, associated with incident dementia<sup>(72)</sup>. The nature of the relationship between LA consumption and cognitive function is inconclusive. A recent study among older Puerto Rican adults found that LA consumption and circulating concentration were not associated with 2-year change in cognitive function, as

assessed using the Mini-Mental-State Exam (MMSE) or an aggregate neurocognitive test score indicative of executive function <sup>(73)</sup>. Similarly, LA intake was not related to cognitive decline in a study among older Dutch men <sup>(74)</sup>. In contrast, greater consumption of total omega-6 FA, primarily composed of LA (90%), was cross-sectionally associated with better score on the Audio Recorded Cognitive Screen test, but not the MMSE <sup>(75)</sup> among Australian adults. Theoretically, ALA may improve cognitive function through reduction in CVD risk <sup>(76)</sup>. Evidence from RCT supports that GLA and LA intake improves total cholesterol <sup>(77)</sup>, which is adversely related to dementia <sup>(78)</sup>.

Inconsistent with our hypotheses, the DFA pattern characterized by greater consumption of long chain SFA, animal based MUFA, and TFA (Factor 1), was not adversely related to global cognitive function. Further, it was positively associated with the DSS test to evaluate psychomotor speed. This DFA pattern was positively correlated with red meat, processed, and organ meat consumption. Although we considered neuroprotective nutrients found in red meat including B6, B12, and niacin, the association with DSS still remained. Additional research is needed to replicate this finding. In particular, longitudinally designed studies should be implemented to overcome the limitations of the cross-sectional analysis used in our study.

Our findings do not support our a priori hypothesis that an omega-3 DFA pattern (Factor 3) would be beneficially associated with cognitive function. Similarly, another cross-sectional study in Australians reported a null association between total omega-3 intake and global cognitive function <sup>(75)</sup>. In contrast, among Puerto Rican adults, total omega-3 FA (EPA, DPA, and DHA) consumption and circulating concentrations were associated with better executive function after 2 years of follow-up <sup>(73)</sup>. This is consistent with evidence from RCT where omega-3 supplementation reduced the rate of cognitive decline among patients with mild to moderate cognitive impairment <sup>(26)</sup>. One possible explanation for the null association observed in our study is that the impact of the very-long-chain omega-3 PUFA may have been offset by ARA intake, which also loaded onto Factor 3. Circulating ARA has been adversely related to cognitive function in prospective studies <sup>(73, 79)</sup>. This omega-6 fatty acid is a direct precursor to proinflammatory eicosanoids, whereas those from EPA and DHA are anti-inflammatory <sup>(27)</sup>. Eicosanoid receptors demonstrate a stronger affinity for ARA-derived eicosanoids, as compared

to those derived from EPA<sup>(27, 80)</sup>. Thus, higher ARA consumption may have blunted the anti-inflammatory potential of the very-long-chain omega-3 PUFA.

Our study has several notable strengths. We used a novel approach of constructing DFA patterns to assess associations with cognitive function. This method allowed us to evaluate the net impact of combinations of individual fatty acids on cognitive function. The large sample size (n=8,942) increased our ability to detect associations. Further, we provide evidence for Hispanic/Latino adults, an underrepresented population in cognitive function research. Our research findings should be interpreted in consideration of some limitations. The cross-sectional design prohibits any causal relationships. For example, reverse causation may be at play if individuals with higher cognitive function choose to consume fatty acids that are thought to be healthy (e.g., omega-3 FA and plant-based MUFA)<sup>(81)</sup>. Another limitation of the dietary data is measurement error, as the data are self-reported. The HCHS/SOL SOLNAS ancillary study validated their intake measures by comparing with biomarkers of energy, protein, sodium and potassium using Doubly Labeled Water, urinary nitrogen, sodium and potassium, and showed substantial under-reporting of energy and protein that varied by BMI and Hispanic/Latino background<sup>(82, 83)</sup>.

Among participants of the HCHS/SOL study, a dietary fatty acid pattern distinguished by greater intakes of short and medium chain SFA was associated with better cognitive function using individual and aggregate measures from a battery of neurocognitive tests. Our results also suggest that intake of plant-based MUFA and PUFA and very-long-chain SFA may benefit global cognitive function and processing speed. Although these results are cross-sectional, they provide evidence that food sources of these fatty acids, including dairy products, vegetable oils, and nuts, as part of an overall healthy dietary pattern, may benefit cognitive function among Hispanic/Latino adults. Future research in similar and additional cohorts should be conducted using prospective study designs to replicate these novel findings.



