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Randomized open-label trial of docosahexaenoic acid–enriched fish oil and fish meal on cognitive and behavioral functioning in Omani children

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ABSTRACT

Objective: This study aimed to examine the effect of docosahexaenoic acid (DHA)–enriched fish oil supplement and meal of grilled fish on cognitive and behavioral functioning manifested as attention-deficit/hyperactivity disorder in primary school students 9 to 10 y of age in Muscat, Oman.

Methods: This randomized open-label trial involved two types of interventions: fish oil supplement or one serving (100 g) of grilled fish per day (Sunday through Friday) for 12 weeks. Red cell total lipid DHA levels were assessed. The Verbal Fluency Test, Buschke Selective Reminding Test, and Trail Making Test were used to measure cognitive functioning. Behavioral functioning was assessed using a standardized Arabic version of the National Initiative for Children's Health Quality Vanderbilt Assessment Scales. All measurements were carried out before and after intervention.

Results: DHA levels increased by 72% and 64% in the fish oil (mean, 3.6%–6.2%) and fish-meal (mean, 3.4%–5.6%) groups, respectively ($P = 0.000$). The Trail Making Test was the only cognitive test that demonstrated marked differences between groups: Median interquartile range difference between pre- and postintervention in the Trail Making Part B score was 61.5 (SE, 19.3, 103.2) in the fish oil versus fish-meal group, 24.5 (SE, –15.2, 74.7, $P = 0.005$). The Vanderbilt Assessment Scales also showed significant differences between groups ($P < 0.001$).

Conclusion: This study contributed to available evidence on the cognitive and behavioral benefits of DHA in healthy school children. Expanding the food fortification program with DHA-enriched fish oil should be considered as part of broader policy to improve child health.

Introduction

The Sultanate of Oman, a country on the southeast corner of the Arabian Peninsula with a long coastline overlooking the Arabian Sea, the Sea of Oman, and the Indian Ocean, is known for its rich fish resources [1]. Although fish is a major national commodity, population intake is minimal [2]. Due to its multiple health benefits, the Ministry of Health is promoting the consumption of fish in its efforts to improve the dietary intake of the population [2].

The abundance in fish of long-chain ω-3 fatty acids, such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), is necessary

SSA recruited, enrolled, and followed up the children; liaised with teachers and parents; oversaw data collection; and reviewed the final manuscript. SA assisted with the study protocol and implementation, and drafted the manuscript. KG and IH contributed to the conception, design, and implementation of the study and reviewed the manuscript. YM assisted in the conceptualization and implementation of the study, developed the proposal, and reviewed the manuscript. LJ reviewed the manuscript. SMA assisted with the implementation of the study, data collection, and statistical analysis. RMM assisted in drafting the manuscript. has contributed significantly in the conception of the study, acquisition of funds, and the refining of the proposal. HSA contributed significantly in the conception of the study.

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for human growth and development. They not only benefit cardiovascular and immune systems but are necessary for the development of the brain and nervous system [3–6]. These are particularly important during brain growth spurts in infancy, early childhood, and adolescence [7]. Promoting consumption of ω-3 fatty acids could be part of a multiprong approach to address concerns raised by parents, teachers, and child welfare advocates about children's school performance and their emotional well-being.

Studies have found that ω-3 fatty acid supplementation benefits cognition (thinking, reasoning, memory), behavior, and school performance among healthy children [7–10]. Supplementation in healthy but underperforming children 7 to 9 y of age in the United Kingdom appears to improve reading and behavior [8]; whereas supplementation among 200 healthy children 8 to 16 y of age in Mauritius resulted in the reduction of behavioral problems [9]. A review of 15 observational and randomized controlled trials in healthy children 4 to 18 y of age reported improvements in learning ability, reading, spelling, and behavior [10]. Studies have demonstrated their efficacy in reducing neurological soft signs, enhancing cognitive functioning, attenuating externalization–internalization disorders, and improving behavior [11]. Moreover, several studies have reported that ω-3 oil supplementation alleviated some attention-deficit/hyperactivity disorder (ADHD)–related symptoms [9,10,12,13].

The benefits of fish consumption on cognitive development is less substantive. A cross-sectional study of Swedish adolescents reported significantly higher grades among participants with more frequent fish intake [3]. A six-country European study of elementary school children reported negative associations of fatty fish consumption with emotional and behavioral problems [14]. The Cape Code Health Study also found high childhood intake of fish associated with some cognitive benefits in adulthood [15].

