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Blood docosahexaenoic acid and eicosapentaenoic acid in vegans: Associations with age and gender and effects of an algal-derived omega-3 fatty acid supplement

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SUMMARY

Background & aims: Several studies have demonstrated that vegetarians and vegans have much lower plasma concentrations of omega-3 fatty acids (i.e., docosahexaenoic and eicosapentaenoic acids) when compared to those who eat fish. The purposes of this study were 1) to define the age and/or sex-specific docosahexaenoic plus eicosapentaenoic acids levels in red blood cell membranes (expressed as a percent of total fatty acids; hereafter the omega-3 index) in long-term vegans, and 2) to determine the effects of a vegetarian omega-3 supplement (254 mg docosahexaenoic plus eicosapentaenoic acids/day for 4 months) on the omega-3 index.

Methods: A sample ($n = 165$) of vegans was recruited, and their omega-3 index was determined using a dried blood spot methodology. A subset of 46 subjects with a baseline omega-3 index of <4% was given a vegetarian omega-3 supplement for 4 months and then retested.

Results: The mean ± SD omega-3 index was 3.7 ± 1.0% which was similar to that of a cohort of omnivores (deployed US soldiers) from a recently-reported study. Among the vegan cohort, the index was significantly higher in females than males (3.9 ± 1.0% vs. 3.5 ± 1.0%; $p = 0.026$) and was directly related to age (p for trend = 0.009). The omega-3 index increased from 3.1 ± 0.6% to 4.8 ± 0.8% ($p = 0.009$) in the supplementation study.

Conclusions: We conclude that vegans have low baseline omega-3 levels, but not lower than omnivores who also consume very little docosahexaenoic and eicosapentaenoic acids. The vegans responded robustly to a relatively low dose of a vegetarian omega-3 supplement.

1. Introduction

The main omega-3 fatty acid in the vegan diet is alpha-linolenic acid (ALA), which is derived from foods such as soybeans, flaxseed and walnuts. ALA is very sparingly and inefficiently converted into the long-chain omega-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).[1,2] Several studies have demonstrated that vegetarians and vegans have much lower plasma concentrations of DHA and EPA when compared to those who eat fish.[3–6] Supplementation with ALA increases plasma EPA to a small extent, but it has little effect on DHA.[2,3]

A substantial body of research (in essentially omnivorous populations) over the past several decades has documented the health benefits of increased omega-3 fatty acid intakes, suggesting that baseline levels could be considered deficient.[7] Because fish and fish oils were, up until recently, the only concentrated sources of preformed DHA and EPA, individuals who do not eat fish or fish oils could be at risk of low omega-3 fatty acid status. Whether this translates into increased risk for disease (e.g., cardiovascular) in vegans is unknown as their risk is already lower than that of omnivores. A recent meta-analysis found a 29% reduction in risk for death from ischemic heart disease and 18% reduction in risk for cancer in vegetarians compared to non-vegetarians,[8] and the EPIC-

Non-standard abbreviations: ANOVA, analysis of variance; ALA, alpha-linolenic acid; ASA24, Automated Self-Administered 24-h Recall; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; RBC EPA + DHA, omega-3 index; RBC, red blood cells.

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Oxford study reported similar benefits in British vegetarians.[9] Until randomized trials with omega-3 fatty acids are conducted in vegetarian/vegan cohorts, the question of whether higher blood levels of these nutrients will reduce risk for disease will remain unanswered. Nevertheless, at our present state of knowledge, it is possible that low omega-3 status does place vegetarians/vegans at increased risk for disease, which then presents a dilemma for these individuals.

There were 2 purposes of this study. The first (Phase 1) was to determine omega-3 status in long-term vegans and to investigate age and/or sex-related differences. We also sought to compare a vegan with an omnivore cohort with respect to omega-3 status. As we were unable to recruit two cohorts simultaneously in this investigation, we have used published data (also from our laboratory) from omnivores who met most of the same inclusion/exclusion criteria as did the vegans.[10] The second purpose was to determine the extent to which omega-3 status can be improved in vegans by the administration of a vegan DHA + EPA supplement (Phase 2). Throughout we have used DHA + EPA content of red blood cells (RBC) expressed as a percent of total RBC fatty acids (hereafter called the omega-3 index[11]), as the biomarker of omega-3 status.

