
Omega-3 PUFA's
(nutritional pharmacology)

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definition

Nutritional Pharmacology/Medicine:

...nutritional pharmacology uses therapeutic doses of basic nutrients (alone or in combination) to address illnesses and disorders. It is effective in addressing diseases of deficiency that may be caused by poor diet or extreme environmental factors. ...

Note: Nutritional Medicine also includes the removal or limiting of various foods to promote health, e.g. low chol, for CHD/diabetes or no gluten (e.g. wheat) for coeliac etc

Food or nutritional elements that correct deficiency diseases

Summary-Table 1.

Disease	Depleted nutrient	Foods that correct deficiency
Scurvy	Ascorbic acid (C)	Citrus fruits
Beriberi	Thiamin (B1)	Brewers Yeast, bran flakes etc
Pellagra	Niacin (B3)	Pinto beans, milk, eggs, banana etc
Megaloblastic anaemia (neuropathy)	Folate Cobalamin (B12)	Greens, orange, brewers yeast etc Animal products (+bacteria)
Night blindness	Retinoic acid (A)	Carrots/Spinach/Broccoli etc
Rickets	Chole/Ergocalciferol (D)	Sunlight Fish-liver oils
Haemorrhagic disease	Vitamin K	Gut bacteria-50% Cabbage/broccoli/lettuce etc.
Microcytic hypochromic Anaemia	Iron	Bran flakes, molasses, Greens, Soy etc
Kwashiorkor	protein	Meat, beans
Osteoporosis/tetany	Ca ⁺⁺	Dairy, greens, Soy, eggs etc

Food or nutritional elements that correct deficiency diseases

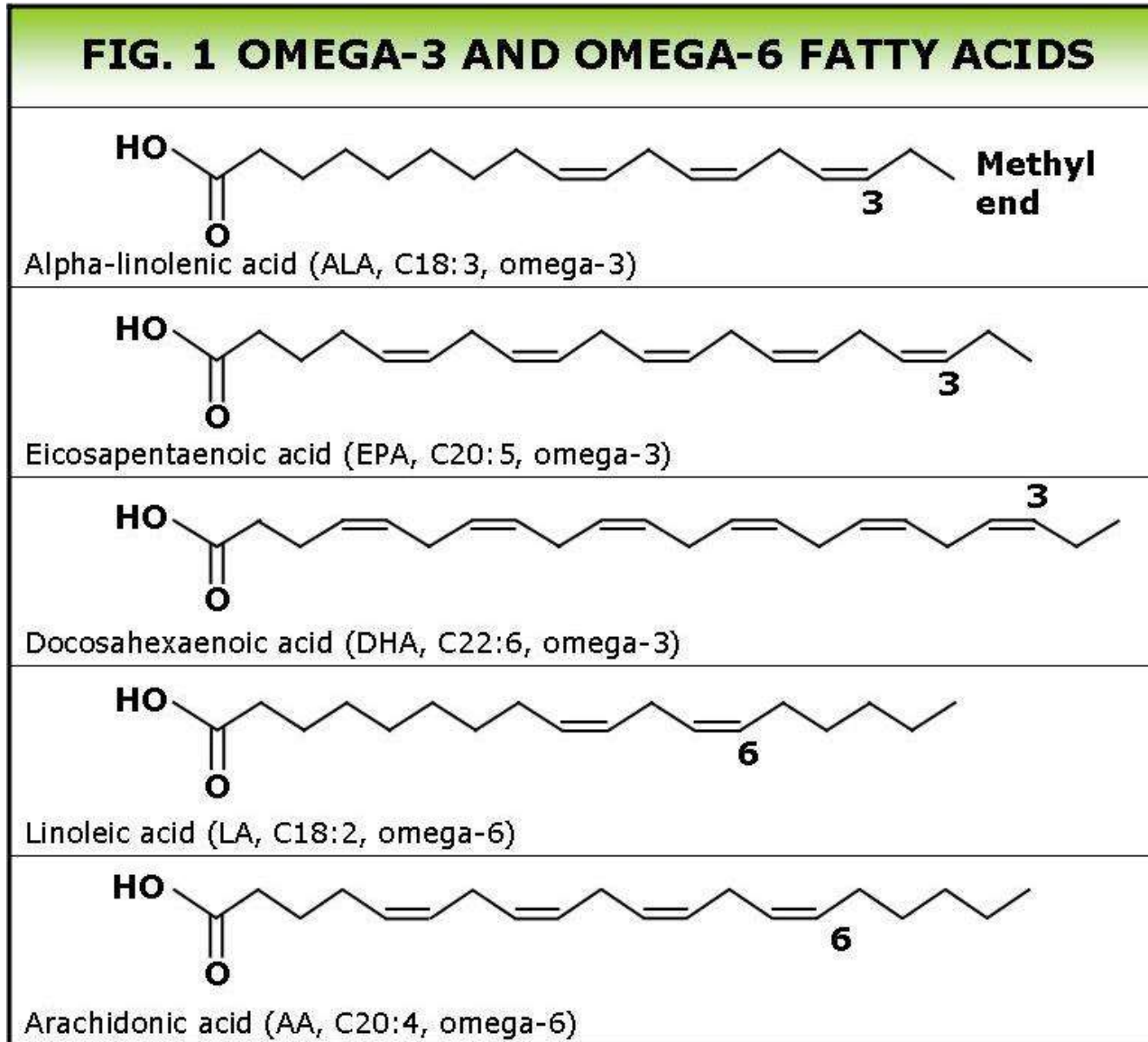
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Mega anaem	<p style="text-align: center;">Under normal physiological conditions, if diet is adequate, no need to supplement with vitamins and minerals</p>	
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Ricke		
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Omega-3 supplementation:
Is there a benefit?

