Twelve Weeks of Additional Fish Intake Improves the Cognition of Cognitively Intact, Resource-Limited Elderly People: A Randomized Control Trial

L. Kühn[1], U.E. MacIntyre[1], C. Kotzé[2], P.J. Becker[3], F.A.M. Wenhold[1]

1. Department of Human Nutrition, Faculty of Health Sciences, University of Pretoria, South Africa; 2. Department of Psychiatry, Faculty of Health Sciences, University of Pretoria, South Africa; 3. Office of the Dean, Faculty of Health Sciences, University of Pretoria, South Africa

Corresponding Author: Lizette Kühn, University of Pretoria Faculty of Health Sciences, Pretoria, Gauteng, South Africa, lizettekuhn24@gmail.com

Abstract

INTRODUCTION: Dietary omega 3 polyunsaturated fatty acids (PUFA) may reduce the risk of dementia. Many studies have investigated PUFA supplementation in high-income countries, yet food-based randomized control trials using omega 3 PUFA rich fish in lower to middle income countries, are lacking.

OBJECTIVE: To determine the effect on cognition of adding either fish or non-fish foods for twelve weeks to an enhanced diet of cognitively intact, independently living, resource-limited elderly people.

DESIGN: Randomized control trial (National Health Trial register: DOH-27-061-6026)

SETTING: Retirement center in urban South Africa.

PARTICIPANTS: Fifty-seven (74% female, mean age: 72±7 years) elderly participants with cognitive function exceeding 22 on the Mini Mental State Examination were randomized into an intervention (n=31) and control (n=26) group.

INTERVENTION: The usual diets of both groups were enhanced with context-appropriate foods to mimic elements of the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet. The intervention group additionally received canned pilchards and fish spread every week amounting to an additional (theoretical) intake of 2.2g omega 3 PUFA daily. The control group received canned meatballs and texturized soya every week.

MEASUREMENTS: Cognition was measured twice before and once after the intervention phase using the Cognitive Abilities Screening Instrument (CASI). Adherence was assessed by a study-specific food frequency questionnaire and red blood cell (RBC) PUFA biomarkers. Data were analyzed using a non-parametric analysis of covariance (ANCOVA) with, and without, bootstrap imputation.

RESULTS: Participants in the intervention group had a significantly higher post intervention (P=0.036) CASI score than the control group, when the model was fitted with imputation and controlled for baseline scores. Participants in the intervention group also had a significantly higher intake of calculated dietary omega 3 PUFA and higher levels of RBC eicosapentaenoic acid and docosapentaenoic acid content than the control group ($P < 0.05$).

CONCLUSION: Twelve weeks of fish intake in the context of a modified MIND diet may improve the cognition of cognitively intact, resource-limited elderly people.

Key words: Fish, cognition, omega 3 fatty acids, elderly, resource-limited, diet.

Introduction

The number of people living with dementia increases annually. Globally, approximately 50 million people are living with dementia of which 60% come from lower to middle income countries (LMIC) (1). Dementia cannot be cured, the focus of the scientific community is thus rather on prevention of the disease (2). Diet is one of the approaches proposed to prevent or delay the onset of cognitive decline (1). Studies investigating diet evolved from single and multi-nutrient foci to food-based and whole diet approaches (3, 4).

The Mediterranean diet is the purported diet of choice for cognitive support (1, 3-5). The Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet combines the Mediterranean diet and the Dietary Approach to Systolic Hypertension (DASH) diet with promising results even with modest adherence (6).

A core element of the MIND diet is fatty fish (6), a good source of omega 3 polyunsaturated fatty acids (PUFA). Among these, the long chain PUFA (LCPUFA) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have received most attention, in relation to cognition (7-10), yet few studies investigated whole foods (11).

The Chicago Health and Aging project found that one or more fish-containing meals per week reduced cognitive decline by 10-30% (12). In the Hordaland Health Study a dose dependent relationship between fish intake and cognition was noted (13). On the other hand, the Doetinchem Cohort study reported no consistent association between fish consumption and absolute cognitive decline after five years (14).

Barberger-Gateau (15) concluded that higher omega 3 PUFA levels in the blood partly enhanced the protective effect of the Mediterranean diet against cognitive decline, indicating possible interactions between nutrients (15). Most food-based studies in high income countries (HIC) rely on salmon, a good source of omega 3 PUFA (16-18) but cost and availability makes this not feasible for people living in LMIC.

To this end, and following previous recommendations (4), we evaluated the effect of a food-based intervention containing omega 3 PUFA-rich fish on the cognition of a resource-limited group of elderly, South African people. In South Africa, canned pilchards and fish spread are affordable and readily available dietary sources of omega 3 PUFA and may be more sustainable than using nutrient supplements. The objective of the study was

therefore to determine the effect on cognition of adding either fish or non-fish foods for twelve weeks to an enhanced diet of cognitively intact, independently living, resource-limited elderly people.