2. Methods

2.1. Subjects

This study was approved by the University of San Diego Institutional Review Board. Subjects were recruited from vegan websites (e.g., vegsource.com, vegnews.com, healthscience.org), with an announcement directing interested individuals to a brief screening questionnaire on the study website. To qualify for the study subjects were required to be 20 years of age or older, vegan (consuming no meat, fish, eggs or dairy) for at least one year and currently not taking any essential fatty acid supplements. Subjects who met these criteria were contacted by study staff and invited to complete a consent form online (at nutritionalresearch.org). After doing so subjects were enrolled in the study and received an email with their personal identification number and password to use to complete the online study demographic questionnaire. This questionnaire included information on age, gender, height, weight, race/ethnic group, education, and length of time on a vegan diet, and nutritional supplements used currently and in the past year. In addition to collecting a blood sample, participants were instructed to complete 3 days of dietary recall online (described below).

Participants who completed the online consent form and study questionnaire were sent an omega-3 index test kit by regular mail. The kit contained a letter welcoming participants to the study and giving general instructions for completing the study. The kit also included blood sample collection instructions, all necessary supplies, a sample collection card with study ID, and a test request form and prepaid return envelope for the blood sample. Participants were instructed to collect a drop of blood from a fingerstick and mail it immediately to the laboratory (OmegaQuant Analytics, Sioux Falls, SD). The samples were analyzed on the day of arrival as described below. (This is the same procedure that was used in the omnivore study noted above.)

A total of 296 people filled out the screening questionnaire and were qualified to participate in Phase 1 of the study. There were an additional 619 who were qualified to participate but, because we had reached the quota of 27 subjects per gender/age group (see Section 2.4), these individuals were put on a waiting list. Of the 296 who were originally qualified for the study, 59 did not complete the online dietary survey within a period of two months. These individuals were notified that they would be removed from the study, and those on the waiting list in the corresponding sex*age groups were invited to participate. Recruitment occurred between February and August of 2012. Enrolled participants received a $20 gift certificate from a national department store chain.

In Phase 2 of the study we invited a sample of Phase 1 participants who had been tested early in Phase 1 and who had an omega-3 index of 4.0% or below to take a vegan omega-3 supplement for 4 months. Of 61 invited individuals, 48 chose to participate. These individuals were sent a 4-month supply of a vegan omega-3 supplement (Life's DHA plus EPA, DSM Nutritional Products, Inc., Parsippany, NJ) providing 172 mg DHA and 82 mg EPA per 0.75 mL. They were instructed to take this amount daily via a graduated bottle dropper. The blood collection protocol used in Phase 1 was repeated after 4 months.

2.2. Fatty acids

The omega-3 index home test kit was used to measure subjects' essential fatty acid levels in a dried blood spot as previously described.[10] Briefly, fatty acids ($n = 24$) are identified using capillary column gas chromatography with an internal-standard-based, three-point calibration curve approach. Upon receipt in the laboratory, paper punches of dried blood are transferred to a reaction vial. Fatty acid methyl esters are generated with boron trifluoride for 10 min at 100 °C, extracted into hexane after the addition of water and analyzed by gas chromatography by using a GC2010 Gas Chromatograph (Shimadzu Corporation, Columbia, MD) equipped with a SP2560, 100-m column (Supelco, Bellefonte, PA). Fatty acids are identified by comparison with a standard mixture of fatty acids (GLC 727, Nucheck Prep, Elysian, MN). The omega-3 index (an erythrocyte-specific metric) is calculated from the dried blood spot EPA + DHA value using an equation determined from a study comparing these two values from 49 subjects. The correlation coefficient between RBC and dried blood spot EPA + DHA was 0.96 ($p < 0.0001$). The laboratory coefficient of variation for the omega-3 index is 5–6%.