Research on the associations of ω-3 fatty acid supplementation and fish consumption and learning and behavior among healthy school children has largely been limited to populations in the West; little is known about other parts of the world. Based on two cross-sectional studies, estimates on the prevalence of ADHD symptoms among Omani school-aged girls and boys are 5.1% and 7.8%, respectively [16,17]. In the present study, we examined the effects of fish and DHA-enriched fish oil supplement on cognitive (verbal ability, learning and remembering, and executive functioning) and behavioral functioning in primary school students living in Muscat, Oman.

Methods

This was a randomized, open-label trial and part of a larger study assessing nutritional status of children and the effect of DHA intake on their health.

The study was approved by the Research Ethics Committee of the Ministry of Health, Sultanate of Oman and the National Research Ethics Committee North West—Haydock, UK. The trial was registered with the ISRCTN Register. Informed and signed consent was obtained from the children's parents or guardians. The study was conducted in accordance with the provisions of the ethical approval of the two ethics committees and the principles of the Helsinki Declaration.

Participants and intervention

Participants were healthy children 9 and 10 y of age attending grade 4 in primary schools in Muscat, the capital of Oman. Children with a known hereditary or chronic medical condition that requires medication or those who were allergic to fish or shellfish were excluded.

DHA was provided either in the form of DHA-enriched fish oil capsules or as a meal of grilled fish. Children in the fish-meal group were given a daily midday lunch snack comprising 100 g of a lightly grilled fish sandwich with some vegetables. Five types of fish, namely grouper, sea bream, king fish, emperor, and snapper were used. It was estimated that 100 g of grilled fish provides 150 to 200 mg of DHA. The meals were prepared tastefully by professional chefs at the Intercontinental City Hotel, Muscat to enhance compliance. Children in the fish oil group were given a capsule containing 403 mg DHA daily during the midday break. The intervention took place for 12 wk during weekdays when school was in session.

Sample size

The sample size for this substudy was based on the Oxford-Durham study, a randomized control trial using ω-3 oil capsule, which found significantly improved reading, spelling, and behavior in a group of 55 school children in each treatment arm [18]. To account for possible drop out, we increased the required number by 20% or 66 in each group.

Outcome measures

The main outcome measures for this study were behavioral (ADHD symptoms) and cognitive functioning. All tests were carried out before and at the end of the intervention at school by trained researchers, undergraduate psychologists trained to dispense the outcome measures uniformly under the supervision of a board-`certified neuropsychologist. Vanderbilt Assessment Scales-Teacher Assessment Scale also known as the National Initiative for Children's Health Quality Vanderbilt Assessment Scales-Teacher Assessment Scale (NICHQ Vanderbilt Assessment Scales) were performed by teachers to quantify the presence of ADHD.

Three tests were used to assess various domains of cognitive functioning including verbal ability, learning and remembering, and executive functioning. To avoid learning effect, different versions of the outcome (verbal fluency test; Buschke Selective Reminding Test) were therefore employed.

The verbal fluency test (also known as Controlled Oral Word Association Test was used to examine lexical ability and initiation speed of verbal responses. The respondents were given 60 s to produce as many unique words as possible within a semantic category such as FAS. In this study, the letters are derived from the Arabic alphabet, *taa, raa*, *waaw* as described elsewhere [19].

The Buschke Selective Reminding Test was used to tap into immediate recall, which represents working memory and attentional capacity [20]. The participants were read a list of 12 words and asked to recall as many as possible in a total of three trials. The scoring represents the mean total items recalled out of the three trials.

Part B of the Trail Making Test was used to assess executive functioning: attention, visual search and scanning, sequencing and shifting, flexibility, ability to execute and modify a plan of action, and ability to maintain two trains of thought simultaneously. The participants were asked to draw lines to connect the circles in an ascending order by alternating between the numbers and letters (i.e., 1-A-2-B-3-C, etc.). These domains generally have been attributed to constitute executive functions [21,22].

A standardized Arabic version of the Vanderbilt Assessment Scales-Teacher Assessment Scale was used to examine behavioral and emotional functioning [23,24]. This tool has 55 questions divided into two sections soliciting symptoms and performance scales based on teachers' observations. The symptoms section contains 47 items that are divided into various subsections: Items 1 to 18 tap into the symptoms of ADHD. The present analysis focused only on the ADHD symptoms. The formula used for scoring Vanderbilt Assessment Scales-Teacher Assessment Scale was detailed elsewhere [25]. The research team taught teachers how to complete Vanderbilt Assessment Scales-

Teacher Assessment Scale by circling only one of the numbers on the scale for each item and basing their answers in reference to the child's behavior over a 6-mo period.

Additionally, students were tested for their intellectual ability using the Coloured Progressive Matrices (CPM), which has been designed for children 5 through 11 y of age. CPM is accorded as culture-free test [26]. It consists of 36 items grouped into three sets. Each item contains a pattern problem with one part removed and between six and eight pictured inserts of which one contains the correct pattern. The child points to the pattern he or she selects as correct. Possible scores, therefore, can range from 0 to 36. For the present study, the raw scores were reported. This test was carried out once during recruitment.