Methods

Study design

The randomized control trial (RCT) consisted of two phases, a no-intervention phase and an intervention phase, each lasting twelve weeks. During the no-intervention phase, normal change in cognition was measured. Two baseline assessments, Baseline 1 Assessment (BL1) before the no-intervention phase and Baseline 2 Assessment (BL2) before the intervention phase were conducted. A post intervention assessment (PI) was conducted after the intervention phase.

Study setting and sample

This study took place at a resource-limited retirement village of urban Gauteng, South Africa. Residents were older than 59 years and included all races/ethnicities. Our study population comprised the independent living residents, living alone or as couples, who had a monthly income of $223 or less per person.

All members of the study population (N=124) were formally invited by letter to attend an information meeting. The basic premise of the study was explained and consent forms, screening forms and study identification numbers provided to potential participants. The resident social worker acted as intermediary between the researcher and the study population. All participants who gave informed consent were included in the sample and kept in the study for as long as they preferred irrespective of whether they met the inclusion criteria. This was to lend food support without obliging anyone to participate and not to embarrass those who did not qualify for the study. The exclusion criteria were applied before analyzing the data. Participants who had sensory impairment influencing administration of assessments, who used specific psychiatric medication or anti-depressants for less than three months, who were allergic or unwilling to eat any of the intervention foods and who had a Mini Mental State Examination (MMSE) score below 22 were excluded. The MMSE cut-off score was included to ensure homogeneity in terms of cognitive function. Participants who were allergic or unwilling to eat the foods were excluded at BL2.

Participants were randomly assigned to the intervention or control groups. An independent moderator, who was blinded to the intervention, used a random number table to assign participants in either group. Randomization took place after the no-intervention phase immediately before the BL2 assessment.

The sample size was calculated a priori using nQuery8 (19). Cognitive function was measured using the Cognitive Abilities Screening Instrument (CASI) (20), which measures cognitive ability on a scale from 0 to 100. Based on a comparable American study (21), we expected participants to score between 70 and 90 points, and considered a mean difference of at least 5 points to be clinically relevant for the intervention group. We further reasoned that adding fish to the diet could be recommended if we observed that cognitive function in intervention group participants improved twice as much as that of people in the control (enhanced diet without fish) group. Since the maximum change in CASI score was unlikely to exceed 15 points, we assumed a conservative standard deviation of 2.5 (15 divided by 6). Since change from BL2 was assessed, an assumed standard deviation of 3.54 (square root of 2 multiplied by 2.5 points) was used. A sample size of 44 participants per group would have 90% power to detect differences based on a two-sided t-test at the 0.05 level of significance.

Pre- and post-intervention assessments

Cognition and function: CASI

The CASI (20, 21) was administered in English or Afrikaans (the native language of approximately 50% of participants). The CASI was translated into Afrikaans by a content specialist (psychiatrist) through forward and backward translation as recommended by Tsang (22) and tested for practicality by the psychiatrist. The content of the instrument was not changed, but different example items were used to test short-term memory at each assessment to prevent a learned response.

Diet: Modified MIND diet focused food frequency questionnaire

In the absence of a validated population specific FFQ, a study specific, 48-item, quantitative FFQ, focusing on foods commonly consumed by the participants and relevant to the MIND diet (6) was developed with the purpose of assessing usual dietary intake and to monitor adherence to the intervention phase. Since the MIND diet originated in the United States of America some of the dietary items were not available or were not affordable for the participants. These inaccessible components were substituted with affordable South African options with comparable nutrient content. For example, nuts were substituted with peanut butter as a source of monounsaturated fatty acids. The FFQ was administered by a registered dietitian using a standardized technique, portion size estimation and food description aids.

Refer to Table 1 for differences between the original MIND and the modified MIND diet as assessed by the study specific FFQ.

Intervention phase

Participants received their weekly food provision from the researcher on the premises of the retirement village. The intervention group and the control group collected food during different time slots on the same day.

Participants in both groups were offered the same basic dietary enhancements. These referred to two 400g cans of

Table 1. Original and modified MIND diet, contextualized for elderly people living in a resource limited South African environment

Original MIND diet	Modified MIND diet	
	Components that stayed the same	**Components that changed**
Whole grains >=3 servings/d	Whole grains >=3 servings/d	
Green leafy vegetables >=6 servings/wk (Kale, collards, greens, spinach, lettuce/tossed salad)		Green leafy vegetables >=6 servings/wk **(As for MIND diet plus cabbage and broccoli)**
Other vegetables >=1 serving/d (Green/red peppers, squash, cooked carrots, raw carrots, broccoli, celery, potatoes, peas or lima beans, tomatoes, tomato sauce, string beans, beets, corn (maize), zucchini/summer squash/eggplant, coleslaw, potato salad)		Other vegetables >= 1 serving/d **(As for MIND diet plus all types of pumpkin and sweet potato)**
Berries >=2 servings/wk Strawberries		Berries >= 2 servings/wk (As for MIND diet plus red/purple/black grapes)
Red meats and products < 4 servings/wk	Red meats and products < 4 servings/wk	
Fish >=1 serving/wk Tuna sandwich, fresh fish as main dish; not fried fish cakes, sticks, or sandwiches		Fish >= 1 serving/wk **(As for MIND diet plus canned pilchards, anchovette fish paste, fish cakes and fingers which were not fried)**
Poultry >=2 servings/wk	Poultry >= 2 servings/wk	
Beans >3 servings/wk Beans, lentils, soybeans		Beans > 3 servings/wk **(As for MIND diet plus texturized soya protein)**
Nuts >5 servings/wk		Nuts > 5 servings/wk **(As for MIND diet plus peanuts and peanut butter)**
Fast/fried food <1 serving/wk	Fast/fried food <1 serving/wk	
Olive oil primary oil		**Canola oil primary oil**
Butter, margarine <1 T/d	Butter, margarine <1 T/d	
Cheese <1 serving/wk	Cheese <1 serving/wk	
Pastries, sweets <5 servings/wk	Pastries, sweets < 5 servings/wk	
Alcohol/wine 1 glass/d	Alcohol/wine 1 glass/d	

