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Validity of Estimated Dietary Eicosapentaenoic Acid and Docosahexaenoic Acid Intakes Determined by Interviewer-Administered Food Frequency Questionnaire Among Older Adults With Mild-to-Moderate Cognitive Impairment or Dementia

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Epidemiologic research is increasingly being focused on elderly persons, many of whom exhibit mild-to-moderate cognitive impairment. This presents a challenge for collection and interpretation of self-reported dietary data. There are few reports on the impact of cognitive function and dementia on the validity of self-reported dietary intakes. Using plasma phospholipid fatty acid profiles as a biomarker of intake, the authors assessed the validity of an interviewer-administered food frequency questionnaire (FFQ) to estimate intakes of 2 marine-based omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), among 273 community-dwelling adults aged $\geq$60 years participating in the Nutrition, Aging, and Memory in Elders Study (Boston, Massachusetts, 2002–2008). Age- and energy-adjusted Pearson correlation coefficients for correlations between dietary intakes and plasma phospholipids were consistent across categories of high and low cognitive function ($r = 0.48$), based on Mini-Mental State Examination score, and were similar across clinically diagnosed categories of normal functioning ($r = 0.49$), mild cognitive impairment ($r = 0.45$), and dementia ($r = 0.52$). The FFQ ranked 78% of subjects to within 1 quartile of their plasma phospholipid EPA + DHA quartile. This frequency was consistently high across all cognitive categories. With interviewer administration, this FFQ seems to be a valid method of assessing dietary EPA + DHA intake in older adults with mild-to-moderate cognitive impairment.

aged; aged, 80 and over; dementia; epidemiologic methods; fatty acids, omega-3; mental recall; nutrition assessment; questionnaires

Abbreviations: DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; FFQ, food frequency questionnaire; IQR, interquartile range; MMSE, Mini-Mental State Examination; MRI, magnetic resonance imaging; NAME, Nutrition, Aging, and Memory in Elders; SD, standard deviation.

With the rapid shift in the age of the US population motivating research on chronic disease risk in older adults, some data collection methods may require special consideration, particularly those used in dietary assessment. The primary challenge in collecting self-reported dietary data in any age group is reliance on the ability of subjects to accurately recall and report their past intakes. However, nearly 25% of community-dwelling elders have some degree of cognitive impairment (1), and 4.5 million persons aged 65 years or older have Alzheimer's disease (2). Thus, the elderly represent a population wherein memory is a critical issue for accurately collecting self-reported data. Because diet is an important modifiable risk factor in decreasing chronic disease risk, it is essential to understand the influence cognitive function may have on the validity of self-reported dietary intakes in impaired or demented persons.

The general cognitive processes relied upon by the main dietary assessment methods have been well described (3). On this basis, the food frequency questionnaire (FFQ) would seem to be the most valid method for use in the

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elderly, because it involves recognition of general patterns of intake, or generic memory, rather than short-term or episodic memory of specific details (4, 5). The latter cognitive processes are known to decline with age (6, 7).

Numerous studies of FFQs in older adults have validated their use (8–12), and in 2 studies investigators have specifically assessed the reproducibility and comparative validity of an FFQ for a number of nutrients by level of cognitive function, using repeated FFQs and either multiple 24-hour recalls or weighed diet records. In one study, Morris et al. (13) reported no significant differences in FFQ performance by level of cognitive function for a number of nutrients, while in the other study, McNeill et al. (14) reported a subtle influence of lower cognitive function on the comparative validity of the FFQ for some nutrients. However, neither study utilized biomarkers of nutrient intake. Thus, the common assumption that impaired elders are unlikely to provide valid dietary intake data remains untested.

The very-long-chain omega-3 fatty acids, specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are increasingly becoming nutritional exposures of interest in observational research on chronic disease risk. Unlike the case for many micronutrients, the direct biochemical measurement of fatty acid status may not be feasible in many research settings or for larger study populations. EPA and DHA are therefore important nutrients of focus for validation studies of dietary assessment methods. Our purpose in this study was to evaluate the effect of cognitive function on the validity of interviewer-administered FFQ estimates of EPA + DHA intake in a population of community-dwelling elders receiving home-care services. The fatty acid composition of plasma phospholipids was used as a biomarker of long-term intake. Mini-Mental State Examination (MMSE) (15) scores were used to assess cognitive function. Clinical consensus diagnoses were used to identify cases of mild cognitive impairment and dementia.