Red cell fatty acid analysis

Fasting blood samples were collected in ethylenediaminetetraacetic acid–treated tube (BD Vacutainer® EDTA tubes) and separated into red cells and plasma by cold (4°C) centrifugation at 1500*g* for 10 min. After removing the plasma, the remaining red cells were washed with saline (0.9%) twice and transferred to another tube. This initial stage of sample preparation was carried out at the Royal Hospital, Oman and subsequently transported to Lipidomics and Nutrition Research Centre, London and kept in a −70°C freezer until analysis. The total red cell lipid was extracted using a mixture of chloroform and methanol, and fatty acid methyl esters were prepared in 15% acetyl chloride in dry methanol solution and separated using a gas-liquid chromatography (HRGC MEGA 2 Series; Fisons Instruments, Milan, Italy) fitted with a BP20 capillary column (25 m × 0.32 mm i.d., 0.25 μm film). Hydrogen was used as a carrier gas and the injector, oven, and detector temperatures were maintained at 250°C, 200°C, and 280°C, respectively. The fatty acid methyl esters were identified by comparing retention time with authentic standards. Peak areas were quantified by a computer chromatography data system (EZChrom Chromatography Data System; Scientific Software, Inc., San Ramon, CA, USA).

Statistical analyses

Group comparisons of outcome measures (mean postintervention score minus baseline score), were carried out. An intention-to-treat (ITT) method was the main statistical analysis. Comparison of mean change from the baseline to the end line, was carried out by calculating the differences in mood scores (mean, SE or median, interquartile range [IQR]) using the student test if normal, otherwise using Mann–Whitney U test. The denominator would be the number randomized. The differences in red cell ω-3 fatty acid levels between two groups were examined using the independent *t* test. The paired *t* test was used to compare the changes in the red cell ω-3 fatty acids within each group. Data was entered in EPIDATA software and analysed using SPSS software.

Results

One hundred thirty-two children, 66 in each group, were randomized to receive either fish oil or a meal containing fish. (Fig. 1 provides the CONSORT flow chart.) Demographic data showed no significant group differences (Table 1), demonstrating appropriate sampling selection. Boys comprised slightly <50% of the sample; the average age of participants was 9.5 y. The reasoning capacity of both groups were within normal range. The children were fairly similar in terms of the birth history and socioeconomic background. Compliance rate was high (97%) with no known side effects (i.e., nausea, loose stools, fish aftertaste) of fish oil supplement reported.

Red cell ω-3 fatty acids

Both groups of children had similar levels of long-chain polyunsaturated ω-3 fatty acids, namely EPA, docosapentaenoic acid (DPA), and DHA in red cells before intervention (Table 2). As expected, fish oil supplement increased the DHA level by 72% compared with preintervention (3.6 ± 1.4 to 6.2 ± 1.5, $P = 0.000$).

