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Review Article

Omega-3/omega-6 fatty acids: The effects on the psychophysical well-being of adolescents and adults

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Abstract

Background: Fatty acids of the omega-3/omega-6 groups are used especially in cases of pregnancy, lactation, and malnutrition. In recent decades, pediatrics has been trying to find out whether the use of omega-3/omega-6 has effects on human growth and neurodevelopment.

Aims: Check the state of the art on the use of omega-3/omega-6 type fatty acids in the diet, in adolescent and adult populations.

Materials and methods: A total of 72 original articles on the topic of human growth and nutrition in pediatrics have been selected on PubMed through September 2022.

Results: In literature, the use of omega-3/omega-6, with greater prevalence in the former group than the latter group, appears to be most effective in hypertension hypothesis, dyslipidemia, and high C-reactive protein values, cardiovascular risk, and neuropathic pain, while appearing to have less impact on neurodegenerative (except in multiple sclerosis) and mental disorders (except in depression). Interesting benefits can be detected when combining omega-3/omega-6 with spirulina algae, chitosan, probiotics, vitamin D, fiber and plant extracts.

Conclusion: Significant evidence emerges on the importance of omega-3 and omega-6 fatty acid supplementation, but important structural shortcomings of research designs still emerge from the published studies; moreover, many studies assume that fatty acid supplementation can have a curative effect on already active diseases, when in fact such prescriptions should be considered as adjuvant therapies to prevent or promote symptomatic regression, precisely because of their anti-inflammatory, antioxidant and immunomodulating virtues. However, there is no concrete and robust evidence of the positive impact on psychological well-being. Future research that can resolve the critical issues highlighted is hoped to promote a better approach to the topic of omega-3/omega-6 supplementation in human health.

Background and aims

Omega-3/Omega-6

Fatty acids are aliphatic monocarboxylic acids derived from or contained in esterified form in a vegetable or animal fat, oil, or wax, and are divided into Short-Chain (SCFA), Medium-Chain (MCFA), Long-Chain (LCFA), or Very Long Chain (VLCFA), depending on the number of carbon atoms present [1]. α-linoleic acid (ALA), cervonic or docosahexaenoic acid (DHA), and thymnodonic or Eicosapentaenoic Acid (EPA) are among the major fatty acids of the omega-3 group, which, together with arachidonic acid (AA) of the omega-6 group, are generally considered to be potent anti-inflammatory antioxidants and immunomodulators [2].

Introductory sources can be both animal (animal oils and fats, fish oil, especially cod liver, herring and oily fish, salmon, and in lesser amounts in cod, trout, and human milk) [3] and plant sources (corn seed oil, sunflower oil, nuts, transgenic Camelina sativa seed oil, CSOs [4,5], the blueberries [6] and microalgae [7]), both in natural and synthetic forms; in

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particular, n-3 PUFAs of marine and plant origin have different effects on erythrocyte fatty acid composition and regulation of glycolipid metabolism [8].

However, the exact dose to be administered has not been determined, although there are studies that emphasize both personalizations of therapy (as is the case with obese people, who may be affected by different assimilation/absorption due to their clinical condition [9]) and use at night, in that in the absence of dietary intake of EPA and DHA, circulating levels of these fatty acids decrease during the nighttime period and reach their lowest point in the morning, and therefore, overnight consumption of n-3 PUFAs, which counteracts this pattern, may have functional significance [10]. One study went on to focus on the assumption that Omega-3 (n-3) Fatty Acid (FA) supplements increase blood concentrations of EPA and DHA and that most supplements on the market are esterified to Triglycerides (TG) or Ethyl Esters (EE), which limits their absorption and may cause gastrointestinal side effects. With this in mind, and intending to compare the 24-hour plasma concentrations of EPA, DHA, and EPA+DHA when provided esterified in Monoglycerides (MAG), this study showed that the plasma concentration of n-3 FA in adults is higher after acute supplementation with n-3 FA esterified in MAG than in EE or TG, suggesting that with a lower dose of n-3 FA MAG, the plasma concentrations of n-3 FA achieved are similar to those achieved after higher doses of n-3 FA esterified in EE or TG [11].

Omega-3/omega-6 in adolescent and adult populations

In the literature, most studies published on the adolescent population focus on allergic disease and metabolic disorders such as diabetes (and its consequences), unlike the adult population, which also broadens the audience to include autoimmune diseases, neurodegenerative disorders, inflammatory and allergic disorders, and many others.

Specifically, in the obese adolescent (as well as in the adult) it has been shown that LCPUFA-ω3 supplementation does not affect body weight [12], although it results in improved muscle tone [13,14] (while reducing linoleylcarnitine [15]) and significant platelet aggregation [16]; on insulin values, studies are conflicting [12,17], however, if omega-3 is combined with acetylsalicylic acid there is an improvement in parameters in diabetes mellitus [18], even in the presence of Duchenne dystrophy [19].

The use of omega-3/omega-6 would also appear to be effective in regulating the effects of metabolic changes that lead to obesity [20], high blood pressure, and dyslipidemia (with little evidence regarding the impact on liver fat [21] (with a preference for DHA + EPA over ALA) [22], unless it is non-alcoholic fatty liver disease [23,24] (in which case it is suggested to add vitamin d3 to the omega-3 formulation [25]).

It has also been shown that the consumption of seed oils high in omega-6 polyunsaturated fat (PUFA), and linoleic acid (LA), contributes to low-grade inflammation, oxidative stress, endothelial dysfunction, and atherosclerosis [26] and not surprisingly, a low serum level of arachidonic acid (AA) was instead associated with an unfavorable functional outcome in patients with acute intracerebral hemorrhage [27].

Recent studies have shown that the combined dietary supplement of DHA / EPA improves the status of triglycerides and HDL, but can increase LDL levels compared to acid α-lipoic acid (ALA) if a low n-6 / n-3 ratio is not maintained [28]. Specifically, PUFAs with a low n-6 / n-3 ratio have been shown to significantly reduce triglyceride concentrations and increase HDL-cholesterol concentrations, while plant-derived n-3 PUFAs significantly reduce total cholesterol and LDL-cholesterol concentrations, and EPA and DHA n-3 PUFAs significantly reduce triglyceride concentrations and increase HDL-C concentrations [29].

Cardiac and vascular diseases have been studied for decades concerning the use of omega-3/omega-6, showing efficacy in cardiovascular risk, atherosclerosis, cardiac arrhythmic disorders, and cardiac ischemic forms, with greater preference for ALA over DHA and EPA and the latter over DHA, although there is a risk of increased fibrous plugin coronary atherosclerotic plaques, but only if supplemental omega-3 intake is < 3.5%, discouraging the combination of DHA + EPA + Acetylsalicylic Acid (although there is discordance) as capable of affecting cyclooxygenase activity in platelets [18,30-40].

Inflammatory diseases, which have high C-reactive protein values, also find benefits when treated with omega-3/omega-6 supplementation, demonstrating greater efficacy of EPA over DHA [41,42].

The therapeutic utility of omega-3/omega-6 use has also been demonstrated concerning the improvement of allergic symptoms of a muscular-tensive, neuropathic [43,44] or autoimmune nature from rheumatoid arthritis [16], and in cystic fibrosis [45], periodontitis [46], sperm motility [47], of male hypotestosteronism in overweight or obese individuals (but only when supplementing with DHA) [48] and the risk of preeclampsia [49,50] and placental disorders, but only in low-risk pregnancies and if supplementation occurs early in pregnancy and not late [51], as well as slowing the outcomes of maculopathy [52] and the disabling symptoms of dry eye syndrome [53].

Concerning about cognitive performance and psychological stability, there are encouraging results in the literature with respect to cognitive function [54] (although it would appear that DHA supplementation has efficacy on attention in ADHD [55-57], EPA supplementation has efficacy on long-term memory, working memory, and problem solving function [58,59], while DHA+EPA has efficacy on executive functions in Alzheimer-type dementia [60]), especially if DHA/EPA supplementation is combined with curcumin [61] and piperine [62]; on the other hand, the positive effect on psychiatric symptoms (anxiety, obsessive, depressive, psychotic and nonpsychotic in bipolar and eating disorders, with a higher positive EPA>DHA ratio for depressive symptoms) [63-80] and neurodegenerative disorders (such as Alzheimer's and Multiple Sclerosis) [81-88], which might be affected by the placebo effect or a slight improvement brought about by the anti-inflammatory and

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oxidative effects of the administered fatty acids, appears less encouraging.

Materials and methods

We searched in PubMed Central, Internet Archive Scholar, CORE, CiteSeerX, Semantic Scholar, and Europe PMC, until September 30, 2022, for meta-analyses, clinical trials, and randomized controlled trials, using the keyword "omega-3/omega-6 fatty acids", "DHA/EPA/ALA/AA", "adolescent" and "adult", content on the abstract and title, have been selected 10,675 useful results, of which 72 original articles were used for the present review as they focused on the topics of growth and neurodevelopment. A single reference (book) related to the analyzed topic from sources outside PubMed was added in the first note. Simple reviews, opinion contributions, or publications in popular volumes were excluded because they were irrelevant or redundant for this paper, and publications that did not present results or statistical samples but only research protocols and proposals, those that did not specifically address the topic of investigation, those with contradictory data, unreliable data, or otherwise with a deficient research design. The search was limited to English-language articles. No limit was placed on the year of publication, covering the time window from 1979 to the present period Figure 1.