MATERIALS AND METHODS

Subjects

Source population. The Nutrition, Aging, and Memory in Elders (NAME) Study was a cross-sectional observational study originally designed to assess the relations between micronutrient status, cognitive impairment, and central nervous system abnormalities among elderly home-care clients aged 60 years or older in Boston, Massachusetts (June 15, 2002–May 31, 2008). The study design and data collection methods have been detailed elsewhere (16). Briefly, subjects in the NAME Study were recruited through 4 home-care agencies collectively serving the towns of Boston, Cambridge, and Somerville, Massachusetts. Persons who agreed to participate were visited in their homes by trained research interviewers and a trained phlebotomist. Interviews included informed consent, a cognitive testing battery, health history and behavior questionnaires, an FFQ, and collection of social and demographic data and information on use of home-care services. Proxy respondents were not utilized during data collection.

Elders who completed all home visits were subsequently invited to participate in a clinical visit, which involved traveling to Tufts Medical Center in Boston. Transportation was provided to all subjects via taxi or wheelchair-accessible van. In addition to cranial magnetic resonance imaging (MRI) scans, 2 clinical examinations were conducted: a neurologic examination by one of 2 board-certified neurologists and a targeted psychiatric examination by a single board-certified psychiatrist. Consensus diagnoses were assigned on the basis of clinical examination data, MRI scans, and cognitive performance results determined from the home interviews. Exclusions from the clinical visit included only those situations where MRI is contraindicated, such as use of a pacemaker. A total of 1,246 subjects enrolled in the NAME Study and 366 further completed the clinical phase of the study, including consensus diagnosis. The institutional review board of Tufts Medical Center approved all protocols and informed consent forms.

FFQ validation study. Subjects for the validation study were drawn from those with a consensus diagnosis ($n = 366$). Subsequent exclusion criteria included a missing FFQ ($n = 6$), insufficient plasma for laboratory analysis (<100 μL; $n = 39$), inability to tolerate the MRI scan ($n = 14$), excessive motion during the MRI scan ($n = 9$), incomplete neurologic examination data ($n = 8$), current dialysis ($n = 2$), and abnormalities revealed by the MRI scan, including brain tumor ($n = 7$), cyst ($n = 4$), dysplasia ($n = 1$), encephalomalasia ($n = 2$), and normal pressure hydrocephalus ($n = 1$), which may have prevented complete quantitative measurement of MRI data. After exclusions, 273 subjects qualified for the validation study.

Plasma phospholipid fatty acid composition

For each participant, a single fasting blood sample was collected in an ethylenediaminetetraacetic acid tube using standard practice, centrifuged immediately during the home visit using a portable centrifuge, and transported to the research laboratory on ice (4°C) within 2 hours. Plasma samples were aliquoted and stored at −70°C. Plasma phospholipid fatty acid analysis was performed by a single technician. The mean duration of storage was 2.4 years (range, 0.7–4.7). Plasma lipids were extracted using a modified version of Folch et al.'s (17) method, and the phospholipid subfraction was isolated by solid-phase extraction using aminopropyl columns (18), saponified, and methylated as previously described (19). The fatty acid methyl esters were analyzed using an Autosystem XL gas chromatograph (Perkin Elmer, Boston, Massachusetts) equipped with a 30-m × 0.25-mm internal diameter (film thickness 0.25 μm) capillary column (HP INNOWAX; Agilent Technologies, Inc., New Castle, Delaware). Peaks of interest were identified by comparison with authentic fatty acid standards (Nu-Chek Prep, Inc., Elysian, Minnesota) and expressed as molar percentage (mol%).

For these analyses, the individual plasma phospholipid fatty acids of interest were EPA (20:5n-3), docosapentaenoic acid (DPA) (22:5n-3), and DHA (22:6n-3). Total concentrations of plasma phospholipid very-long-chain omega-3 fatty acids were computed by summing data on

these 3 fatty acids (EPA + DPA + DHA). DPA was included in the total, since it is the biochemical product of EPA elongation and desaturation in humans.

Dietary intake

Investigators in the NAME Study utilized the Harvard semiquantitative FFQ to estimate dietary intake (20, 21). The FFQ included 4 questions on fish and seafood consumption: ''canned tuna fish'' (3–4 ounces (85–113 g)), ''dark meat fish'' (e.g., mackerel, salmon, sardines, bluefish, and swordfish (3–5 ounces (85–142 g))), ''other fish'' (3–5 ounces (85–142 g)), and ''shrimp, lobster, or scallops'' (as a main dish). Each food item had 9 possible categories of frequency ranging from never or less than once per month to 6 or more times per day. Information on use of either cod-liver oil or omega-3 fatty acid supplements was obtained as part of the FFQ in the form of yes/no questions. Completed questionnaires were sent to Harvard University's Channing Laboratory (Boston, Massachusetts) for processing and nutrient computation. Details on the computation of EPA and DHA intakes from this FFQ have been published elsewhere (22). This FFQ has been shown to be well suited to the investigation of fish consumption (23), and using biomarkers of intake, it has been shown to reflect EPA and DHA intakes in men and women (24, 25).