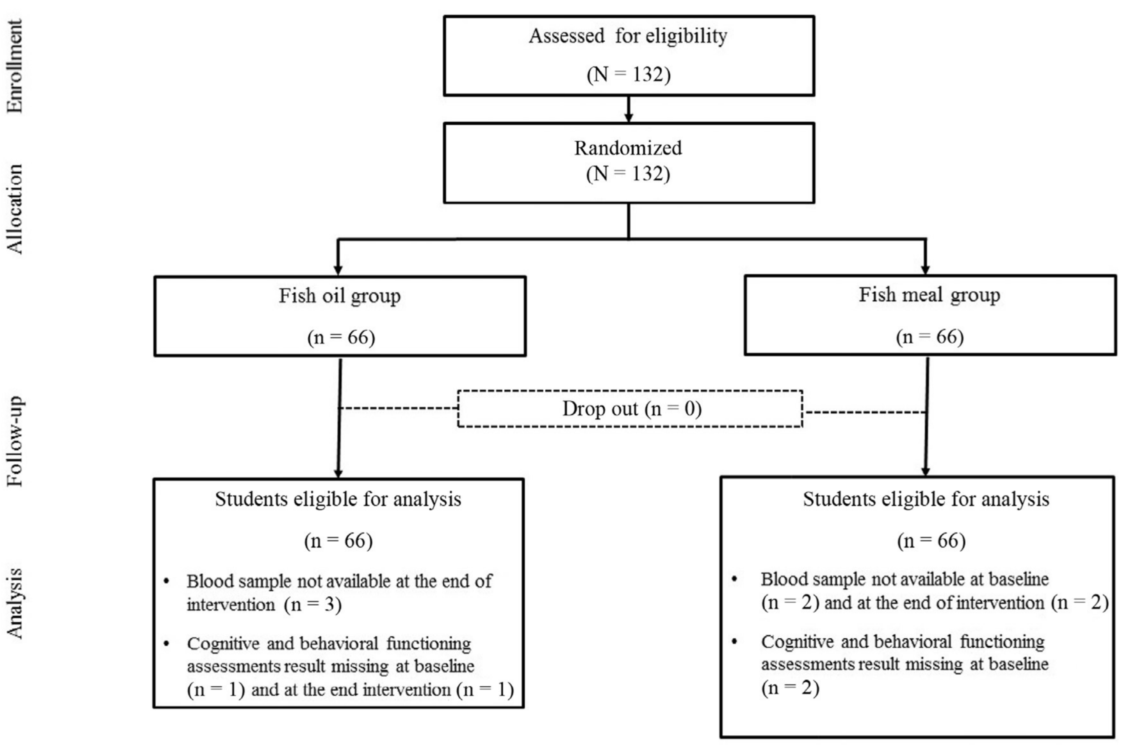

Fig. 1. CONSORT flow diagram of study participants.

Table 1
Description of study participants

	Fish oil group (n = 66)	Fish-meal group (n = 66)
Boys (%)	40.9	45.5
Mean age (y; mean ± SD)	9.58 ± 0.4	9.56 ± 0.5
Intellectual functioning (colored progressive matrices; mean ± SD)	27.6 ± 6.2	29.4 ± 5.5
Birth history		
Anthropometric measures at birth (mean ± SD)		
Mean weight at birth (kg; mean ±SD)	3.09 ± 0.4	3.11 ± 0.5
Mean length at birth (cm; mean ± SD)	50.6 ± 3.8	50.5 ± 5.7
Problems during pregnancy (%)		
None	75.4	61.1
Gestational diabetes	11.5	19.4
Hypertension	1.6	8.3
Iron deficiency anemia	3.3	2.8
Other	8.2	8.3
Birth-related issues (%)		
None	87.5	87.7
Cesarean delivery	7.8	7.7
Low birth weight	1.6	4.6
Preterm baby	1.6	0
Other	1.6	0
Parental consanguinity		
First degree	28.1	23.1
Second degree	10.9	16.9
Distantly	15.6	9.2
No relationship	45.3	50.8
Parental socioeconomic background		
Mother's education (%)		
Preparatory or less	6.3	4.5
Secondary	25.0	37.9
More than secondary	18.8	21.2
Mother's employment status (%)		
Employed	7.9	8.1
Not employed	92.1	91.9
Father's education (%)		
Preparatory or less	9.4	6.2
Secondary	25	30.8
More than secondary	20.3	15.4
Father's employment status (%)	87.5	87.7
Employed	12.5	12.3
Not employed		
Mean household monthly income (Omani Rial; mean ± SD)	1376 ± 788	1406.7 ± 875.4

Similarly, the DHA level was 64% higher in the fish-meal group (3.4 ± 1.4 to 5.6 ± 1.2, $P = 0.000$). However, the proportional increase was significantly higher in the fish oil group ($P = 0.014$) than in the fish-meal group. Interestingly, the sum of long-chain ω-3 fatty acids between the two groups did not differ after intervention, as the slightly lower level of DHA in children from the fish-meal group was compensated by the higher proportion of DPA. Although arachidonic acid (ARA) was positively associated with the ω-3 fatty acid index postintervention in both groups (fish oil $r = 0.394$, $P < 0.0001$; fish meal $r = 0.213$, $P < 0.05$, data not shown); the association of total ω-6 fatty acid with ω-3 fatty acid was observed only in the fish oil group (fish oil $r = 0.414$, $P < 0.0001$; fish meal $r = -0.032$, $P > 0.05$).

Cognitive functioning

Of the three tests for cognitive function presented in Table 3, the Trail Making Test for executive functioning was the only one that demonstrated marked differences between the groups. The median IQR difference between pre- and postintervention in the Trail Making Part B score was 61.5 (19.3, 103.2) in the fish oil group and was markedly lower in the fish-meal group, 24.5 (−15.2, 74.7). Thus, the fish oil group had significantly higher change than the fish-meal group ($P = 0.005$).

Emotional and behavioral functioning

The Vanderbilt Assessment Scales measuring symptoms of ADHD demonstrated marked differences between groups. The mean (SE) score for the fish oil group at the pretest was 22.1 (2), whereas this was 23 (2.4) at the post-test. Similarly, the corresponding values for the fish-meal group were 25.7 (2.2) and 18 (2.1). Although the fish oil group saw an improvement (mean, 1.4, SE 1.6), a marked decrease was observed in the fish-meal group (mean, −7.2, SE 0.7).