Results, discussion and limitations

In the medical literature, omega-3/omega-6 supplementation is advisable, with proper precautions and specific purposes, although to date, the reference dietary intakes have not yet been established with certainty, and published studies have important structural shortcomings, such as frequent small sample sizes for each category evaluated, questionable quality of included studies, and technical error, as well as the noncomparability of blood levels of omega-3 long-chain polyunsaturated fatty acids and the possible influence of genetic factors (such as in the case of the presence of the APOEε4 -APOE4-allele that accelerates the oxidation of omega-3 polyunsaturated fatty acids -PUFAs- or

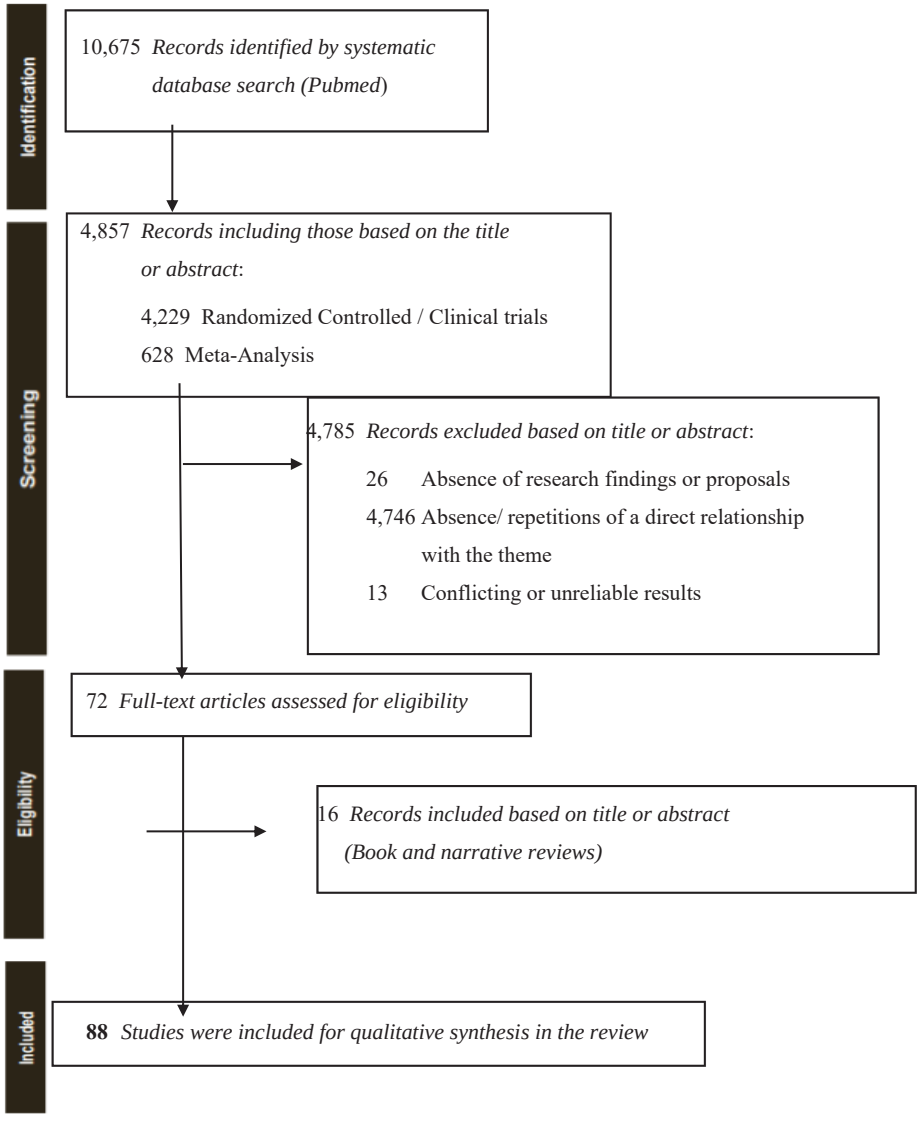

Figure 1: Prisma model.

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in the hypothesis of the minor allele of rs3834458 in FADS2 that results in lower delta-6 desaturase activity leading to increased ALA and decreased EPA, DPA and DHA in the blood) and environmental. These limitations could qualitatively affect the conclusive results.

The use of omega-3/omega-6, with greater prevalence in the former group than the latter group, appears to be most effective in hypertension hypothesis, dyslipidemia, and high C-reactive protein values, although there is still debate about efficacy on inflammatory factors such as interleukin (IL)-6 and tumor necrosis factor (TNF)-α.

The impact on cardiovascular risk brought about by the addition of omega-3 to statin therapy also appears to be nonsignificant, although studies often consider only high-risk patients and not all other subjects as well, according to a rationale opposite to prevention, in fact leading to a potential bias that would lead one to believe on their no efficacy, when in fact they could have a preventive efficacy (even reduced or potential) on cardiovascular risk. In particular, studies show differentiation by type of morbid condition, modulating the prescription according to the specific clinical profile of the patient, since fatty acids of animal origin do not have the same function and effectiveness as those of marine and plant origin; in fact: if the former are more effective in reducing systolic blood pressure and dyslipidemia, the latter are better suited to intervene in erythrocyte fatty acid composition and regulation of glycolipid metabolism; if DHA has a greater anti-inflammatory effect, on the metabolic and nervous system, EPA has greater impact in the cardiovascular system and depressive and mood symptoms, but their DHA + EPA combination may not be suitable in the presence of coronary atherosclerotic plaques (as long as a low n-6/n-3 ratio is maintained), hypercholesterolemia with high LDL, coronary ischemic heart disease, and the presence of cardiac arrhythmias, and in such cases ALA supplementation is better; DHA + EPA + aspirin is always discouraged, because they might affect the activity of cyclooxygenase in platelets, and promote thrombotic episodes, in more predisposed individuals (smoking, obesity, dyslipidemia, genetic thrombophilia, and taking birth control pills).

In obesity then, the clinical picture becomes more complicated, as the factors at play are multiple, complex, and interlinked, although one study has nonetheless demonstrated a clinical benefit in the administration of DHA+EPA, as well as the use of spirulina algae, chitosan, probiotics, vitamin D, fiber, and plant extracts, to promote moderate weight loss, under controlled dietary intake.

The same discourse can also be applied to psychiatric symptomatology, which is affected as much by exact drug therapy as by the exact daily intake of the omega-3 supplement taken (as there is high subjective variability in the response to the supplement in erythrocytes plasma, and whole blood depending on different doses), but also to neurodegenerative diseases such as Alzheimer's, which appear to be unaffected by DHA/EPA supplementation as much as glucose-insulin ratio, malnutrition, and hypovitaminosis; the exception appears to be Multiple Sclerosis, in which omega-3 and fish oil supplementation have beneficial effects on reducing relapse rates, inflammatory markers, and improving quality of life. Evidence on psychological well-being is not robust, although there are studies already cited that point to secondary effects in certain neurodegenerative pathologies and in anxiety and mood states Table 1.

Table 1: Cohort studies. Meta: Meta-analysis. Sys = Systematic review. R = Randomized Study. Only R considers the total study participants; Meta and Sys refer to the number of studies.

Author (Year)	Objectives	Type	Key Results and Conclusions
Simopoulos AP, et al. [2]	The importance of the ratio of omega-6/omega-3 essential fatty acids	Sys: 101	A lower ratio of omega-6/omega-3 fatty acids is more desirable to reduce the risk of many of the high-prevalence chronic diseases in Western societies, as well as in developing countries, that are exported to the rest of the world.
Yang J, et al. [3]	DHA/EPA and oxidative stress	M: 21	It remains controversial whether n-3 PUFAs are effective in counteracting oxidative stress. On the other hand, data suggest that n-3 PUFA supplementation may be effective in the early stages of NAFLD, but not in patients with more severe NAFLD or NASH.
West AL, et al. [4]	DHA/EPA in CSO	R: 36	The incorporation into blood lipids of EPA and DHA consumed in the form of CSOs was equivalent to that of BFO and such transgenic vegetable oils are an adequate dietary source of EPA and DHA in humans.
Schwab US, et al. [5]	Camelina Sativa Oil	R: 79	A diet enriched in CSO improves serum lipid profile as compared with a diet enriched in FF or LF in subjects with impaired fasting glucose, with no differences in glucose metabolism or concentrations of inflammatory markers.
McNamara RK, et al. [6]	Omega-3 and blueberry	R: 65	The FO and BB groups reported fewer cognitive symptoms, and the BB group showed better memory discrimination, indicating that supplementation improved cognition. The cognitive benefit in the BB group was associated with the presence of urinary anthocyanins reflecting recent BB intake but not anthocyanin metabolites. However, combined FO + BB treatment was not associated with cognitive improvement as expected.
Dawczynski C, et al. [7]	Omega-3 and treatment of rheumatoid arthritis	R: 38	DHA supplementation with microalgae improves disease activity in patients with RA along with a shift in the balance of AA- and DHA-derived lipid mediators toward an anti-inflammatory/pro-remedial state
Liu H, et al. [8]	Effects of marine-derived and plant-derived omega-3 polyunsaturated fatty acids	R: 180	Perilla oil supplementation reduced FBG, while fish oil supplementation reduced TG level. PUFA n-3s of marine and plant origin have different effects on erythrocyte fatty acid composition and regulation of glycolipid metabolism.