What are Omega-3 PUFA

- omega-3 fatty acids also referred to as ω -3 fatty acids or n-3 fatty acids, are a family of poly unsaturated fatty acids (PUFA's) that have in common a carbon-carbon double bond in the n-3 position.
 - Omega-3 fatty acids are considered one of the 'essential' fatty acids as they must be obtained from the diet as the body can not make the raw material.
 - There are 3 types of omega-3 PUFA's in humans; alpha linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)
 - ALA is found in triglycerides, in cholesteryl esters, and in very small amounts in phospholipids.
 - EPA is found in cholesteryl esters and phospholipids.
 - DHA is found mostly in phospholipids.
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Omega-3 structure



How much omega-3 is needed in the diet?

A small amount of $n-3$ in the diet (~1% of total calories) enabled normal growth in animals and children. Increasing the amount had little to no additional effect on growth.

Landis W. FASEB Journal 6 (8): 2530–2536 (1992)

Gross pathology due to absolute deficiency in omega-3 is likely rare

Nutritional elements that affect sub-clinical disease processes

Summary-Table .

Sub-clinical pathology	Associated dysfunction	Associated disease(s)	Nutritional element
Endocrine dysfunction	↓ Oestrogen receptor signalling	Menopausal symptoms, (Breast cancer)	Phytoestrogens
Immune dysfunction	Cytokine activation, Inflammation	Rheumatoid arthritis, autoimmune diseases, psoriasis	Omega-3 PUFA
G.I.T. dysfunction	Reduced motility, irritation, bacterial dysbiosis	Constipation, coeliac disease, IBS, bowel toxicity	Soluble Fibre
Oxidative stress	↑ damage to lipids, proteins, DNA	Plays important role in: vascular diseases (CHD, stroke), cancer, COPD, neurodegeneration, Aging process	polyphenols

Omega-3 PUFA

Effective for:

- depression
 - cardiovascular disease,
 - inflammatory and autoimmune diseases
-