In the NAME Study, the FFQ was interviewer-administered in subjects' homes, which allowed specific details about food items and vitamin supplements to be obtained and confirmed. By interviewer convention, individual food items left blank during the field interview were subsequently coded as ''never'' being consumed and were assigned the lowest category of frequency. For these analyses, the total estimated daily intakes (mg/day) of EPA and DHA from the FFQ were used as the dietary variables of interest. EPA and DHA were considered individually, and data were summed for total EPA + DHA intake.

Self-reported frequency of fish consumption, expressed as number of servings per week for the 4 individual fish/seafood questions, was also used to explore the validity of type of fish consumed. Two collapsed categories of fish consumption were created by grouping items according to similar (higher or lower) very-long-chain omega-3 fatty acid content. The ''fatty fish'' category was created by summing weekly servings of ''dark meat fish'' and ''canned tuna fish.'' The ''lean fish'' category was created by summing weekly servings of ''other fish'' and ''shrimp, lobster, or scallops.'' The ''total fish'' variable was created by summing weekly servings of all 4 fish/seafood items.

Cognitive function and consensus diagnosis

The MMSE (15) was administered to all subjects in the NAME Study during the first home interview. This widely used assessment tool briefly tests subjects in the areas of orientation, registration, attention, recall, language, and visual construction and provides a general indication of level of cognitive functioning. Possible scores range from 0 to 30. Participation in the NAME Study required an MMSE score of 10 or more; scores below 10 indicate severe cognitive impairment. For these analyses, an MMSE score cutoff of $\leq$24 points was used to define lower cognitive function. An MMSE score cutoff less than 24 or 25 points has been commonly used to indicate a mild-to-moderate degree of cognitive impairment (26).

Clinical consensus diagnosis meetings, which included the study psychiatrist, neuropsychologist, neurologist, and neuroradiologist, were convened to establish clinical diagnoses for each clinical participant. For diagnoses of possible or probable Alzheimer's disease, the NINCDS-ADRDA [National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association] criteria (27) were used, and for diagnoses of possible or probable vascular dementia, the NINDS-AIREN [National Institute of Neurological Disorders and Stroke–Association Internationale pour la Recherche et l'Enseignement en Neurosciences] criteria (28) were used. *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (29), criteria were used in the diagnosis of other dementias, and the diagnosis of mild cognitive impairment was based on international working group criteria (30, 31). For these analyses, subjects were grouped by 3 broad diagnoses: normal functioning (no impairment, no dementia), mild cognitive impairment (cognitively impaired but no dementia), and dementia (any type; possible or probable).

Statistical analysis

The validation sample included 273 subjects with completed home visits, FFQs, MRI scans, neurologic examinations, and consensus diagnoses. All data were analyzed using SAS, version 9.1 (SAS Institute Inc., Cary, North Carolina). Distributions of data on fatty acid variables (plasma phospholipid and dietary) were evaluated and were log(e)-transformed to achieve normality. General descriptive statistics, mean values with standard deviations, median values with interquartile ranges (25th–75th percentiles), and frequencies were used to characterize basic descriptive variables, dietary intake of EPA + DHA, plasma phospholipid fatty acid concentrations, and weekly servings of fish. Comparisons between subgroups were conducted using chi-squared tests for categorical variables and independent sample *t* tests or analysis of variance for continuous variables. Fish consumption (servings/week) was nonnormally distributed, and differences between groups were tested using Kruskal-Wallis tests.

Pearson partial correlation coefficients were used to assess associations between intakes of EPA, DHA, or total EPA + DHA (all as mg/day) and their plasma phospholipid counterparts (mol%), and Spearman partial correlation coefficients were used to assess associations between fish consumption (servings/week) and plasma phospholipid total very-long-chain omega-3 fatty acid content (mol%). All correlations were adjusted for age, total energy intake, and use of omega-3-containing oils (in correlations of fish consumption).

Subjects were also ranked by energy-adjusted quartile of total EPA + DHA intake and by quartile of total plasma phospholipid very-long-chain omega-3 fatty acid content. The residuals method (32) was used to adjust for energy

intake prior to ranking of dietary EPA + DHA intake. Differences between dietary and plasma phospholipid rankings were calculated for each subject, and the frequency (percentage) of being classified into the same quartile, within 1 quartile, or within 3 quartiles is reported. All analytic results were determined first for all subjects and then stratified by MMSE category and consensus diagnosis category.

Regression models were used to assess the linear association between dietary EPA + DHA (as an independent predictor) and total plasma phospholipid very-long-chain omega-3 fatty acids (as the dependent outcome) after adjustment for age, sex, race, total energy intake, and home-care agency. Interaction terms for dietary EPA + DHA intake crossed with either MMSE category or consensus diagnosis were added to the adjusted regression models of all subjects to determine whether the associations between dietary and plasma phospholipid very-long-chain omega-3 fatty acids differed significantly by cognitive outcome category.