Discussion

To our knowledge, this one of the first studies in the Arab world to examine the benefits of long-chain polyunsaturated ω-3 fatty acid consumption, DHA in particular, on cognitive and behavioral functioning among healthy school children. The findings, particularly the significantly greater benefit of fish oil consumption compared with fish, adds to the available evidence largely from North America and western Europe [3,7,8,10,14]. Studies have generally shown global cognitive improvement (attention and concentration, learning and remembering, executive functioning) among children taking ω-3 fatty acid supplements [12,27,28]. This 12-wk intervention study suggests improvement in verbal fluency and executive functioning in all children; however, significantly greater improvement was seen only with executive functioning among those who consumed the ω-3 oil supplement 5 d/wk than in those who consumed fish. Previous studies have linked executive functioning to perceptual motor speed, visual searching and sequencing, and the ability to make alternating conceptual shifts, planning and goal-directed behavior [29]. They also have suggested that ω-3 fatty acid supplement has the potential to affect executive functioning [7,30,31]. A related study found that ω-3 fatty acid supplementation mitigates vitamin D deficiency prevalence in Omani school

Table 2
Red cell total lipid EPA (20:5ω3), DPA (22:5ω3), DHA (22:6ω3), and sum of ω-3 LC PUFA levels before and after intervention*

	Fish oil group (n = 66)†				Fish-meal group (n = 64)‡			
	EPA	DHA	DPA	Sum of ω-3 LC PUFAs	EPA	DHA	DPA	Sum of ω-3 LC PUFAs
Before intervention	0.3 ± 0.1	3.6 ± 1.4	0.9 ± 0.3	4.8 ± 1.7	0.3 ± 0.1	3.4 ± 1.4	1 ± 0.3	4.7 ± 1.8
After intervention	0.4 ± 0.1 [a]	6.2 ± 1.5 [c]	1 ± 0.2	7.6 ± 1.8 [c]	0.4 ± 0.2 [§, b]	5.6 ± 1.2 [§, c]	1.4 ± 0.3 [§, c]	7.4 ± 1.5 [c]

DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosahexaenoic acid; LC PUFA, long-chain polyunsaturated fatty acids.
Values with superscript letters (a, b, c) significantly different from the values measured before intervention at $P < 0.05$, $P < 0.01$, and $P < 0.0001$, respectively (paired sample *t* test, two-tailed).
*Values are expressed as mean (% of total fatty acids identified) ± SD.
†The mean value for the “After intervention” was based on 63 participants as blood samples were not available from 3.
‡Blood samples were not available from two children at baseline and two at the end of intervention.
§Significantly different from those of fish oil group at $P < 0.05$ and $P < 0.0001$ (independent sample *t* test, 2-tailed).

Table 3
Cognitive and behavioral functioning assessments

	Fish oil group		Fish-meal group		Mean difference of change between groups (95% CI)	*P*-value
	Mean/Median	SE/IQR	Mean/Median	SE/IQR		
Verbal fluency test						
ITT						
Pre	9.0	6.0/12.0	7.0	5.0/10.0		
Post	12.0	9.0/15.5	11.5	7.0/16.0		
Difference	−4.0	−6.5/0.5	−3.5	−6.2/−2.0	NA	0.235*
Buschke Selective Reminding Test						
ITT						
Pre	24.9	0.4	23.6	0.5		
Post	25.3	0.4	23.2	0.6		
Difference	−0.4	0.5	0.1	0.6	−0.5 (−2.2 to 1.2)	0.548
Trail Making—Part B						
ITT						
Pre	184.0	139.5/232.5	183.5	135.5/219.2		
Post	111.0	85.0/145.0	142.0	98.5/194.2		
Difference	61.5	19.3/103.2	24.5	−15.2/74.7	NA	0.005*
Vanderbilt Assessment Scales-Teacher Assessment Scale						
ITT						
Pre	22.1	2.0	25.7	2.2		
Post	23.0	2.4	18.0	2.1		
Difference	1.4	1.6	−7.2	0.7	8.6 (5 to 12.2)	<0.001

IQR, interquartile range; ITT, intention to treat; NA, not applicable.
*P-value based on Mann–Whitney test.

children [32]. Thus, consideration should be made for a child-focused program of food fortification.

