Cognitive performance among the elderly and dietary fish intake: the Hordaland Health Study¹–³

Eha Nurk, Christian A Drevon, Helga Refsum, Kari Solvoll, Stein E Vollset, Ottar Nygård, Harald A Nygaard, Knut Engedal, Grethe S Tell, and A David Smith

ABSTRACT
Background: Increasing evidence suggests that cognitive impairment and dementia in older subjects might be influenced by a diet including seafood.
Objective: The objective was to examine the cross-sectional relation between intake of different amounts of various seafood (fish and fish products) and cognitive performance.
Design: The subjects (n = 2031 subjects; 55% women), aged 70–74 y, were recruited from the general population in Western Norway and underwent cognitive testing. A cognitive test battery included the Kendrick Object Learning Test, Trail Making Test (part A), modified versions of the Digit Symbol Test, Block Design, Mini-Mental State Examination, and Controlled Oral Word Association Test. Poor cognitive performance was defined as a score in the highest decile for the Trail Making Test and in the lowest decile for all other tests.
Results: Subjects whose mean daily intake of fish and fish products was ≥10 g/d (n = 1951) had significantly better mean test scores and a lower prevalence of poor cognitive performance than did those whose intake was <10 g/d (n = 80). The associations between total intake of seafood and cognition were strongly dose-dependent; the maximum effect was observed at an intake of ≈75 g/d. Most cognitive functions were influenced by fish intake. The effect was more pronounced for nonprocessed lean fish and fatty fish.
Conclusions: In the elderly, a diet high in fish and fish products is associated with better cognitive performance in a dose-dependent manner. Am J Clin Nutr 2007;86:1470–8.

KEY WORDS Cognitive deficit, cognition, elderly, fish, fish oils, processed fish, seafood

INTRODUCTION
Modern studies of the role of nutrition in cognition among the elderly began in the 1980s and were reviewed by Rosenberg and Miller (1). In 1997 Grant (2) highlighted the possible role of diet in the development of Alzheimer disease (AD). After the initiation of large-scale observational epidemiologic studies in the Netherlands in the 1990s (3), it was suggested that the intake of fish might protect the elderly from developing cognitive impairment or dementia (4, 5). This idea has been supported by several independent studies (2, 6–12) that have led to a debate about whether modification of the diet might be one way to prevent cognitive decline and dementia in the elderly (13, 14). It is clearly important to resolve the question of whether such a relatively simple change in lifestyle as eating more fish can reduce the burden on the individual and on society of cognitive decline and dementia in the elderly (15). Although intervention studies ultimately will be required to answer this question, it is possible to test some hypotheses by additional observational studies.

The purpose of this cross-sectional study on community-dwelling elderly people was to seek answers to the following questions: 1) Is the intake of fish and fish products associated with better cognitive performance? 2) Is dietary intake of seafood associated with the performance of all, or only some, cognitive abilities? 3) Is there any relation between the type of seafood product consumed and cognitive test results? and 4) Is there any relation between the amount of fish consumed and cognitive test results? We had the opportunity to examine these issues among >2000 elderly men and women, who represented a subset of subjects within the Hordaland Health Study (HUSK).

SUBJECTS AND METHODS
Study population
The HUSK study was conducted from 1997 to 1999 as a collaboration between the University of Bergen, University of Oslo, local health services, and the Norwegian Institute of Public Health. In a subsample of the study, 4338 individuals born in 1925–1927 who had participated in the Hordaland Homocysteine Study (16) in 1992–1993, were invited to participate in HUSK to examine age effects. Recruitment into the Cognitive Substudy is described on the Web (Internet: www.uib.no/isf/husk).
Association Test (access to semantic memory) (23) is a test of
Abridged version of the Controlled Oral Word Association
with cognitive impairment (22).

as the full version when the purpose is to identify elderly subjects
memory, backward spelling, and performing a 3-stage command
repeating, writing, copying, instantaneous recall, short-term
(m-MMSE; global cognition) (21) covers various aspects of cog-
ceptual speed) (20) is regarded as a measure of focused attention,

Modified version of the Digit Symbol Test
The modified version of the Digit Symbol Test (m-DST; per-
ceptual speed) (20) is regarded as a measure of focused attention, visuo
motor coordination, and psychomotor speed. In the present
version, the number of correct matches between digits and sym
bols in 30 s was recorded.