RESULTS

Subjects in the validation group were significantly younger (a mean age of 73.4 years (standard deviation (SD), 8.1) vs. 75.6 years (SD, 8.7); $P < 0.001$) than the remaining NAME population. A higher proportion were high school graduates (79.1% vs. 62.8%; $P < 0.0001$), and a lower proportion had MMSE scores less than or equal to 24, indicative of cognitive impairment (31.9% vs. 39.8%; $P < 0.05$). Functional disability was also lower in the validation group as measured by the Activities of Daily Living Scale (33) (8.9 points (SD, 7.4) vs. 11.6 points (SD, 8.6); $P < 0.0001$). These differences probably reflect the travel required for participation in the clinical visit. However, no significant differences were seen for sex, race, dietary intakes of total energy, total fat, and EPA + DHA, or frequency of fish consumption between validation study participants and the remaining NAME Study cohort (data not shown).

Within the validation group, subjects with a consensus diagnosis of dementia were significantly older than the mildly impaired or normal subjects, although mean age was not significantly different between MMSE categories (Table 1). Race was significantly different across groups; a higher proportion of elders in the low-MMSE and dementia groups were nonwhite. Predictably, MMSE scores differed significantly by consensus diagnosis category, with persons in the dementia group having the lowest scores. No significant difference in selected dietary variables was seen, and the proportions of home-delivered meal recipients (those receiving meals at least once per month) were similar across groups. Among all subjects, median numbers of servings per week for the 4 individual fish items were 0.0 (interquartile range (IQR), 0.00–0.47) for dark meat fish, 0.47 (IQR, 0.00–1.00) for canned tuna fish, 0.47 (IQR, 0.00–1.00) for other fish, and 0.00 (IQR, 0.00–0.47) for shrimp, lobster, or scallops. These distributions were statistically similar across all cognitive categories (data not shown). Use of supplements containing n-3 fatty acids (cod-liver oil or omega-3 fatty acids) was low overall ($n = 19$). However, supplement use was highest among persons in the high-MMSE and normal-diagnosis groups. Levels of plasma phospholipid total very-long-chain omega-3 fatty acids did not differ significantly by cognitive group, although fish-oil users had significantly higher plasma concentrations of phospholipid total very-long-chain omega-3 fatty acids than nonusers (6.7 mol% (SD, 2.0) vs. 4.5 mol% (SD, 1.7); $P < 0.0001$).

Pearson partial correlation coefficients, adjusted for age and total energy intake, showed moderately strong associations between FFQ estimates of dietary EPA + DHA intake and plasma phospholipid total very-long-chain omega-3 fatty acid concentrations ($r = 0.48$), which remained consistent when stratified by cognitive and diagnosis categories (Table 2). Correlation coefficients ranged from 0.45 in the mild cognitive impairment group to 0.52 in the dementia group. Correlation coefficients were moderately strong for associations between estimated dietary DHA and plasma phospholipid DHA in the whole group and across the cognitive and diagnosis categories. Estimated dietary EPA displayed weaker associations with plasma phospholipid EPA in all groups, ranging from 0.29 in the low-MMSE group to 0.43 in the dementia group, possibly because of the lower concentration of EPA than DHA in the plasma phospholipid fraction. Correlation coefficients were comparable in men and women (data not shown).

Associations between estimated dietary EPA + DHA and plasma phospholipid total very-long-chain omega-3 fatty acid concentrations were significant after adjustment for age, sex, race (white/nonwhite), total energy intake, and home-care agency (Table 3). Similar β estimates were seen across the cognitive status categories after stratification, and the amounts of variation accounted for by the models (R^2) were similar in all groups but the dementia group. In that group, the adjusted model accounted for 10% more variation in plasma phospholipid very-long-chain omega-3 fatty acids than in the high-MMSE group and nearly 12% more than in the normal-diagnosis group. P values from formal tests for interaction between dietary intake of EPA + DHA and cognitive function were not significant ($P = 0.16$ for MMSE category interaction, $P = 0.81$ for consensus diagnosis interaction), confirming that the association between FFQ estimated dietary intake of EPA + DHA and plasma phospholipid very-long-chain omega-3 fatty acids was not modified by cognitive status.

We explored the ability of the FFQ to accurately rank individuals according to their intake by examining the cross-classification agreement between quartiles of estimated EPA + DHA intake and quartiles of plasma phospholipid very-long-chain omega-3 fatty acid concentration. More than two-thirds of subjects were ranked into the same quartile or an adjacent quartile. After stratification, slightly higher proportions of participants in the low-MMSE (81.6%) and dementia (80.7%) groups were ranked in the same quartile or an adjacent quartile, relative to those with higher functioning (Table 4). Extreme misclassification (opposite quartile) was less than 5% overall and ranged from 1.6% in the dementia group to 7.3% in the mild cognitive impairment group.