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## **Conflict of Interest**

The authors have no relevant conflicts of interest to report.

## **Authorship**

NAK and SJB: created the study concept and design, analyzed the data, interpreted data, and wrote the manuscript; CMP: assisted in data analysis; SA and TS: assisted in developing the study design, data interpretation, and manuscript writing; JS, SEN, HMG, YM-R, DS-A, LCG, MLD, LVN, TE, MDG, AEM, KLT, and RCK: contributed to data interpretation and critical revisions to the manuscript. All authors have read and approved this manuscript.

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## TABLES

**Table 1.** Factor loadings of dietary fatty acid patterns<sup>†</sup>

Fatty Acid	Mean $\pm$ SD		Dietary Fatty Acid Pattern			
	g or mg <sup>‡</sup>	% of energy	Factor 1	Factor 2	Factor 3	Factor 4
<b>Saturated Fatty Acids</b>						
Butyric (4:0), mg/d	428 $\pm$ 148	0.22 $\pm$ 0.067	0.23	0.89*	0.08	-0.07
Caproic (6:0), mg/d	229 $\pm$ 86	0.12 $\pm$ 0.039	0.16	0.92*	0.04	-0.06
Caprylic (8:0), mg/d	211 $\pm$ 80	0.11 $\pm$ 0.036	0.11	0.95*	0.04	-0.03
Capric (10:0), mg/d	358 $\pm$ 119	0.18 $\pm$ 0.051	0.24	0.96*	0.04	-0.05
Lauric (12:0), mg/d	640 $\pm$ 268	0.32 $\pm$ 0.12	0.16	0.80*	-0.02	-0.01
Myristic (14:0), g/d	1.73 $\pm$ 0.55	0.87 $\pm$ 0.2	0.44*	0.87*	0	-0.06
Palmitic (16:0), g/d	11.4 $\pm$ 3.4	5.65 $\pm$ 0.7	0.83*	0.36*	-0.06	0.22
Margaric (17:0), mg/d	69.4 $\pm$ 21.2	0.035 $\pm$ 0.008	0.43*	0.32	0.19	0.19
Stearic (18:0), g/d	4.99 $\pm$ 1.56	2.48 $\pm$ 0.37	0.85*	0.36*	-0.09	0.14
Arachidic (20:0), mg/d	103 $\pm$ 31	0.051 $\pm$ 0.009	0.05	0.03	0.08	0.89*
Behenic (22:0), mg/d	57.4 $\pm$ 23.2	0.029 $\pm$ 0.008	0.03	0.09	0.04	0.80*
<b>Monounsaturated Fatty Acids</b>						
Myristoleic (14:1), mg/d	83.3 $\pm$ 33.2	0.042 $\pm$ 0.014	0.48*	0.12	-0.02	0.02
Palmitoleic (16:1), g/d	1.08 $\pm$ 0.33	0.54 $\pm$ 0.084	0.83*	-0.05	0.24	0.07
Oleic (18:1), g/d	21.9 $\pm$ 6.8	10.8 $\pm$ 1.41	0.63*	-0.03	-0.08	0.62*
Gadoleic (20:1), mg/d	178 $\pm$ 55	0.09 $\pm$ 0.016	0.39*	-0.19	0.43*	0.51*
Erucic (22:1), mg/d	11.3 $\pm$ 4.5	0.006 $\pm$ 0.002	0.17	0.04	0.71*	0.07
Plant MUFA, g/d	10.9 $\pm$ 3.5	5.41 $\pm$ 1.03	0.02	-0.13	0.01	0.76*
Animal MUFA, g/d	12.6 $\pm$ 3.9	6.29 $\pm$ 1.06	0.88*	0.17	0.11	0.05
<b>Polyunsaturated Fatty Acids</b>						
Linoleic (18:2), g/d	12.1 $\pm$ 3.9	0.65 $\pm$ 0.12	0.18	-0.16	0.03	0.71*
Linolenic (18:3), g/d	1.31 $\pm$ 0.44	0.014 $\pm$ 0.007	0.10	0.05	0.03	0.71*
Parinaric (18:4), mg/d	1.3 $\pm$ 0.29	0.013 $\pm$ 0.006	-0.09	0.22	0.75*	0.09