Abbreviations: d – day, wk – week, T – tablespoon; Serving sizes as in original MIND diet

baked beans every week, 400g peanut butter at weeks one, four, seven and ten, and 750ml canola oil at weeks one, five and nine. We additionally enhanced each group's diet with foods that primarily differed in fatty acid content. Every week, the intervention group was offered two 410g cans of pilchards and 75g of fish paste. The control group was offered two 410g cans of beef-chicken meatballs and a 200g packet of texturized soya protein. Apart from omega 3 PUFA content, the foods had similar macronutrient composition as gleaned from the labels on the cans, resulting in an additional intake of 2.2g of omega 3 PUFA per day for the intervention group if they consumed all the foods offered. Previous studies suggest that the anti-inflammatory effect of EPA occurs with intakes of between 1.35 – 2.7g/day and whilst total omega 3 PUFA has anti-inflammatory effects with intakes of 2g/day (8).

Both groups perceived the study foods to be excessive and chose not to take all the foods weekly. The foods taken were recorded by the researcher and actual intake of foods was assessed by a food frequency questionnaire (FFQ).

In this study, compliance was defined as the participants' commitment to collect study foods. Compliance was monitored by recording the participant's number each time he or she collected food. Each participant was requested to record their intake of study foods on a record sheet and hand in empty containers. Participants who returned their containers and/or record sheets were entered into a monthly draw (twice during the three month intervention). The prizes (two per month – one for the intervention group and one for the control group) included treats such as bubble bath, soap and coffee mugs, which were sponsored by the researcher. None of the prizes exceeded the value of $12.

Adherence was defined as the participants' commitment to ingest study foods and not to exchange study foods with participants from the other group. Adherence was measured by assessing dietary intake using the study-specific FFQ and by testing biomarkers (RBC-total omega 3 LCPUFA, -EPA, -DHA and –DPA and omega 6 arachidonic acid) before and after the intervention phase. Samples were analyzed using

gas chromatography. Relative percentages of individual fatty acid derivatives (% w/w) were calculated as a proportion of all fatty acids as per the unpublished protocol of the Centre of Excellence for Nutrition at North-West University.

Data management and statistical considerations

The psychometrist scored the CASI using a pre-programmed Excel spreadsheet. Pre-programmed Excel spreadsheets were also used to score the modified MIND diet out of 15 and to estimate omega 3 PUFA intake from information extracted from the study-specific FFQ. Omega 3 PUFA content from manufacturer labels and the USDA (23) food databases (the South African food composition tables are incomplete in terms of fatty acid content) were used. All data were checked by the researcher before statistical analysis.

Only data from participants who performed the BL2 assessment, irrespective of whether they participated in the no-intervention phase were used. New participants at BL2 were introduced to increase sample size.

Data were analyzed in STATA 15 (24). Two sided testing was done at the 0.05 level of significance. Demographic characteristics of the participants were descriptively. A two-sided test was used to measure within group variance in CASI scores. The different domains of the CASI showed little variance and were only descriptively analyzed. A two-sided t-test was used to test for differences in total MIND diet score and the differences in MIND diet categories (dietary characteristics) between the two groups. The intervention and control groups were compared at BL2 using a two-sided t-test with equal variances.

To predict the effect of the dietary intervention, the two groups were compared using non-parametric analysis of covariance (ANCOVA) with bootstrap estimation and BL2 values of education category and omega 3 PUFA supplementation as covariates. The outcome variables included CASI score, MMSE score, MIND diet score, omega 3 PUFA intake and RBC omega 3 PUFA. This analysis was repeated with imputation (BL2 values carried forward) where PI data were missing.

