n–3 Fatty acid proportions in plasma and cognitive performance in older adults1–3

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ABSTRACT
Background: Very-long-chain n–3 polyunsaturated fatty acids (n–3 PUFAs) are suggested to be related to cognitive performance in older adults. However, limited data exist on the association between n–3 PUFAs and performance in specific cognitive domains.

Objective: We evaluated the association between plasma n–3 PUFA proportions and cognitive performance in 5 cognitive domains and determined whether plasma n–3 PUFA proportions predict cognitive change over 3 y.

Design: We used data from the FACIT trial, in which participants received folic acid or placebo capsules for 3 y. Fatty acid proportions in plasma cholesteryl esters at baseline were measured in 807 men and women aged 50–70 y. Cognitive performance for memory, sensorimotor speed, complex speed, information-processing speed, and word fluency was assessed at baseline and after 3 y. The cross-sectional analyses were based on all 807 participants; the longitudinal analyses were based only on 404 participants in the placebo group.

Results: Higher plasma n–3 PUFA proportions predicted less decline in sensorimotor speed (multiple linear regression coefficient, z score = 0.31; 95% CI: 0.06, 0.57) and complex speed (0.40; 95% CI: 0.10, 0.70) over 3 y. Plasma n–3 PUFA proportions did not predict 3-y changes in memory, information-processing speed, or word fluency. The cross-sectional analyses showed no association between plasma n–3 PUFA proportions and performance in any of the 5 cognitive domains.

Conclusions: In this population, plasma n–3 PUFA proportions were associated with less decline in the speed-related cognitive domains over 3 y. These results need to be confirmed in randomized controlled trials. 


KEY WORDS Cognitive performance, n–3 polyunsaturated fatty acids, n–3 fatty acids, cognitive decline, older adults

INTRODUCTION
A decline in cognitive performance over time is observed in the general elderly population (1). However, the extent and rate of this decline can vary considerably between individuals (1). There is increasing scientific interest in the hypothesis that very-long-chain n–3 polyunsaturated fatty acids (n–3 PUFA), as present in fish or fish oil, explain part of this interindividual variation and are beneficial for the maintenance of cognitive performance in adults.

Several observational studies, conducted among older adults, have examined the association between n–3 PUFAs and cognitive performance (2–9). Some authors have reported that lower dietary intake or lower plasma or erythrocyte proportions of n–3 PUFAs were indeed associated with cognitive impairment and cognitive decline (2–4, 8, 9); others have reported no such associations (5–7). Some of these studies also evaluated the association between fish consumption and cognitive performance and reported a lower risk of cognitive impairment (3) and slower cognitive decline (7, 8) or a trend toward a lower risk of cognitive decline (5) with increasing fish intakes. The inconsistency of these findings may be due to various factors: differences in sample size, heterogeneity of study populations, different methods of estimating n–3 PUFA intakes, or the wide variety of the applied cognitive tests.

Cognitive function in older adults declines with different rates in specific cognitive domains (10). Domain-specific information is valuable because it provides insight into the specific cognitive functions that may be associated with n–3 PUFAs. However, most of the studies in this field define a global measure of overall cognitive performance (2, 4–8), rather than report performance in specific cognitive domains separately. Cognitive deficits in a specific domain may or may not be detected by such generalized measures of cognitive performance, and this may explain the inconsistent results between studies.

Only 2 studies conducted in middle-aged persons have addressed the association between n–3 PUFAs and cognitive performance in different domains (3, 9). Beydoun et al (9) showed that higher proportions of plasma n–3 PUFA reduced the risk of decline in verbal fluency, whereas Kalmijn et al (3) showed that a higher intake of fatty fish and n–3 PUFAs was associated with a lower risk of impaired psychomotor speed. However, this latter

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study used dietary assessments to evaluate n−3 PUFA intake, a method that relies on accuracy of memories and awareness of food intake; no plasma fatty acid proportions were available. Moreover, because this study was solely cross-sectional, it was not possible to evaluate the association between n−3 PUFA consumption and cognitive change over time.

The present study assessed whether plasma n−3 PUFA proportions predict changes in cognitive performance over 3 y in 5 cognitive domains in older adults living in the Netherlands.