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Arachidonic (20:4), mg/d	140 ± 39	0.039 ± 0.015	0.28	-0.17	0.75*	0.04
Eicosapentaenoic (20:5), mg/d	26.9 ± 13.2	6.02 ± 0.93	-0.03	0.06	0.86*	0.01
Docosapentaenoic (22:5), mg/d	24.1 ± 9.7	0.0007 ± 0.0002	-0.14	0.01	0.88*	-0.01
Docosahexaenoic (22:6), mg/d	76 ± 28.8	0.07 ± 0.016	-0.03	0.01	0.96*	0
Trans Fatty Acids						
Trans-hexadecenoic (16:1), mg/d	32.9 ± 12.5	0.016 ± 0.004	0.67*	0.07	-0.01	0.07
Elaidic (18:1), g/d	1.98 ± 0.71	0.99 ± 0.25	0.63*	0.18	0.04	-0.01
Linolelaidic (18:2), mg/d	330 ± 111	0.16 ± 0.034	0.59*	0.28	-0.07	0.15

<sup>†</sup>Dietary fatty acid patterns were derived using principal components analysis; SFA, Saturated Fatty Acids; MUFA, Monounsaturated Fatty Acids; PUFA, Polyunsaturated Fatty Acids; Variation explained by DFA patterns 1, 2, 3 and 4 were 8.1%, 4.8%, 4.1%, and 2.3%, respectively; \*Factor loadings greater than 0.35.

<sup>‡</sup>Values expressed as grams or mg per 2000 kcals.

**Table 2.** Age and sex adjusted characteristics by dietary fatty acid pattern score (quintile) (n=8942)<sup>†</sup>

	Factor 1 (quintile)			Factor 2 (quintile)			Factor 3 (quintile)			Factor 4 (quintile)		
	1	3	5	1	3	5	1	3	5	1	3	5
	n=1788	n=1788	n=1788	n=1788	n=1788	n=1788	n=1788	n=1788	n=1788	n=1788	n=1788	n=1788
Age, years	57.9 ± 0.35	56.2 ± 0.32	54.5 ± 0.27**	55 ± 0.29	56.3 ± 0.30	57.4 ± 0.37**	55.7 ± 0.32	56 ± 0.32	56.6 ± 0.32	55.1 ± 0.29	56.2 ± 0.32	56.9 ± 0.30*
Female, %	32.2	43.7	58.5**	68.3	49	20.0**	53	44	42.0**	48.9	43.6	41.7
Hispanic/Latino Background, %												
Central American	8	6.6	4.7**	11.6	5.8	3.4**	5.1	6.4	5.9**	7.6	7.2	4.6**
Cuban	23.3	34.8	18.9	32.6	27	24	56.1	22.7	5	5.5	19.2	55.1
Dominican	22.8	5.2	2.1	9.6	9.5	5.7	0.7	4.8	24.9	14.1	8.8	3.6
Mexican	22.8	29.1	43.5	28.3	34.6	30.2	22.2	38.2	31.8	39	36.2	20.3
Puerto Rican	13.1	16.3	23.2	8.4	14.9	30.7	12.4	19.9	20.7	22.7	19.2	10.3
South American	8.4	5.9	3.3	5.7	6.4	4.7	1.8	4.8	9.6	7.1	6.8	3.9
>One/Other	1.7	2.2	4.3	3.8	1.8	1.4	1.7	3.2	2	4.1	2.6	2.2
Study Site, %												

Bronx	40.1	19.6	19.2**	17.3	25.5	36.4*	7.6	20	52.0**	47.6	25.3	7.9**
Chicago	11.7	13.1	14.1	20.3	12.9	5.4	15.2	14.4	6.6	15.9	14.9	7
Miami	34.6	45.1	26.3	44.6	35.9	30.1	65.5	33.9	11.2	10.3	30.3	66.4
San Diego	13.6	22.2	40.4	17.8	25.8	28.1	11.7	31.7	30.2	26.2	29.5	18.7
Education, %												
< High School	40.8	35.5	37.9	39.5	39.8	38.4	34.8	36	44.3*	44.2	37.4	30.7**
High School	20.5	24.4	20	22.8	20.2	20.8	21.7	24.5	20.4	22.9	20	23.6
> High School	38.7	40	42.1	37.7	40	40.9	43.5	39.5	35.2	32.9	42.7	45.7
Household income > \$30,000, %	27.2	29.4	34.8*	28.2	31.3	27.1	25.6	33.8	29.6*	30.6	30.5	28.1
Diabetes, %	26.3	23.7	25.1	26	22.9	24.8	28.1	26	20.9*	24.9	26.4	26.3
Cardiovascular Disease, %	6.6	6.2	7.3	8.2	8.7	5.3	7.9	7.1	7.8	6.7	7.9	7.7
Hypertension, %	43.1	43.6	44.6*	38.8	43.3	47	42.3	41.9	44.8	39.1	42.5	47.4
CES-D score	7.03 ± 0.24	7.28 ± 0.22	7.49 ± 0.22	7.18 ± 0.24	7.28 ± 0.21	7.91 ± 0.33	7.62 ± 0.23	7.21 ± 0.22	7.33 ± 0.3	7.52 ± 0.21	7.23 ± 0.31	7.08 ± 0.22
Physical activity, MET-mins/d	597 ± 34	529 ± 31	515 ± 30	603 ± 36	510 ± 29	531 ± 30	533 ± 32	555 ± 37	568 ± 28	643 ± 37	510 ± 26	483 ± 25*