Block Design
The Block Design (m-BD; visuospatial skills) (20) tests visuo
spatial and motor skills. The short form, used in the present study,
cluded 4 of the 10 patterns (patterns 1, 2, 5, and 6) in the full test.
Every correct matching gives 4 points; thus, a possible maximum score
on the m-BD short form is 16.

Modified version of the Mini-Mental State Examination
A modified version of the Mini-Mental State Examination
(m-MMSE; global cognition) (21) covers various aspects of cog
nitive function, including orientation to time and place, naming,
repeating, writing, copying, instantaneous recall, short-term
memory, backward spelling, and performing a 3-stage command
(22). The m-MMSE consists of 12 of the 20 items in the full
version of the MMSE and has been shown to be just as effective
as the full version when the purpose is to identify elderly subjects
with cognitive impairment (22).

Abridged version of the Controlled Oral Word Association
Test
The abridged version (S-task) of the Controlled Oral Word
Association Test (access to semantic memory) (23) is a test of
verbal fluency and psychomotor speed. The subjects were re
quired to generate as many words as possible beginning with the
letter S within 60 s. The maximum possible score is theoretically
infinite; in our subjects it was 39.

Dietary habits
To assess habitual food consumption, a modified version of a
comprehensive food-frequency questionnaire created at the De
partment of Nutrition, University of Oslo (24, 25), was handed
out on the day of the examination and filled out later at home by
the participants and then mailed to the HUSK Project Centre in
Bergen. The questionnaire included 169 food items that were
grouped according to Norwegian meal patterns. It was designed
to obtain information on usual food intake during the past year.
The frequency of consumption was given per day, week, or
month. The portion sizes were given as household measures or
units such as slices or pieces.

Fish intake included sandwich spread and fish intake as a part
of a main meal. Questions related to sandwich spread were as
follows: How many slices of bread with the following spreads do
you eat per week: tinned mackerel in tomato paste, smoked
mackerel, pilchard, pickled herring, anchovies or similar fish,
salmon, or trout? All these questions had 11 categories (0, 0.5, 1,
Questions related to fish intake as a main meal were 2-fold,
related to frequency of intake and to the typical amount of intake
per meal. The frequency of fish intake included 9 categories (0,
<1, 1, 2, 3, 4, 5–6, 7–8, and ≥9 times/mo). The amount of fish
intake was categorized into 5 categories that differed according
to type of product: fishcakes, fish pudding, and fish balls (from
1 to ≥5 units); fish fingers (from 1–2 to ≥10 pieces); boilded cod,
coalfish, and haddock (from 1 to ≥5 pieces); fried cod, coalfish,
or haddock (from 1 to ≥5 pieces); fresh, salt-cured, or smoked
herring (from 1 to ≥5 fillets); fresh or smoked mackerel (from
0.5 to ≥3 fillets); salmon or trout (both wild and farmed) (from
1 to ≥5 steaks); and fish stew, fish soup, and fish au gratin (from
1–2 to ≥9 dl). In the data analyses, the main meal was divided
into 3 different categories: fatty fish (herring, mackerel, salmon,
and trout), lean fish (cod, coalfish, and haddock), and processed
fish (fish cakes, fish pudding, fish balls, fish fingers, fish stew,
fish soup, and fish au gratin). The last category, “processed fish,”
is imprecise in terms of nutritional value.

The questionnaire also included questions about dietary sup
plement intake, in which the product names of the most used
supplements in Norway were considered. Use of cod liver oil and
fish oil was reported as “seasonal use” (during the whole year or
only winter half of the year), frequency per week, and amount per
time.

Dichotomous variables were created for different types of fish
and fish products. Individuals who reported use of certain prod
ucts in the abovementioned categories were considered as users,
whereas all those who reported that they never ate that product
were considered nonusers. To identify the individuals who never
ate any fish and fish products (including fish either as sandwich
spread or as part of main meals, cod liver oil, and other fish oils),
all dichotomous variables were combined. The amount of fish
and fish products in grams per day was calculated by using a food
database and software system developed at the Department of
Nutrition, University of Oslo (Kostberegningssystem, version
3.2; University of Oslo, Oslo, Norway). Calculations of total
intake of fish and fish products also included intake of cod liver
of CVD (limited to some important CVD variables), and tHcy were cofactors.

