igennus
HEALTHCARE NUTRITION
Be kind to your health™

Clinical guide

Nutritional interventions for managing mood disorders

Overview

Omega-3 deficiency and elevated homocysteine levels are key risk factors for a wide range of psychiatric and neurological disorders. Changes in nutrient intake, coupled with lifestyle changes and hyper stimulation of both the innate immune system and the HPA-axis (stress-mediating pathway) leads to modulation of immune and inflammatory pathways central to the initiation and development of mood disorders. Elevated homocysteine and low omega-3 levels increase inflammation and disrupt neurotransmitter synthesis.

Treatment protocol for depression

It is clear from fatty acid intervention studies that when individuals are recruited irrespective of their omega-3 baseline levels and then treated with fixed doses (ignoring the large inter-individual variability in omega-3 uptake), the treatment outcomes derived from omega-3 supplementation can vary considerably. *Key* to successful intervention is the understanding and acknowledgement that we are metabolically unique individuals with highly personal nutrition requirements. As such, at Igennus we focus on omega-3 interventions to optimise therapeutic outcomes at an individual level rather than endorsing a 'one size fits all' dosing regimen. When baseline omega-3 levels and body weight are taken into account, together with client biomarker results from the Opti-O-3 test, it is possible to personalise dosing to bring clients' omega-3 levels into the desired ranges quickly and efficiently.

Dosing chart

The Opti-O-3 biomarker test is highly effective when used in conjunction with our therapeutic range of supplements. By identifying the specific dose required for an individual to achieve an omega-3 index of ≥8% and an AA to EPA ratio of 1.5-3:1, it offers the ideal solution to personalised nutrition. When it is not possible to use the Opti-O-3 biomarker test, we suggest the following minimum doses.

Product	Dose	Duration
Pharmepa RESTORE	Minimum 2 x 1 capsule daily (1000 mg EPA)	6 months minimum
Homocysteine Control	3 x 1 tablet daily	6 months
Pharmepa MAINTAIN	3 x 1 capsule daily (1000 mg EPA & DHA)	from 6 months onwards or once symptoms subside
Homocysteine Control	2-3 x 1 tablet daily	from 6 months onwards

Notes

- Capsules and tablets should be taken as a split-dose and **with food** for optimum absorption and to improve bioavailability
- Pharmepa RESTORE may be the most effective long-term management strategy for some depressed clients and this is considered perfectly safe
- At 6 months, if the client is happy with their level of improvement, move on to 3 x Pharmepa MAINTAIN daily
- Homocysteine Control is designed as a co-therapy and thus supplementation with Pharmepa (RESTORE & MAINTAIN) should take priority for managing depression when use of both products is not possible

Contraindications

Omega-3 thins the blood and can decrease blood pressure. Whilst it is perfectly safe to take alongside anticoagulant or antihypertensive medication we recommend that the patient inform their doctor.
Side effects: taking capsules with meals can help decrease the likelihood of fishy aftertaste, belching, nausea and loose stools occasionally experienced when taking high dose omega-3.
Warnings: pregnant or lactating women should consult their doctor before taking any food supplement.

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Mechanisms of action of depression management protocol

- Regulates neurotransmitter function (serotonin, dopamine, melatonin)
- Improves cell signalling and transduction, receptors density regulation
- Increases antioxidant (glutathione) levels
- Improves methylation processes
- Reduces cortisol levels
- Restores a healthy AA to EPA ratio to regulate inflammation
- Restores and maintains a healthy omega-3 index
- Neuroprotective actions through maintenance of cell membrane integrity

The science

- Polyunsaturated fat (PUFA) biosynthesis is down-regulated in major depressive disorder, reflected by the significantly low levels of omega-3 observed in patients.
- The AA to EPA ratio correlates positively with inflammation and depression symptom severity.
- Increased levels of prostaglandin E2 (PGE2) directly activates the HPA-axis, increases cortisol and drives the production of inflammatory mediators. Abnormal HPA-axis activity is routinely observed in patients with major depressive disorder.
- Cortisol and inflammatory cytokine production increase the risk of developing depression via increasing kynurenine production.
- The chronic up-regulation of the kynurenine pathway reduces tryptophan and serotonin and elevates production of quinolinic acid, which has potent neurotoxic effects.
- Magnetic resonance imaging (MRI) scans show brain grey matter abnormalities in major depression, bipolar disorder and schizophrenia.
- Pro-inflammatory cytokines increase serotonin transporter (SERT) activity (involved in recycling serotonin for reuse), thus further reducing overall serotonin activity.
- A low omega-3 index (EPA + DHA) appears to play a causal role in the development of mood disorders.
- Treatment with omega-3 results in an improvement in the AA to EPA ratio, omega-3 index and subsequently in depression scores.
- The AA to EPA ratio and omega-3 index are important biomarkers of depression risk and severity.
- Interferon (IFN) treatment in hepatitis C patients is known to induce depression in approximately 40% of patients. Genetic variations in the COX2 and PLA2 genes increase the risk of IFN-α-induced depression. Omega-3 EPA and DHA deficiency has been associated with an increased risk of IFN-induced depression.
- EPA increases both EPA and DHA erythrocyte levels and prevents IFN-α-induced depression.
- EPA directly competes with AA, inhibits COX2 enzyme activity and reduces PGE2 synthesis; this reduces pro-inflammatory cytokine production and down-regulates the IDO enzyme cascade and the production of potentially neurodamaging metabolites.
- EPA influences both the production and function of neurotransmitters known to play a role in the symptoms of depression, such as serotonin (involved in mood, emotion, sleep and appetite).
- EPA plays a direct role in protecting the brain and nerves from dietary and/or stress-related damage.
- The ratio of EPA to DHA is of significance when establishing the efficacy of a supplement in the treatment of depression. The higher the content of EPA in relation to DHA, the greater the efficacy.
- EPA must be in excess of DHA to show benefits in depressed patients for the duration of the initial 'treatment' phase.
- Supplements containing EPA ≥ 60% of total EPA + DHA content, in a dose range of up to 2,200

mg/day of EPA in excess of DHA, are clinically effective against primary depression, with those studies using pure EPA at a dose of 1g/daily the most efficacious.

- A 2013 study directly comparing EPA and DHA found 1g pure EPA to be significantly more effective than 1g DHA in treating depressive symptoms.
- Studies show that EPA is as effective as the most commonly prescribed antidepressants in the treatment of depression.
- EPA isolate is safe and effective when used in combination with conventional antidepressants.
- The use of pure EPA as a standalone natural treatment is particularly effective in individuals who do not respond to conventional pharmaceutical medication.
- Using EPA in re-esterified triglyceride (rTG) form ensures delivery of highly concentrated EPA, but also optimises bioavailability – key factors that have the potential to influence therapeutic outcomes.
- Deficiency in folate and vitamin B12 results in elevated serum homocysteine, which causes a decrease in SAMe, followed by impaired methylation and, consequently, impaired metabolism of neurotransmitters, including serotonin.
- Elevated homocysteine leads to increased oxidative stress and neurotoxicity, which may promote the development of depression.
- Homocysteine recycling to cystathionine requires vitamin B6 (pyridoxal-5-phosphate); cystathionine is further metabolised to cysteine and, finally, to the antioxidant glutathione. Low levels of glutathione are accompanied by an increase in oxidative stress and increased inflammation. This may play a role in the pathophysiology of neuro-immune disorders, including depression.
- Omega-3 fatty acids up-regulate homocysteine metabolism. Omega-3 deficiency is associated with elevated homocysteine levels. Benefits attributed to EPA in the treatment of depression may therefore be in part via homocysteine regulation.