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Fisk ML, et al. [9]	Omega-3 and adipose tissue inflammation	R: 84	Reduced expression of genes responsible for fatty acid activation and metabolism may contribute to an inflammatory profile of oxylipins and limit the effects of LC n-3 PUFAs in obesity. Individualized supplementation of LC n-3 PUFAs based on obesity status may be necessary.
Jackson PA, et al. [10]	Diurnal rhythm of plasma EPA and DHA in healthy adults	R: 21	In the absence of dietary intake of EPA and DHA, circulating levels of these fatty acids decrease during the overnight period and reach their lowest point in the morning. Consumption of n-3 PUFAs at night, which counteracts this pattern, may have functional significance.
Chevalier L, et al. [11]	DHA/EPA and blood concentrations	R: 22	The plasma concentration of n-3 FA in adults is higher after acute supplementation with n-3 FA esterified in MAG than in EE or TG.
Lòpez-Alarcòn M, et al. [12]	Omega-3 and body weight and insulin resistance in pubertal children with obesity	R: 366	LCPUFA-ω3 supplementation does not affect body weight or insulin in adolescents with obesity.
Rondanelli M, et al. [13]	DHA/EPA on fat-free mass and physical performance in elderly	Meta: 14	N-3 EPA + DHA supplementation could be a promising strategy to improve muscle quality and prevent or treat fragility.
Huang YH, et al. [14]	Effects of Omega-3 Fatty Acids on Muscle Mass, Muscle Strength, and Muscle Performance	Meta: 10	A long period of omega-3 fatty acid supplementation can improve walking speed.
Guo X-F, et al. [15]	Clinical implications in DHA/EPA supplementation on the inflammatory mediators	Meta: 20	Intervention with EPA significantly reduced systolic blood pressure, especially in subjects with dyslipidemia. The aggregate effect indicated that supplemental DHA exerted a significant reduction in diastolic blood pressure in subjects with dyslipidemia.
Tomic-Smiljanic M, et al. [16]	DHA/EPA and AR	R: 60	Co-administration of concentrated fish oil with supplementation may reduce platelet aggregation in adults with RA.
Abbott KA, et al. [17]	DHA and insulin resistance	R: 73	DHA-enriched fish oil reduces insulin resistance in overweight and obese adults.
Holub A, et al. [18]	The effects of aspirin and N-3 fatty acids on telomerase activity in adults with diabetes mellitus	R: 30	Aspirin harms aging in diabetics who have relatively high EPA and DHA ingestion.
Rodrìguez-Cruz M, et al. [19]	DHA/EPA and Duchenne muscular dystrophy	R: 28	Taking Omega-3 long-chain polyunsaturated fatty acids (Ω-3LCPUFA, 2.9 g/day) for 6 months probably slows the progression of muscle loss, decreases fat mass, and reduces IR in boys with DMD.
Gonzàlez-Becerra K, et al. [20]	DHA/EPA and metabolic diseases	M: 24	Consumption of fatty acids such as n-3 PUFAs: EPA and DHA, and MUFAs: oleic acid and palmitoleic acid has been associated with improved metabolic. Fatty acids can regulate gene expression by modifying epigenetic mechanisms and, consequently, have a positive or negative impact on metabolic outcomes.
Parker HM, et al. [21]	DHA/EPA and Hepatic fat	R: 50	Omega-3 PUFAs do not appear to be an effective agent for reducing liver fat in overweight men. The factors that determine the health benefits of omega-3 PUFA supplementation at the individual level need to be clarified.
Zhou Q, et al. [22]	Effects of DHA/EPA on IL-6	R: 123	Supplementation improves lipid and IL-6 status. The α-linolenic acid (ALA) supplement is not necessary.
Song L, et al. [23]	DHA/EPA and hepatic steatosis in non-alcoholic fatty liver disease	R: 96	Co-supplementation of phytosterol esters (PS) and EPA + DHA could increase the effectiveness of the treatment of hepatic steatosis.
Guo X-F, et al. [24]	Compare EPA, DPA, and DHA incorporated into red blood cells, phospholipids, plasma PLs, plasma triglycerides, and plasma cholesterol ester fractions	R: 12	Supplementation with DPA and DHA significantly increased the levels of sphingosine 1-phosphate and 15-deoxy-Δ12,14-prostaglandin A1 compared with the olive oil group. In addition, supplementation with EPA and DHA significantly reduced the levels of linoleylcarnitine, compared with the olive oil group.
Yang J, et al. [25]	DHA/EPA and oxidative stress	Meta: 21	It remains controversial whether n-3 PUFAs are effective in counteracting oxidative stress. On the other hand, data suggest that n-3 PUFA supplementation may be effective in the early stages of NAFLD, but not in patients with more severe NAFLD or NASH.
Hennig B, et al. [26]	High-energy diets, fatty acids and endothelial cell function: implications for atherosclerosis	R: 66	Omega-6 fatty acids, and especially linoleic acid, cause endothelial cell dysfunction most markedly as well as can potentiate TNF-mediated endothelial cell injury.
Takahashi J, et al. [27]	DHA/EPA and acute intracerebral hemorrhage	R: 133	A lower serum level of AA has been associated with an unfavorable functional outcome in patients with ICH. AA may be an important biomarker of severity among patients with ICH.
Chen H, et al. [28]	DHA/EPA vs ALA on cardiometabolic disorders	Meta: 14	Dietary supplementation of EPA/DHA improved TG and HDL status, but increased LDL levels compared with ALA.
Li N, et al. [29]	Low n-6/n-3 ratio	R: 1,368	Low n-6/n-3 ratio PUFAs significantly reduced TG concentration and increased HDL-C concentration. The beneficial effects of low n-6/n-3 ratio PUFAs on TG, TC, HDL-C, and LDL-C concentrations increased with time. However, plant-derived n-3 PUFAs significantly reduced TC and LDL-C concentrations, while EPA- and DHA-derived n-3 PUFAs significantly reduced TG concentration and increased HDL-C concentration.
Youjia D, et al. [30]	Modulation of endothelial cell responses and vascular function by dietary fatty acids	S: 59	This review summarizes the results of studies that have examined the acute and chronic effects of dietary fatty acids on endothelial function and vascular properties in humans, as well as the potential mechanisms by which n-3 polyunsaturated fatty acids regulate endothelial function.
Chen X, et al. [31]	Omega-3 and rs3834458 Single Nucleotide Polymorphism in FADS2	Meta: 5	The minor allele of rs3834458 in FADS2 may result in decreased delta-6 desaturase activity leading to increased ALA and decreased EPA, DPA, and DHA in the blood.
Guo X-F, et al. [32]	Effects of EPA and DHA on blood pressure and inflammatory factors	Meta: 20	The present meta-analysis provides substantial evidence that EPA and DHA have independent (blood pressure) and shared (CRP concentration) effects on risk factors of chronic diseases, and high-quality RCTs with multi-center and large simple-size should be performed to confirm the present findings.