For comparison between the groups of fish and fish product intake, the chi-square test or the univariate analysis of variance was used. Adjusted mean cognitive scores by intake of various types of seafood were obtained from the univariate analysis of variance. Multinomial logistic regression analysis (adjusted for the same variables) with fish and fish products intake as the independent variable, and the number of tests with poor results as the dependent variable, was applied to find risk ratios for poor cognitive performance by using subjects without poor test performance as the reference group. Gaussian generalized additive regression models, as implemented in S-PLUS 6.2 for WINDOWS (Insightful Corporation, Seattle, WA), were used to generate graphic representations of the dose-response relations, with the use of both models. On the y axis, the model generated a reference value of zero that approximately corresponds to the value of cognitive test score associated with the mean of the average total fish intake in grams per day for all subjects. Multiple linear regression analyses were used to examine significant associations between the cognitive test scores and average of total fish intake. Except for generalized additive models, all statistical analyses were performed by using the STATISTICAL PACKAGE FOR THE SOCIAL SCIENCES 12.0 for WINDOWS (SPSS Inc, Chicago, IL). P values <0.05 were considered significant.

RESULTS

Our study population had an overall high fish intake. Only 2% reported that they never ate fish and fish products (Table 1). The mean total intake of fish and fish products among consumers was

<table>
<thead>
<tr>
<th>Type of fish and fish product</th>
<th>Prevalence (n = 2031)</th>
<th>Mean intake (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish sandwich†</td>
<td>1314 (64.7)</td>
<td>16.0 (14.9, 17.1)</td>
</tr>
<tr>
<td>Main meal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatty fish‡</td>
<td>1579 (77.7)</td>
<td>18.6 (17.7, 19.6)</td>
</tr>
<tr>
<td>Lean fish§</td>
<td>1852 (91.2)</td>
<td>39.3 (38.0, 40.6)</td>
</tr>
<tr>
<td>Processed fish¶</td>
<td>1893 (93.2)</td>
<td>16.9 (16.4, 17.5)</td>
</tr>
<tr>
<td>Any type of fish as part of a main meal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>65 (3.2)</td>
<td>—</td>
</tr>
<tr>
<td>≤1 time/mo</td>
<td>8 (0.4)</td>
<td>—</td>
</tr>
<tr>
<td>2–3 times/mo</td>
<td>51 (2.4)</td>
<td>—</td>
</tr>
<tr>
<td>1 time/wk</td>
<td>45 (2.2)</td>
<td>—</td>
</tr>
<tr>
<td>&gt;1 time/wk</td>
<td>1862 (91.8)</td>
<td>—</td>
</tr>
<tr>
<td>Cod liver oil and fish oil</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Winter half year</td>
<td>397 (19.5)</td>
<td>2.6 (2.4, 2.8)</td>
</tr>
<tr>
<td>All year round</td>
<td>436 (21.5)</td>
<td>5.6 (5.2, 5.9)</td>
</tr>
<tr>
<td>All fish and fish products combined</td>
<td>1990 (98.0)</td>
<td>85.4 (83.0, 87.8)</td>
</tr>
</tbody>
</table>

† Mackerel, pilchard, pickled herring, anchovies, salmon, or trout as a sandwich spread.
‡ Herring, mackerel, salmon, or trout as part of a main meal.
§ Cod, coalfish, or haddock as part of a main meal.
¶ Fish balls, fish cakes, fish fingers, fish stew, fish soup, or fish au gratin as part of a main meal.

The study population had an overall high fish intake. Only 2% reported that they never ate fish and fish products (Table 1). The mean total intake of fish and fish products among consumers was
Comparison of subjects who reported consumption of seafood with those who did not

Because the number of subjects who never ate fish and fish products was small (n = 41), we also included those with a low total intake (<10 g/d) in the group defined as “nonconsumers.” Characteristics of the study population by intake of any type of fish and fish products are presented in Table 2. The proportions of women and subjects with low education (≤9 y) were significantly higher among subjects who consumed <10 g/d of any type of fish or fish product. The mean scores on all 6 cognitive tests were significantly better for those who ate any type of fish or fish product. The prevalence of poor cognitive performance was 2–3 times lower in those who reported eating seafood than in those who did not report eating seafood, independent of the cognitive test used. The proportion of subjects with poor scores on more than one cognitive test was greater in subjects who did not eat fish and fish products (27%) than in those who did (11%; P < 0.001).