SUBJECTS AND METHODS

Subjects

For this study we used data from the FACIT study, a randomized placebo-controlled trial investigating the effect of folic acid supplementation on cognitive performance, carotid intima-media thickness, and hearing, which was approved by the Wageningen University Medical Ethics Committee (11). The baseline measurements, which included cognitive testing, were conducted between 2000 and 2001. In this study, 819 men and postmenopausal women aged 50–70 y were randomly assigned to either folic acid (n = 406) or placebo (n = 413) treatment for 3 y. Participants were originally included in this study if they had plasma total homocysteine concentrations ≥15 μmol/L and ≤26 μmol/L and serum vitamin B-12 concentrations ≥200 pmol/L.

In our analyses, we excluded 8 participants from whom insufficient amounts of blood could be obtained, 3 participants who did not give permission for the fatty acid analyses, and 1 participant who did not perform the cognitive tests, which resulted in a total of 807 participants.

Assessment of cognitive performance

Cognitive performance was assessed by using a concise battery of 5 cognitive tests. These tests are reported to be sensitive enough to detect small cognitive differences with aging (10, 12–16). These tests have no ceiling effect and are therefore presumed to be sensitive and robust in detecting cognitive impairment, even at middle age.

Concept Shifting Test

The Concept Shifting Test evaluates the ease of switching between 2 psychological concepts (16). On each of 4 test cards, 16 small circles are grouped in a larger circle. The small circles are either empty or contain a number or a letter and are randomly arranged in the larger circle. First, subjects were asked to cross out circles with numbers in chronologic order (subtask A), then circles with letters in alphabetical order (subtask B), and finally circles with either letters or numbers in chronologic and alphabetical order (subtask C). The final task was to cross out empty circles (subtask O). The time needed to complete each of the 4 tasks was recorded.

Stroop Color-Word Test

The Stroop Color-Word Test is considered to be a general measure of cognitive flexibility and executive functioning (12). Subjects were first asked to read the names of colors (subtask I) and subsequently to name color blocks (subtask II). Finally, participants were asked to name the color of the ink in which the words were printed, rather than reading the word (subtask III). The time needed to complete each of the 3 tasks was recorded.

Word Learning Test

The Word Learning Test evaluates the declarative memory, the part of the memory used for specific facts or experiences (13). Fifteen monosyllabic words in a fixed sequence were visually presented in 3 subsequent trials, with a recall procedure immediately following each presentation (immediate recall). Twenty minutes after the last trial, participants were again asked to recall the memorized words (delayed recall). In each trial, the number of correctly recalled words was recorded.

Letter Digit Substitution Test

The Letter Digit Substitution Test evaluates the general speed of visual information processing (14). Nine different letters are coupled with 9 different numbers in a key on top of the form. Participants were asked to copy the corresponding number by each letter as quickly as possible. The number of correctly filled in numbers in 90 s was recorded.

Verbal Fluency Test

The Verbal Fluency Test measures the ability to recollect as many words in a specific category as possible from memory (15). Participants were asked to name as many animals as possible in 60 s. The number of different animal names was recorded.

To compare the results of the different cognitive tests, we transformed the raw test scores of all participants into z scores: $z = \frac{x - \bar{x}}{S}$.

For the cross-sectional analyses, we used the means and SDs of the baseline scores to calculate the z scores. For the longitudinal analyses, the means and SDs at baseline and at follow-up were pooled to calculate the grand mean ± SD per test; this grand mean ± SD was used to calculate z scores at both time points. This latter step was necessary because both the follow-up scores and the baseline scores are included in the statistical model and therefore have to refer to the same z distribution.

The z scores were clustered into 5 cognitive domains, which had been established a priori; they were denoted as sensorimotor speed, complex speed, memory, information-processing speed, and word fluency (11). Sensorimotor speed was calculated by averaging the z scores on the O, A, and B subtests of the Concept Shifting Test and subtest I of the Stroop Color-Word Test. Complex speed was composed of subtest C of the Concept Shifting test and subtest III of the Stroop Color-Word test. Signs of sensorimotor speed and complex speed scores were inverted so that they reflected above average performance if positive and below average performance if negative. Memory was calculated by averaging the z scores of the total, maximum, and delayed recall scores of the Word Learning Test. Information-processing speed was composed of the z score of the Letter Digit Substitution test, and word fluency was composed of the z score of the verbal fluency test.