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Nicholls SJ, et al. [33]	Clinical implications of DHA/EPA supplementation on the cardio risk	R: 13,078	Among patients at high cardiovascular risk treated with statins, the addition of omega-3 CA, compared with corn oil, to usual baseline therapies resulted in no significant difference in the composite outcome of major adverse cardiovascular events.
Khan SU, et al. [34]	DHA/EPA and cardiorisk	Meta: 149,051	Omega-3 FA reduced cardiovascular mortality and improved cardiovascular outcomes. The reduction in cardiovascular risk was more evident with EPA monotherapy than with EPA+DHA.
Abdelhamid AS, et al. [35]	DHA/EPA and cardiorisk	Meta: 86	Moderate and low certainty evidence suggests that increasing LCn3 slightly reduces the risk of mortality and coronary events and reduces serum triglycerides (evidence mainly from supplementation studies). Increasing ALA slightly reduces the risk of cardiovascular events and arrhythmia.
Kita U, et al. [36]	DHA/EPA and FCT	R: 130	EPA or EPA+DHA therapy in addition to strong statin therapy for the presence of coronary atherosclerotic plaques did not significantly increase fibrous cap (FCT) in noncellular plaques compared with strong statin therapy alone, but significantly increased FCT in patients with thinner FCT.
Alfaddagh A, et al. [37]	DHA/EPA and coronary artery plaque	R: 218	The addition of EPA and DHA to statins prevented coronary plaque progression in nondiabetic subjects with mean LDL-C <80 mg/Dl when an omega-3 index ≥4% was achieved. A low omega-3 index of <3.43% identified nondiabetic subjects at risk of coronary plaque progression despite statin therapy. These results highlight the importance of measuring plasma omega-3 fatty acid levels at the beginning and conclusion of the study. Aiming for an omega-3 index ≥4% maximizes cardiovascular benefit.
Xu B, et al. [38]	ALA and ischemic heart disease	R: 8,866	The benefit of ALA for IHD and its major risk factors. DHA, DPA, and EPA had no association with IHD but were partially associated with increased cardiometabolic risk factors.
Block RC, et al. [39]	DHA/EPA and aspirin	R: 2,500	The role of omega-3 (n3) fatty acids [EPA/DHA] and low-dose aspirin in the primary prevention of ischemic cardiovascular disease (CVD) is controversial. Because omega-3 fatty acids (n3) and aspirin affect cyclooxygenase activity in platelets, there could be a clinically relevant effect of aspirin in combination with a particular level of n3 fatty acids present in any individual.
Gallini A, et al. [40]	DHA/EPA and psychiatric treatment	R: 1,680	Low blood DHA-EPA concentration has been independently associated with psychotropic drug use. Future studies are needed to assess whether a low DHA-EPA concentration in the RBC is a risk marker for psychotropic drug use in older adults and to better understand the underlying pathophysiological mechanisms.
Macintosh BA, et al. [41]	DHA/EPA and pain	R: 178	DHA/EPA administration is effective in reducing neuropathic and muscular-tensive pain, precisely because of its anti-inflammatory efficacy.
Ramsden CE, et al. [42]	DHA/EPA and headache	R: 182	H3-L6 and H3 interventions altered bioactive mediators implicated in headache pathogenesis and reduced headache frequency and severity but did not significantly improve quality of life.
Galàn-Arriero I, et al. [43]	The role of Omega-3 and Omega-9 fatty acids in the treatment of neuropathic pain after neurotrauma	Sys: 32	Bioactive Omega-9 monounsaturated fatty acids, such as oleic acid (OA) and 2-hydroxy oleic acid (2-OHOA), also show therapeutic effects in neurotrauma models. These FAs reduce noxious hyperreflexia and pain-related anxiety behavior following peripheral nerve injury and improve sensorimotor function following spinal cord injury (SCI), including facilitation of descending inhibitory antinociception.
Pham TL, et al. [44]	Docosanoid signaling modulates corneal nerve regeneration	Sys: 34	Treating corneas with pigment epithelium-derived factor plus DHA increases nerve regeneration, wound healing, and tear secretion.
Watson H, et al. [45]	DHA/EPA and cystic fibrosis	Meta: 23	Regular omega-3 supplements may provide some limited benefits for people with cystic fibrosis with relatively few adverse effects: however, the quality of evidence on all outcomes was very low.
Stando M, et al. [46]	DHA/EPA and paradontitis	R: 30	Dietary intervention with high doses of omega-3 PUFAs during nonsurgical therapy may have potential benefits in the management of periodontitis.
Hosseini B, et al. [47]	DHA/EPA and male infertility	Meta: 3	Omega-3 fatty acid supplementation in infertile men resulted in a significant improvement in sperm motility and DHA concentration in seminal plasma.
Abbott KA, et al. [48]	DHA and levels of testosterone	R: 61	DHA-enriched fish oil supplementation increases testosterone levels in overweight and obese men.
Zhou SJ, et al. [49]	DHA and preeclampsia	R: 2399	DHA supplementation of 800 mg/day in the second half of pregnancy does not reduce the risk of GDM or preeclampsia.
Bakouei F, et al. [50]	DHA/EPA and preeclampsia	Meta: 67	N-3 fatty acid supplements are an effective strategy to prevent the incidence of preeclampsia in women with low-risk pregnancies.
Carvajal JA, et al. [51]	LCPUFA and deep placentation disorders	Sys: 118	It is postulated that DHA supplementation, early in pregnancy, may reduce the incidence of deep placentation disorders
Zhong Y, et al. [52]	DHA/EPA and maculopathy	Meta: 11	Increased dietary intake of ω-3 polyunsaturated fatty acids (PUFAs), particularly DHA and EPA, was associated with a reduced risk of early age-related macular degeneration (AMD subtype), while other types of fatty acids (AF) did not present significant results. Further research is needed to explore the potential association between dietary FA, plasma levels of FA, and the advanced subtype of AMD.
Downie LE, et al. [53]	DHA/EPA and dry eye disease	M: 34	The results of this review suggest a possible role of long-chain omega-3 supplementation in the management of dry eye disease, although the evidence is uncertain and inconsistent.
van der Wurff ISM, et al. [54]	DHA/EPA and cognition	M: 33	Daily supplementation of ≥450 mg DHA + EPA per day and an increase in O3I to >6% makes efficacy on cognition more likely in children and adolescents.
Chang JPC, et al. [55]	DHA/EPA and ADHD	R: 92	High-dose eicosapentaenoic acid (EPA) improves attention and vigilance in children and adolescents with attention deficit hyperactivity disorder (ADHD) and low endogenous EPA levels.

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Checa-Ros A, et al. [56]	Early monitoring of fatty acid profile in children with attention deficit	R: 40	The cognitive effects of omega-3 polyunsaturated fatty acids (ω-3 PUFAs) might make them helpful in attention deficit/hyperactivity disorder (ADHD). However, the results derived from supplementation studies in children depend on the respective combinations and the study period. We aimed to investigate the serum fatty acid profile, attention scores, and tolerability in a group of ADHD children after receiving methylphenidate (MPH) and ω-3 PUFAs for 1 month.
Emery S, et al. [58]	DHA/EPA and cognitive tests	Meta: 29	Subgroup analyses identified beneficial effects of formulations rich in eicosapentaenoic acid (EPA) but not docosahexaenoic acid (DHA) in the domains of long-term memory, working memory, and problem-solving.
Kosti RI, et al. [60]	Omega 3 and executive functions	Meta: 12	The protection offered by fish intake against cognitive decline is exhausted by intakes above 2 servings/week and is probably related to the impact of EPA and DHA on an individual's executive functions, although questions remain about the mechanisms linking short- and long-term effects.
Kuszewski JC, et al. [61]	Omega-3 and curcumin	R: 126	Improvements in processing speed following fish oil supplementation in middle-aged and elderly men could be mediated by improvements in circulatory function. The mechanisms underlying the cognitive benefits observed with curcumin are unknown.
Khairani S, et al. [62]	Curcumin-Piperine	Sys: 46	Curcumin is a potent antioxidant, that damages parasite DNA, and may promote an immune response against Plasmodium by increasing reactive oxygen species (ROS), while piperine is also a potent antioxidant that potentiates the effects of curcumin.
Liao Y, et al. [63]	Clinical implications in DHA/EPA supplementation on depression condition	Meta: 26	Current evidence supports the finding that omega-3 PUFAs with EPA ≥60% at a dosage of ≤1 g/d would have beneficial effects on depression.
van der Burg, et al. [64]	DHA/EPA and depression	R:158	Changes in fatty acid levels from a nutraceutical combination containing EPA and DHA provide a biomarker of response in the treatment of depression
Guu TW, et al. [65]	Guidelines for Omega-3 Fatty Acids in the Treatment of Major Depressive Disorder	Guidelines	The key practice guidelines contend that: (1) clinicians and other practitioners are advised to conduct a clinical interview to validate clinical diagnoses, physical conditions, and measurement-based psychopathological assessments in the therapeutic settings when recommending n-3 PUFAs in depression treatment; (2) concerning formulation and dosage, both pure eicosapentaenoic acid (EPA) or an EPA/docosahexaenoic acid (DHA) combination of a ratio higher than 2 (EPA/DHA >2) are considered effective, and the recommended dosages should be 1-2 g of net EPA daily, from either pure EPA or an EPA/DHA (>2:1) formula; (3) the quality of n-3 PUFAs may affect therapeutic activity; and (4) potential adverse effects, such as gastrointestinal and dermatological conditions, should be monitored, as well as obtaining comprehensive metabolic panels
Robinson DG, et al. [66]	DHA/EPA and psychotic patients	R: 50	Adjuvant omega-3 treatment is a potential option for symptoms of depression and anxiety in people with recent-onset psychosis.
Li W, et al. [67]	DHA/EPA and mood disorders	R: 108	Abnormalities in emotional network organization observed in high-risk depressed youth can be modified through fish oil supplementation.
McPhilemy G, et al. [68]	DHA/EPA and bipol sindrome	R: 80	Despite a slight reduction in hypomania scores in the omega-3 PUFA group compared with the placebo, we find little evidence that omega-3-PUFA supplementation shows prophylactic benefit in BD.
Zhang M-M, et al. [69]	Omega-3 and depressive symptoms	Meta: 8	A significant effect of omega-3 FA on perinatal depression was found. Omega-3s with a higher ratio of EPA/DHA (≥1.5) had significant efficacy in both mild-to-moderate gravid depression and postpartum depression, with a low incidence of side effects.
Satogami K, et al. [70]	DHA/EPA and eating disorders	Meta: 8	Eating disorders were associated with significantly higher levels of palmitoleic acid and oleic acid on the red blood cell membrane and lower levels of adrenic acid, arachidonic acid, and total omega-6 fatty acids. In addition, PUFA supplements were associated with a benefit on body weight outcomes but not on disease severity and mood symptoms in interventional studies.
Bianchi VE, et al. [81]	Effect of nutrition on neurodegenerative diseases	Sys: 21	Omega-3 and -6, and vitamin supplementation seem to be less effective in protecting against neuron degeneration. Insulin activity is a prevalent factor contributing to brain health while malnutrition is correlated with the higher development of dementia and mortality.
AlAmmar WA, et al. [82]	DHA/EPA and multiple sclerosis	Sys: 7	Supplementation of omega-3 and fish oils has beneficial effects on reducing relapse rate, and inflammatory markers, and improving the quality of life for MS patients.
Tomaszewski N, et al. [83]	DHA/EPA and APOE Genotype	R: 275	The lower increase in plasma DHA/AA and EPA/AA in APOE□4/□4 carriers after DHA supplementation reduces brain intake and affects the efficacy of DHA supplementation.
Chen X, et al. [87]	Effects of the rs3834458 Single Nucleotide Polymorphism in FADS2 on Levels of n-3 Long-chain Polyunsaturated Fatty Acids	Meta: 12	This meta-analysis indicates that a minor allele of rs3834458 in FADS2 may result in the lower activity of delta-6 desaturase leading to higher ALA and lower EPA, DPA, and DHA in blood.
Scholtz SA, et al. [88]	DHA in pregnancy differentially modulates arachidonic acid and DHA status across FADS genotypes in pregnancy	R: 205	DHA but not the placebo decreased the ARA status of minor allele homozygotes of both FADS SNPs but not major allele homozygotes at delivery.