Ethical approval

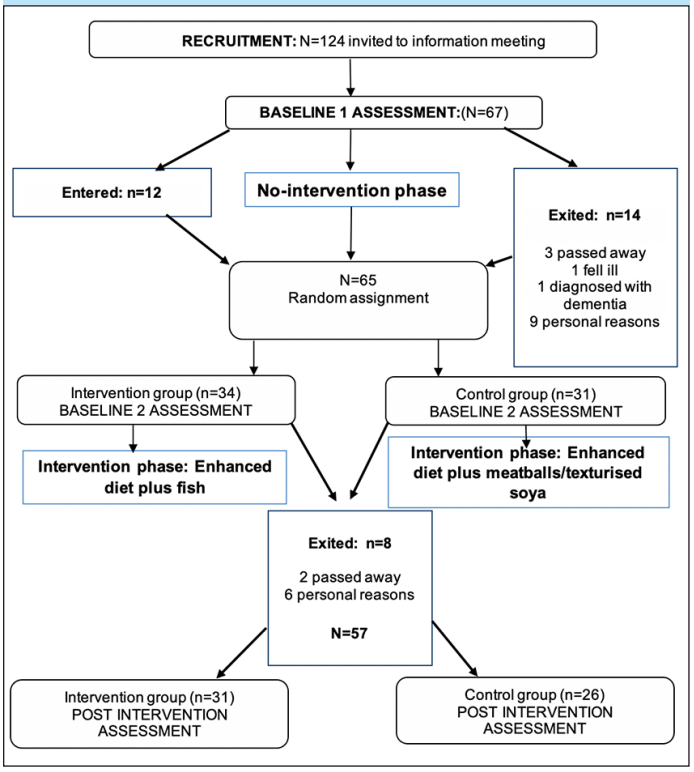
The Research Ethics Committee of the Faculty of Health Sciences, University of Pretoria approved the study (542/2017). All participants gave informed consent.

Results

Demographic characteristics

In total, 57 participants (intervention n=31; control n=26) completed the PI assessment. Figure 1 outlines study design and flow of participants through the study. Table 2 presents demographic data over the course of the study. The two groups presented with similar demographic characteristics.

Figure 1. Flow of participants



The female participants comprised 74% of the sample. The mean age of the whole group was 72±7 years.

Outcomes

Table 3 shows the means of the main outcome variables and the variables which were used to measure adherence after non-parametric ANCOVA with and without imputation was applied.

3.2.1 Cognition

At BL2, before the intervention, both groups had similar total CASI scores (P=0.43). Participants in both groups recorded higher total CASI scores at BL2 than at BL1 (Figure 2). Between BL2 and PI the CASI scores increased, with participants in the intervention group scoring on average 2.3 points higher than participants in the control group (P=0.04).

Of the CASI domains, only visual construction stood out: Participants in the intervention group scored significantly higher (P=0.02) following the intervention (8.81±1.54 versus 7.54±2.42 out of 10).

3.2.2 Diet

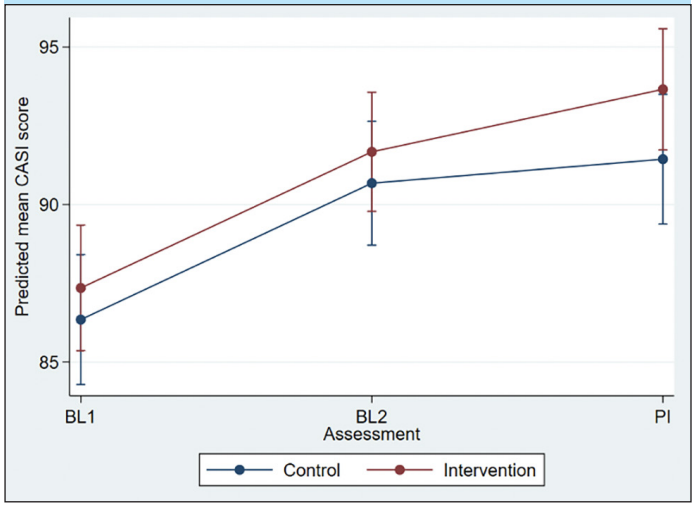
Both groups had similar MIND diet scores out of 15 at BL1 and BL2 namely 8±1.27 and 8±1.48 respectively. At PI, the control group recorded a significantly higher mean diet score when values were not imputed (P=0.04). Participants in the two groups consumed different specific food components at BL1 and PI. At BL1, the intervention group had a better score for legumes (P=0.01) and sweets (P=0.04). At PI, the control group scored better for poultry intake (P=0.01).