The cognitive tests were derived from the Maastricht Aging Study, a prospective study on the determinants of cognitive aging (17). Additionally, we included the Mini-Mental State Examination (MMSE) (18). The MMSE was not one of our outcome measures, but we used it to compare our study population with other study populations and to enable the exclusion of persons with suspected dementia (score: <24 points). We adopted this widely used cutoff point, because population studies investigating the MMSE as a screening test for dementia reported this cutoff point to be a good compromise between sensitivity and specificity (19, 20).
Trained research assistants administered the cognitive tests during a 40-min session using standard test protocols. All participants performed the tests after an overnight fast followed by a standardized breakfast without coffee or tea. Cognitive testing was repeated after 3 y by using parallel versions of the tests used at baseline to prevent learning effects. We did not use a parallel version of the Verbal Fluency Test, because a valid parallel version of this test is not available.

Assessment of plasma n–3 PUFAs

Venous blood was collected after an overnight fast in one 10-mL Vacutainer tube (Becton Dickinson and Co., Franklin Lakes, NJ) containing EDTA as anticoagulant. The samples were centrifuged, and the obtained plasma was stored within 2 h at −80 °C until analyzed. Fatty acids in plasma cholesteryl esters were measured as described previously (21). We calculated plasma n–3 PUFAs by adding up the proportions of eicosapentaenoic acid (EPA), docosapentaenoic acid, and docosahexaenoic acid (DHA).

Assessment of potential confounders

Participants completed questionnaires on demographic variables, which were reviewed by a research assistant in the presence of the participant. Level of education was divided into 3 groups according to the highest level attained: primary education, junior vocational training, and senior vocational or academic training. We assessed alcohol and fish consumption during the preceding 3 mo with a food-frequency questionnaire and estimated physical activity using the Physical Activity Scale for the Elderly. Height and weight were measured to calculate body mass index (in kg/m²). The ApoE genotype was determined by the polymerase chain reaction–based restriction fragment length polymorphism method and restriction enzyme digestion with Hha I. The apolipoprotein ε4 allele is involved in neuropathology and is the major known genetic risk factor for Alzheimer disease (22). We divided ApoE genotype according to the absence of the apolipoprotein ε4 allele or the presence of 1 or 2 apolipoprotein ε4 alleles.

Statistical analyses

We assessed the association between n–3 PUFAs and cognitive performance with multiple linear regression analysis, with possible confounders based on previously published associations and associations with exposure and outcomes (change in the β coefficient ≥ 10%) in the current data set. We applied base-10 logarithmic transformation of n–3 PUFAs concentrations, because the distribution was skewed to the right. Logarithmic transformation disabled interpretation on a ratio scale and implied interpretation in terms of 10-fold multiplications.

Longitudinal analyses

We present the longitudinal association between n–3 PUFAs and cognitive performance after 3 y only for the 404 participants that received placebo capsules, because the folic acid treatment has been shown to improve performance in memory, information-processing speed, and sensorimotor speed (11) and appeared to be an effect modifier in our data set. We used one-sample t tests to determine whether cognitive performance significantly changed over 3 y. We used multiple linear regression analysis to investigate the association between n–3 PUFAs concentrations (independent) measured at baseline and cognitive performance in z scores (dependent) in 5 different domains after 3 y, with adjustment for baseline cognitive performance scores. We examined whether potential confounders (age, sex, level of education, erythrocyte folate concentrations, alcohol intake, physical activity, smoking, body mass index, number of apolipoprotein ε4 alleles, depression, diabetes mellitus, and cardiovascular disease) were associated both with plasma n–3 PUFAs and cognitive performance and substantially attenuated the association when added to the model. The final model was adjusted for age, sex, level of education (3 categories), erythrocyte folate concentrations, and alcohol intake. We chose to correct for baseline cognitive performance in contrast with calculating change scores, because change scores do not control for baseline imbalances and may therefore lead to regression-to-the-mean (23). Nevertheless, analysis of the change scores yielded similar results with regard to the P values.

Cross-sectional analyses

We used multiple linear regression analyses to investigate the association between n–3 PUFAs concentrations (independent) and cognitive performance in z scores (dependent) at baseline in the 5 different cognitive domains. We evaluated the same potential confounders as in the longitudinal analyses, and the final model was adjusted for age, sex, level of education (3 categories), erythrocyte folate concentrations, and alcohol intake.