Antiinflammatory

Omega-3 Fatty Acids

alpha-linolenic acid
(flax, chia, hemp)

stearidonic acid
(black currant oil)

eicosatetraenoic acid

eicosapentaenoic acid
EPA
(fish, krill)

docosapentaenoic acid
DPA

docosahexaenoic acid
DHA
(fish, krill algae)

Δ 6-desaturase
(cofactors – B3, B6, Mg, Zn, Vit C)
Enzyme inhibited by alcohol,
trans fats, diabetes,
hyperinsulinism.

elongase
(cofactor – B6)

Δ 5-desaturase
(cofactors – B3, Zn, Vit C)

cyclo-oxygenase
5-lipoxygenase

3-Series
Prostaglandins &
Thromboxanes,
5-Series
Leukotrienes

2-Series
Prostaglandins &
Thromboxanes,
4-Series
Leukotrienes

elongase

docosanoids

Omega-6 Fatty Acids

linoleic acid
(sunflower, safflower, corn)

gamma-linolenic acid
GLA
(borage, black currant, evening
primrose)

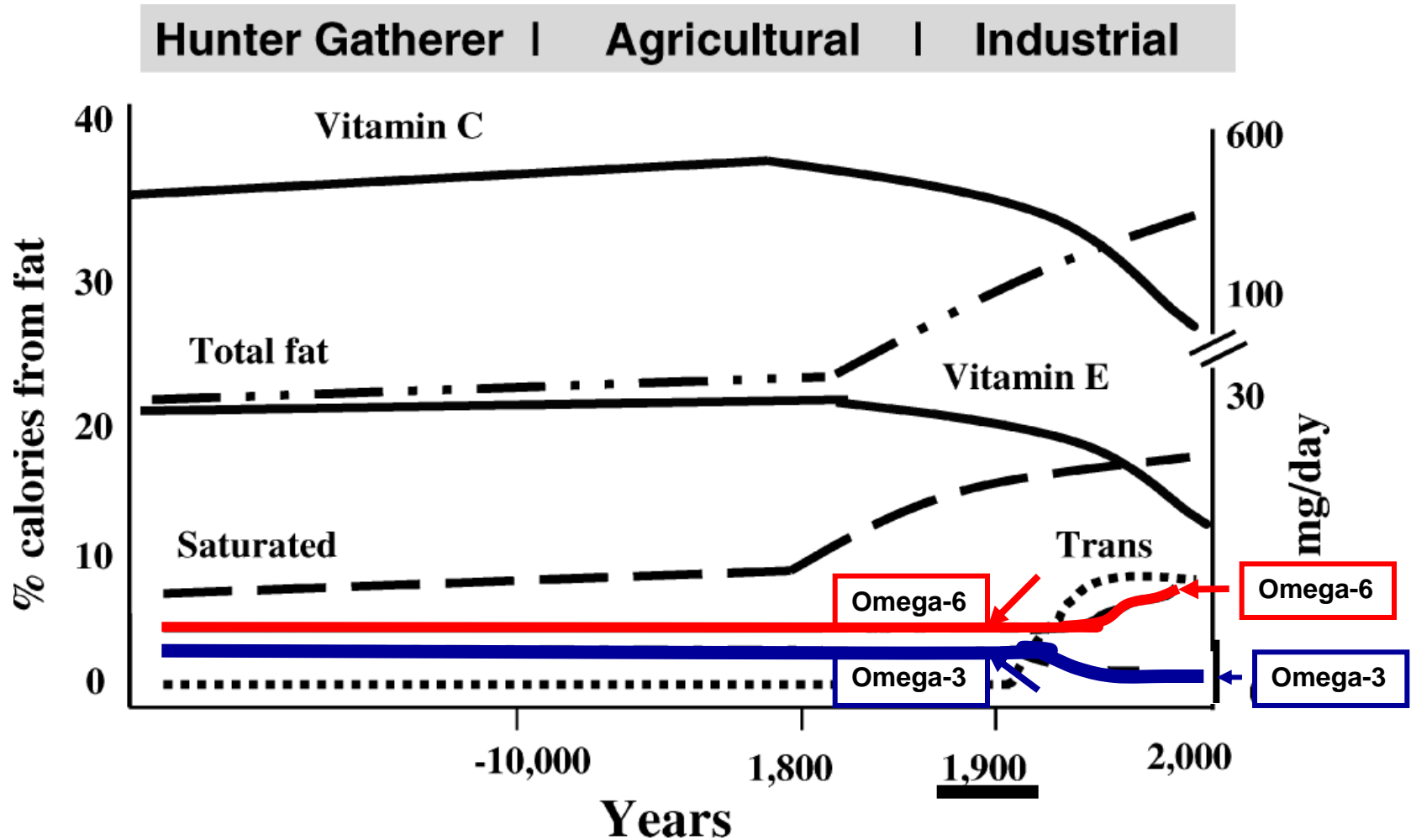
dihomo-gamma-linolenic
acid – DHGLA

arachidonic acid
(meat, eggs, dairy)

Proinflammatory

Omega-3 metabolism