Current Smoker, %	15.5	21.1	23.2	25.7	17.6	18.6	28.3	18.9	12.2**	21	18.3	22.1
Diet <sup>‡</sup>												
Total Energy, kcal/d	1941 ± 19.6	1956 ± 14.7	1787 ± 14.9**	1960 ± 17.4	1941 ± 17.0	1811 ± 12.7**	2216 ± 12.0	1913 ± 12.9	1575 ± 11.5**	1909 ± 18.2	1888 ± 15.7	1922 ± 14.1
Fat, % of energy	27.7 ± 0.11	30.2 ± 0.08	32.1 ± 0.07**	29.6 ± 0.11	29.9 ± 0.09	30.8 ± 0.10**	30.9 ± 0.08	30.3 ± 0.07	29.1 ± 0.13**	28.4 ± 0.09	29.8 ± 0.09	31.8 ± 0.07**
Saturated	8.62 ± 0.04	10.2 ± 0.04	11.7 ± 0.06**	9.11 ± 0.04	10.1 ± 0.04	11.6 ± 0.05**	10.2 ± 0.05	10.3 ± 0.05	10.3 ± 0.07	9.87 ± 0.06	10.2 ± 0.06	10.4 ± 0.05**
Monounsaturated	10.2 ± 0.06	11.6 ± 0.05	13.1 ± 0.05**	11.7 ± 0.07	11.6 ± 0.05	11.7 ± 0.06*	11.7 ± 0.06	11.7 ± 0.06	11.7 ± 0.08	10.4 ± 0.05	11.5 ± 0.04	12.9 ± 0.05**
Polyunsaturated	6.53 ± 0.05	6.85 ± 0.03	7.0 ± 0.03**	6.97 ± 0.05	6.77 ± 0.05	6.63 ± 0.03**	6.63 ± 0.04	6.82 ± 0.04	7.09 ± 0.05**	5.76 ± 0.021=	6.76 ± 0.03	7.82 ± 0.03**
Trans fat	0.913 ± 0.008	1.15 ± 0.009	1.43 ± 0.012**	1.06 ± 0.011	1.16 ± 0.012	1.28 ± 0.012**	1.11 ± 0.013	1.2 ± 0.012	1.21 ± 0.014**	1.14 ± 0.014	1.19 ± 0.012	1.12 ± 0.012**
Vegetables, s/d	2.21 ± 0.03	2.25 ± 0.03	2.33 ± 0.03*	2.34 ± 0.03	2.26 ± 0.02	2.14 ± 0.03**	2.05 ± 0.02	2.23 ± 0.03	2.53 ± 0.04**	2.02 ± 0.03	2.27 ± 0.04	2.51 ± 0.03**
Fruit, servings/d	1.72 ± 0.04	1.25 ± 0.03	1.27 ± 0.03**	1.41 ± 0.03	1.42 ± 0.04	1.24 ± 0.03**	1.05 ± 0.03	1.31 ± 0.03	1.79 ± 0.04**	1.61 ± 0.03	1.39 ± 0.03	1.14 ± 0.03**