Statistical significance was defined as \( P < 0.05 \). The statistical analyses were conducted by using SAS version 9.1.3 (Statistical Analysis Software; SAS Institute, Cary, NC).

RESULTS

The mean age of the participants was 60 y at baseline, 72% of the participants were male, 77% of the participants completed junior/senior vocational training or academic training, and the median alcohol intake was approximately one drink per day. The geometric mean plasma n–3 PUFA proportion was 1.57% of total fatty acids, with an interquartile range of 1.18–2.04% of total fatty acids. The median MMSE score at baseline was 29, and the range was 15–30 points (Table 1). Seven participants scored <24 out of 30 points on the MMSE. However, the exclusion of these 7 participants did not substantially change the results; hence, we present all results including these subjects. There were no differences in baseline characteristics of participants between the cross-sectional and the longitudinal analyses. The fatty acid profiles of the participants are shown in Table 2.

Change in cognitive performance over 3 y (longitudinal analyses)

Four participants did not return for the cognitive measurements after 3 y, because they died (\( n = 2 \)) or suffered from severe illnesses (\( n = 2 \)). Sensorimotor speed, complex speed, and information-processing speed declined significantly over 3 y. The mean (±SD) 3-y change in z scores was \(-0.10 \pm 0.46\) for sensorimotor speed, \(-0.07 \pm 0.53\) for complex speed, and \(-0.15 \pm 0.51\) for information-processing speed. Participants improved on memory over 3 y; the mean (±SD) 3-y change in z scores was \(0.34 \pm 0.73\) for memory, because of procedural learning effects (Table 3).
Higher concentrations of plasma n−3 PUFA concentrations significantly predicted less decline over 3 y in cognitive performance scores in the domains of sensorimotor speed and complex speed (Table 3). The change in sensorimotor speed improved by a z score of 0.31 (95% CI: 0.06, 0.57) for each 1% change in log-transformed n−3 PUFA proportions. This translates to an improvement in z score of 0.31 for every 10-fold multiplication in n−3 PUFA proportions. For example, this implies that a person with 2.0% n−3 PUFA of total fatty acid proportions in plasma has 9% less decline in sensorimotor speed than does a person with 1.0% n−3 PUFA of total fatty acids in plasma. The change in complex speed improved with a z score of 0.40 (95% CI: 0.10, 0.70) for every 10-fold multiplication in n−3 PUFA concentrations. This corresponds to an increase in z score of 0.12 for every doubling in n−3 PUFA proportions. This implies that a person with 2.0% n−3 PUFA of total fatty acid proportions in plasma has 12% less decline in complex speed than does a person with 1.0% n−3 PUFA of total fatty acids in plasma. Thus, higher plasma n−3 PUFA concentrations at baseline predicted less decline in scores of sensorimotor speed and complex speed over 3 y. These associations were present after adjustments for baseline cognitive performance, age, sex, level of education, erythrocyte folate status, and alcohol consumption. n−3 PUFA concentrations at baseline did not predict changes in memory (regression coefficient: 0.17; 95% CI: −0.23, 0.57), information-processing speed (0.14; −0.14, 0.42), or word fluency (0.36; −0.10, 0.82) over 3 y (Table 3). The results were similar when we evaluated the association between plasma DHA concentrations and 3-y cognitive change in all 5 cognitive domains (data not shown). Furthermore, plasma proportions of n−6 PUFAs (the sum of linoleic acid, γ-linolenic acid, and arachidonic acid) did not predict 3-y changes in any of the 5 cognitive domains (data not shown).

Cognitive performance (cross-sectional analyses)

Multiple linear regression analysis showed no significant linear associations between plasma n−3 PUFA concentrations and performance in any of the 5 cognitive domains. Higher plasma n−3 PUFA proportions were not significantly associated with better performance in sensorimotor speed (regression coefficient: 0.01; 95% CI: −0.26, 0.29), complex speed (0.07; −0.24, 0.38), memory (0.20; −0.15, 0.55), information-processing speed (0.04; −0.32, 0.41), or word fluency (0.18; −0.20, 0.57) after adjustments for age, sex, level of education, erythrocyte folate concentrations, and alcohol consumption (Table 4). The results were similar when we evaluated the association between plasma DHA concentrations and cognitive performance in all 5 cognitive domains (data not shown). Furthermore, plasma proportions of n−6 PUFAs (the sum of linoleic acid, γ-linolenic acid, and arachidonic acid) were not significantly associated with cognitive performance at baseline in any of the 5 cognitive domains (data not shown).