2.3. Dietary assessments

In Phase 1 dietary intake data were collected and analyzed using the Automated Self-Administered 24-h Recall (ASA24) system, version 1, developed by the National Cancer Institute, Bethesda, MD. ASA24 is a freely available, web-based software tool.[12] It consists of a respondent web site used by participants to enter recall data and a researcher web site to manage study logistics and obtain analyses. The format and design of the Respondent Web site are modeled on the interviewer-administered Automated Multiple Pass Method 24-h recall developed by the US Department of Agriculture. Nutrient intakes were calculated by the ASA24 program based on the USDA's Food and Nutrient Database for Dietary Studies. Participants were instructed to complete at least two, and if possible three, days of dietary recall with a separation of 2–3 days between each recall. Regular reminders were sent to participants who did not complete the recalls within a month of enrollment in the study.

The ASA24 database did not include chia and hemp seeds, two food sources of ALA that might be consumed on a regular basis by vegans. These were therefore included in the online study survey, and the ALA provided was calculated as the grams of hemp/chia seed per teaspoon × frequency per week × grams ALA per teaspoon.

2.4. Statistical analysis

In phase 1, participants were initially stratified into five age categories by gender (20–39, 40–59, 60–69, 70–79, and 80+).

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Recruitment by internet proved to be difficult for those aged 70 and above, therefore the age categories of 70–79 and 80+ were collapsed. A sample size of at least 10 participants in each of the 8 age/gender group would provide 80% power to detect an effect size of 0.4 (Cohen's f) when testing the interaction term between sex and age group (4 degree of freedom test) for the omega-3 index in a two-way factorial analysis of variance (ANOVA) with a two-sided significance level of 0.05 (G*Power software v. 3.1.3). One of our cells had a sample size of 10 while the rest of the groups ranged between 17 and 26.

Descriptive statistics were computed for key study variables and included means, and standard deviations for continuous variables, and frequencies and percentages for categorical ones. Years of formal education was censored at 17 for those having greater than a college education. Race/ethnicity is self-reported as Asian, Black, Hispanic, Pacific Islander, or White.

Those with at least one day of dietary recall were included in analyses involving dietary variables. These variables were averaged across the available days (ranging from 1 to 5 days). Study participants were included in the analysis if they completed the survey, and contributed data for the blood analysis and/or the dietary recall.

To address the question of whether there were differences in the omega-3 index by age group, one-way analysis of variance was utilized, and the linear trend in mean omega-3 index across the age groups was formally assessed though a statistical contrast. To formally assess the question of whether there were mean differences in the omega-3 index by gender, a two-sample independent groups *t*-test was utilized]. Two-way ANOVA examined the question of whether mean omega-3 index varied by both age group and gender, and their interaction, as well as the linear trend across the age groups. Spearman correlation coefficients were computed and tested to determine whether there were associations between omega-3 index and both dietary intake of ALA and body mass index; analysis of covariance was used to assess these relationships controlling for age.

To address the question of whether there are differences in the omega-3 index between this vegan cohort and a group of omnivores (also not taking omega-3 supplements whose blood was analyzed using the same laboratory methods as those used with the vegans), we used data from 78 US soldiers deployed in Iraq.[10] Only blood fatty acids present at 0.5% or more of total in either cohort were included in the analysis. Fatty acid percentages were compared by two-sample *t*-test.

All statistical analysis was generated using SAS software, (Version 9.3, SAS Institute Inc., Cary, NC, USA). The significance level was set at two-sided 0.05, and the comparison of fatty acid levels with the US soldiers utilized a Bonferroni adjustment accounting for the number of fatty acids reported (0.05/15 fatty acids = 0.0036).

