

Omega-3 fatty acids in the treatment of psychiatric disorders.

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FROM ABSTRACT:

The importance of omega-3 fatty acids for physical health is now well recognised and there is increasing evidence that omega-3 fatty acids may also be important to mental health.

The two main omega-3 fatty acids in fish oil, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have important biological functions in the CNS.

DHA is a major structural component of neuronal membranes, and changing the fatty acid composition of neuronal membranes leads to functional changes in the activity of receptors and other proteins embedded in the membrane phospholipid.

EPA has important physiological functions that can affect neuronal activity.

Epidemiological studies indicate an association between depression and low dietary intake of omega-3 fatty acids, and biochemical studies have shown reduced levels of omega-3 fatty acids in red blood cell membranes in both depressive and schizophrenic patients.

Five of six double-blind, placebo-controlled trials in schizophrenia, and four of six such trials in depression, have reported therapeutic benefit from omega-3 fatty acids in either the primary or secondary statistical analysis, particularly when EPA is added on to existing psychotropic medication.

Individual clinical trials have suggested benefits of EPA treatment in borderline personality disorder and of combined omega-3 and omega-6 fatty acid treatment for attention-deficit hyperactivity disorder.

The evidence to date supports the adjunctive use of omega-3 fatty acids in the management and treatment of unresponsive depression and schizophrenia.

As these conditions are associated with increased risk of coronary heart disease and diabetes mellitus, omega-3 fatty acids should also benefit the physical state of these patients.

THESE AUTHORS ALSO NOTE:

"The importance of omega-3 fatty acids for physical well-being had been recognized for several decades."

Omega-3 fatty acids have anti-inflammatory, antithrombotic, antiarrhythmic and hypolipidaemic effects.

Omega-3 fatty acids are beneficial in the prevention and treatment of physical illnesses ranging from coronary heart disease to rheumatoid arthritis.

"Homo sapiens evolved in an omega-3 rich nutritional environment."

"Over the last century, dietary intake of omega-3 fatty acids has declined, whereas there has been an increase in the amount of omega-6 fatty acids."

"This altered balance of fatty acids is regarded as detrimental to the health of the population." **[Key Point]**

Omega-3 fatty acids are important not only for physical health but also for brain development and function. **[Key Point]**

There is an increasing interest in the use of omega-3 fatty acids for the treatment of mental health problems.

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are the most important omega-3 fatty acids in relation to brain function.

Alpha-linolenic acid (ALA) omega-3 is also essential and must be obtained from the diet. [Important: most fish oil omega-3 supplements do not contain ALA, yet it is essential as are EPA and DHA. They must all come from the diet.]

Metabolizing EPA and DHA from ALA is "very inefficient" and therefore EPA and DHA must come from food sources; "the main food providing EPA and DHA is fish, and the fish in turn obtain these omega-3 fatty acids by eating algae." [Very Important for strict vegetarians].

"Highly purified [supplemental] EPA and DHA are now available"

"Omega-3 fatty acids have important effects on brain function."

DHA is a major structural component of nerve cell membranes.

Altering the lipids of the nerve cell membranes "leads to functional changes in the activity of receptors and other proteins embedded in the membrane phospholipid." [Very Important Point: altering the function of the membrane bound proteins and receptors, alters the coupling with hormones and neurotransmitters, increasing the need for drugs.]

EPA is not present in nerve cell membranes, but functions as a precursor for eicosanoids and a modulator of cytokines.

The first study showing that omega-3s are helpful in the treatment of mental disorder was published in 1981.

Omega-3s are reduced in the membranes of patients with schizophrenia and depression.

"Fish oil consumption correlates not only with rates of depression, but also with rates of bipolar disorder, homicide and postnatal depression."

Schizophrenics taking high doses of EPA all improved, whereas those treated with DHA did not differ from placebo in their therapeutic response. [Important, with schizophrenia the most critical omega-3 is EPA, not DHA].

Studies on schizophrenics tend to dose at 2 to 4 g/d of EPA for 3 months. Improvements are seen in both schizophrenia symptoms, "but also in tardy dyskinesia, which is a movement disorder seen particularly in schizophrenic patients treated long-term with older antipsychotic drugs."