DISCUSSION

This study among older adults showed that higher plasma proportions of n−3 PUFA significantly predicted less decline in the sensorimotor speed and complex speed cognitive domains over 3 y than did lower proportions of n−3 PUFAs. We observed
no significant associations between plasma n–3 PUFA proportions and 3-y changes in memory, information-processing speed and word fluency. The cross-sectional analyses showed no significant associations between plasma n–3 PUFA proportions and performance in any of the 5 cognitive domains.

A major strength of our study is that we assessed cognitive performance longitudinally using an extensive cognitive battery under standardized test conditions. This battery is reported to be sensitive enough to detect small cognitive differences in this age range (10, 12–16), and it provided us with specific information on performance in various cognitive domains. These are 2 important advantages compared with commonly used dementia screening tools, such as the MMSE. A second strength is that we used plasma cholesteryl ester proportions of n–3 PUFA as a marker of dietary intake. Plasma cholesteryl ester proportions are generally considered an objective and valid estimate of the dietary intake of fatty acids during the prior weeks (24) and have the advantage of taking individual absorption into account (25).

Moreover, additional data on dietary intake of fish from a food-frequency questionnaire indicated that baseline dietary fish intake correlated well with dietary fish intake after 3 y (Spearman correlation coefficient: 0.79; P < 0.001). Therefore, we assume that participants did not change their dietary intake of fish, and n–3 PUFA proportions in plasma were stable over this period. Finally, close follow-up of the subjects reduced the chance of missing values on outcome variables; only 4 participants (1%) in the placebo group did not return for the cognitive function measurements after 3 y.

A possible limitation of this study was that the participants did not represent a random sample of the Dutch older adult population. We performed observational analyses in a population that was selected specifically for participation in a randomized controlled trial. Hence, selective participation may have affected the generalizability of our results. Our participants had relatively high plasma homocysteine concentrations and low serum vitamin B–12 concentrations. Therefore, it could be possible that they represent a group of people with relatively unhealthy dietary habits, such as a lower dietary intake of fish. However, the range of plasma n–3 PUFA proportions in our study population was comparable with that of other large studies in older adult populations (25, 26). Furthermore, although we used an extensive test battery to assess cognitive performance, we cannot exclude the possibility that a more detailed cognitive assessment might have revealed associations undetected by the current tests.

We observed that higher plasma proportions of n–3 PUFA significantly predict less decline in scores of sensorimotor speed and complex speed over 3 y; however, this finding was not confirmed in the cross-sectional analyses. One could argue that the inconsistency between the cross-sectional and the longitudinal findings may be explained by differences between the populations because the longitudinal analyses were performed in the placebo group only. However, there were no differences in the baseline characteristics of the participants in cross-sectional and longitudinal analyses. Moreover, the cross-sectional analyses still yielded no associations when restricted to the placebo group only.

Because our analyses were performed in a population of normal aging participants with no signs of cognitive disorder or dementia (with the exception of 7 participants with an MMSE score <24), it is difficult to determine whether an improvement of 9% in sensorimotor speed and 12% in complex speed for every doubling in plasma n–3 PUFA proportions is clinically relevant. Moreover, there is considerable debate in the literature about whether or not cognitive decline is the beginning of a broad spectrum of cognitive changes leading to dementia. To determine the relevance of our findings, we considered our results along with those from other observational studies in comparable populations (Table 5). Our longitudinal associations are in line with earlier findings by Morris et al (7), in which the annual rate

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### Table 3

Results of the longitudinal analyses: change in cognitive performance over 3 y (left side of dotted line) and differences in 3-y cognitive change per 10-fold multiplication in plasma cholesteryl ester n–3 polyunsaturated fatty acid concentrations (right side of dotted line) in 400 Dutch older adults.