3. Results

3.1. Phase 1

Of those who qualified and were eligible, 178 completed the online consent form and survey, 167 sent in a blood sample and 146 completed at least one 24-h dietary recall. The omega-3 index was available from 166 participants (one blood sample was not analyzed for technical reasons). The analysis that examined the relationship between dietary intake of ALA and blood levels of omega-3 fatty acids included 141 subjects who had completed the survey, sent in their blood sample and completed at least one 24-h dietary recall. Dietary recalls ($n = 143$) were available for 1–5 days (2.7 ± 0.9 days).

Fifty-two percent of participants were female and 92% were white (Table 1). Age ranged from 22 to 85 years (years). Seven percent had a high school education or less, while 46% had post-college graduate education. Body mass index was 22.7 ± 3.7 kg/m^2 (range 16.4–41.2) and years as a vegan ranged from 1 to 52 (12.8 ± 10.7).

The mean omega-3 index was 3.7 ± 1.0% (Table 2), and it was significantly higher in females than males (females = 3.9% ± 1.0% vs. males = 3.5% ± 1.0%; $p = 0.026$). The omega-3 index was directly and linearly related with age, with means of 3.5%, 3.6%, 4.0%, and 4.0% for the youngest to the oldest age groups (linear trend $p = 0.009$; Fig. 1). Further adjusted for dietary ALA as the sole covariate in the regression model, the linear trend between age group and the omega-3 index became non-significant ($p = 0.18$). In two-way ANOVA, the gender by age group interaction was not significant ($p = 0.13$), and the main effects model supported the gender ($p = 0.023$) effect and age group linear trend ($p = 0.010$).

Intakes of EPA and DHA from dietary recalls were very low (EPA 1.5 ± 3.5 and DHA 2.8 ± 10.1 mg/day), whereas the intake of ALA averaged 3.40 ± 2.54 g/day. The omega-3 index was not correlated with dietary ALA ($r = 0.075$, $p = 0.53$), nor with BMI ($r = 0.074$, $p = 0.34$). These non-significant relationships persisted when controlling for age ($p = 0.95$ and $p = 0.81$, respectively). There was a strong relationship between age and ALA intake ($r = 0.23$, $p = 0.003$).

Demographics and levels of 14 blood fatty acids were compared between the vegans and the US soldiers. The subset of vegans included in this comparison was a mean of 7 years older than the soldiers and had more years of education (Table 3). The vegans had significantly ($p < 0.003$) higher levels of EPA and docosapentaenoic acid (22:5n3, DPA) than the soldiers. Vegan DHA levels, however, were non-significantly lower ($p = 0.015$; did not reach the adjusted level of 0.003) as was the omega-3 index ($p = 0.95$). As for the omega-6 fatty acids, arachidonic acid (20:4n6) was slightly lower in the vegans, but linoleic acid (18:2n6) was similar between groups. *Trans* fatty acids (18:1 and 18:2 isomers) were lower in the vegans (see Table 4).

3.2. Phase 2

Pre- and post-results were available for 46 individuals (2 post-blood tests were lost in the mail). The omega-3 index increased from 3.1 ± 0.6% to 4.8 ± 0.8% ($p < 0.001$; Fig. 2). Of 46 subjects with a pre-supplementation omega-3 index of <4%, 40 (87%) achieved an Index of >4% after supplementation.

Table 1
Demographic characteristics for participants in phase 1 ($N = 167$).

	Female	Male
Age		
20–39	25	21
40–59	26	26
60–69	19	23
70+	17	10
Education		
HS or less (11–12)	8	4
Some college (13–16)	36	43
Post-college (17+)	43	33
Race		
Asian	2	3
Black	1	0
Hispanic	3	3
Pacific Islands	0	1
White	81	73
Total	87	80

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Table 2
Baseline blood fatty acids[a] and the Omega-3 Index in 166 vegan subjects.