Conclusion

Significant evidence emerges regarding the importance of omega-3 and omega-6 fatty acid supplementation in pregnancy and lactation, malnutrition states, inflammatory diseases, cardiac and vascular risk, neurodegenerative disorders, and mental disorders. However, while several findings are promising, important structural shortcomings of the research

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designs still emerge from the published studies; moreover, many studies assume that fatty acid supplementation can have a curative effect on already active diseases, when in fact such prescriptions should be considered as adjuvant therapies to prevent or promote symptomatic regression, precisely because of their anti-inflammatory, antioxidant and immunomodulatory virtues. Such findings could be capable of undermining the research results. However, there is no concrete and robust evidence of the positive impact on psychological well-being. Future research that can resolve the critical issues noted is hoped, to promote a better approach to the topic of omega-3/omega-6 supplementation, in human health.

References

1. Arienti G. Le basi molecolari della nutrizione. Piccin. 2003.
2. Simopoulos AP. The importance of the ratio of omega-6/omega-3 essential fatty acids. Biomed Pharmacother. 2002 Oct;56(8):365-79. doi: 10.1016/s0753-3322(02)00253-6. PMID: 12442909.
3. Yang S, Lin R, Si L, Li Z, Jian W, Yu Q, Jia Y. Cod-Liver Oil Improves Metabolic Indices and hs-CRP Levels in Gestational Diabetes Mellitus Patients: A Double-Blind Randomized Controlled Trial. J Diabetes Res. 2019 Dec 28;2019:7074042. doi: 10.1155/2019/7074042. PMID: 31956660; PMCID: PMC6949680.
4. West AL, Miles EA, Lillycrop KA, Han L, Sayanova O, Napier JA, Calder PC, Burdge GC. Postprandial incorporation of EPA and DHA from transgenic Camelina sativa oil into blood lipids is equivalent to that from fish oil in healthy humans. Br J Nutr. 2019 Jun;121(11):1235-1246. doi: 10.1017/S0007114519000825. Epub 2019 Apr 12. PMID: 30975228; PMCID: PMC6658215.
5. Schwab US, Lankinen MA, de Mello VD, Manninen SM, Kurl S, Pulkki KJ, Laaksonen DE, Erkkilä AT. Camelina Sativa Oil, but not Fatty Fish or Lean Fish, Improves Serum Lipid Profile in Subjects with Impaired Glucose Metabolism-A Randomized Controlled Trial. Mol Nutr Food Res. 2018 Feb;62(4). doi: 10.1002/mnfr.201700503. Epub 2018 Jan 31. PMID: 29272068.
6. McNamara RK, Kalt W, Shidler MD, McDonald J, Summer SS, Stein AL, Stover AN, Krikorian R. Cognitive response to fish oil, blueberry, and combined supplementation in older adults with subjective cognitive impairment. Neurobiol Aging. 2018 Apr;64:147-156. doi: 10.1016/j.neurobiolaging.2017.12.003. Epub 2017 Dec 12. PMID: 29458842; PMCID: PMC5822748.
7. Dawczynski C, Dittrich M, Neumann T, Goetze K, Welzel A, Oelzner P, Völker S, Schaible AM, Troisi F, Thomas L, Pace S, Koeberle A, Werz O, Schlattmann P, Lorkowski S, Jahreis G. Docosahexaenoic acid in the treatment of rheumatoid arthritis: A double-blind, placebo-controlled, randomized cross-over study with microalgae vs. sunflower oil. Clin Nutr. 2018 Apr;37(2):494-504. doi: 10.1016/j.clnu.2017.02.021. Epub 2017 Mar 6. PMID: 28302406.
8. Liu H, Wang F, Liu X, Xie Y, Xia H, Wang S, Sun G. Effects of marine-derived and plant-derived omega-3 polyunsaturated fatty acids on erythrocyte fatty acid composition in type 2 diabetic patients. Lipids Health Dis. 2022 Feb 10;21(1):20. doi: 10.1186/s12944-022-01630-0. PMID: 35144649; PMCID: PMC8832668.
9. Fisk HL, Childs CE, Miles EA, Ayres R, Noakes PS, Paras-Chavez C, Kuda O, Kopecký J, Antoun E, Lillycrop KA, Calder PC. Modification of subcutaneous white adipose tissue inflammation by omega-3 fatty acids is limited in human obesity-a double blind, randomised clinical trial. EBioMedicine. 2022 Mar;77:103909. doi: 10.1016/j.ebiom.2022.103909. Epub 2022 Mar 2. PMID: 35247847; PMCID: PMC8894262.
10. Jackson PA, Husberg C, Hustvedt SO, Calder PC, Khan J, Avery H, Forster J, Kennedy DO. Diurnal rhythm of plasma EPA and DHA in healthy adults. Prostaglandins Leukot Essent Fatty Acids. 2020 Mar;154:102054. doi: 10.1016/j.plefa.2020.102054. Epub 2020 Jan 15. PMID: 32018166.
11. Chevalier L, Vachon A, Plourde M. Pharmacokinetics of Supplemental Omega-3 Fatty Acids Esterified in Monoglycerides, Ethyl Esters, or Triglycerides in Adults in a Randomized Crossover Trial. J Nutr. 2021 May 11;151(5):1111-1118. doi: 10.1093/jn/nxaa458. PMID: 33564872; PMCID: PMC8112767.
12. Chevalier L, Vachon A, Plourde M. Pharmacokinetics of Supplemental Omega-3 Fatty Acids Esterified in Monoglycerides, Ethyl Esters, or Triglycerides in Adults in a Randomized Crossover Trial. J Nutr. 2021 May 11;151(5):1111-1118. doi: 10.1093/jn/nxaa458. PMID: 33564872; PMCID: PMC8112767.
13. Rondanelli M, Perna S, Riva A, Petrangolini G, Di Paolo E, Gasparri C. Effects of n-3 EPA and DHA supplementation on fat free mass and physical performance in elderly. A systematic review and meta-analysis of randomized clinical trial. Mech Ageing Dev. 2021 Jun;196:111476. doi: 10.1016/j.mad.2021.111476. Epub 2021 Mar 26. PMID: 33781784.
14. Rondanelli M, Perna S, Riva A, Petrangolini G, Di Paolo E, Gasparri C. Effects of n-3 EPA and DHA supplementation on fat free mass and physical performance in elderly. A systematic review and meta-analysis of randomized clinical trial. Mech Ageing Dev. 2021 Jun;196:111476. doi: 10.1016/j.mad.2021.111476. Epub 2021 Mar 26. PMID: 33781784.
15. Guo XF, Tong WF, Ruan Y, Sinclair AJ, Li D. Different metabolism of EPA, DPA and DHA in humans: A double-blind cross-over study. Prostaglandins Leukot Essent Fatty Acids. 2020 Jul;158:102033. doi: 10.1016/j.plefa.2019.102033. Epub 2019 Nov 12. PMID: 31740197.
16. Tomic-Smiljanic M, Vasiljevic D, Lucic-Tomic A, Andjelkovic N, Jakovljevic V, Bolovich S, Veselinovic M. Influence of different supplementation on platelet aggregation in patients with rheumatoid arthritis. Clin Rheumatol. 2019 Sep;38(9):2443-2450. doi: 10.1007/s10067-019-04569-3. Epub 2019 May 10. PMID: 31076942.
17. Abbott KA, Burrows TL, Acharya S, Thota RN, Garg ML. DHA-enriched fish oil reduces insulin resistance in overweight and obese adults. Prostaglandins Leukot Essent Fatty Acids. 2020 Aug;159:102154. doi: 10.1016/j.plefa.2020.102154. Epub 2020 Jun 13. PMID: 32563863.
18. Holub A, Mousa S, Abdolahi A, Godugu K, Tu XM, Brenna JT, Block RC. The effects of aspirin and N-3 fatty acids on telomerase activity in adults with diabetes mellitus. Nutr Metab Cardiovasc Dis. 2020 Sep 24;30(10):1795-1799. doi: 10.1016/j.numecd.2020.06.014. Epub 2020 Jun 25. PMID: 32723580; PMCID: PMC7494550.
19. Holub A, Mousa S, Abdolahi A, Godugu K, Tu XM, Brenna JT, Block RC. The effects of aspirin and N-3 fatty acids on telomerase activity in adults with diabetes mellitus. Nutr Metab Cardiovasc Dis. 2020 Sep 24;30(10):1795-1799. doi: 10.1016/j.numecd.2020.06.014. Epub 2020 Jun 25. PMID: 32723580; PMCID: PMC7494550.
20. González-Becerra K, Ramos-Lopez O, Barrón-Cabrera E, Riezu-Boj JI, Milagro FI, Martínez-López E, Martínez JA. Fatty acids, epigenetic mechanisms and chronic diseases: a systematic review. Lipids Health Dis. 2019 Oct 15;18(1):178. doi: 10.1186/s12944-019-1120-6. PMID: 31615571; PMCID: PMC6792183.
21. Parker HM, Cohn JS, O'Connor HT, Garg ML, Caterson ID, George J, Johnson NA. Effect of Fish Oil Supplementation on Hepatic and Visceral Fat in Overweight Men: A Randomized Controlled Trial. Nutrients. 2019 Feb 23;11(2):475. doi: 10.3390/nu11020475. PMID: 30813440; PMCID: PMC6413081.
22. Zhou Q, Zhang Z, Wang P, Zhang B, Chen C, Zhang C, Su Y. EPA+DHA, but not ALA, Improved Lipids and Inflammation Status in Hypercholesterolemic Adults: A Randomized, Double-Blind, Placebo-Controlled Trial. Mol Nutr Food Res. 2019 May;63(10):e1801157. doi: 10.1002/mnfr.201801157. Epub 2019 Apr 23. Erratum in: Mol Nutr Food Res. 2020 Apr;64(7):e2070012. PMID: 30900815.
23. Song L, Zhao XG, Ouyang PL, Guan Q, Yang L, Peng F, Du H, Yin F, Yan W, Yu WJ, Yan H. Combined effect of n-3 fatty acids and phytosterol esters on alleviating hepatic steatosis in non-alcoholic fatty liver disease subjects: a double-blind placebo-controlled clinical trial. Br J Nutr. 2020 May 28;123(10):1148-1158. doi: 10.1017/S0007114520000495. Epub 2020 Feb 14. PMID: 32054543.