Evidence for progressive imbalance in omega-3:omega-6 intake



Hypothetical scheme of fatty acid (x6, x3, trans and total) intake (as percent of calories from fat) and intake of vitamins E and C (mg/d). Data were extrapolated from cross-sectional analyses of contemporary hunter-gatherer populations and from longitudinal observations and their putative changes during the preceding 100 years.

adapted from; *Exp Biol Med* 2008;233(6):674-88.

Ω 6 : Ω 3 ratios and depression

Evidence:

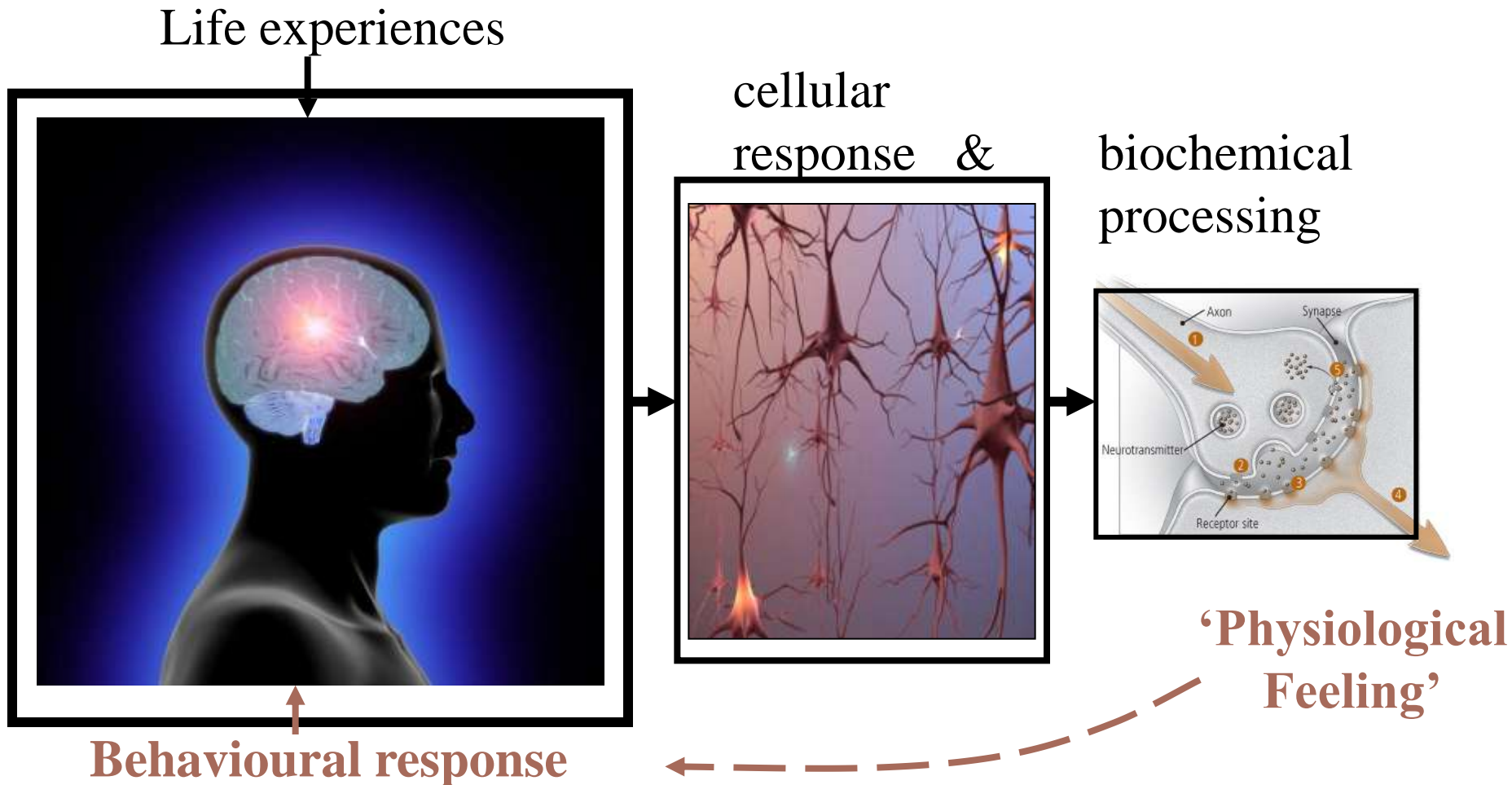
- **Study 1:** An initial correlation was found between low seafood intake and mood disorders ¹²
- **Study 2:** An increased in positive mood in adults was observed following supplementation with EPA/DHA studies ^{13,14}
- **Study 3:** Omega-3 supplementation significantly reduced plasma noradrenalin concentrations compared to control (double blind placebo controlled trial) ¹⁵.