In a systematic review and meta-analysis of randomized, placebo-controlled trials examining ω-3 fatty acid supplementation among children with ADHD, Bloch and Qawasmi [33] concluded that ω-3 fatty acid supplementation attenuates the ADHD symptoms. Other systematic reviews and meta-analyses had similar findings [34,35]. It is interesting to note that ADHD has been suggested to manifest de-executive disorder [36]. Some of the spectrum of deficits in children with ADHD includes impaired self-regulation or poor impulse control, lack of planning or goal-directed behavior [37–39]. Pending further scrutiny, this study suggests that ADHD-related symptoms are amenable with ω-3 fatty acid supplementation. The retrospective Cape Cod Health Study found that increased fish consumption was associated with increased odds of children having ADHD-related symptoms but showed no other meaningful associations to childhood learning and behavior disorders [40]. They observed that it may be because of insufficient fish consumption or the type of fish consumed. It is possible that the present study's finding of increased teacher-observed ADHD-related symptoms with fish consumption may be due to insufficient fish consumption; in our study, the fish provided around 150 to 200 mg DHA, <50% the amount provided by the supplements.

The positive correlation seen between ARA and ω-3 fatty acids corresponds with observations made in other studies [41,42]. For example, Luxwolda et al. found a bell curve relationship between erythrocyte ω-3 fatty acid and ARA [41]. It appears that the incorporation of ω-3 and ω-6 long-chain polyunsaturated fatty acids into cell membrane is highly regulated and the balance between the two fatty acid families is critical for orderly structural organization and function of cellular and subcellular membranes. *At the same time, studies have found that ARA supplementation improves infant neurodevelopment, including cognition and language development* [42–44]. *Further studies are required to better understand the role of ARA in normal growth and development.*

The findings from this study have several limitations. First, the amount of ω-3 fatty acids was not the same across the two groups; the fish oil capsules were likely to have uniform nutritional contents; whereas the ω-3 fatty acid levels of the variety of the fish served were not examined. These discrepancies could act as a confounder for the present comparison. According to a meta-analysis of 21 cohort studies reported by Zhang et al. [45], both capsule supplementation and fish appear to be associated with lower risk for cognitive impairment, there is no established linear dose–response relation in the existing literature. In another meta-analysis, it was suggested that ω-3 fatty acid capsules have a greater potential for enhancing cognitive performance, especially in growing children [46]. Future studies should aim to establish the optimal intake of ω-3 fatty acids for optimum effect of cognitive and behavioral functioning in children; preferably using a double-blind study methodology rather than an open-label one as used in this study and with varying amounts of ω-3 fatty acids. Second, ADHD symptoms were solicited by the Vanderbilt Assessment Scales-Teacher Assessment Scale, which has not been standardized for use with the Omani population. These symptoms were solicited using a checklist rather than a clinician-based semistructured interview. The development of a reliable and valid Arabic version of these scales would greatly improve confidence in the measure, particularly if this process of standardization were carried out with an eye toward the cultural specificities relevant to the Omani school population. Finally, students were only recruited from Muscat, the capital area, thus results cannot be generalized to the Omani population.

This small intervention study contributes to available evidence on the cognitive and behavioral benefits in healthy school children of ω-3 fatty acid consumption, particularly as a supplement. However, further research is required to determine optimal intake. Given these benefits, public health authorities should not only continue to promote fish consumption but may wish to consider enhancing the food fortification program as part of broader policy to improve the health of children and their performance in school.