To explore the ability of the population to accurately report the type of fish consumed, we used Spearman partial correlations. In the whole group, ''dark meat fish'' was the individual type most strongly correlated with plasma

Table 1. Characteristics[a] of Participants According to MMSE Score Cutoff and Clinical Consensus Diagnosis, NAME Study, Boston, Massachusetts, 2002–2008

Characteristic	All Subjects (n = 273)	Cognitive Function[b]		Consensus Diagnosis[c]		
		High Function (n = 186)	Low Function (n = 87)	Normal (n = 129)	Mild Cognitive Impairment (n = 82)	Dementia (n = 62)
Mean age, years	73.4 (8.1)	72.9 (8.1)	74.4 (8.1)	72.6 (8.0)	72.5 (7.5)	76.3 (8.5)**
Sex, % female	74.0	72.6	77.0	78.3	72.0	67.7
Race, % white	62.3	71.0	43.7***	70.5	56.1	53.2*
Education, % high school graduates	79.1	86.6	63.2***	80.6	84.2	69.4
Mean MMSE score	25.8 (3.1)	27.5 (1.6)	22.2 (2.1)***	27.2 (2.5)	25.6 (2.6)	23.0 (2.6)***
Home-care agency, %						
A	27.1	27.4	26.4	28.7	23.2	29.0
B	30.8	25.3	42.5	22.5	39.0	37.1
C	20.2	21.0	18.4	20.2	22.0	17.7
D	22.0	26.3	12.6	28.7	15.9	16.1
Home-delivered meals, % yes	58.3	58.1	58.8	56.7	58.4	61.7
Mean total energy intake, kcal/day	1,844 (591)	1,828 (617)	1,878 (532)	1,859 (614)	1,770 (594)	1,910 (532)
Mean total fat intake, % of energy	30.4 (6.7)	30.5 (6.9)	30.3 (6.3)	30.8 (6.6)	29.9 (7.0)	30.3 (6.5)
Mean saturated fat intake, % of energy	10.6 (2.9)	10.7 (3.1)	10.6 (2.5)	10.7 (2.9)	10.5 (3.1)	10.6 (2.6)
Mean EPA intake, mg/day	104 (115)	108 (124)	95.2 (91.4)	105 (121)	101 (117)	107 (98.9)
Mean DHA intake, mg/day	206 (174)	209 (182)	199 (157)	211 (175)	200 (185)	203 (161)
Use of fish oil, no. (%)	16 (7.0)	16 (8.6)	3 (3.5)	12 (9.3)	4 (4.9)	3 (4.8)
Median fish consumption, servings/week						
Fatty fish (dark meat + tuna)	0.94 (0.47–1.47)	0.94 (0.47–1.47)	1.00 (0.47–1.47)	0.94 (0.47–1.47)	1.00 (0.47–1.47)	0.94 (0.47–1.47)
Lean fish (other + shrimp)	0.47 (0.47–1.00)	0.47 (0.47–1.00)	0.47 (0.00–1.00)	0.47 (0.00–1.00)	0.47 (0.00–1.00)	1.47 (0.00–1.00)
Total fish (all types)	1.47 (0.94–2.94)	1.47 (0.94–2.94)	1.47 (0.94–3.00)	1.47 (0.94–2.94)	1.47 (0.94–3.00)	1.94 (0.94–3.00)
Mean plasma phospholipid level, mol%						
EPA (20:5n-3)	0.80 (0.67)	0.79 (0.64)	0.83 (0.75)	0.85 (0.74)	0.75 (0.69)	0.76 (0.48)
DPA (22:5n-3)	0.77 (0.20)	0.77 (0.21)	0.78 (0.18)	0.78 (0.22)	0.75 (0.20)	0.79 (0.15)
DHA (22:6n-3)	3.09 (1.17)	3.06 (1.13)	3.17 (1.26)	3.03 (1.19)	3.15 (1.20)	3.15 (1.11)

Abbreviations: DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; MMSE, Mini-Mental State Examination; NAME, Nutrition, Aging, and Memory in Elders.

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.0001$ (t test, analysis of variance test for trend, or chi-squared test for significant difference between cognitive function groups or between consensus diagnosis groups).

[a] Data on continuous variables are presented as mean values with standard deviations in parentheses; data on categorical variables are presented as frequencies. Data on fish consumption are presented as median values with interquartile ranges (25th–75th percentile).

[b] High and low cognitive function were defined by MMSE scores of >24 points or ≤24 points, respectively.