Citation: Perrotta G (2023) Omega-3/omega-6 fatty acids: The effects on the psychophysical well-being of adolescents and adults. Int J Clin Endocrinol Metab 9(1): 008-018. DOI: https://dx.doi.org/10.17352/ijcem.000057

24. Guo XF, Wang C, Yang T, Ma WJ, Zhai J, Zhao T, Xu TC, Li J, Liu H, Sinclair AJ, Li D. The effects of fish oil plus vitamin D_3 intervention on non-alcoholic fatty liver disease: a randomized controlled trial. Eur J Nutr. 2022 Jun;61(4):1931-1942. doi: 10.1007/s00394-021-02772-0. Epub 2022 Jan 24. PMID: 35067753.

25. Yang J, Fernández-Galilea M, Martínez-Fernández L, González-Muniesa P, Pérez-Chávez A, Martínez JA, Moreno-Aliaga MJ. Oxidative Stress and Non-Alcoholic Fatty Liver Disease: Effects of Omega-3 Fatty Acid Supplementation. Nutrients. 2019 Apr 18;11(4):872. doi: 10.3390/nu11040872. PMID: 31003450; PMCID: PMC6521137.

26. Hennig B, Toborek M, McClain CJ. High-energy diets, fatty acids and endothelial cell function: implications for atherosclerosis. J Am Coll Nutr. 2001 Apr;20(2 Suppl):97-105. doi: 10.1080/07315724.2001.10719021. PMID: 11349944.

27. Takahashi J, Sakai K, Sato T, Takatsu H, Komatsu T, Mitsumura H, Murakami H, Iguchi Y. Serum arachidonic acid levels is a predictor of poor functional outcome in acute intracerebral hemorrhage. Clin Biochem. 2021 Dec;98:42-47. doi: 10.1016/j.clinbiochem.2021.09.012. Epub 2021 Oct 6. PMID: 34624254.

28. Chen H, Deng G, Zhou Q, Chu X, Su M, Wei Y, Li L, Zhang Z. Effects of eicosapentaenoic acid and docosahexaenoic acid versus α-linolenic acid supplementation on cardiometabolic risk factors: a meta-analysis of randomized controlled trials. Food Funct. 2020 Mar 26;11(3):1919-1932. doi: 10.1039/c9fo03052b. PMID: 32175534.

29. Li N, Jia M, Deng Q, Wang Z, Huang F, Hou H, Xu T. Effect of low-ratio n-6/n-3 PUFA on blood lipid level: a meta-analysis. Hormones (Athens). 2021 Dec;20(4):697-706. doi: 10.1007/s42000-020-00248-0. Epub 2020 Oct 29. PMID: 33123975.

30. Du Y, Taylor CG, Zahradka P. Modulation of endothelial cell responses and vascular function by dietary fatty acids. Nutr Rev. 2019 Jun 22:nuz026. doi: 10.1093/nutrit/nuz026. Epub ahead of print. PMID: 31228246.

31. Chen H, Deng G, Zhou Q, Chu X, Su M, Wei Y, Li L, Zhang Z. Effects of eicosapentaenoic acid and docosahexaenoic acid versus α-linolenic acid supplementation on cardiometabolic risk factors: a meta-analysis of randomized controlled trials. Food Funct. 2020 Mar 26;11(3):1919-1932. doi: 10.1039/c9fo03052b. PMID: 32175534.

32. Guo XF, Li KL, Li JM, Li D. Effects of EPA and DHA on blood pressure and inflammatory factors: a meta-analysis of randomized controlled trials. Crit Rev Food Sci Nutr. 2019;59(20):3380-3393. doi: 10.1080/10408398.2018.1492901. Epub 2019 Feb 4. PMID: 29993265.

33. Nicholls SJ, Lincoff AM, Garcia M, Bash D, Ballantyne CM, Barter PJ, Davidson MH, Kastelein JJP, Koenig W, McGuire DK, Mozaffarian D, Ridker PM, Ray KK, Katona BG, Himmelmann A, Loss LE, Rensfeldt M, Lundström T, Agrawal R, Menon V, Wolski K, Nissen SE. Effect of High-Dose Omega-3 Fatty Acids vs Corn Oil on Major Adverse Cardiovascular Events in Patients at High Cardiovascular Risk: The STRENGTH Randomized Clinical Trial. JAMA. 2020 Dec 8;324(22):2268-2280. doi: 10.1001/jama.2020.22258. PMID: 33190147; PMCID: PMC7667577.

34. Khan SU, Lone AN, Khan MS, Virani SS, Blumenthal RS, Nasir K, Miller M, Michos ED, Ballantyne CM, Boden WE, Bhatt DL. Effect of omega-3 fatty acids on cardiovascular outcomes: A systematic review and meta-analysis. EClinicalMedicine. 2021 Jul 8;38:100997. doi: 10.1016/j.eclinm.2021.100997. PMID: 34505026; PMCID: PMC8413259.

35. Abdelhamid AS, Brown TJ, Brainard JS, Biswas P, Thorpe GC, Moore HJ, Deane KH, Summerbell CD, Worthington HV, Song F, Hooper L. Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2020 Feb 29;3(3):CD003177. doi: 10.1002/14651858.CD003177.pub5. PMID: 32114706; PMCID: PMC7049091.

36. Kita Y, Watanabe M, Kamon D, Ueda T, Soeda T, Okayama S, Ishigami K, Kawata H, Horii M, Inoue F, Doi N, Okura H, Uemura S, Saito Y. Effects of Fatty Acid Therapy in Addition to Strong Statin on Coronary Plaques in Acute Coronary Syndrome: An Optical Coherence Tomography Study. J Am Heart Assoc. 2020 Aug 18;9(16):e015593. doi: 10.1161/JAHA.119.015593. Epub 2020 Aug 1. PMID: 32805184; PMCID: PMC7660823.

37. Alfaddagh A, Elajami TK, Saleh M, Mohebali D, Bistrian BR, Welty FK. An omega-3 fatty acid plasma index ≥4% prevents progression of coronary artery plaque in patients with coronary artery disease on statin treatment. Atherosclerosis. 2019 Jun;285:153-162. doi: 10.1016/j.atherosclerosis.2019.04.213. Epub 2019 Apr 13. PMID: 31055222; PMCID: PMC7963401.

38. Xu B, Xu Z, Xu D, Tan X. Effect of n-3 polyunsaturated fatty acids on ischemic heart disease and cardiometabolic risk factors: a two-sample Mendelian randomization study. BMC Cardiovasc Disord. 2021 Nov 8;21(1):532. doi: 10.1186/s12872-021-02342-6. PMID: 34749668; PMCID: PMC8576934.

39. Block RC, Shearer GC, Holub A, Tu XM, Mousa S, Brenna JT, Harris WS, Tintle N. Aspirin and omega-3 fatty acid status interact in the prevention of cardiovascular diseases in Framingham Heart Study. Prostaglandins Leukot Essent Fatty Acids. 2021 Jun;169:102283. doi: 10.1016/j.plefa.2021.102283. Epub 2021 Apr 24. PMID: 33964664; PMCID: PMC8159885.