<table>
<thead>
<tr>
<th>3-y Change in Cognitive Performance</th>
<th>Regression Coefficient (95% CI)</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Performance at baseline</td>
<td>Performance after 3 y</td>
<td>P</td>
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<table>
<thead>
<tr>
<th>Cognitive domains</th>
<th>Regression coefficient (95% CI)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Sensorimotor speed (z score)²</td>
<td>0.02 ± 0.84</td>
<td>0.02</td>
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<tr>
<td>Complex speed (z score)⁴</td>
<td>0.00 ± 0.88</td>
<td>0.00</td>
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<tr>
<td>Memory (z score)</td>
<td>−0.21 ± 0.88</td>
<td>−0.14 ± 0.10</td>
</tr>
<tr>
<td>Information-processing speed (z score)²</td>
<td>0.03 ± 1.01</td>
<td>0.00 ± 0.95</td>
</tr>
<tr>
<td>Word fluency (z score)</td>
<td>0.03 ± 1.01</td>
<td>0.00 ± 0.95</td>
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</table>

¹ Left side of dotted line: change in cognitive performance over 3 years was tested with one-sample t tests. Right side of dotted line: multiple linear regression analyses, adjusted for baseline cognitive performance, age, sex, level of education, erythrocyte folate concentrations, and alcohol consumption.
² Data were available for 399 participants.
³ Data were available for 395 participants.
⁴ Data were available for 391 participants.
⁵ Data were available for 390 participants.

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### Table 4

Results of the cross-sectional analyses: differences in cognitive performance per 10-fold multiplication in plasma cholesteryl ester n–3 polyunsaturated fatty acid concentrations in 807 Dutch older adults.

<table>
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<tr>
<th>Cognitive domains</th>
<th>Regression coefficient (95% CI)</th>
<th>P</th>
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</table>

1 Multiple linear regression analyses, adjusted for age, sex, level of education, erythrocyte folate concentrations, and alcohol consumption.
2 Data available for 800 participants.
3 Data available for 801 participants.
4 Data available for 804 participants.
of overall cognitive decline was reduced by 10–13% in persons who consumed one or more fish meals per week compared with those with a less than weekly consumption. Furthermore, 2 reports from the Zutphen Elderly study reported less cognitive decline with high fish consumption (5, 8), although these findings were not statistically significant in one of these studies (5).

Two other studies have examined the role of n-3 PUFAs in cognitive performance in older adult populations in observational and intervention studies with sensitive cognitive outcome measurements that provide domain-specific information (37). These studies should preferably be conducted with sensitive cognitive test batteries. However, in the latter 2 studies, the number of participants experiencing cognitive decline was small. A recent study by Beydoun et al (9) showed that higher plasma concentrations of n-3 PUFAs reduced the risk of decline in verbal fluency but not in psychomotor speed or memory. Therefore, more observational studies in this population within a normal range of plasma n-3 PUFA concentrations using an extensive battery of cognitive tests are welcome to verify the direction and size of the association. Subsequently, randomized controlled trials with n-3 PUFA supplementation should help to clarify the importance of the observed associations.

One way to describe the predictive value of n-3 PUFAs in affecting cognitive changes is to express it in terms of another predictor in the linear regression model, such as chronologic age. For example, we can calculate the average number of years that participants are cognitively younger by using the ratio between the regression coefficients associated with the plasma n-3 PUFA concentrations and age in years (10). Thus, a doubling in plasma n-3 PUFA concentrations in our statistical model gives a person a hypothetical 3-y decline in cognitive performance of someone 4.5 y younger for sensorimotor speed (0.09/−0.02 = −4.5 y) or 12 y younger for complex speed (0.12/−0.01 = −12 y). However, we have to keep in mind that these regression equations are derived from observational data; therefore, we can make no direct inferences on causality. Moreover, these numbers are reflective of our specific population only.

We have shown in a population of Dutch older adults that higher plasma proportions of n-3 PUFAs are associated with less decline in 3-y cognitive performance in sensorimotor speed and complex speed but not in memory, information-processing speed, and word fluency. Further examination of the role of n-3 PUFA concentrations in cognitive performance in older adult populations in observational and intervention studies seems justified. These studies should preferably be conducted with sensitive cognitive outcome measures that provide domain-specific information.