Table 2. Demographic characteristics, at different assessments, of participants

Characteristic	Baseline 1 (N=53)		Baseline 2 (N=65)			Post Intervention (N=57)	
	Intervention group (n=27)	Control group (n=26)	Intervention group (n=34)	Control group (n=31)	P-value[a]	Intervention group (n=31)	Control group (n=26)
Sex, n (%)							
Male	7 (25.9)	7 (26.9)	9 (26.5)	8 (25.8)	1.00[b]	8 (52.8)	7 (26.9)
Female	20 (74.1)	19 (73.1)	25 (73.5)	23 (74.2)		23 (74.2)	19 (73.1)
Age, mean (SD) (years)	71.8 (4.5)	73.6 (5.8)	70.9 (4.8)	73.6 (6.5)	0.07[c]	71.0 (5.0)	74.1 (5.5)
Education category, n (%)							
Gr 8-10[d]	17 (63.0)	15 (57.7)	21 (61.8)	15 (48.4)	0.32[b]	18 (58.0)	14 (53.9)
Post Gr 10[d]	10 (37.0)	11 (42.3)	13 (38.2)	16 (51.6)		13 (41.9)	12 (46.2)
Smoking, n (%)							
Yes	4 (14.8)	6 (23.1)	7 (20.6)	7 (22.6)	1.00[b]	6 (19.4)	4 (15.4)
No	23 (85.2)	20 (76.9)	27 (79.4)	24 (77.4)		25 (80.7)	22 (84.6)
Omega 3 PUFA supplementation, n (%)							
Yes	5 (18.5)	2 (7.7)	6 (17.7)	4 (12.9)	0.43[b]	5(16.1)	3 (11.5)
No	22 (81.5)	24 (92.3)	28 (82.4)	27 (87.1)		26 (83.9)	23 (88.5)
Using chronic medication >3 months, n (%)	27 (100)	26 (100)	34 (100)	31 (100)	-	31 (100)	26 (100)

a. P-value to indicate comparability of intervention and control groups before onset of intervention; b. Fisher's exact test; c. Two-sided t-test; d. Gr 8-10: South African standard grades pertaining to the first three years of secondary school (usually aged 13 -16 years.Post Gr10:Any educational level past the first three years of secondary school (may include education past the secondary level)

Figure 1. Estimated mean CASI score of intervention and control group at baseline 1 (BL1), baseline 2 (BL2) and post-intervention (PI) using imputation



Estimated mean omega 3 PUFA intake differed significantly between the two groups at PI, where the intervention group had a higher intake of total omega 3 LCPUFA, EPA, DPA and DHA (for all: P<0.001).

Biomarkers as measure of adherence

At PI, both groups had similar mean total RBC LCPUFA. Participants in the intervention group had significantly higher levels of mean EPA (P=0.004) and DPA (P=0.013) both with and without the imputation. As the intervention group received fish concentrated in both EPA and DPA, the increase in concentration suggests adherence.

Discussion

In this study of independent-living, elderly people in a resource constrained setting, a RCT was used to show that supplementing diet with fish resulted in improved cognition, especially in the visual construction domain. Participants who ate fish also had higher levels of EPA and DPA, which may explain their improved cognition. Internationally, the Mediterranean diet is recommended for cognitive support (1). The cost of the Mediterranean diet may be prohibitive, and be difficult to follow if people are not used to including Mediterranean diet foods in their usual eating pattern. In this study, the intervention was based on the MIND diet, a variation of the Mediterranean diet specifically aimed at neurocognitive support (6). Currently, there are no international or national reference values of omega 3 PUFA and LCPUFA intake aimed specifically at cognitive support. The initial target intake of omega 3 PUFA was 2.2.g/day, which seemed to improve cognition in similar studies (10, 16, 25-27). Affordable food products that could deliver the amount of omega 3 PUFA were identified. The intervention phase lasted for twelve weeks, similar to other studies (16, 31) and was not extended due to cost, logistics and to prevent food fatigue. Although food fatigue was initially a concern, there was no decrease in the amount of foods that participants took towards the end of the study. The compilation of a recipe book has been proposed to support fish intake as part of usual diet following the intervention phase. The current study was a short term study and additional intake was modest, but improved cognition was still recorded in the intervention group.

Improved cognition has been associated with the MIND diet. Interestingly in this study, participants had better than expected CASI scores, scoring close to 90 at BL1 and close to 92 at BL2, leaving little room for improvement during the

Table 3. The effect of additional fish intake on cognitive ability and other variables of participants: Predicted means with and without imputation, and considering various covariates