40. Gallini A, Yrondi A, Cantet C, Poncet M, Vellas B, Schmitt L, Andrieu S. Red Blood Cell Omega-3 Fatty Acid Composition and Psychotropic Drug Use in Older Adults: Results from the MAPT Study. J Nutr Health Aging. 2019;23(9):805-812. doi: 10.1007/s12603-019-1252-4. PMID: 31641729..

41. MacIntosh BA, Ramsden CE, Honvoh G, Faurot KR, Palsson OS, Johnston AD, Lynch C, Anderson P, Igudesman D, Zamora D, Horowitz M, Gaylord S, Mann JD. Methodology for altering omega-3 EPA+DHA and omega-6 linoleic acid as controlled variables in a dietary trial. Clin Nutr. 2021 Jun;40(6):3859-3867. doi: 10.1016/j.clnu.2021.04.050. Epub 2021 May 12. PMID: 34130033; PMCID: PMC8293619.

42. Ramsden CE, Zamora D, Faurot KR, MacIntosh B, Horowitz M, Keyes GS, Yuan ZX, Miller V, Lynch C, Honvoh G, Park J, Levy R, Domenichiello AF, Johnston A, Majchrzak-Hong S, Hibbeln JR, Barrow DA, Loewke J, Davis JM, Mannes A, Palsson OS, Suchindran CM, Gaylord SA, Mann JD. Dietary alteration of n-3 and n-6 fatty acids for headache reduction in adults with migraine: randomized controlled trial. BMJ. 2021 Jun 30;374:n1448. doi: 10.1136/bmj.n1448. PMID: 34526307; PMCID: PMC8244542.

43. Galán-Arriero I, Serrano-Muñoz D, Gómez-Soriano J, Goicoechea C, Taylor J, Velasco A, Ávila-Martín G. The role of Omega-3 and Omega-9 fatty acids for the treatment of neuropathic pain after neurotrauma. Biochim Biophys Acta Biomembr. 2017 Sep;1859(9 Pt B):1629-1635. doi: 10.1016/j.bbamem.2017.05.003. Epub 2017 May 8. PMID: 28495596.

44. Pham TL, Bazan HEP. Docosanoid signaling modulates corneal nerve regeneration: effect on tear secretion, wound healing, and neuropathic pain. J Lipid Res. 2021;62:100033. doi: 10.1194/jlr.TR120000954. Epub 2021 Feb 6. PMID: 32788291; PMCID: PMC7933495.

45. Watson H, Stackhouse C. Omega-3 fatty acid supplementation for cystic fibrosis. Cochrane Database Syst Rev. 2020 Apr 10;4(4):CD002201. doi: 10.1002/14651858.CD002201.pub6. PMID: 32275788; PMCID: PMC7147930.

46. Stańdo M, Piatek P, Namiecinska M, Lewkowicz P, Lewkowicz N. Omega-3 Polyunsaturated Fatty Acids EPA and DHA as an Adjunct to Non-Surgical Treatment of Periodontitis: A Randomized Clinical Trial. Nutrients. 2020 Aug 27;12(9):2614. doi: 10.3390/nu12092614. PMID: 32867199; PMCID: PMC7551834.

47. Hosseini B, Nourmohamadi M, Hajipour S, Taghizadeh M, Asemi Z, Keshavarz SA, Jafarnejad S. The Effect of Omega-3 Fatty Acids, EPA, and/or DHA on Male Infertility: A Systematic Review and Meta-analysis. J Diet Suppl. 2019;16(2):245-256. doi: 10.1080/19390211.2018.1431753. Epub 2018 Feb 16. PMID: 29451828.

48. Hosseini B, Nourmohamadi M, Hajipour S, Taghizadeh M, Asemi Z, Keshavarz SA, Jafarnejad S. The Effect of Omega-3 Fatty Acids, EPA, and/or DHA on Male Infertility: A Systematic Review and Meta-analysis. J Diet Suppl. 2019;16(2):245-256. doi: 10.1080/19390211.2018.1431753. Epub 2018 Feb 16. PMID: 29451828.

49. Zhou SJ, Yelland L, McPhee AJ, Quinlivan J, Gibson RA, Makrides M. Fish-oil supplementation in pregnancy does not reduce the risk of gestational

Citation: Perrotta G (2023) Omega-3/omega-6 fatty acids: The effects on the psychophysical well-being of adolescents and adults. Int J Clin Endocrinol Metab 9(1): 008-018. DOI: https://dx.doi.org/10.17352/ijcem.000057

diabetes or preeclampsia. Am J Clin Nutr. 2012 Jun;95(6):1378-84. doi: 10.3945/ajcn.111.033217. Epub 2012 May 2. PMID: 22552037.

50. Bakouei F, Delavar MA, Mashayekh-Amiri S, Esmailzadeh S, Taheri Z. Efficacy of n-3 fatty acids supplementation on the prevention of pregnancy induced-hypertension or preeclampsia: A systematic review and meta-analysis. Taiwan J Obstet Gynecol. 2020 Jan;59(1):8-15. doi: 10.1016/j.tjog.2019.11.002. PMID: 32039806.

51. Carvajal JA. Docosahexaenoic acid supplementation early in pregnancy may prevent deep placentation disorders. Biomed Res Int. 2014;2014:526895. doi: 10.1155/2014/526895. Epub 2014 Jun 12. PMID: 25019084; PMCID: PMC4082939.

52. Zhong Y, Wang K, Jiang L, Wang J, Zhang X, Xu J, Yao K. Dietary fatty acid intake, plasma fatty acid levels, and the risk of age-related macular degeneration (AMD): a dose-response meta-analysis of prospective cohort studies. Eur J Nutr. 2021 Sep;60(6):3013-3027. doi: 10.1007/s00394-020-02445-4. Epub 2021 Jan 19. PMID: 33469697.

53. Downie LE, Ng SM, Lindsley KB, Akpek EK. Omega-3 and omega-6 polyunsaturated fatty acids for dry eye disease. Cochrane Database Syst Rev. 2019 Dec 18;12(12):CD011016. doi: 10.1002/14651858.CD011016.pub2. PMID: 31847055; PMCID: PMC6917524.

54. van der Wurff ISM, Meyer BJ, de Groot RHM. Effect of Omega-3 Long Chain Polyunsaturated Fatty Acids (n-3 LCPUFA) Supplementation on Cognition in Children and Adolescents: A Systematic Literature Review with a Focus on n-3 LCPUFA Blood Values and Dose of DHA and EPA. Nutrients. 2020 Oct 12;12(10):3115. doi: 10.3390/nu12103115. PMID: 33053843; PMCID: PMC7599612.

55. van der Wurff ISM, Meyer BJ, de Groot RHM. Effect of Omega-3 Long Chain Polyunsaturated Fatty Acids (n-3 LCPUFA) Supplementation on Cognition in Children and Adolescents: A Systematic Literature Review with a Focus on n-3 LCPUFA Blood Values and Dose of DHA and EPA. Nutrients. 2020 Oct 12;12(10):3115. doi: 10.3390/nu12103115. PMID: 33053843; PMCID: PMC7599612.

56. Checa-Ros A, Haro-García A, Seiquer I, Molina-Carballo A, Uberos-Fernández J, Muñoz-Hoyos A. Early monitoring of fatty acid profile in children with attention deficit and/or hyperactivity disorder under treatment with omega-3 polyunsaturated fatty acids. Minerva Pediatr. 2019 Aug;71(4):313-325. doi: 10.23736/S0026-4946.18.04975-7. Epub 2018 Nov 7. PMID: 30419741.

57. Perrotta G. Attention Deficit Hyperactivity Disorder: definition, contexts, neural correlates and clinical strategies. J Addi Adol Beh. 2019; 2(1). doi: 10.31579-007/2688-7517/08.

58. Emery S, Häberling I, Berger G, Walitza S, Schmeck K, Albert T, Baumgartner N, Strumberger M, Albermann M, Drechsler R. Omega-3 and its domain-specific effects on cognitive test performance in youths: A meta-analysis. Neurosci Biobehav Rev. 2020 May;112:420-436. doi: 10.1016/j.neubiorev.2020.02.016. Epub 2020 Feb 15. PMID: 32070694.

59. Perrotta G. Executive functions: definition, contexts and neuropsychological profiles. J. Neuroscience and Neurological. 2019; 4(3). doi: 10.31579/2578-8868/077.

60. Kosti RI, Kasdagli MI, Kyrozis A, Orsini N, Lagiou P, Taiganidou F, Naska A. Fish intake, n-3 fatty acid body status, and risk of cognitive decline: a systematic review and a dose-response meta-analysis of observational and experimental studies. Nutr Rev. 2022 May 9;80(6):1445-1458. doi: 10.1093/nutrit/nuab078. PMID: 34605891.

61. Kuszewski JC, Howe PRC, Wong RHX. Evaluation of Cognitive Performance following Fish-Oil and Curcumin Supplementation in Middle-Aged and Older Adults with Overweight or Obesity. J Nutr. 2020 Dec 10;150(12):3190-3199. doi: 10.1093/jn/nxaa299. PMID: 33097947.