Fatty acids	Mean	SD
14:0	0.69%	0.44%
16:0	22.41%	1.65%
18:0	14.38%	1.02%
18:1trans	0.42%	0.25%
18:1n9	17.51%	2.00%
18:2trans	0.53%	0.41%
18:2n6	19.19%	2.65%
18:3n3	0.55%	0.31%
20:3n6	2.15%	0.55%
20:4n6	11.68%	1.89%
20:5n3	0.63%	0.29%
22:4n6	2.16%	0.57%
22:5n3	2.00%	0.49%
22:6n3	2.44%	0.84%
Omega-3 Index[b]	3.73%	1.02%

[a] Includes only fatty acids present at >0.4% of total fatty acids.
[b] The omega-3 index is the estimated erythrocyte EPA + DHA level and is derived from whole blood DHA + EPA levels by application of a regression equation as described previously.[10]

4. Discussion

This study surveyed the omega-3 index in long-term vegans and examined sex- and age-related differences. Assuming an omega-3 index of <4% to be undesirable, 64% of the cohort fell into this category, 27% were <3% and 1% was <2%. Thus, a substantial number of vegan subjects have low omega-3 status. Interestingly, two subjects had an index of >8%, the proposed cardioprotective level,[11] underscoring the marked metabolic variability possible between individuals. We observed an increase in the index with age, which has been observed before in omnivore populations[13] and has typically been explained by increased fish intake with aging. This obviously cannot be the case in the present cohort of vegans. The explanation for this observation here is unclear, but the fact that the inclusion of the ALA intake into the model eliminated the significant relationship between age and the omega-3 index suggests that increasing ALA intakes with age may have contributed to the correlation between age and the index. Whether the higher ALA intake was responsible for the higher omega-3 index cannot be known from these cross sectional observations. We found that women had higher omega-3 indexes than men. This too has been reported previously and is presumed to be due to enhanced synthesis of EPA and DHA from ALA in pre-menopausal women.[14] Overall, the omega-3 index was not correlated with dietary ALA intake, suggesting that post-intake processes (e.g., absorption, synthetic enzyme activities, clearance, etc.) are more determinants of the omega-3 index than dietary ALA.

There have been several previous head-to-head studies comparing omega-3 status in omnivores (meat-eaters) and vegans/vegetarians, and most were reviewed by Sanders in 2009.[6] Some have used plasma or plasma lipid classes[4,5] whereas others have used RBCs.[3,15–18] In the largest sample reported to date, plasma levels of EPA + DHA (percent of total fatty acids) were 1.0% in 232 vegans and 2.4% in 196 meat-eaters.[5] In the four prior studies that measured RBC EPA + DHA in vegans, levels averaged between 1% and 3.8% (Table 5) compared with 3.7% in the present US study. As all these studies were performed in different countries in different labs, dietary, genetic, laboratory methodologic, and/or demographic/lifestyle factors may be responsible for these differences. Typically, RBC EPA + DHA was about 50–60% lower than in a comparator group of omnivores.

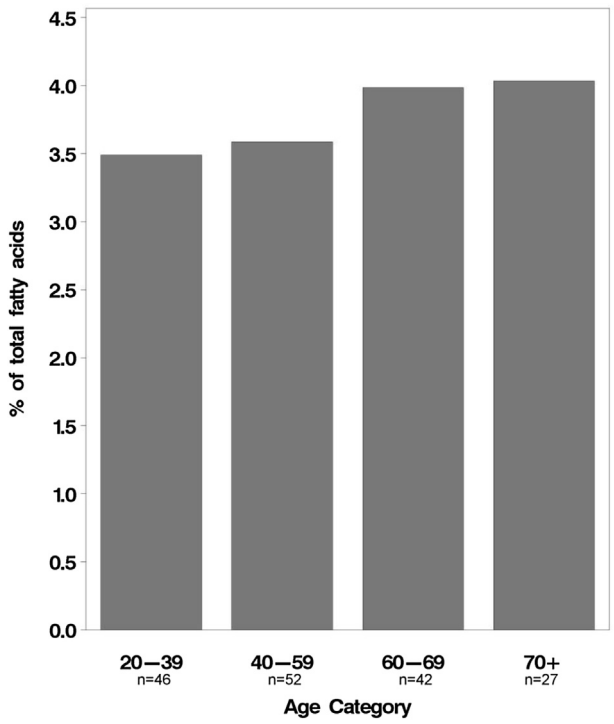

Fig. 1. Linear trend in baseline omega-3 index by age group for participants in Phase 1. *P* for trend = 0.009.