Mechanism of action:

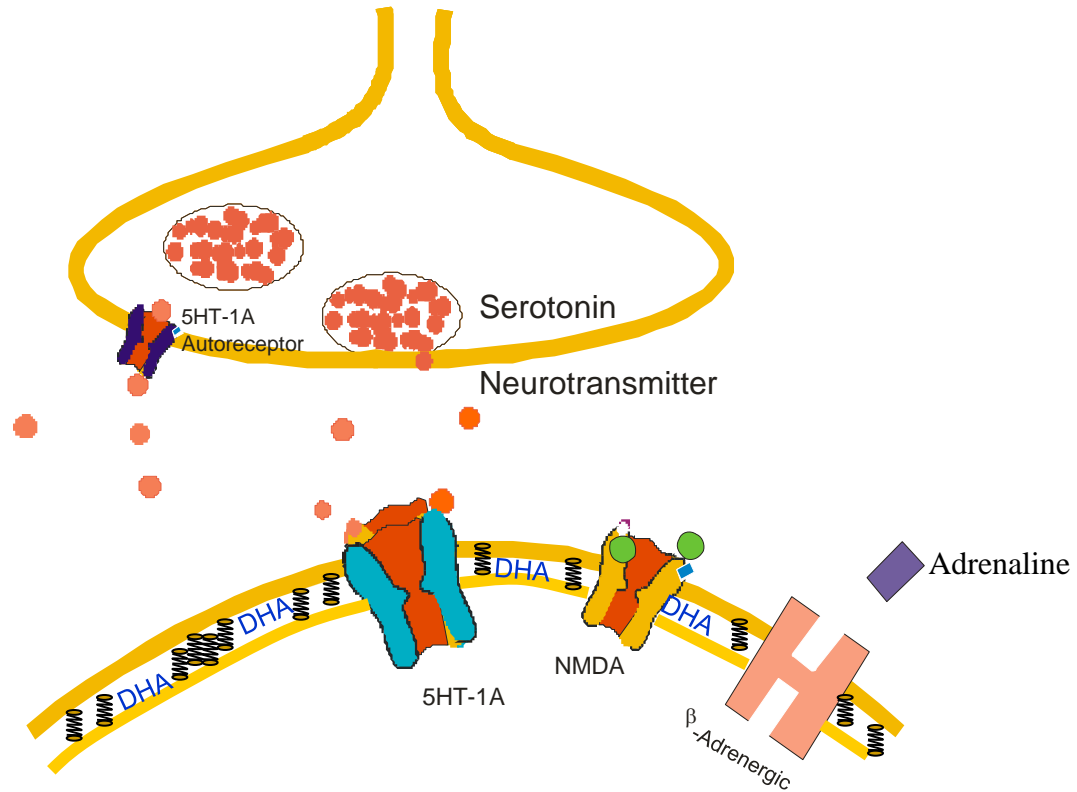
- cerebral cortex, retina, and testis and sperm are particularly rich in DHA.
- Thought that as DHA is one of the most abundant components of the brain's structural lipids DHA in the membrane promotes receptor function and activity.