Variable (total score or unit)		Observations[a]	Predicted mean (95% CI)		Intervention vs Control		Covariates					
		N	Intervention group	Control group	Estimated effect	P – value[b]	Estimated effect (variable at BL2)[c]	P – value[b]	Estimated effect (Education)	P – value[b]	Estimated effect (n3 supplements)	P – value[b]
Total CASI (100)	With imputation	64	93.36 (91.80; 95.10)	91.10 (89.23; 93.09)	2.26	0.04*	0.65	0.00*	2.95	0.00*	-0.54	0.63
	Without imputation	56	93.68 (91.93; 95.32)	91.54 (89.25; 93.66)	2.14	0.07	0.56	0.00*	3.18	0.00*	0.08	0.95
Total MIND diet (15)	With imputation	64	8.44 (8.06; 8.76)	8.93 (8.51; 9.35)	-0.48	0.07	0.41	0.00*	-0.13	0.64	0.21	0.44
	Without imputation	56	8.47 (8.06; 8.86)	9.05 (8.57; 9.53)	-0.58	0.04*	0.40	0.00*	-0.11	0.71	0.36	0.15
Total omega 3 LCPUFA intake (mg)	With imputation	62	1359.92 (1164.49; 1588.79)	724.01 (561.722; 896.45)	635.91	0.00*	0.88	0.00*	205.26	0.12	-84.81	0.65
	Without imputation	55	1416.24 (1212.98; 1702.41)	774.11 (604.80; 1008.86)	642.12	0.00*	0.75	0.01*	149.32	0.33	-42.63	0.87
EPA intake (mg)	With imputation	63	498.60 (377.01; 636.58)	134.42 (71.68; 203.50)	364.17	0.00*	0.74	0.01*	-56.22	0.36	3.89	0.97
	Without imputation	55	534.10 (402.33; 677.86)	149.08 (59.09; 223.37)	385.02	0.00*	0.73	0.02*	-91.81	0.18	58.99	0.64
DPA intake (mg)	With imputation	62	4.45 (3.09; 6.06)	1.33 (0.63; 1.98)	3.13	0.00*	-0.13	0.78	-0.63	0.45	0.24	0.86
	Without imputation	55	5.03 (3.37; 6.76)	1.38 (0.45; 2.10)	3.65	0.00*	-0.40	0.50	-0.47	0.64	-0.05	0.98
DHA intake (mg)	With imputation	62	294.87 (242.78; 356.33)	106.55 (74.82; 134.65)	188.32	0.00*	0.52	0.02*	-26.49	0.38	15.58	0.75
	Without imputation	54	318.59 (249.21; 369.15)	121.94 (67.06; 137.13)	196.65	0.00*	0.29	0.22	-49.45	0.16	29.96	0.62
RBC Total Omega 3 LCPUFA (%w/w)	With imputation	56	5.91 (5.35; 6.35)	5.60 (4.97; 6.10)	0.32	0.33	0.36	0.047*	-0.47	0.15	0.94	0.03*
	Without imputation	41	5.73 (5.25; 6.37)	5.53 (4.59; 6.25)	0.20	0.70	0.14	0.67	-0.37	0.38	1.38	0.07
RBC EPA (%w/w)	With imputation	55	0.34 (0.27; 0.41)	0.24 (0.19; 0.26)	0.11	0.00*	0.89	0.00*	-0.04	0.33	-0.00	0.97
	Without imputation	42	0.37 (0.29; 0.44)	0.25 (0.18; 0.28)	0.12	0.01*	0.79	0.00*	-0.07	0.14	-0.01	0.88
RBC DPA (%w/w)	With imputation	56	1.44 (1.36; 1.53)	1.31 (1.24; 1.40)	0.14	0.01*	0.65	0.00*	-0.8	0.16	0.08	0.32
	Without imputation	41	1.43 (1.31; 1.50)	1.25 (1.14; 1.35)	0.18	0.01*	0.50	0.00*	-0.07	0.27	0.07	0.43
RBC DHA (%w/w)	With imputation	56	3.87 (3.48; 4.24)	3.74 (3.38; 4.15)	0.13	0.59	0.39	0.01*	-0.27	0.23	0.64	0.05
	Without imputation	42	3.63 (3.24; 4.16)	3.72 (3.19; 4.17)	-0.09	0.79	0.19	0.38	-0.23	0.44	0.80	0.08

a. Number of observations differ due to missing data; b. P-value derived from non-parametric ANCOVA with covariates (score of relevant outcome variable at BL2, education category and Omega 3 supplement intake); c. Score of relevant outcome variable at BL2 served as covariate; *Significant P-values (P<0.05); Abbreviations: CASI – Cognitive Abilities Screening Instrument, BL1 – Baseline 1 Assessment, BL2 – Baseline 2 Assessment, DHA – Docosahexaenoic Acid, DPA – Docosapentaenoic Acid, EPA – Eicosapentaenoic Acid, PI – Post Intervention Assessment, RBC – Red Blood Cell

intervention phase. The increase in total CASI score between BL1 and BL2 may be attributed to a few factors. Participants may have had an improved sense of wellbeing due to receiving more attention and interacting with people. Participants may have recognized that the instruments were testing cognition, causing them to focus and concentrate better. The participants could potentially have learned about specific brain supportive foods at BL1 and adjusted their diet accordingly. Although the CASI was developed for epidemiological studies, there was little time between the two assessments, only twelve weeks. It is likely that participants could still remember the questions from the previous assessment. The CASI was, however, developed to accommodate repeated assessments (20). In the Fins-Teens study, repeated cognitive tests resulted in a learning effect, but the learning effect was equally distributed across both groups which allowed researchers to detect an intervention effect when comparing groups (16).

Following the intervention phase, all participants showed a small but still significantly improved total CASI score. Improved CASI scores in both groups were expected because both groups received baseline diets enhanced with canola oil, peanut butter and baked beans (Table 1). Despite the enhanced baseline diets, the intervention group, which received fish products, had higher CASI scores (+2.3 points) indicating the superiority of fish as a source of omega 3 PUFA.

