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HEALTHCARE NUTRITION
Be kind to your health™

# Clinical guide

## Nutritional interventions for managing neurodevelopmental disorders

### Overview

Neurodevelopmental disorders are associated with various dysfunctions in cognition, learning, communication and behaviour, and include: attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), dyspraxia and dyslexia. Evidence suggests that neurodevelopmental disorders are the result of genetic and environmental factors which, when present together in early life, result in neurological and cognitive dysfunction. Breakdowns in several neurotransmitter pathways, disturbances in neurotransmission and dysfunction of the hypothalamus-pituitary-adrenal (HPA) axis activity are all associated with the development and progression of neurodevelopmental disorders. Deficiencies in key micronutrients (including zinc and magnesium, important for neurotransmission), coupled with deficiencies or imbalances in the long-chain omega-3 fatty acids, have also been implicated in their predisposition and development. Omega-3 supplementation is an effective treatment method, especially for ADHD – with high EPA to DHA ratios essential for producing the most beneficial effects. The use of pure EPA has been shown to be a highly effective therapy for ADHD, in particular for those individuals resistant to commonly used pharmaceuticals, with greater improvements observed in combination with micronutrients – specifically zinc, magnesium and vitamin B6. Oxidative stress and dysregulation of cellular redox activity has also been observed in neurodevelopmental disorders, particularly autism, with ubiquinol proving a useful tool in reducing symptom severity.

## Treatment protocol for neurodevelopmental disorders

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 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 charts

**Adults and adolescents (12+)**

| Product | Dose | Duration |
|---|---|---|
| Pharmepa RESTORE<br>Pharmepa MAINTAIN | 2 capsules daily<br>3 capsules daily | 6 months or more<br>from 6 months if symptoms have improved |
| Neurobalance | 2 x 3 tablets daily | Ongoing |
| VESIsorb Ubiquinol-QH | 1 capsule daily | Ongoing |

**Children aged 8-12**

| Product | Dose | Duration |
|---|---|---|
| Vegepa | 3-4 capsules daily | 6 months – reduce by 1-2 at this point if symptoms have improved |
| Neurobalance | 2 x 2 tablets daily | Ongoing |
| VESIsorb Ubiquinol-QH | 1 capsule daily | Ongoing |

**Children aged 4-8**

| Product | Dose | Duration |
|---|---|---|
| Vegepa | 3-4 capsules daily | 6 months – reduce by 1-2 at this point if symptoms have improved |
| Neurobalance | 1-2 x 2 tablets daily | Ongoing |
| VESIsorb Ubiquinol-QH | 1 capsule daily | Ongoing |

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## Notes

- Capsules and tablets should be taken as a split-dose **and with food** for optimum absorption and to improve bioavailability
- At 6 months, if client is happy with level of improvement, reduce the dosage accordingly
- Should symptoms show signs of recurrence, increase the dosage accordingly

## Mechanisms of action of neurodevelopmental disorders treatment protocol

- Restores optimal long-chain omega-3 status
- Restores optimal omega-6 to omega-3 ratio
- Protects neurotransmitter synthesis and function
- Reduces inflammation
- Supports neurotransmitter synthesis and function
- Reduces high oxidative stress levels and subsequent lipid peroxidation
- Helps alleviate the damage associated with poor antioxidant function
- Helps restore VDAC function

## 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.

## The science

- Deficiencies of the long-chain polyunsaturated fatty acids (PUFA) are related to neurodevelopmental disorders.
- Delta-6-desaturase (FADS2) enzyme presents a major rate-limiting step in the biosynthesis of polyunsaturated fatty acids (PUFA) and variants in the genes coding FADS2 have been found to correlate with neurodevelopmental disorders.
- Inadequate dietary supply of omega-3 fatty acids and increased activity of phospholipase A2 results in cell membranes becoming depleted of omega-3, leading to deficiencies; both correlate with neurodevelopmental disorders.
- EPA protects cell membrane integrity by reducing the production of phospholipase A2, thereby reducing EPA and DHA loss from phospholipids.
- Increasing erythrocyte omega-3 levels via dietary supplementation improves behaviour, attention and literacy in children with ADHD. Additional benefits appear to be derived when combining EPA with the omega-6 fatty acid GLA.
- A 2012 pilot trial supplementing treatment-resistant children with EPA and GLA in combination (using Vegepa®) found statistically significant improvements in 10 out of 11 behavioural measures of ADHD in children whose parents reported no previous improvements in behaviour and learning with methylphenidate and standard behaviour therapy for six months or more.
- Brain-derived neurotrophic factor (BDNF) is involved in survival, differentiation, and synaptic plasticity of several neuronal systems, including dopaminergic pathways.
- Dysregulation of BDNF is linked to neurodevelopmental disorders and is a key target for omega-3 supplementation.
- Circulating levels of inflammatory cytokines are directly correlated with behavioural problems in children with ADHD. Omega-3 supplementation decreases plasma inflammatory mediators and oxidative stress in children with ADHD.
- Low levels of zinc can impede normal neurotransmitter function and deficiencies are common in neurodevelopmental disorders, with zinc supplementation leading to improvement in symptoms.
- Deficiencies in vitamin B6 and magnesium are also common in neurodevelopmental disorders and lead to low neurotransmitter production, as well as to accumulation of the tryptophan metabolite kynurenine, which is associated with disturbances in neurotransmission.
- Supplementation with vitamin B6 combined with magnesium has been shown to improve symptoms relating to ASD and ADHD, and more so when used in combination with omega-6 (GLA) and omega-3 fatty acids (EPA ± DHA).
- 100 mg of ubiquinol daily results in significant improvements in autism symptoms. This is thought to be due to its role in reducing high oxidative stress levels and subsequent lipid peroxidation, both of which are heavily associated with autism.
- Antibodies to voltage-dependent anion channel (VDAC) and subsequent reduced VDAC redox activity have been found to correlate with expression of autism; ubiquinol supplementation may thus be helpful in restoring both VDAC function and autism symptoms.