How does this work: [Mood sensation]

- Interaction between environment (social) and brain biology



Brain biology



How much omega-3 do we need in the diet to promote health benefits?

Omega-3 index:

Adequate omega-3 levels are being ingested when DHA plus EPA exceed eight percent (8%) of the total membrane fatty acids

Harris WS. *Pharmacol Res*;55:217-223 (2007)

Are our children getting enough?

Adolescent health study 2008-2011:

Brain Biology Food and Mood



Australasian
Research Institute



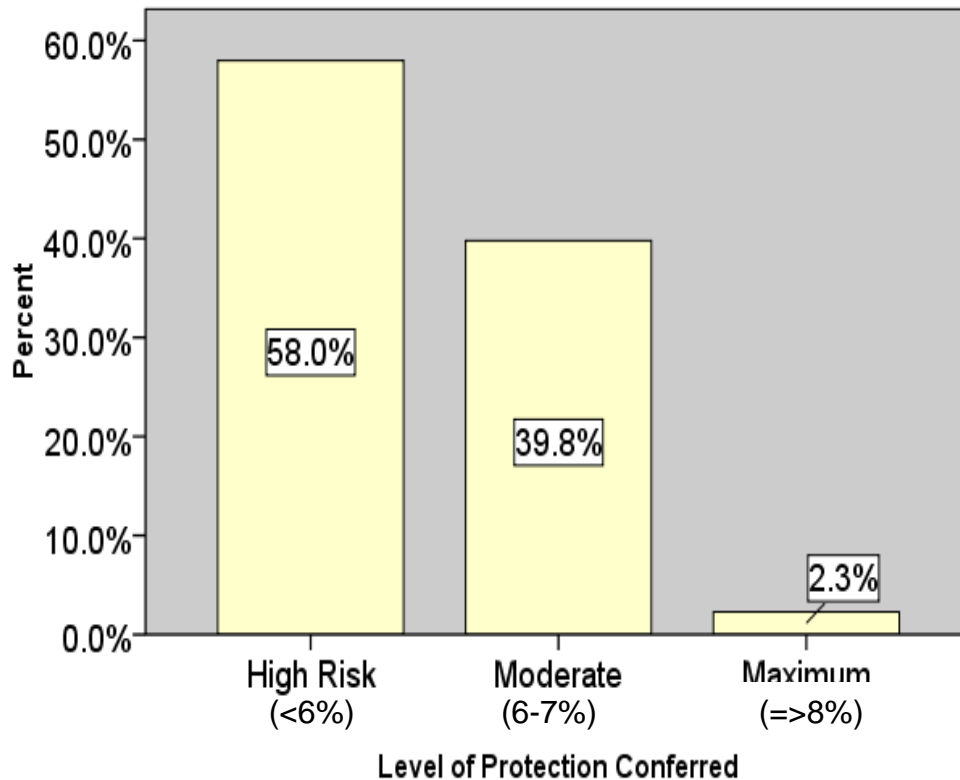
UNSW
THE UNIVERSITY OF NEW SOUTH WALES



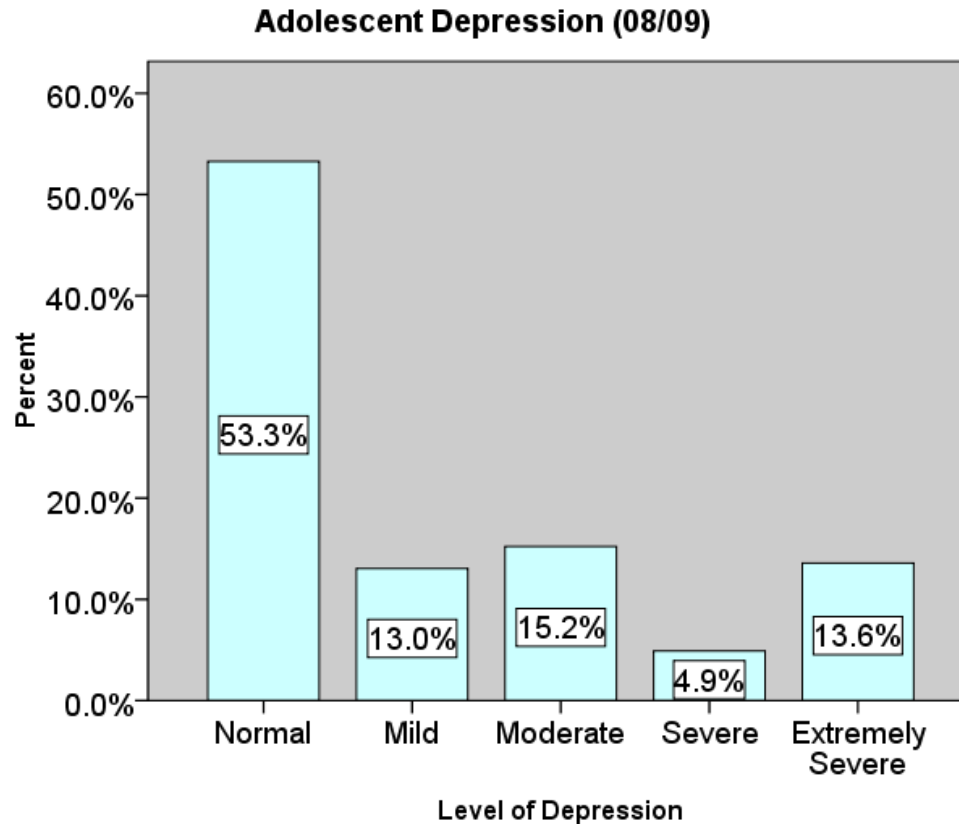


Adolescent health study:

Adolescent Omega-3 Index (09)



These results show that 6 out of 10 children are not benefiting from the protective effects of omega-3 against CVD



This study so far reveal that a significant number of children within our region are experiencing severe to extremely severe levels of:
stress (29%), **anxiety** (26%) and **depression** (19%)

Ω 3 and cardiovascular disease

Evidence:

- **Study 1:** 95 consecutive patients with their first AMI and 17 controls were assessed. A significant correlation between serum n-3 polyunsaturated fatty acid levels and the extent of coronary soft plaques and calcification was observed in AMI patients ¹⁹.
- **Meta analysis:** 29 RCT for high risk CVD patients:
.... the evidence to date suggests that omega-3 fatty acids may result in a modest reduction in mortality and restenosis ¹⁸

Mechanism of action:

- Increased Ω -6: Ω -3 promotes eicosanoid metabolic products from AA such as; prostaglandins, thromboxanes, leukotrienes, hydroxy fatty acids, and lipoxins ¹⁶. As these are very active in small quantities large amounts will contribute to the formation of thrombus and atheromas ¹⁷.