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Added sugar, % of energy	13 ± 0.18	12.8 ± 0.14	12.4 ± 0.17*	11.8 ± 0.16	13 ± 0.14	13.7 ± 0.18**	12.8 ± 0.16	13.1 ± 0.16	12.1 ± 0.16*	14 ± 0.21	12.8 ± 0.15	11.2 ± 0.09**
Alcohol, g/d	0.275 ± 0.02	0.271 ± 0.01	0.25 ± 0.01	0.312 ± 0.02	0.258 ± 0.01	0.233 ± 0.01**	0.264 ± 0.02	0.261 ± 0.01	0.267 ± 0.01	0.349 ± 0.02	0.252 ± 0.01	0.215 ± 0.01**
Vitamin B6, mg/d	2.15 ± 0.02	2.02 ± 0.01	2.06 ± 0.02**	2.12 ± 0.02	2.07 ± 0.01	1.98 ± 0.01**	1.87 ± 0.01	2.03 ± 0.01	2.34 ± 0.02**	2.07 ± 0.02	2.09 ± 0.01	2.05 ± 0.01*
Vitamin B12, mg/d	4.69 ± 0.06	4.85 ± 0.05	5.48 ± 0.07**	4.49 ± 0.06	4.99 ± 0.05	5.41 ± 0.06**	4.51 ± 0.05	4.98 ± 0.07	5.68 ± 0.07**	4.99 ± 0.08	5.15 ± 0.07	4.88 ± 0.05*
Niacin, mg/d	23.8 ± 0.13	23.7 ± 0.12	24.5 ± 0.16**	24.5 ± 0.13	23.8 ± 0.12	23.5 ± 0.14**	22.1 ± 0.10	23.6 ± 0.11	26.7 ± 0.16**	23.2 ± 0.17	24 ± 0.13	24.6 ± 0.11**

<sup>†</sup>Values are age and sex adjusted mean ± SE and proportions estimated using survey procedures. Survey linear and logistic regression were used to compare means and proportions between factor score categories (quintiles). \* $P_{F\text{-test}} < 0.05$  and \*\* $P_{F\text{-test}} < 0.0001$  indicate significant differences across dietary fatty acid categories (factor score quintile).

<sup>‡</sup>Dietary intake variables are expressed per 2000 kcal/d, unless otherwise indicated.

**Table 3.** Adjusted mean of global cognitive function score by dietary fatty acid pattern quintile (n=8,942)

Dietary Fatty Acid Patterns <sup>†</sup>	Dietary Fatty Acid Factor Score (Quintile) <sup>‡,§</sup>					$P_{F\text{-test}}$	$\beta \pm SE^{\S, \parallel}$	$P$
	1	2	3	4	5			
	n=1778	n=1789	n=1788	n=1789	n=1788			
Factor 1	-0.058 ± 0.17	-0.034 ± 0.17	-0.013 ± 0.18	-0.029 ± 0.18	0.005 ± 0.17	0.36	0.018 ± 0.011	0.12
Factor 2	-0.034 ± 0.17 <sup>a</sup>	-0.029 ± 0.17 <sup>a</sup>	0.036 ± 0.17 <sup>a,b</sup>	0.012 ± 0.17 <sup>a,b</sup>	0.077 ± 0.17 <sup>b</sup>	0.008	0.037 ± 0.012	0.003
Factor 3	-0.018 ± 0.17	0.062 ± 0.16	0.038 ± 0.17	-0.008 ± 0.17	-0.031 ± 0.16	0.044 <sup>  </sup>	-0.012 ± 0.016	0.45
Factor 4	-0.11 ± 0.18	-0.069 ± 0.19	-0.0081 ± 0.18	-0.038 ± 0.18	-0.038 ± 0.18	0.08	0.022 ± 0.011	0.05

<sup>†</sup>Dietary fatty acid patterns were characterized by: long chain (13 to 20 C) SFA and MUFA, as well as animal-based MUFA and TFA (Factor 1); short (<6 C) and medium chain SFA (6-12 C) (Factor 2); animal-based omega-3 PUFA (EPA, DPA, and DHA), but also the omega-6 PUFA arachidonic acid (Factor 3); and long-chain plant-based MUFA, as well as PUFA found in plant food sources (linoleic and linolenic acid) (Factor 4).

<sup>‡</sup>Values represent the adjusted mean ± SE neurocognitive test z-score by factor score quintile. Differences in cognitive function score between factor score quintiles were examined using survey linear regression with factor scores treated categorically and neurocognitive test scores continuously. Tukey's post-hoc tests were used for pairwise comparisons. Values with different letters are significantly different ( $P < 0.05$ ).