The authors’ responsibilities were as follows—CD: analyzed and interpreted the data, directed the blood sample assays, and drafted the manuscript; JD, PV, and OvdR: designed the FACIT study and collected the data; JD,

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**TABLE 5**

Cross-sectional and longitudinal studies examining the association between n-3 polyunsaturated fatty acids (PUFAs) and cognitive performance in older adults

<table>
<thead>
<tr>
<th>First author</th>
<th>Study population</th>
<th>n-3 PUFA</th>
<th>Cognitive tests</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-sectional studies</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Conquer et al (2)</td>
<td>Cognitive impairment (n = 36); no cognitive impairment (n = 19); age: 77–83 y</td>
<td>Plasma phospholipids</td>
<td>1 SD below age norm on 6 tests</td>
<td>Lower n-3 PUFA concentrations in cognitively impaired group</td>
</tr>
<tr>
<td>Kalmijn et al (3)</td>
<td>Cognitive impairment (n = 163); no cognitive impairment (n = 1450); age: 45–70 y</td>
<td>FFQ</td>
<td>Lowest 10% on overall cognition, speed, flexibility, memory</td>
<td>Higher n-3 PUFA and fish intakes associated with lower risk of overall cognitive impairment and speed</td>
</tr>
<tr>
<td>Kalmijn et al (5)</td>
<td>Cognitive impairment (n = 153); no cognitive impairment (n = 323); age: 64–89 y</td>
<td>Dietary history method</td>
<td>MMSE (cutoff score ≤25)</td>
<td>n-3 PUFA and fish intakes not associated with cognitive impairment</td>
</tr>
<tr>
<td>Laurin et al (6)</td>
<td>Cognitive impairment (n = 43); no cognitive impairment (n = 79); age: ≥65 y</td>
<td>Plasma phospholipids</td>
<td>Diagnosis based on Zaudig’s criteria</td>
<td>No difference in n-3 PUFA concentrations between groups</td>
</tr>
<tr>
<td>van Gelder et al (8)</td>
<td>Elderly men (n = 210); age: 70–89 y</td>
<td>Dietary history method</td>
<td>MMSE</td>
<td>No difference in cognition between categories of fish consumers</td>
</tr>
<tr>
<td>Longitudinal studies</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Kalmijn et al (5)</td>
<td>Cognitive decline (n = 51); no cognitive decline (n = 291); age: 64–89 y; follow-up: 3 y</td>
<td>Dietary history method</td>
<td>MMSE (drop &gt;2 points)</td>
<td>n-3 PUFA and fish intakes not associated with cognitive decline</td>
</tr>
<tr>
<td>Laurin et al (6)</td>
<td>Incident cognitive impairment (n = 16); no cognitive impairment (n = 52); age: ≥65 y, follow-up: ≥5 y</td>
<td>Plasma phospholipids</td>
<td>Diagnosis based on Zaudig’s criteria</td>
<td>n-3 PUFA concentrations not different between groups. Higher EPA concentrations in cognitive impaired group</td>
</tr>
<tr>
<td>Heude et al (4)</td>
<td>Cognitive decline (n = 27); no cognitive decline (n = 219); age: 63–74 y; follow-up: ≥5 y</td>
<td>Erythrocyte membranes</td>
<td>MMSE (drop ≥2 points)</td>
<td>Higher n-3 PUFA concentrations associated with lower risk of cognitive decline</td>
</tr>
<tr>
<td>Morris et al (7)</td>
<td>Community residents (n = 3718); age: ≥65 y; follow-up: 6 y</td>
<td>FFQ</td>
<td>Sum of scores on 4 tests</td>
<td>Higher fish intake, but not n-3 PUFA intake, associated with slower cognitive decline</td>
</tr>
<tr>
<td>van Gelder et al (8)</td>
<td>Elderly men (n = 210); age: 70–89 y; follow-up: 5 y</td>
<td>Dietary history method</td>
<td>MMSE</td>
<td>Higher fish intake and n-3 PUFA intake associated with slower cognitive decline</td>
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<tr>
<td>Beydoun et al (9)</td>
<td>Cognitive decline (n = 140); no cognitive decline (n = 2111); age: 50–65 y; follow-up: 6 y</td>
<td>Plasma phospholipids and cholesteryl esters</td>
<td>RCI &lt; −1.645 on overall cognition, memory, psychomotor speed, verbal fluency</td>
<td>Higher n-3 PUFA concentrations associated with lower risk of decline in verbal fluency</td>
</tr>
</tbody>
</table>

1 EPA, eicosapentaenoic acid; FFQ, food-frequency questionnaire; MMSE, Mini-Mental State Examination; RCI, reliable change index.
2 Results adjusted for confounding factors as reported in original article.
5 East Boston tests of immediate and delayed recall, MMSE, and Symbol Digit Modalities Test.

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REFERENCES