In multivariate models including adjustments for sex, ApoE ε4 variant allele, education, history of some important CVD variables, and thcy, the overall results changed moderately (data not shown), but because of missing data the significance was reduced for mean test scores (Table 2).

Compared with users of fish and fish products, the nonusers had a somewhat poorer health status. The prevalence of several diseases was significantly higher among those who did not eat fish and fish products than among those who did (epilepsy: 5.5% compared with 0.8%, P = 0.015; asthma: 19.5% compared with 9.1%, P = 0.005; chronic bronchitis: 14.5% compared with 6.7%, P = 0.036; and osteoporosis: 20.3% compared with 11.0%, P = 0.034). We found no significant differences in the prevalence of history of some important CVD variables, diabetes, renal diseases, liver diseases, arthritis, thyroiditis, depression, psoriasis, or some other skin diseases between those who reported eating and those not eating fish and fish products (data not shown).

Cognitive scores in relation to type of fish and fish products

We studied the associations between cognitive performance and the main types of consumed seafood, ie, fatty fish, lean fish, processed fish, fish sandwich, and fish or cod liver oil. The adjusted mean cognitive test scores by different types of fish and fish products intake are presented in Table 3. Subjects who ate fatty fish or lean fish as their main meal performed significantly better in 5 of the 6 tests than did those who did not eat fatty fish or lean fish. Intake of processed fish as part of a main meal was associated with significantly better mean scores in 3 cognitive tests: KOLT, m-BD, and m-MMSE. Similarly, those who ate fish sandwiches performed better on 3 tests (m-DST, m-BD, and S-task). In contrast, those who ate fish oils performed better only in the S-task.

Dose-response relations between intake of seafood and cognitive function

In this population there were very few subjects who did not eat any type of fish or fish products. However, there was a considerable range in the amounts of fish eaten, which allowed us to

### Table 2

<table>
<thead>
<tr>
<th>Characteristics of the participants by intake of any type of seafood (fish and fish products)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intake of any type of seafood</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Sex (male)</td>
</tr>
<tr>
<td>Education ≤9 y</td>
</tr>
<tr>
<td>KOLT score</td>
</tr>
</tbody>
</table>
| Poor test score, ≤25
| TMT-A score                                    | 1944     | 55.7 (54.2, 57.2) | 80              | 66.9 (59.7, 74.2) |
| Poor test score, ≥111
| m-DST score                                    | 1942     | 10.4 (10.2, 10.6) | 80              | 9.1 (8.1, 10.0) |
| Poor test score, ≤5
| m-BD score                                     | 1939     | 15.1 (15.0, 15.2) | 79              | 14.3 (13.8, 14.8) |
| m-MMSE score                                   | 1931     | 11.5 (11.5, 11.6) | 79              | 11.2 (11.0, 11.4) |
| Poor test score, ≤10
| S-task score                                   | 1944     | 15.3 (15.0, 15.5) | 80              | 13.2 (12.0, 14.4) |
| Poor test score, ≤8

1 KOLT, Kendrick Object Learning Test; m-BD, modified version of Block Design; m-DST, modified version of Digit Symbol Test; m-MMSE, modified version of Mini-Mental State Examination; S-task, from the Controlled Oral Word Association Test; TMT-A, part A of the Trail Making Test.
2 Adjusted for sex.
3 Pearson’s chi-square or univariate ANOVA adjusted for sex.
4 Univariate ANOVA adjusted for sex, apolipoprotein E ε4 variant allele, education, history of cardiovascular disease, and plasma total homocysteine.
5 n; % in parentheses (all such values).
6 ε; 95% CIs in parentheses (all such values).
7 Cutoff points for poor cognitive score were set at approximately the 10th percentile, except for TMT-A, for which the 90th percentile was used.

≈85 g/d. About four-fifths of the population ate fatty fish as part of a main course, whereas even more reported having lean fish and processed fish for a main course. Nearly 2 of 3 subjects consumed fish as a sandwich spread, and >2 of 5 reported intake of cod liver oil or other fish oils.
investigate the dose-response relation between total intake of any type of fish and fish products and cognitive function. The results of all the cognitive tests improved with increasing intake of seafood up to 70–80 g/d and then leveled off (Figure 1). Linear regression analyses adjusted only for sex indicated that dose-response associations were significant for all cognitive tests. In the multiple-adjusted analyses, most of the relations remained significant (KOLT, m-DST, m-BD, and m-MMSE).