<sup>§</sup>Models are adjusted for age (years), sex (M/F), energy intake (kcal/d), physical activity (MET-min/d), education (< high school, high school or equivalent, > high school), Hispanic/Latino background (Central American, Cuban, Dominican, Mexican, Puerto Rican, South



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American, and multiple/other/missing), field site (Bronx, Chicago, Miami, San Diego), CES-D score, type 2 diabetes (y/n), CVD (y/n), current smoker (y/n), hypertension (y/n), household income (< \$30,000 or not), and dietary intakes of fruits (servings/d/kcal), vegetables (servings/d/kcal), alcohol (servings/d/kcal), added sugar (% of energy/d), B12 (mg/d/kcal), B6 (mg/d/kcal), and niacin (mg/d/kcal).

<sup>¶</sup>In post-hoc analyses, we did not observe significant differences in global cognitive function score between Factor 3 Dietary Fatty Acid Pattern quintiles, however there was a suggestion of difference comparing Quintile 1 vs 2 ( $P=0.08$ ).

<sup>¶¶</sup>Values are adjusted  $\beta \pm SE$  and can be interpreted as the SD change in neurocognitive test score per one SD change in factor score. Analyses were conducted using survey linear regression treating each dietary fatty acid pattern score as a continuous variable.

**Table 4.** Associations between dietary fatty acid patterns and individual neurocognitive tests (n=8,942)

Dietary Fatty Acid Patterns <sup>†</sup>	Neurocognitive Test	$\beta \pm SE^{\ddagger}$		
		Standardized	Unstandardized	<i>P</i>
Factor 1	Word Fluency	0.027 ± 0.016	0.19 ± 0.18	0.11
	Digit Symbol Substitution	0.040 ± 0.013	0.54 ± 0.17	0.003
	B-SEVLT-Sum	0.009 ± 0.020	0.051 ± 0.11	0.65
	B-SEVLT-Recall	-0.005 ± 0.016	-0.013 ± 0.047	0.76
Factor 2	Word Fluency	0.031 ± 0.016	0.23 ± 0.11	0.057
	Digit Symbol Substitution	0.042 ± 0.015	0.56 ± 0.20	0.007
	B-SEVLT-Sum	0.040 ± 0.019	0.23 ± 0.11	0.03
	B-SEVLT-Recall	0.036 ± 0.017	0.11 ± 0.050	0.04
Factor 3	Word Fluency	-0.002 ± 0.026	-0.013 ± 0.18	0.94
	Digit Symbol Substitution	-0.019 ± 0.018	-0.25 ± 0.24	0.29
	B-SEVLT-Sum	-0.009 ± 0.019	-0.050 ± 0.11	0.63
	B-SEVLT-Recall	-0.018 ± 0.020	-0.051 ± 0.058	0.37
Factor 4	Word Fluency	0.018 ± 0.015	0.13 ± 0.11	0.23
	Digit Symbol Substitution	0.052 ± 0.013	0.70 ± 0.18	0.0001
	B-SEVLT-Sum	0.011 ± 0.017	0.059 ± 0.095	0.54

B-SEVLT-Recall	0.007 ± 0.017	0.020 ± 0.049	0.70
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<sup>†</sup>Dietary fatty acid patterns were characterized by: long chain (13 to 20 C) SFA and MUFA, as well as animal-based MUFA and TFA (Factor 1); short (<6 C) and medium chain SFA (6-12 C) (Factor 2); animal-based omega-3 PUFA (EPA, DPA, and DHA), but also the omega-6 PUFA arachidonic acid (Factor 3); and long-chain plant-based MUFA, as well as PUFA found in plant food sources (linoleic and linolenic acid) (Factor 4).

<sup>‡</sup>Survey linear regression was used to examine associations with factor and neurocognitive test scores treated as continuous variables. Models are adjusted for age (years), sex (M/F), energy intake (kcal/d), physical activity (MET-min/d), education (< high school, high school or equivalent, > high school), Hispanic/Latino background (Central American, Cuban, Dominican, Mexican, Puerto Rican, South American, and multiple/other/missing), field site (Bronx, Chicago, Miami, San Diego), CES-D score, type 2 diabetes (y/n), CVD (y/n), current smoker (y/n), hypertension (y/n), household income (< \$30,000 or not), and dietary intakes of fruits (servings/d/kcal), vegetables (servings/d/kcal), alcohol (servings/d/kcal), added sugar (% of energy/d), B12 (mg/d/kcal), B6 (mg/d/kcal), and niacin (mg/d/kcal).