[c] Clinical diagnosis of normal functioning, mild cognitive impairment, or dementia as determined by consensus diagnostic criteria.

phospholipid very-long-chain omega-3 fatty acids, and the collapsed category of ''fatty fish'' was more strongly correlated than ''lean fish'' (Table 5). However, upon stratification by cognitive and diagnosis categories, some qualitative differences emerged. In the low-MMSE and dementia groups, correlations were similar for all 4 individual fish/seafood questions, despite known relative differences in EPA and DHA content. Consistent with this observation, the collapsed categories of fatty and lean fish were similarly correlated in the low-MMSE group, while lean fish was more strongly correlated than fatty fish in the dementia group. These relative inaccuracies in fish type, however, seemed to be less evident in the summary ''total fish'' variable, which was more strongly associated with plasma phospholipid very-long-chain omega-3 fatty acid content in the low-MMSE and dementia groups than in the other groups.

Table 2. Correlations[a] Between Estimated Dietary Intakes of Individual and Total Very-Long-Chain Omega-3 Fatty Acids From a Food Frequency Questionnaire (mg/day) and Their Plasma Phospholipid Counterparts (mol%), According to MMSE Score Cutoff and Clinical Consensus Diagnosis, NAME Study, Boston, Massachusetts, 2002–2008

Omega-3 Fatty Acid[b]	All Subjects (n = 273)	Cognitive Function[c]		Clinical Diagnosis[d]		
		High Function (n = 186)	Low Function (n = 87)	Normal (n = 129)	Mild Cognitive Impairment (n = 82)	Dementia (n = 62)
EPA	0.37	0.40	0.29	0.38	0.35	0.43
DHA	0.48	0.48	0.51	0.49	0.48	0.50
Total[e]	0.48	0.48	0.47	0.49	0.45	0.52

Abbreviations: DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; MMSE, Mini-Mental State Examination; NAME, Nutrition, Aging, and Memory in Elders.

[a] Pearson partial correlation coefficients adjusted for age and total energy intake.

[b] Data on all dietary (mg/day) and plasma phospholipid (mol%) fatty acid variables were log(e)-transformed.

[c] High and low cognitive function were defined by MMSE scores of >24 points or ≤24 points, respectively.

[d] Clinical diagnosis of normal functioning, mild cognitive impairment, or dementia as determined by consensus diagnostic criteria.

[e] All very-long-chain omega-3 fatty acids; corresponds to EPA + DHA for diet and EPA + DPA + DHA for plasma phospholipids.

DISCUSSION

Using data from a population of elderly home-care clients with clearly defined differences in cognitive function and dementia status, we found moderately strong correlations between dietary intake of EPA + DHA, estimated from an interviewer-administered FFQ, and the total very-long-chain omega-3 fatty acid content of plasma phospholipids. Our results were consistent in subjects with lower cognitive function (MMSE score ≤ 24) and those clinically diagnosed with mild cognitive impairment or dementia. These results suggest that the FFQ, in the context of interviewer administration, may be a valid method of assessing very-long-chain omega-3 fatty acid intake in mildly-to-moderately impaired elderly adults.

In mild-to-moderate cognitive impairment and dementia and, to a lesser extent, in normal aging, *episodic memory* or recall of specific details becomes reduced, while *recognition* or generic memory is generally maintained (6, 7). Because FFQs rely on the ability to recognize and report usual dietary routines rather than more specific details of individual meals (3, 4), we hypothesized that the FFQ would be a valid method of collecting dietary intake data in mildly-to-moderately cognitively impaired elderly persons. Our results support this hypothesis.

Our results are also consistent with biomarker-based validations of this FFQ conducted in populations of non-cognitively impaired adults. Coefficients for the correlation between FFQ estimates of omega-3 fatty acid intake (percentage of total fat) and adipose tissue concentrations have been reported for postmenopausal women (EPA + DHA, r = 0.48) (24), male health professionals (EPA only, r = 0.47) (25), and older African-American prostate cancer patients (EPA + DHA, r = 0.43) (34). In a study of older Costa Rican adults, Baylin et al. (35) reported lower correlations between adipose tissue concentrations and dietary EPA (r = 0.15) and DHA (r = 0.18), possibly because of infrequent fatty fish consumption in the population. Correlations between diet and erythrocyte membrane concentrations of EPA and DHA have been reported in 2 analyses of middle-aged participants in the Nurses' Health Study (for EPA, r = 0.38 and for DHA, r = 0.56 (36); for EPA, r = 0.32 and for DHA, r = 0.55 (37)). Correlations between estimated DHA and EPA intakes

Table 3. Prediction of Plasma Phospholipid Total Very-Long-Chain Omega-3 Fatty Acid Content From Estimated Dietary Intake of EPA + DHA in Multivariate Models[a], According to MMSE Score Cutoff and Clinical Consensus Diagnosis, NAME Study, Boston, Massachusetts, 2002–2008

	No. of Subjects	Model Statistic		
		β Estimate	P Value	Model R^2
All subjects	273	0.157	<0.0001	0.273
Cognitive function[b]				
High	186	0.146	<0.0001	0.303
Low	87	0.177	<0.0001	0.282
Clinical diagnosis[c]				
Normal	129	0.171	<0.0001	0.287
Mild cognitive impairment	82	0.137	0.0006	0.273
Dementia	62	0.160	<0.0001	0.403

Abbreviations: DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; MMSE, Mini-Mental State Examination; NAME, Nutrition, Aging, and Memory in Elders.