### DISCUSSION

In a large population-based study of elderly people, we found that consumers of fish and fish products had better cognitive function than did nonconsumers and, notably, that the associations between fish and fish product intake and cognition were dose-dependent. We also observed that the effect of fish on cognition differed according to the type of fish and fish product consumed.

### TABLE 3

<table>
<thead>
<tr>
<th>Food and cognitive test</th>
<th>Intake of fish or fish product</th>
<th>n</th>
<th>Mean (95% CI)</th>
<th>n</th>
<th>Mean (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td></td>
<td></td>
<td>Never or &lt;10 g/d</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fatty fish</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KOLT</td>
<td>1494</td>
<td>35.7 (35.3, 36.1)</td>
<td>429</td>
<td>34.3 (33.7, 35.0)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>TMT-A</td>
<td>1490</td>
<td>54.8 (53.1, 56.4)</td>
<td>430</td>
<td>59.7 (56.7, 62.8)</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>m-DST</td>
<td>1489</td>
<td>10.5 (10.3, 10.7)</td>
<td>429</td>
<td>10.1 (9.7, 10.4)</td>
<td>0.030</td>
<td></td>
</tr>
<tr>
<td>m-BD</td>
<td>1488</td>
<td>15.1 (15.0, 15.2)</td>
<td>427</td>
<td>14.8 (14.6, 15.0)</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>m-MMSE</td>
<td>1482</td>
<td>11.5 (11.5, 11.6)</td>
<td>426</td>
<td>11.5 (11.4, 11.6)</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>S-task</td>
<td>1490</td>
<td>15.4 (15.2, 15.7)</td>
<td>430</td>
<td>14.5 (14.0, 15.0)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lean fish</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KOLT</td>
<td>1751</td>
<td>35.6 (35.2, 35.9)</td>
<td>172</td>
<td>33.3 (32.1, 34.5)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>TMT-A</td>
<td>1748</td>
<td>55.1 (53.6, 56.6)</td>
<td>172</td>
<td>64.4 (58.5, 68.2)</td>
<td>0.005</td>
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<tr>
<td>m-DST</td>
<td>1746</td>
<td>10.5 (10.3, 10.7)</td>
<td>172</td>
<td>9.7 (9.1, 10.3)</td>
<td>0.011</td>
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<tr>
<td>m-BD</td>
<td>1744</td>
<td>15.1 (15.0, 15.2)</td>
<td>171</td>
<td>14.6 (14.3, 14.9)</td>
<td>0.005</td>
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<tr>
<td>m-MMSE</td>
<td>1738</td>
<td>11.5 (11.5, 11.6)</td>
<td>170</td>
<td>11.4 (11.3, 11.5)</td>
<td>0.07</td>
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<tr>
<td>S-task</td>
<td>1748</td>
<td>15.3 (15.1, 15.6)</td>
<td>172</td>
<td>14.3 (13.5, 15.0)</td>
<td>0.009</td>
<td></td>
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<tr>
<td></td>
<td>Processed fish</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>KOLT</td>
<td>1779</td>
<td>35.5 (35.1, 35.9)</td>
<td>144</td>
<td>34.1 (32.8, 35.3)</td>
<td>0.033</td>
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<tr>
<td>TMT-A</td>
<td>1775</td>
<td>55.5 (54.0, 57.0)</td>
<td>145</td>
<td>60.3 (55.1, 65.6)</td>
<td>0.08</td>
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<tr>
<td>m-DST</td>
<td>1773</td>
<td>10.5 (10.3, 10.7)</td>
<td>145</td>
<td>9.9 (9.2, 10.5)</td>
<td>0.07</td>
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<tr>
<td>m-BD</td>
<td>1770</td>
<td>15.1 (15.0, 15.2)</td>
<td>145</td>
<td>14.5 (14.1, 14.8)</td>
<td>0.001</td>
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<tr>
<td>m-MMSE</td>
<td>1765</td>
<td>11.5 (11.5, 11.6)</td>
<td>143</td>
<td>11.4 (11.3, 11.5)</td>
<td>0.034</td>
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</tr>
<tr>
<td>S-task</td>
<td>1775</td>
<td>15.2 (15.0, 15.5)</td>
<td>145</td>
<td>15.4 (14.6, 16.3)</td>
<td>0.66</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fish sandwich</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KOLT</td>
<td>1252</td>
<td>35.6 (35.2, 36.1)</td>
<td>671</td>
<td>34.9 (34.3, 35.5)</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>TMT-A</td>
<td>1248</td>
<td>55.1 (53.3, 56.9)</td>
<td>672</td>
<td>57.3 (54.8, 59.7)</td>
<td>0.17</td>
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<tr>
<td>m-DST</td>
<td>1247</td>
<td>10.6 (10.4, 10.8)</td>
<td>671</td>
<td>10.1 (9.8, 10.4)</td>
<td>0.013</td>
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<tr>
<td>m-BD</td>
<td>1245</td>
<td>15.1 (15.0, 15.3)</td>
<td>670</td>
<td>14.9 (14.7, 15.1)</td>
<td>0.023</td>
<td></td>
</tr>
<tr>
<td>m-MMSE</td>
<td>1243</td>
<td>11.6 (11.5, 11.6)</td>
<td>665</td>
<td>11.5 (11.4, 11.5)</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>S-task</td>
<td>1248</td>
<td>15.5 (15.2, 15.8)</td>
<td>672</td>
<td>14.7 (14.3, 15.1)</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cod liver oil and fish oil</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KOLT</td>
<td>785</td>
<td>35.8 (35.2, 36.3)</td>
<td>1138</td>
<td>35.1 (34.7, 35.6)</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>TMT-A</td>
<td>785</td>
<td>54.7 (52.5, 57.0)</td>
<td>1135</td>
<td>56.7 (54.8, 58.6)</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>m-DST</td>
<td>784</td>
<td>10.5 (10.2, 10.8)</td>
<td>1134</td>
<td>10.4 (10.1, 10.6)</td>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td>m-BD</td>
<td>783</td>
<td>15.1 (14.9, 15.2)</td>
<td>1132</td>
<td>15.0 (14.9, 15.2)</td>
<td>0.62</td>
<td></td>
</tr>
<tr>
<td>m-MMSE</td>
<td>783</td>
<td>11.6 (11.5, 11.6)</td>
<td>1125</td>
<td>11.5 (11.5, 11.6)</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>S-task</td>
<td>785</td>
<td>15.7 (15.4, 16.1)</td>
<td>1135</td>
<td>14.9 (14.6, 15.2)</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