Table 3
Demographic characteristics for the male vegans, 20–54 years of age [matching the age range of the comparator group of US Soldiers deployed in Iraq[10]].

	Vegans ($n = 40$)	Soldiers ($n = 78$)	*P*-value
Age (mean ± SD)	38 ± 9	31 ± 7	0.0002
Education			<0.0001
High school or less	2 (5%)	14 (18%)	
Some college	26 (65%)	64 (82%)	
Post-college	12 (30%)	0	
Race			NS
Asian	3 (8%)	1 (1%)	
Black	0 (0%)	4 (5%)	
Hispanic	1 (3%)	5 (6%)	
White	36 (90%)	68 (87%)	

Table 4
Blood fatty acid profiles (percent of total fatty acids) for the male vegans, 20–54 years of age [matching the age range of the comparator group of US Soldiers deployed in Iraq[10]].

Fatty acids	Vegans ($n = 40$)	Soldiers ($n = 78$)
14:0	0.76 ± 0.64	0.83 ± 0.36
16:0	22.39 ± 1.44	23.21 ± 1.27*
18:0	14.28 ± 1.08	14.38 ± 0.83
18:1trans	0.38 ± 0.25	1.26 ± 0.55*
18:1n9	17.95 ± 1.88	16.16 ± 1.33*
18:2trans	0.51 ± 0.33	0.90 ± 0.18*
18:2n6	18.70 ± 2.68	18.50 ± 1.91
18:3n3	0.49 ± 0.21	0.32 ± 0.13*
20:3n6	2.08 ± 0.42	1.97 ± 0.42
20:4n6	11.95 ± 1.90	12.94 ± 1.65
20:5n3 (EPA)	0.56 ± 0.22	0.40 ± 0.18*
22:4n6	2.44 ± 0.49	2.34 ± 0.44
22:5n3	2.02 ± 0.48	1.51 ± 0.27*
22:6n3 (DHA)	2.28 ± 0.70	2.61 ± 0.65
Omega-3 Index[a]	3.48 ± 0.81	3.47 ± 0.72

*$p < 0.0033$, Bonferroni adjustment 0.05/15 tests.
[a] Calculated erythrocyte EPA + DHA content.

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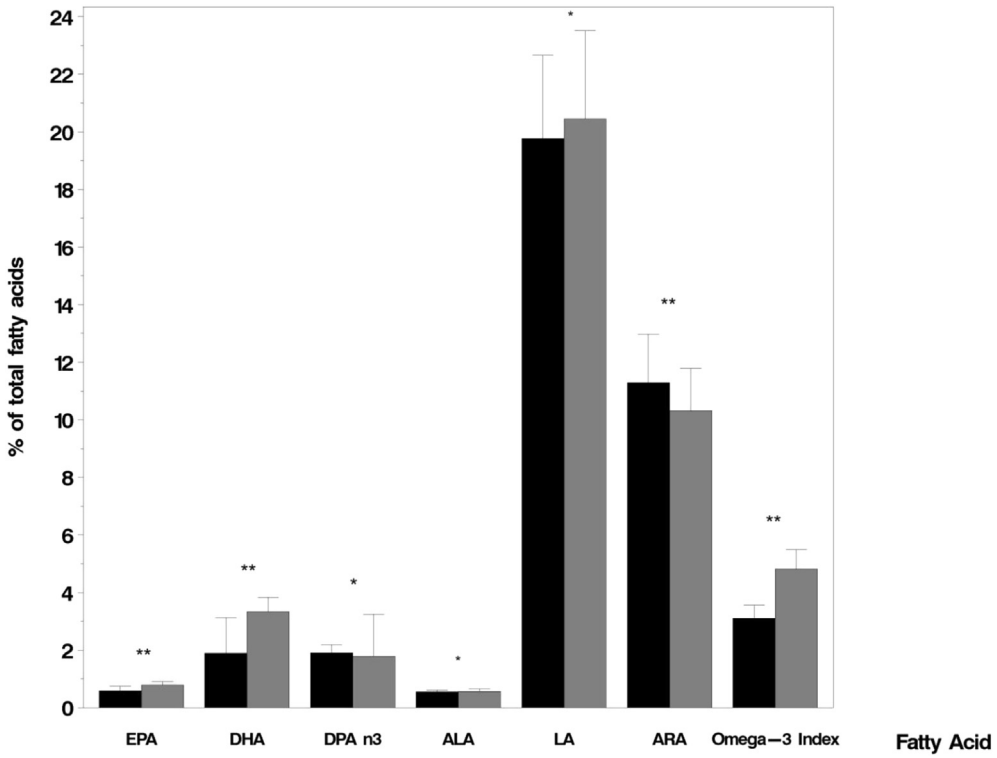