Patients given EPA "required significantly lower dosages of antipsychotic medication to produce the same clinical benefit, and they also experienced substantially less cognitive decline than those given placebo."

"Double blind, placebo-controlled trials on omega-3 fatty acid treatments have been conducted in borderline personality disorder, obsessive-compulsive disorder and attention-deficit hyperactivity disorder (ADHD)."

In borderline personality disorder, 1 gm of EPA per day was superior to placebo in diminishing aggression as well as the severity of depressive symptoms.

DHA also has an anti-aggression effect.

Studies using combinations of fish oil and evening primrose oil [which contains the omega-6 gamma-linolenic acid] "have shown a significant treatment effect relative to placebo on ADHD symptoms."

Consumption of one fish meal a week is associated with a reduced risk of Alzheimer's disease.

Levels of omega-3 fatty acids are reduced in the cell membranes of patients with schizophrenia and depression.

There is a relationship between dietary intake of fish and the prevalence of depression [Increased fish consumption reduced depression rates.]

Increased dietary consumption of saturated fat and sugar increase rates of schizophrenia.

Omega-3 fatty acids, especially EPA, are capable of modulating the severity of schizophrenia.

“In treatment studies for both schizophrenia and depression, current evidence suggests that EPA rather than DHA is the effective agent.”

“It has been suggested that EPA is working as an inhibitor of phospholipase A2, which is known to be elevated in patients with schizophrenia.”

[Background:

- 1) Phospholipase A2 is an enzyme that cleaves essential fatty acids out of membranes; this is bad, and increases schizophrenia.
- 2) Phospholipase A2 is a protein, and therefore is coded for by a gene in one's DNA.
- 3) Schizophrenia is often found in families, suggesting a genetic link.
- 4) A proposed genetic link in schizophrenia is overexpression of the gene that codes for phospholipase A2.
- 5) Drugs like lithium inhibit the activity of phospholipase A2, and this helps schizophrenic patients. However, lithium drugs have many serious side effects.
- 6) The theory is that dosing schizophrenic patients with EPA replenished membrane EPA faster than phospholipase A2 cleaves it from the membrane, allowing schizophrenic patients to function more normally without or with a minimum of drugs like lithium, avoiding the lithium side effects.]

It has also been suggested that schizophrenia is a pro-inflammatory condition, and that there are increased levels of proinflammatory cytokines in schizophrenic patients. “This, EPA could be acting through an anti-inflammatory effect.” Cox-2 inhibitors benefit schizophrenics, [and cox-2 inhibitors reduce the conversion of the omega-6 fatty acid arachidonic acid into the pro-inflammatory eicosanoid prostaglandin E2. EPA also inhibits the conversion of arachidonic acid into prostaglandin E2.]

The US FDA recognizes the safety of fish oil up to a dose of 3 g/d of EPA plus DHA.

Other benefits of omega-3 fatty acids are particularly related to cardiovascular disease, and both depression and schizophrenic patients have a substantially increased risk of coronary artery disease.

Antipsychotic drugs elevate plasma triglyceride levels, and these elevated levels can be normalized during treatment with omega-3 fatty acids.

“Omega-3 fatty acids generally do not appear to have clinically significant effects on bleeding time, but caution has been urged when using these preparations in higher doses, or for patients with pre-existing haemorrhagic disorders or those on anticoagulant treatment.”

“There are concerns about contamination of fish with dioxins, dioxin-like compounds and methyl mercury.”

“The evidence suggests that doses of 1-2 g/day, particularly of EPA, are required. This level cannot be safely attained by diet alone.” [NOTE: If one is taking the omega-3 combination EPA/DHA in the recommended ratio of 2/1, the ratio would be 2000 mg EPA / 1000 mg DHA for a total of 3000 mg EPA/DHA per day.]

“Fish oil preparations available from health food stores and pharmacists are of variable quality and composition, and are potentially unsafe in high dosage because of contaminants that vary between products. Pharmaceutical grade omega-3 fatty acid preparations will deliver the necessary quantity of omega-3 fatty acids within the dosages that are already prescribed for lipid and cardiovascular disorders.”