1 KOLT, Kendrick Object Learning Test; m-BD, modified version of Block Design; m-DST, modified version of Digit Symbol Test; m-MMSE, modified version of Mini-Mental State Examination; S-task, from the Controlled Oral Word Association Test; TMT-A, part A of Trail Making Test. The univariate ANOVA was adjusted for sex, apolipoprotein E ε4 variant allele, education, history of cardiovascular disease, and plasma total homocysteine.

2 Herring, mackerel, salmon, or trout as part of a main meal.

3 Cod, coalfish, or haddock as part of a main meal.

4 Fish balls, fish cakes, fish fingers, fish stew, fish soup, or fish au gratin as part of a main meal.

5 Mackerel, pilchard, pickled herring, anchovies, salmon, or trout as a sandwich spread.

Number of poor test scores in relation to fish intake

The association between intake of different types of seafood and the number of tests yielding poor scores in an individual participant is presented in Table 4. A diet including fish or fish products was associated with a low risk of having ≥4 tests with poor scores. The risk decreased by as much as 80% when all types of fish and fish products were combined.
FIGURE 1. Associations between different cognitive tests scores and intake of any type of fish or fish product (including fish oils) obtained by Gaussian generalized additive regression models. The solid lines represent the estimated dose-response curves; the shaded areas represent the 95% CIs. Multiple adjustments included sex, apolipoprotein E ε4 variant allele, education, history of cardiovascular disease, and plasma total homocysteine. P values are from corresponding multiple linear regression analyses. KOLT, Kendrick Object Learning Test; m-BD, modified version of Block Design; m-DST, modified version of Digit Symbol Test; m-MMSE, modified version of Mini-Mental State Examination; S-task, from the Controlled Oral Word Association Test; TMT-A, part A of the Trail Making Test.
TABLE 4
Cross-sectional associations between habitual intake of different types of seafood (fish and fish products) during the previous year and the number of cognitive tests with poor scores