Fig. 2. The effects of 254 mg/d of omega-3 fatty acids in 46 vegan subjects on the omega-3. The omega-3 index and other selected blood fatty acids measured before (black) and after (gray) 12 weeks of supplementation. Abbreviations: EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; DPA; docosapentaenoic acid; ALA, alpha-linolenic acid; LA, linoleic acid; ARA, arachidonic acid; Omega-3 Index, the sum of EPA + DHA. $^{*}p < 0.05$; $^{**}p < 0.001$.

Similarly, the mean omega-3 index in the vegan subjects studied here (3.7%) was lower than that seen in other non-vegan cohorts in which RBC fatty acids were reported. For example, it was 4.7% in about 160,000 presumably omnivorous outpatients in the US having blood tested at a clinical laboratory.[13] Average indexes in other US cohorts were 5.7% in the Framingham Offspring Study,[19] and 4.6% in a group of about 900 patients with stable coronary disease.[20] In another cohort of 21 non-fish oil supplementing, low fish intake outpatients from Kansas City the average omega-3 index was 3.4%.[21]

Here we included as a comparator population a group of 78 US service members (virtually all males) deployed in Iraq who were eating Army rations (definitely not vegetarian cuisine). They were chosen because they were tested using the same dried blood spot method as was used here and because they met similar inclusion/exclusion criteria as the vegans (except, of course, being vegan). This afforded an opportunity to compare full blood fatty acid patterns not just the omega-3 index. We found that EPA and DPA (the latter being an elongation product of the former) were both significantly higher in the vegans than in the soldiers, but DHA (and the omega-3 index) were not different. In other words, absent a simultaneous, direct comparison between vegans and omnivores using the same dried blood spot methodology, it appears that vegans are no different from omnivores who also consume very little omega-3. Based on this comparison, the vegans may even produce more EPA (and DPA), from their presumably higher ALA intake. It should be noted that the vegan subset was older and more well-educated than the soldier comparators, and both of these factors have been associated with higher omega-3 status.[13,22] Perhaps not surprisingly, *trans* fatty acid levels were lower in the vegan cohort, presumably due to a higher intake of products containing partially-hydrogenated vegetable oils in Army rations.

Table 5
Comparison of red blood cell EPA + DHA (percent of total fatty acids) in vegans and controls in previous studies.

Population	Vegans	Controls	Description of controls
British[16]	2.0% ($n = 22$)	6.4% ($n = 22$)	"not on special diets"; matched on age, sex, height, SES status, ethnicity
Austrian[3]	1.0% ($n = 37$)	2.2% ($n = 23$)	Self-defined omnivore by questionnaire
Dutch[17]	2.3% ($n = 12$)	4.5% ($n = 76$)	"adult omnivores"
Finnish[18]	3.8% ($n = 8$)	8.1% ($n = 11$)	"normal mixed diet"; controls reported an average of 2 fish meals per week
US (present study)	3.5% ($n = 40$)	3.5% ($n = 78$)	US Soldiers deployed in Iraq[10]