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References

[1] Sahay A, Ali SM, Gupta A, Goes JI. Ocean color satellite determinations of phytoplankton size class in the Arabian Sea during the winter monsoon. Remote Sens Environ 2017;198:286–96.
[2] Alasfoor DH, Rajab H, Al Rassasi B. Food based dietary guidelines, technical background and description. Muscat (Oman): Oman Ministry of Health; 2007.
[3] Kim JL, Winkvist A, Aberg MA, Aberg N, Sundberg R, Torén K, et al. Fish consumption and school grades in Swedish adolescents: a study of the large general population. Acta Paediatr 2010;99:72–7.
[4] Fotuhi M, Mohassel P, Yaffe K. Fish consumption, long-chain omega-3 fatty acids and risk of cognitive decline or Alzheimer disease: a complex association. Nat Rev Neurol 2009;5:140.
[5] Cooper RE, Tye C, Kuntsi J, Vassos E, Asjherson P. Omega-3 polyunsaturated fatty acid supplementation and cognition: a systematic review and meta-analysis. J Psychopharmacol 2015;29:753–63.
[6] Grosso G, Pajak A, Marventano S, Castellano S, Galvano F, Bucolo C. Role of omega-3 fatty acids in the treatment of depressive disorders: a comprehensive meta-analysis of randomized clinical trials. PLoS ONE 2014;9. e96905.
[7] Stonehouse W. Does consumption of LC omega-3 PUFA enhance cognitive performance in healthy school-aged children and throughout adulthood? Evidence from clinical trials. Nutrients 2014;6:2730–58.
[8] Richardson AJ, Burton JR, Sewell RP, Spreckelsen TF, Montgomery P. Docosahexaenoic acid for reading, cognition and behavior in children aged 7–9 years: a randomized, controlled trial (the DOLAB Study). PLoS ONE 2012;7. e43909.
[9] Raine A, Portnoy J, Liu J, Mahoomed T, Hibbeln JR. Reduction in behavior problems with omega-3 supplementation in children aged 8–16 years: a randomized, double-blind, placebo-controlled, stratified, parallel-group trial. J Child Psychol Psychiatry 2015;56:509–20.
[10] Kuratko CN, Barrett EC, Nelson EB, Salem Jr N. The relationship of docosahexaenoic acid (DHA) with learning and behavior in healthy children: a review. Nutrients 2013;5:2777–810.
[11] Dunstan JA, Dixon GN, Simmer K, Prescott SL. Cognitive assessment of children at age 2(1/2) years after maternal fish oil supplementation in pregnancy: a randomised controlled trial. Arch Dis Child Fetal Neonatal Ed 2008;93:F45–50.
[12] Richardson AJ. Omega-3 fatty acids in ADHD and related neurodevelopmental disorders. Int Rev Psychiatry 2006;18:155–72.
[13] Richardson AJ, Puri BK. A randomized double-blind, placebo-controlled study of the effects of supplementation with highly unsaturated fatty acids on ADHD-related symptoms in children with specific learning difficulties. Prog Neuropsychopharmacol Biol Psychiatry 2002;26:233–9.
[14] Gispert-Llaurado M, Perez-Garcia M, Escribano J, Closa-Monasterolo R, Luque V, Grote V, et al. Fish consumption in mid-childhood and its relationship to neuropsychological outcomes measured in 7–9 year old children using a NUTRIMENTHE neuropsychological battery. Clin Nutr 2016;35:1301–7.
[15] Butler LJ, Janulewicz PA, Carwile JL, White RF, Winter MR, Aschengrau A. Childhood and adolescent fish consumption and adult neuropsychological performance: an analysis from the Cape Cod Health Study. Neurotoxicol Teratol 2017;61:47–57.
[16] Al-Sharbati M, Adawi SA, Al-Hussaini AA, Lawati SA, Martin R. ADHD in Omani schoolgirls. J Am Acad Child Adolesc Psychiatry 2004;43:132–3.
[17] Al-Sharbati M, Al-Adawi S, Lawati SA, Al-Mshefri F. Hyperactivity in a sample of Omani schoolboys. J Atten Disord 2008;12:264–9.
[18] Richardson AJ, Montgomery P. The Oxford-Durham study: a randomized, controlled trial of dietary supplementation with fatty acids in children with developmental coordination disorder. Pediatrics 2005;115:1360–6.
[19] Al-Ghatani AM, Obonsawin M, Al Moutaery KR. Normative data for the two equivalent forms of the Arabic verbal fluency test. Pan Arab J Neurosurg 2009;13:57–65.
[20] Al-Adawi S, Braidy N, Essa M, Al-Azri F, Hussain S, Al-Sibani N, et al. Cognitive profiles in patients with multi-infarct dementia: an Omani study. Dement Geriatr Cogn Disord Extra 2014;4:271–82.
[21] Espy KA, Cwik MF. The development of a trial making test in young children: the TRAILS-P. Clin Neuropsychol 2004;18:411–22.
[22] Lezak MD, Howieson DB, Bigler ED, Tranel D. Neuropsychological assessment. 5th ed New York: Oxford University Press; 2012.
[23] American Academy of Pediatrics. Caring for children with ADHD: a resource toolkit for clinicians. Itasca (IL): Author; 2008.
[24] Pliszka S. Issues AWGoQ. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 2007;46:894–921.