<table>
<thead>
<tr>
<th>Daily intake of ≥10 g/d seafood</th>
<th>0 (n = 1318)</th>
<th>1–3 (n = 534)</th>
<th>≥4 (n = 39)</th>
<th>Overall P²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Fatty fish</td>
<td>1.00</td>
<td>0.79 (0.62, 1.00)</td>
<td>0.053</td>
<td>0.44 (0.23, 0.87)</td>
</tr>
<tr>
<td>Lean fish</td>
<td>1.00</td>
<td>0.75 (0.52, 1.06)</td>
<td>0.11</td>
<td>0.28 (0.13, 0.61)</td>
</tr>
<tr>
<td>Processed fish</td>
<td>1.00</td>
<td>0.71 (0.49, 1.05)</td>
<td>0.08</td>
<td>0.26 (0.12, 0.59)</td>
</tr>
<tr>
<td>Fish sandwich</td>
<td>1.00</td>
<td>0.72 (0.58, 0.89)</td>
<td>0.003</td>
<td>0.44 (0.23, 0.85)</td>
</tr>
<tr>
<td>Cod liver oil and fish oil</td>
<td>1.00</td>
<td>0.83 (0.67, 1.03)</td>
<td>0.08</td>
<td>0.41 (0.18, 0.90)</td>
</tr>
<tr>
<td>Any type of fish or fish oil</td>
<td>1.00</td>
<td>0.63 (0.36, 1.09)</td>
<td>0.10</td>
<td>0.19 (0.07, 0.50)</td>
</tr>
</tbody>
</table>

¹ All values were adjusted for sex, apolipoprotein E ε4 variant allele, education, history of cardiovascular disease, and plasma total homocysteine.
² Multinomial logistic regression (intake of fish product as dichotomous variable).
³ Across all categories, univariate ANOVA.
⁴ Herring, mackerel, salmon, or trout as part of a main meal.
⁵ Cod, coalfish, or haddock as part of a main meal.
⁶ Fish balls, fish cakes, fish fingers, fish stew, fish soup, or fish au gratin as part of a main meal.
⁷ Mackerel, pilchard, pickled herring, anchovies, salmon, or trout as a sandwich spread.

Prevalence of participants who reported eating seafood

The proportion of participants who reported eating fish and fish products and the mean daily fish intake were higher in our population than in populations in previous studies (5, 11, 12). Despite the relatively low fish intake in previous studies, all suggested that fish eaters exhibit better cognitive performance than do nonconsumers (5, 11, 12). Our study, in a population who reported eating a lot of fish, allowed us to investigate the associations between fish intake and cognition variables in more detail.

Intake of seafood and cognitive test performance

We found that fish eaters had significantly better results on all cognitive tests than did nonconsumers. Most of these associations remained significant after adjustment for several nonnutritional factors (sex, ApoE ε4 variant allele, education, history of some important CVD variables, and tHcy) with a proven association with cognition. Moreover, the prevalence of poor scores, independent of the cognitive test used, was significantly lower among those who reported eating than in those who reported not eating fish and fish products.

The population-based Rotterdam Study was one of the first large prospective studies to show that fish consumption is associated with a reduced risk of dementia, particularly of AD (4). The favorable effect of fish consumption was observed at a relatively low intake (from ≈20 g/d) (4, 5). Other prospective studies (6–8) showed that subjects who consumed seafood at least once a week had a significantly lower risk of developing dementia or AD in the following 4–7 y. In contrast, an evidence-based study (31) focusing on the role of n–3 fatty acids reported that fish consumption was only weakly associated with a reduced risk of cognitive impairment and had no association with cognitive decline.

The associations between different types of fish and impaired cognitive outcome have been little studied. Huang et al (9) observed that the consumption of fatty fish was associated with a greater reduction in risk of dementia and AD than was eating lean fish. In the present study, the effects of fatty and lean fish intake on cognitive test performance were comparable. However, when the significance level was restricted to P < 0.001 in the multiple-adjusted model, only the association between lean fish intake and the KOLT remained.