In Phase 2, we found that a relatively low dose of EPA + DHA (243 mg per day) significantly raised the omega-3 index. The mean absolute increase here was 1.7% over 4 months. This compares favorably to an observed increase of 1.8% in a group of 23 omnivores given 300 mg EPA + DHA for 5 months.[23] In another study, 850 mg of EPA + DHA ethyl esters raised the omega-3 index by 1.5% after 2 months of supplementation.[24] Although not head-to-head studies, blood samples were measured using the same method in all 3 of these studies. In a German study with an algal DHA-only supplement, 940 mg/d for 2 months was reported to raise the omega-3 index from 4.8% to 8.4% in 87 vegetarians.[15] All of these findings suggest that vegans respond to supplemental omega-3 fatty acids in the same way that omnivores do.

Omega-3 treatment reduces risk for CHD death[25] but these data are from omnivorous populations, and whether vegans would derive similar benefit is unclear. It is well-known that cardiovascular risk in vegans/vegetarians is significantly reduced compared to omnivore controls,[8,9] and thus at present, there is no direct

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evidence that raising the omega-3 index would confer additional health benefits over and above their already-protective vegan diet.

More than the risk of cardiovascular disease, a concern raised by these results is that chronic low omega-3 levels among vegans could lead to depression[26] or neurologic decline in later life.[27] In a large study of 800 military suicides, the risk of death was 62 percent higher in those with low DHA levels.[28] With increased DHA demands of the baby, nursing vegan mothers may be at increased risk for post-partum depression.

Epidemiological and animal studies also suggest that omega-3 fatty acids are protective against cognitive decline.[29] Decreases in plasma DHA are associated with cognitive decline in healthy elderly and Alzheimer's patients and higher DHA intake and plasma levels are inversely correlated with increased relative risk of Alzheimer's disease.[30] However, if started early enough in life and maintained for sufficient years, some evidence suggests that it may be protective. For example, Witte et al. showed that omega-3 supplementation improved executive function[31] in healthy elderly subjects. A low omega-3 index was associated with poorer executive function in the cohort of soldiers included in this report.[10] Higher levels of blood DHA are associated with greater cognitive function scores and brain volume.[31,32] The consistency of the epidemiological findings suggests that a lifetime DHA insufficiency may put vegans at increased risk for cognitive dysfunction.

Strengths of this study included a relatively large (compared with past studies, Table 5) sample of US vegans, an objective measure of omega-3 status, and the combination of both cross-sectional and interventional components. The study also had several limitations. We did not include a control group in Phase 2, nor did we conduct analyses accounting for potential confounding variables such as race, genetic polymorphisms, or concomitant medication interactions. As noted earlier, a contemporaneous comparison group of omnivores was not included. The sample was self-selected and thus may not be truly representative of the population of interest. We also found the particular dietary intake website we used was quite difficult for many subjects to use. This led to fewer average completions than the goal of three per subject. Hence, our fatty acid intake data may be questionable although the intakes we report are reasonable for vegans. There was no objective measure of adherence to the supplementation guidelines in Phase 2. Since subjects were taking their omega-3 fatty acids by eye-dropper, actual doses likely varied considerably, and how, exactly the subjects consumed the dose of <1 mL per day is also unknown (i.e., directly on the tongue, mixed in other foods, dispersed in juice, etc.).

We conclude that a majority of long-term vegans appear to be relatively deficient in DHA and EPA, but whether this leads to adverse health consequences is unclear. It is possible that low-dose supplementation with algae-sourced DHA and EPA may mitigate the potential adverse effects of deficiency in this population. All of these issues require additional investigation.

Author contributions

All authors contributed to the study design. In addition, BS and KSK collaborated on the first draft of the manuscript, and KSK also oversaw the conduct of the study. TAS performed statistical analysis and edited the manuscript, and WSH performed blood analysis and edited the manuscript. All authors read and approved the final manuscript.

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Conflict of interest

WSH is the President of OmegaQuant Analytics, LLC, which provided the fatty acid analyses for this study. The other authors have no conflicts of interest to declare.

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