[a] All results were adjusted for age, sex, race, total energy intake, and home-care agency. The dependent variable was plasma phospholipid EPA + DPA + DHA (mol%) concentration; the independent predictor was estimated dietary EPA + DHA intake (mg/day). Data on both plasma and dietary fatty acid variables were log(e)-transformed.

[b] High and low cognitive function were defined by MMSE scores of >24 points and ≤24 points, respectively.

[c] Clinical diagnosis of normal functioning, mild cognitive impairment, or dementia as determined by consensus diagnostic criteria.

Table 4. Cross-Classification Agreement Between Energy-adjusted Quartiles of EPA + DHA Intake and Quartiles of Plasma Phospholipid Total Very-Long-Chain Omega-3 Fatty Acid Concentration, According to MMSE Score Cutoff and Clinical Consensus Diagnosis, NAME Study, Boston, Massachusetts, 2002–2008

Cross-Classification Agreement[a]	All Subjects (n = 273)		Cognitive Function[b]				Clinical Diagnosis[c]					
			High Function (n = 186)		Low Function (n = 87)		Normal (n = 129)		Mild Cognitive Impairment (n = 82)		Dementia (n = 62)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0 (same quartile)	115	42.1	82	44.1	33	37.9	58	45.0	37	45.1	20	32.3
0 or ±1 (same quartile or adjacent quartile)	213	78.0	142	76.4	71	81.6	102	79.1	61	74.4	50	80.7
±3 (opposite quartile)	12	4.4	10	5.4	2	2.3	5	3.9	6	7.3	1	1.6

Abbreviations: DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MMSE, Mini-Mental State Examination; NAME, Nutrition, Aging, and Memory in Elders.

[a] Agreement was computed as the difference between a subject's diet quartile rank and that subject's plasma quartile rank. A difference of 0 represents the same quartile, a difference of 0 or ±1 represents the same quartile or an adjacent quartile, and a difference of ±3 represents the opposite quartile; results for a difference of ±2 are not reported. Dietary intake was adjusted for total energy intake using the residuals method.

[b] High and low cognitive function were defined by MMSE scores of >24 points or ≤24 points, respectively.

[c] Clinical diagnosis of normal functioning, mild cognitive impairment, or dementia as determined by consensus diagnostic criteria.

(g/day) and plasma phospholipid concentrations (for EPA, $r = 0.19$; for DHA, $r = 0.38$) have also been reported among middle-aged men and women in the Atherosclerosis Risk in Communities Study (38). Data in our unique population are comparable to those in these reports and suggest that this FFQ, with interviewer administration, performs equally well despite the measurable cognitive impairments in our study population.

Reporting of type of fish consumed appeared less accurate in the lower cognitive function and dementia diagnosis

Table 5. Correlations[a] Between Self-reported Fish Consumption (servings/week) and Plasma Phospholipid Very-Long-Chain Omega-3 Fatty Acid Concentrations (mol%), According to MMSE Score Cutoff and Clinical Consensus Diagnosis, NAME Study, Boston, Massachusetts, 2002–2008

Fish Consumption[b]	All Subjects (n = 273)	Cognitive Function[c]		Clinical Diagnosis[d]		
		High Function (n = 186)	Low Function (n = 87)	Normal (n = 129)	Mild Cognitive Impairment (n = 82)	Dementia (n = 62)
FFQ item						
Dark meat fish	0.36	0.40	0.29	0.39	0.37	0.29
Canned tuna fish	0.13	0.08	0.25	0.13	0.10	0.21
Other fish	0.21	0.17	0.32	0.21	0.18	0.30
Shrimp, lobster, or scallops	0.08	0.02	0.19	−0.04	0.09	0.27
Collapsed category						
Fatty fish (dark + tuna)	0.30	0.29	0.33	0.34	0.30	0.24
Lean fish (other + shrimp)	0.20	0.15	0.32	0.15	0.17	0.36
Total fish (all types)	0.36	0.31	0.47	0.35	0.32	0.47

Abbreviations: FFQ, food frequency questionnaire; MMSE, Mini-Mental State Examination; NAME, Nutrition, Aging, and Memory in Elders.