[25] Wamithi S, Ochieng R, Njenga F, Akech S, Macharia WM. Cross-sectional survey on prevalence of attention deficit hyperactivity disorder symptoms at a tertiary care health facility in Nairobi. Child Adolesc Psychiatry Ment Health 2015;9:1.
[26] Kazem AM, Alzubiadi AS, Yousif YH, Aljamail FA, Al-Mashhdany SI, Alkharusi HA, et al. Psychometric properties of Raven's Colored Progressive Matrices for Omani children aged 5 through 11 years. J Soc Behav Person 2007;35:1385–98.
[27] Campoy C, Escolano-Margarit MV, Anjos T, Szajewska H. Omega 3 fatty acids on child growth, visual acuity and neurodevelopment. Br J Nutr 2012;107 (Suppl. 2):S85–106.
[28] McNamara RK, Asch RH, Lindquist DM, Krikorian R. Role of polyunsaturated fatty acids in human brain structure and function across the lifespan: an update on neuroimaging findings. Prostaglandins Leukot Essent Fatty Acids 2017. https://doi.org/10.1016/j.plefa.2017.05.001. [E-pub ahead of print].
[29] D'Ascoli TA, Mursu J, Voutilainen S, Kauhanen J, Tuomainen TP, Virtanen JK. Association between serum long-chain omega-3 polyunsaturated fatty acids and cognitive performance in elderly men and women: the Kuopio Ischaemic Heart Disease Risk Factor Study. Eur J Clin Nutr 2016;70:970–5.
[30] Sheppard KW, Cheatham CL. Omega-6 to omega-3 fatty acid ratio and higher-order cognitive functions in 7- to 9-y-olds: a cross-sectional study. Am J Clin Nutr 2013;98:659–67.
[31] Dalton A, Wolmarans P, Wittuhn RC, van Stuijvenberg ME, Swanevelder SA, Smuts CM. A randomised control trial in schoolchildren showed improvement in cognitive function after consuming a bread spread, containing fish flour from a marine source. Prostaglandins Leukot Essent Fatty Acids 2009;80:143–9.
[32] Al-Ghannami SS, Sedlak E, Hussein IS, Min Y, Al-Shmmkhi SM, Al-Oufi HS, et al. Lipid-soluble nutrient status of healthy Omani school children before and after intervention with oily fish meal or re-esterified triacylglycerol fish oil. Nutrition 2016;32:73–8.
[33] Bloch MH, Qawasmi A. Omega-3 fatty acid supplementation for the treatment of children with attention-deficit/hyperactivity disorder symptomatology: systematic review and meta-analysis. J Am Acad Child Adolesc Psychiatry 2011;50:991–1000.
[34] Hawkey E, Nigg JT. Omega-3 fatty acid and ADHD: blood level analysis and meta-analytic extension of supplementation trials. Clin Psychol Rev 2014;34:496–505.
[35] Cooper RE, Tye C, Kuntsi J, Vassos E, Asherson P. The effect of omega-3 polyunsaturated fatty acid supplementation on emotional dysregulation, oppositional behaviour and conduct problems in ADHD: a systematic review and meta-analysis. J Affect Disord 2016;190:474–82.
[36] Shue KL, Douglas VI. Attention deficit hyperactivity disorder and the frontal lobe syndrome. Brain Cogn 1992;20:104–24.
[37] Barkley RA. Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. Psychol Bull 1997;121:65–94.
[38] Suzuki K, Okumura Y, Kita Y, Oi Y, Yamashita Y, Goto T, et al. Excessive hemodynamic activity in the superior frontal cortex during the flanker task in children with attention deficit hyperactivity disorder. Neuroreport 2017;28:828–32.
[39] Sonuga-Barke EJ, Brandeis D, Cortese S, Daley D, Ferrin M, Holtmann M, et al. Nonpharmacological interventions for ADHD: systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. Am J Psychiatry 2013;170:275–89.
[40] Carwile JL, Janulewicz P, Butler L, Aschengrau A. Childhood fish consumption and learning and behavioral disorders. Int J Environ Res Public Health 2016;13:1069.
[41] Luxwolda MF, Kuipers RS, Smit EN, Velzing-Aarts FV, Dijck-Brouwer DA, Muskiet FA. The relation between the omega-3 index and arachidonic acid is bell shaped: synergistic at low EPA+DHA status and antagonistic at high EPA+DHA status. Prostaglandins Leukot Essent Fatty Acids 2011;85:171–8.
[42] Devlin AM, Chau CMY, Dyer R, Matheson J, McCarthy D, Yurko-Mauro K, et al. Developmental outcomes at 24 months of age in toddlers supplemented with arachidonic acid and docosahexaenoic acid: results of a double blind randomized, controlled trial. Nutrients 2017;9:975.
[43] Hadley KB, Forsyth S, Ryan AS, Salem N. The essentiality of arachidonic acid in infant development. Nutrients 2016;8:216.
[44] Carlson SE, Colombo J. Docosahexaenoic acid and arachidonic acid nutrition in early development. Adv Pediatr 2016;63:453–71.
[45] Zhang Y, Chen J, Qiu J, Li Y, Wang J, Jiao J. Intakes of fish and polyunsaturated fatty acids and mild-to-severe cognitive impairment risks: a dose-response meta-analysis of 21 cohort studies. Am J Clin Nutr 2016;103:330–40.
[46] Jiao J, Li Q, Chu J, Zeng W, Yang M, Zhu S. Effect of n-3 PUFA supplementation on cognitive function throughout the life span from infancy to old age: a systematic review and meta-analysis of randomized controlled trials. Am J Clin Nutr 2014;100:1422–36.