These results compare well with the findings of the previously referred to Chicago Health and Aging project which found a significant decrease in cognitive decline when one or more fish meal per week was consumed (12). Similarly the Hordaland Health Study indicated improved cognitive performance in those that consumed fish and fish products of more than 10g/day (13). The current study results are supported by the findings of two trials in preschool children which also showed improvement in cognition after dietary supplementation with oily fish (18, 27). Although the study population was much older and the study fish restricted to pilchards and fish spread (more affordable options than the salmon and mackerel used in the other trials) cognition still improved.

In this study, it was estimated that the intervention group consumed twice as much total omega 3 LCPUFA (1360mg) than the control group (720mg) and four times as much dietary EPA (500mg) than the control group (130g). Both groups received canola oil, and therefore consumed similar amounts of alpha-linolenic acid (ALA). When the intervention group's total omega 3 LCPUFA (1360mg) and ALA (550mg) intake were combined, the total omega 3 PUFA intake was approximately 1900mg per day. It was estimated that the intervention group consumed about 86% of the planned intake.

The main strength of this study was its randomized control trial design in an under-researched target group, with evidence of compliance. This study was also food rather than supplement based.

This study had a number of limitations. The small sample size influenced the power and did not allow for any attrition. The final size of the sample at PI was 57 (intervention n=31 control n=26). Had the SD of the CASI score been the assumed 3.54 and the t-test one sided, the power would have been 83.59% with the current sample.

Cognitive ability was measured using a screening tool - and not a full neuropsychological battery – and may have missed improvements. A non-validated FFQ was used. Our study was also a short term intervention, which may not be enough time to see improvements but previous studies have also used interventions of similar duration (17,27). Control over all the actions of the participants was impossible and the researcher had to rely on honesty when participants reported their intake. The possibility that participants shared their foods existed. Personal contact and weekly follow-up possibly supported honesty to an extent. Also the motivation behind the flexible principle of only taking foods that they prefer was also aimed at supporting intake. Participants were resource limited and had restrained budgets, which made the sharing of food more challenging. The adherence to intake of omega 3 foods was measured through the biomarkers.

Cost prohibited independent chemical analysis of the intervention foods. Also insight into the interaction between nutrients and study foods (enhancement versus experimental food) may be lacking (4).

Conclusion

The current study points to the potential role of diet in cognitive functioning of elderly people living in a LMIC. Involvement in a dietary study and dietary enhancement (informed by some of the MIND principles) for twelve weeks, slightly improved the cognitive functioning of all the elderly participants, yet those that received fish improved significantly more than those receiving the control diet.

Acknowledgements: Residents, management and personnel from the retirement village where the study was conducted Ampath Laboratories, Centre of Excellence for Nutrition at the North-West University (NWU), Lucky Star, Shoprite Checkers, Southern Oil.

Conflict of interest: No conflict of interest.

Ethical standard: The Research Ethics Committee of the Faculty of Health Sciences, University of Pretoria approved the study (542/2017). All participants gave informed consent. National Health Trial register: DOH-27-061-6026

References

1. Livingston G, Huntley J, Sommer, Ballard A, Ames D, Ballard C, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet. 2020; 396(10248):413-46. doi:10.1016/S 0140-6736(20)30367-6
2. Cessari M, Azzolino D, Arosio B, Canevelli M. Nutritional interventions for early dementia. J Nutr Health Aging. 2021;25(5);688-691.
3. Van de Rest O, Berendsen AM, Havenman-Nies A, De Groot LCPGM. Dietary patterns, cognitive decline and dementia: a systematic review. Adv Nutr. 2015; 6:6154-168. doi: 10.3945/an.114.007617
4. Bowman GL, Dodge HH, Guyonnet S, Zhou N, Donohue J, Bichsel A, et al. A blood-based nutritional risk index explains cognitive enhancement and decline in the multidomain Alzheimer prevention trial. Alzheimers Dement (N Y). 2019; 5:953-63. doi:10.1016/j.trci.2019.11.004
5. Hosking DE, Eramudugolla R, Cherbuin N, Anstey KJ et al. MIND not Mediterranean diet related to 12-year incidence of cognitive impairment in an Australian longitudinal cohort study. Alzheimers Dement. 2019; 15(4):581-9. doi:10.1016/j.jalz.2018.12.011
6. Morris MC, Tangney CC, Wang Y, Sacks FM, Bennet DA, Aggarwal NT. MIND diet associated with reduced incidence of Alzheimer's disease. Alzheimers Dement. 2015; 11(9):1007-1014. doi:10.1016/j.jalz.2015.04.011
7. Janssen CIF, Kiliaan AJ. Long-chain polyunsaturated fatty acids (LCPUFA) from genesis to senescence: the influence of LCPUFA on neural development, aging, and neurodegeneration. Prog Lipid Res. 2014; 53:1–17. doi:10.1016/j.plipres.2013.10.002
8. Calder PC. Marine omega-3 fatty acids and inflammatory processes: effects, mechanisms and clinical relevance. Biochim Biophys Acta. 2015; 1851(4):469-84. doi:10.1016/j.bbalip.2014.08.010