Ω 3 and immune/inflammatory disease

Evidence:

- **Study 1:** Blood samples from 43 older adults (mean age = 66.67, SD=10.09) provided data on PUFAs and TNF- α , IL-6, and sIL-6r. Depressive symptoms were assessed by the CES-D. **Results:** Depressive symptoms and n -6: n -3 ratios worked together to enhance proinflammatory cytokines beyond the contribution provided by either variable alone. **Conclusion:** Diets with high n -6: n -3 PUFA ratios may enhance risk for both depression and inflammatory diseases ²⁰.
- **Review:** Ingestion of dietary supplements of n -3 fatty acids has been consistently shown to reduce both the number of tender joints & morning stiffness in patients with **Rheumatoid A**. Minimum daily dose of 3 g eicosapentaenoic and docosahexaenoic acids for 12 weeks required ²¹.

Ω 3 and immune/inflammatory disease

Mechanism of action:

- Activation the transcription factor nuclear factor kappa B (NF- κ B) upregulates proinflammatory cytokine production. EPA and DHA, can substantially decrease TNF- α expression by blocking NF- κ B activation ²⁰.
- Higher levels of *n*-3 PUFAs are associated with lower serum levels of the inflammatory cytokines IL-6 and TNF- α ²².

Omega-3 rich vegetarian foods

Source	Total Essential Fatty acids g	Ω-6 g	Ω-3 g	Ratio Ω6:Ω3
Flaxseed oil 1 tbsp (14g)	8.9	1.7	7.2	1:4
Flaxseed ground 1 tbsp (7g)	2.0	0.4	1.6	1:4
Hulled hemp seeds 1 tbsp (10g)	3.9	3.0	0.9	3:1
Rapeseed oil 1 tbsp (14g)	3.9	2.6	1.3	2:1
Walnuts 1oz (28g)	13.2	10.7	2.5	4:1

Omega-3 seafood

Sources of EPA and DHA in Diet and Omega-3 FA Therapy

Fish	Amount (g) in 3 oz Serving	Serving Amount Required to Provide 1 g of EPA/DHA
Mackerel	0.34–1.57	2–8.5
Herring	1.71–1.81	1.5–2.0
Salmon	0.68–1.83	1.5–4.5
Trout	0.84–0.98	3.0–3.5
Catfish	0.1–2.0	15–20
Flounder/Sole	0.42	7
Cod	0.1–0.24	12.5–23
Tuna, fresh	0.24–1.28	2.5–12
Supplements	Amount (g) in 1 g Capsule	Capsules Required to Provide 1 g of EPA/DHA
Cod liver oil	0.19	5.0
Fish body oil	0.30	3.0
Omega-3 FA concentrate	0.50	2.0
Prescription omega-3 FA	0.85	1.0

Kris-Etherton, et al. *Circulation*. 2002;105:2747-2757

Additional Notes:

- Flaxseed oil does deliver the greatest amounts of omega 3 fatty acids,
- Whole flaxseeds contain fibre and important compounds such as lignans which can have additional health benefits.
- Flaxseeds must always be crushed in order to ensure nutrient availability.
- Rapeseed oil is a good source of omega 3 fatty acids but it should not be heated and preferably only used as cold-pressed.
- Both essential fatty acids can easily generate free radicals once they are subjected to heat, light and oxygen.
- Green leafy vegetables can also add to your ALA intake (e.g. broccoli has 0.13g per 100g and cabbage 0.11g per 100g).

Adapted from:

<http://www.vegsoc.org/info/omega3.html>

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