62. Khairani S, Fauziah N, Wiraswati HL, Panigoro R, Setyowati EY, Berbudi A. The Potential use of a Curcumin-Piperine Combination as an Antimalarial Agent: A Systematic Review. J Trop Med. 2021 Oct 11;2021:9135617. doi: 10.1155/2021/9135617. PMID: 34671402; PMCID: PMC8523290.

63. Liao Y, Xie B, Zhang H, He Q, Guo L, Subramanieapillai M, Fan B, Lu C, McIntyre RS. Efficacy of omega-3 PUFAs in depression: A meta-analysis. Transl Psychiatry. 2019 Aug 5;9(1):190. doi: 10.1038/s41398-019-0515-5. Erratum in: Transl Psychiatry. 2021 Sep 7;11(1):465. PMID: 31383846; PMCID: PMC6683166.

64. van der Burg KP, Cribb L, Firth J, Karmacoska D, Mischoulon D, Byrne GJ, Bousman C, Stough C, Murphy J, Oliver G, Berk M, Ng CH, Sarris J. EPA and DHA as markers of nutraceutical treatment response in major depressive disorder. Eur J Nutr. 2020 Sep;59(6):2439-2447. doi: 10.1007/s00394-019-02090-6. Epub 2019 Sep 25. PMID: 31555976.

65. Guu TW, Mischoulon D, Sarris J, Hibbeln J, McNamara RK, Hamazaki K, Freeman MP, Maes M, Matsuoka YJ, Belmaker RH, Jacka F, Pariante C, Berk M, Marx W, Su KP. International Society for Nutritional Psychiatry Research Practice Guidelines for Omega-3 Fatty Acids in the Treatment of Major Depressive Disorder. Psychother Psychosom. 2019;88(5):263-273. doi: 10.1159/000502652. Epub 2019 Sep 3. PMID: 31480057.

66. Robinson DG, Gallego JA, John M, Hanna LA, Zhang JP, Birnbaum ML, Greenberg J, Naraine M, Peters BD, McNamara RK, Malhotra AK, Szeszko PR. A potential role for adjunctive omega-3 polyunsaturated fatty acids for depression and anxiety symptoms in recent onset psychosis: Results from a 16 week randomized placebo-controlled trial for participants concurrently treated with risperidone. Schizophr Res. 2019 Feb;204:295-303. doi: 10.1016/j.schres.2018.09.006. Epub 2018 Sep 19. PMID: 30241990; PMCID: PMC6402999.

67. Li W, Lei D, Tallman MJ, Patino LR, Gong Q, Strawn JR, DelBello MP, McNamara RK. Emotion-Related Network Reorganization Following Fish Oil Supplementation in Depressed Bipolar Offspring: An fMRI Graph-Based Connectome Analysis. J Affect Disord. 2021 Sep 1;292:319-327. doi: 10.1016/j.jad.2021.05.086. Epub 2021 Jun 5. PMID: 34139404; PMCID: PMC8282765.

68. McPhilemy G, Byrne F, Waldron M, Hibbeln JR, Davis J, McDonald C, Hallahan B. A 52-week prophylactic randomised control trial of omega-3 polyunsaturated fatty acids in bipolar disorder. Bipolar Disord. 2021 Nov;23(7):697-706. doi: 10.1111/bdi.13037. Epub 2021 Jan 10. PMID: 33340432.

69. Zhang MM, Zou Y, Li SM, Wang L, Sun YH, Shi L, Lu L, Bao YP, Li SX. The efficacy and safety of omega-3 fatty acids on depressive symptoms in perinatal women: a meta-analysis of randomized placebo-controlled trials. Transl Psychiatry. 2020 Jun 17;10(1):193. doi: 10.1038/s41398-020-00886-3. PMID: 32555188; PMCID: PMC7299975.

70. Satogami K, Tseng PT, Su KP, Takahashi S, Ukai S, Li DJ, Chen TY, Lin PY, Chen YW, Matsuoka YJ. Relationship between polyunsaturated fatty acid and eating disorders: Systematic review and meta-analysis. Prostaglandins Leukot Essent Fatty Acids. 2019 Mar;142:11-19. doi: 10.1016/j.plefa.2019.01.001. Epub 2019 Jan 11. PMID: 30773209..

71. Perrotta G. Anxiety disorders: definitions, contexts, neural correlates and strategic therapy. J Neurol Neurosci. 2019; 6(1):046.

72. Perrotta G. Neural correlates in eating disorders: Definition, contexts and clinical strategies. J Pub Health Catalog. 2019; 2(2):137-148.

73. Perrotta G. Post-traumatic stress disorder: Definition, contexts, neural correlations and cognitive-behavioural therapy. J Pub Health Catalog. 2019; 2(2):40-7.

74. Perrotta G. Sleep-wake disorders: Definition, contexts and neural correlations. J Neurol Psychol. 2019; 7(1):09.

75. Perrotta G. Depressive disorders: Definitions, contexts, differential diagnosis, neural correlates and clinical strategies. Arch Depress Anxiety. 2019; 5(2):009-033, DOI: 10.17352/2455-5460.000038.

76. Perrotta G. Panic disorder: definitions, contexts, neural correlates and clinical strategies. Curr Tr Clin & Med Sci. 2019; 1(2).CTCMS.MS.ID.000508.

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77. Perrotta G. Obsessive-Compulsive Disorder: definition, contexts, neural correlates and clinical strategies. Journal of Neurology. 2019; 08-16.

78. Perrotta G. Behavioral addiction disorder: definition, classifications, clinical contexts, neural correlates and clinical strategies. J Addi Adol Beh. 2019; 2(1). doi: 10.31579/ JARAB.19/007.

79. Perrotta G. Bipolar disorder: definition, differential diagnosis, clinical contexts and therapeutic approaches. J. Neuroscience and Neurological Surgery. 2019; 5(1), DOI: 10.31579/2578-8868/097.

80. Perrotta G. Suicidal risk: definition, contexts, differential diagnosis, neural correlates and clinical strategies. J. Neuroscience and Neurological Surgery. 2020; 6(2):114. DOI: 10.31579/2688-7517/114.

81. Bianchi VE, Herrera PF, Laura R. Effect of nutrition on neurodegenerative diseases. A systematic review. Nutr Neurosci. 2021 Oct;24(10):810-834. doi: 10.1080/1028415X.2019.1681088. Epub 2019 Nov 4. PMID: 31684843.

82. AlAmmar WA, Albeesh FH, Ibrahim LM, Algindan YY, Yamani LZ, Khattab RY. Effect of omega-3 fatty acids and fish oil supplementation on multiple sclerosis: a systematic review. Nutr Neurosci. 2021 Jul;24(7):569-579. doi: 10.1080/1028415X.2019.1659560. Epub 2019 Aug 28. PMID: 31462182.

83. Tomaszewski N, He X, Solomon V, Lee M, Mack WJ, Quinn JF, Braskie MN, Yassine HN. Effect of APOE Genotype on Plasma Docosahexaenoic Acid (DHA), Eicosapentaenoic Acid, Arachidonic Acid, and Hippocampal Volume in the Alzheimer's Disease Cooperative Study-Sponsored DHA Clinical Trial. J Alzheimers Dis. 2020;74(3):975-990. doi: 10.3233/JAD-191017. PMID: 32116250; PMCID: PMC7156328.

84. Perrotta G. Alzheimer's disease: definition, contexts, neural correlates, strategies and clinical approaches. J Aging Stud Ther. 2019; 104:1(1). doi: 10.16966/ jast.

85. Perrotta G. Parkinson's disorder: definition, contexts, neural correlates, strategies and clinical approaches. J Neurosci Neurol Surg. 2019; 4(5). doi: 10.31579/2578-8868/079.

86. Perrotta G. General overview of "human dementia diseases": definitions, classifications, neurobiological profiles and clinical treatments. Gerontol & Geriatric stud. 2020; 6(1). GGS.000626. doi: 10.31031/GGS.2020.06.000626.

87. Chen X, Wu Y, Zhang Z, Zheng X, Wang Y, Yu M, Liu G. Effects of the rs3834458 Single Nucleotide Polymorphism in FADS2 on Levels of n-3 Long-chain Polyunsaturated Fatty Acids: A Meta-analysis. Prostaglandins Leukot Essent Fatty Acids. 2019 Nov;150:1-6. doi: 10.1016/j.plefa.2019.08.005. Epub 2019 Aug 24. PMID: 31487670.

88. Scholtz SA, Kerling EH, Shaddy DJ, Li S, Thodosoff JM, Colombo J, Carlson SE. Docosahexaenoic acid (DHA) supplementation in pregnancy differentially modulates arachidonic acid and DHA status across FADS genotypes in pregnancy. Prostaglandins Leukot Essent Fatty Acids. 2015 Mar;94:29-33. doi: 10.1016/j.plefa.2014.10.008. Epub 2014 Nov 7. PMID: 25500337; PMCID: PMC4339528.

Citation: Perrotta G (2023) Omega-3/omega-6 fatty acids: The effects on the psychophysical well-being of adolescents and adults. Int J Clin Endocrinol Metab 9(1): 008-018. DOI: https://dx.doi.org/10.17352/ijcem.000057