9. Yurko-Mauro K, McCarthy D, Rom D, Nelson EB. Ryan AS, Blackwell A, et al. Beneficial effects of docosahexaenoic acid on cognition in age-related cognitive decline. Alzheimers Dement. 2010; 6(6):456-64. doi:10.1016/j.jalz.2010.01.013
10. Dangour AD, Allen E, Elbourne D, Fletcher A, Richards M, Uauy R. Fish consumption and cognitive function among older people in the UK: Baseline data from the OPAL study. J Nutr Health Aging. 2009; 13(3):198-202. doi:10.1007/s12603-009-0057-2
11. Cao L, Tan L, Wang H, Zhu X, Jiang T, Lu H, et al. Dietary patterns and risk of dementia: a systematic review and meta-analysis of cohort studies. Mol Neurobiol. 2016; 53(9):6144-54. doi:10.1007/s12035-015-9156-4
12. Morris MC, Evan DA, Tagney CC, Bienias JL, Wilson RS. Fish consumption and cognitive decline with age in a large community study. Arch Neurol. 2005; 62(12):1849-53. doi:10.1001/archneur.62.12.noc50161
13. Nurk E, Drevon CA, Refsum H, Soovoll K, Vollset SE, Nygart O, et al. Cognitive performance among the elderly and dietary fish intake: the Hordaland Health Study. Am J Clin Nutr. 2007; 86(5):1470-8. doi:10.1093/ajcn/86.5.1470
14. Nooyens AC, Van Gelder BM, Bueno-de-Mesquita HB, Van Boxtel MP, Verschuren WM. Fish consumption, intake of fats and cognitive decline at middle and older age: the Doetinchem Cohort Study. Eur J Nutr. 2018; 57(4):1667-75. doi:10.1007/s00394-017-1453-8
15. Barberger-Gateau P, Feart C, Samieri C. Mediterranean diet and cognitive decline: what role for omega-3 polyunsaturated fatty acids? OCL. 2011; 18(4):224-227. doi:10.1051/ocl.2011.0388
16. Skotheim S, Dahl L, Handeland K, Foryland L, Lie O, Oyen J, et al. Design of the FINS-TEENS study: A randomized controlled trial assessing the impact of fatty fish on cognitive performance in adolescents. Scand J Public Health. 2017; 45(6):621-9. doi:10.1177/1403494817717408
17. Van de Rest O, Geleijnse JM, Kok FJ, Van Staveren WA, Dullemeijer C, Olderikkert MG, et al. Effect of fish oil on cognitive performance in older subjects: a randomized, controlled trial. Neurology. 2008; 71(6):430–8. doi:10.1212/01.wnl.0000324268.45138.86
18. Demmelmair H, Oyen J, Pickert T, Rauh-Pfeiffer A, Stormark KM, Graff IE, Oyvind L, et al. The effect of Atlantic salmon consumption on the cognitive performance of preschool children – A randomized controlled trial. Clin Nutr. 2019; 38(6):2558-68. doi:10.1016/j.clnu.2018.11.031
19. nQuery(2017). Sample Size and Power Calculation. "Statsols" (Statistical Solutions Ltd), Cork, Ireland
20. Teng LE, Hasegawa K, Homma A, Yukimuchi I, Larson E, Graves A, et al. The Cognitive Abilities Screening Instrument (CASI): a practical test for cross-cultural epidemiological studies of dementia. Int Psych Geriat. 1994; 6(1):45-55. doi:10.1017/S1041610294001602
21. McCurry SM, Edland SD, Teri L, Kukull WA, Bowen JD, Mccormick WC et al. The Cognitive Abilities Screening Instrument (CASI): data from a cohort on 2524 cognitively intact elderly. Int Psych Geriat. 1999; 14(10):882-888.
22. Tsang S, Royse C, Terkawi A. Guidelines for developing, translating, and validating questionnaire in perioperative and pain medicine. Saudi J Anaesth. 2017; 11(Suppl1):S80-9. doi:10.4103/sja.SJA_203_17
23. U.S. Department of Agriculture, Agricultural Research Service. FoodData Central, 2019. Fdc.nal.usda.gov
24. Stata Release 15, StataCorp, College Station, Texas, 2017.
25. Jaremka LM, Derry HM, Bornstein R, Prakash RS, Peng J, Belury MA, et al. Omega 3 supplementation and loneliness-related memory problems: secondary analyses of a randomized controlled trial. Psychosom Med. 2014; 76(8):650-58. doi:10.1097/PSY.0000000000000104
26. Danthiir V, Hosking DE, Nettelbeck, Vincent AD, Wilson C, O'Callaghan N, et al. An 18-mo randomized, double-blind, placebo-controlled trial of DHA-rich fish oil to prevent age-related cognitive decline in cognitively normal older adults. Am J Clin Nutr. 2018; 105(5):754-62. doi: 10.1093/ajcn/nqx077
27. Oyen J, Kvestad I, Midtbo LK, Graff IE, Hysing M, Stormak KM, et al. Fatty fish intake and cognitive function: FINS-KIDS, a randomized controlled trial in preschool children. BMC Medicine. 2018; 16(1):41. doi:10.1186/212916-018-1020-z