In contrast with another study (32), we observed that intake of fish oils had a beneficial effect only on the S-task. In the groups who reported consuming processed fish and fish sandwiches, the associations were inconsistent, possibly because cooking and preparation methods influence the nutritive value of the meal (9). Thus, our most consistent finding was related to total intake of fish and fish products. In line with this, we found that those who reported consuming ≥10 g seafood/d were protected against having multiple tests with poor scores. A reduction of up to 80% in the risk of having poor scores on ≥4 tests was found in those who reported eating ≥10 g seafood/d compared with those who reported eating less or no seafood.

Dose-response relation

Although few subjects never ate seafood, there was a wide span in intake. Using dose-response curves, we observed that the performance on all 6 of the cognitive tests, adjusted for sex, improved with increasing total fish intake up to 70–80 g/d and reached a plateau thereafter. The dose-response relations remained significant in all except the TMT-A and S-task after multiple adjustments, which indicated the robustness of these associations. A dose-response relation was suggested in an earlier study (9), in which the hazard ratio for dementia decreased with the number of servings per week of fatty fish.

Cognitive test abilities

The protective effect of eating fish and fish products extended to almost all of the tested cognitive abilities. Notably, the test of global cognitive ability, the m-MMSE, was frequently not affected by individual types of seafood. However, as with the other tests, a strong dose-response relation was found with the combined intake of any type of fish or fish oil. Few other studies have examined fish intake in relation to specific cognitive abilities in the elderly, but one report described a positive effect of eating
fatty fish on processing speed, but not on tests of memory or flexibility (11). Another study found that the BD and the DST scores were higher in consumers of fish oil (32).

Strengths and limitations of the study

The strengths of this study included a large population-based sample with a relatively high consumption of fish and fish products and inclusion of 6 different tests to study cognitive performance. The food-frequency questionnaire used was validated in several studies, including the correlation between self-reported dietary intake of fish and essential n−3 fatty acids in plasma phospholipids among 579 men and women (25) and 14-d weighed diet records with the intakes calculated from the food-frequency questionnaire in a group of 38 elderly women (24).

One limitation of dietary studies is errors in estimates of nutrients (11, 14, 31). Thus, it is possible to over- or underestimate true associations with outcomes. In addition, lack of a uniform quantification of fish intake makes comparisons between different studies difficult.

Because 77.3% of the study participant volunteered for cognitive testing, recruitment bias may have been an issue. Several differences between those who underwent and who did not undergo cognitive testing were reported earlier (33). However, the dietary habits were similar, and the difference in total fish intake was only 0.3 g/d (P = 0.91).

Cognition in the elderly is shaped by long-term exposures (34, 35). Thus, an important limitation of this study was its cross-sectional design. Furthermore, subjects with impaired cognition may have altered their diet as a consequence of a change in their cognitive status, although the direction of such a change is not predictable. In addition, self-reported dietary data collected from subjects who are cognitively impaired or demented may be less reliable. However, participants in the present study were not seriously impaired, and we do not believe this to have a major effect on our findings. Last but not least, foods are not consumed individually but as part of a diet; therefore, confounding by other food items is always an issue in studies using dietary assessments.

Conclusion

In a population-based study, we showed that intake of fish and fish products is associated with better performance across several cognitive abilities and that the associations are strongly dose-dependent. We also observed that the effect depends on the type of fish consumed. Our data indicate the need for additional studies in which more details about the type or species of fish and methods of preparation should be taken into account. Nevertheless, because this and earlier studies have shown that fish intake is associated with better cognition, the next question is what component of fish makes it good for the brain? Studies of n−3 fatty acids (36), niacin (37), and any other factor known to be enriched in fish are needed to answer this question.

We are grateful to E Blomdal (University of Bergen, Norway) and Gunnar Åmlid for their excellent support with the literature and the questionnaires. The authors’ responsibilities were as follows—HR, SEV, and GST: participated in the study design and the organization of data collection; KE, HAN, and ADS: assisted with the design and organization of the cognitive substudy; KS: assessed food intakes and helped develop the food-frequency questionnaire; CAD: helped develop the food-frequency questionnaire; EN: conducted the statistical analysis and wrote the first draft of the manuscript; and EN, CAD, HR, KS, SEV, ON, HAN, KE, GST, and ADS: interpreted the results and contributed to the study design and the writing of the paper. None of the authors had any financial conflicts of interest.

REFERENCES