“It is the opinion of these reviewers that nutritional advice, including advice on consumption of fish, should form part of the holistic management of all patients with mood disorders and schizophrenia.”

“It is the opinion of these reviewers that the prescription of omega-3 fatty acids is justified for depressive and schizophrenic patients who have not responded optimally to standard treatments. Many patients choose such approaches for themselves, and clinicians should at least be aware of the evidence base and be able to give sensible advice.”

KEY POINTS FROM DAN MURPHY

- 1) Omega-3 fatty acids are important for physical and mental health.
- 2) The two main omega-3 fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are found primarily in fish oil.
- 3) DHA is a major structural component of neuronal membranes. Its fluidity [from an incredible 6 double bonds] allows for optimal shape and function of membrane bound proteins and receptors.
- 4) Omega-3 treatment benefits borderline personality disorder and attention-deficit hyperactivity disorder.
- 5) Omega-3 fatty acids have anti-inflammatory, antithrombotic, antiarrhythmic and hypolipidaemic effects.
- 6) Omega-3 fatty acids are beneficial in the prevention and treatment of physical illnesses ranging from coronary heart disease to rheumatoid arthritis.
- 7) “*Homo sapiens* evolved in an omega-3 rich nutritional environment.”

- 8) "Over the last century, dietary intake of omega-3 fatty acids has declined, whereas there has been an increase in the amount of omega-6 fatty acids." "This altered balance of fatty acids is regarded as detrimental to the health of the population." **[Key Point]**
- 9) Omega-3 fatty acids are important not only for physical health but also for brain development and function. **[Key Point]**
- 10) The omega-3 alpha-linolenic acid (ALA) is also essential and must be obtained from the diet. [Important: most fish oil omega-3 supplements do not contain ALA, yet it is essential as are EPA and DHA. They must all come from the diet.]
- 11) Metabolizing EPA and DHA from ALA is "very inefficient" and therefore EPA and DHA must come from food sources.
- 12) "Omega-3 fatty acids have important effects on brain function." DHA is a major structural component of nerve cell membranes.
- 13) "Fish oil consumption correlates not only with rates of depression, but also with rates of bipolar disorder, homicide and postnatal depression."
- 14) Schizophrenics taking high doses of EPA all improved, whereas those treated with DHA did not differ from placebo in their therapeutic response. [Important, with schizophrenia the most critical omega-3 is EPA, not DHA].
- 15) Studies using combinations of fish oil and evening primrose oil [which contains the omega-6 gamma-linolenic acid] "have shown a significant treatment effect relative to placebo on ADHD symptoms."
- 16) Increased dietary consumption of saturated fat and sugar increase rates of schizophrenia.
- 17) Omega-3 fatty acids, especially EPA, are capable of modulating the severity of schizophrenia.
- 18) "In treatment studies for both schizophrenia and depression, current evidence suggests that EPA rather than DHA is the effective agent."
- 19) The US FDA recognizes the safety of fish oil up to a dose of 3 g/d of EPA plus DHA.
- 20) Omega-3 fatty acids do not appear to have clinically significant effects on bleeding time, but caution should be used for those with pre-existing hemorrhagic disorders or those on anticoagulant drugs.

- 21) Fish is contaminated with dioxins, dioxin-like compounds and methyl mercury. Because of contaminants, optimal levels of omega-3s cannot be safely attained by diet alone.
- 22) Taking the omega-3 combination EPA/DHA in the recommended ratio of 2/1, would be 2000 mg EPA / 1000 mg DHA for a total of 3000 mg EPA/DHA per day.
- 23) One should also take alpha-linolenic acid omega-3 (as it is also essential) and gamma-linolenic acid omega-6. [This is why I like the Nutri-West formula, as it contains EPA, DHA, ALA, and GLA. Their phone number is (**800-443-3333**)]
- 24) Fish oil supplements must be pharmaceutical grade for safe high-dose consumption, and health food store preparations may not be of this pure quality.
- 25) Advice on fish consumption should form part of the holistic management of all patients with mood disorders and schizophrenia.
- 26) The prescription of omega-3 fatty acids is justified for depressive and schizophrenic patients.