[a] Spearman partial correlation coefficients adjusted for age, total energy intake, and use of fish-oil supplements (yes/no).

[b] There were 4 fish/seafood consumption items on the FFQ: "canned tuna fish"; "dark meat fish," which included salmon, mackerel, sardines, swordfish, and bluefish; "other fish," which included any other variety of fin fish; and "shrimp, lobster, or scallops." Two collapsed categories were created: "fatty fish" is the summation of "canned tuna" and "dark meat fish"; "lean fish" is the summation of "other fish" and "shrimp, lobster, or scallops." "Total fish" represents the summation of all 4 FFQ items.

[c] High and low cognitive function were defined by MMSE scores of >24 points or ≤24 points, respectively.

[d] Clinical diagnosis of normal functioning, mild cognitive impairment, or dementia as determined by consensus diagnostic criteria.

groups. This may indicate a reduced ability of these persons to recall specific details on food items consumed. Correlations with ''total fish'' were not weaker; thus, the ability to self-report overall *frequency* of consumption, the general pattern of intake, appeared to be preserved. Despite these differences, our results are consistent with a previous report of associations between self-reported fish consumption using this FFQ and biomarkers of very-long-chain omega-3 fatty acids. In middle-aged women in the Nurses' Health Study, *r* values for correlation between total fish intake (servings/week) and whole plasma or erythrocyte membrane concentrations of very-long-chain omega-3 fatty acids were 0.35 and 0.42, respectively (37).

The NAME Study had several strengths with regard to the investigation of cognitive function and the validity of dietary self-reports in older adults. Thirty-two percent of the NAME validation sample met the definition of impaired cognitive function, based on MMSE scores less than or equal to 24. This large proportion allowed us to assess the data on the basis of a commonly used and clinically relevant cutoff score. Additionally, we had large proportions of subjects with clinical diagnoses of dementia (23%) and mild cognitive impairment (30%). While MMSE scores, and thus cognitive functioning, are known to be significantly lower in subjects with dementia, the two do not necessarily coexist in individuals. In our sample, 52% of the low-MMSE group was also clinically diagnosed with dementia, whereas 21% was clinically normal. Thus, we were able to assess the impact of cognitive functioning as well as clinical disease on the validity of the FFQ to estimate EPA and DHA intakes.

One important difference from previous validation studies of this FFQ was our use of interviewer administration. The NAME population was entirely composed of elderly home-care clients who had some degree of functional disability or chronic disease and a wide range of educational backgrounds. Proxy respondents were not utilized during data collection, since the majority of subjects (72%) lived alone. Interviewer administration was used to maximize the completeness of the FFQ data in all possible subgroups and to ensure that physical disability would not affect completion or mailing of the form. While our results cannot be generalized to populations in which the FFQ is self-administered, we expect that interviewer administration was one factor responsible for our consistently strong results across cognitive groups.

Limitations of our results include the inability to generalize our findings to more severely impaired persons. The low MMSE scores in our sample were indicative of only mild-to-moderate impairment (the range was 16–24 in the low group), while severe impairment is represented by MMSE scores closer to and below 10. However, we would not expect the FFQ to perform similarly well among severely impaired persons. Our use of a widely used cognitive screening tool, the MMSE, does allow our findings to be interpreted in many populations and research settings.

We were also limited by our use of a single fasting blood sample as a biomarker for long-term dietary intake. Plasma phospholipid fatty acid composition reflects dietary intake over the previous 1–2 months (39), and measurements at multiple time points would have better reflected long-term intake of dietary EPA + DHA and matched the time frame captured by the FFQ. However, because our analysis was an ancillary addition to an existing observational study, we were unable to obtain fatty acid profile data beyond the single blood drawing. Correlation coefficients observed in the current analysis may be underestimates of the true associations.

We confined our analyses to dietary very-long-chain omega-3 fatty acids. This decision was based upon the potential importance and utility of the results (direct measurement of fatty acid status in most research settings is not feasible), as well as the unique opportunity provided by the narrow distribution of these fatty acids in the food supply. The known relative differences in concentrations of very-long-chain omega-3 fatty acids between types of fish (i.e., fatty vs. lean) allowed us to explore possible differences in the self-reporting of information stored as generic memory (reporting a regular pattern of intake) as compared with episodic memory (recall of specific details of intake). Caution may be required when the analytic focus of research is an individual food item (i.e., a specific type of fish) rather than total estimated intake of a nutrient.

Our data suggest that interviewer administration of the FFQ may be a valid method of estimating EPA + DHA intake among community-dwelling elders regardless of the presence of mild-to-moderate cognitive impairment or a diagnosis of dementia. Whether this conclusion can be extended to other nutrient intakes is yet to be determined.

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