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HEALTHCARE NUTRITION

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Clinical nutrition for neurodevelopmental disorders

Overview

The childhood disorders known collectively as *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 mental/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.[1, 2] 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. [3, 4] The use of omega-3 supplementation is widely recognised as an effective treatment, especially for ADHD – with the ratio of EPA to DHA within dietary supplements directly linked to the efficacy of the treatment regime. [5] The use of pure EPA has been shown to be a highly effective therapy for ADHD, [6] in particular for those individuals resistant to commonly used pharmaceuticals, [7] with greater improvements observed in combination with micronutrients – specifically zinc, magnesium and vitamin B6. [8-10] Oxidative stress and dysregulation of cellular redox activity has also been observed in neurodevelopmental disorders, particularly autism, with ubiquinol proving a useful tool in providing antioxidant and redox support, as well as reducing symptom severity.[37]

Omega-3 and neurodevelopmental disorders

Clinical and biochemical evidence suggests that deficiencies of the long-chain polyunsaturated fatty acids (PUFA) are related to neurodevelopmental disorders, as lower omega-3 blood levels and a higher omega-6 to omega-3 ratio (specifically AA to EPA) are consistently observed in both children and adolescents with the condition when compared with healthy controls. [9-11] The 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, in particular in ADHD. This strongly suggests a pathogenic role of endogenous variations in PUFA metabolism in ADHD and new research suggests that the ratio between omega-3 long-chain PUFA levels and desaturase enzyme activity may provide valuable insights into the biological factors that contribute to ADHD. [12]

The enzyme phospholipase A2 (PLA2) is responsible for releasing omega-3 from cell membrane phospholipids. An inadequate dietary supply of the omega-3 needed for replenishing cells levels and increased activity of PLA2 results in cell membranes becoming depleted of omega-3, leading to deficiencies; both have been found to correlate with neurodevelopmental disorders. [11] In reducing the production of phospholipase A2, EPA protects cell membrane integrity by reducing EPA and DHA loss from phospholipids. [12] Increasing erythrocyte omega-3 levels via dietary supplementation improves behaviour, attention and literacy in children with ADHD.[13, 14] Additional benefits appear to be derived when combining EPA with the omega-6 fatty acid GLA.

For example, a 2012 pilot trial supplementing treatment-resistant children (who have not responded to conventional treatment with Ritalin) with two Vegepa E-EPA-70 capsules daily showed significant improvements in both behaviour and academic learning. Of those children taking Vegepa E-EPA 70, 81.2% showed significant statistical improvements in restlessness, 87.5% in aggressiveness and 70.8% in anger control. Furthermore, 83.3% showed statistically significant improvements in cooperation with both parent and teachers, with 77.1% of children showing improved educational functioning and academic performance. Whilst some improvements were observed within three months, the most marked improvements were observed after six months of supplementation.[7] This was the first study of its kind to demonstrate the effectiveness of EPA and GLA in combination, in children with ADHD whose parents reported no improvements in behaviour and learning with Ritalin and standard behaviour therapy for six months or more.

In addition to direct replenishment of cellular omega-3, EPA plays a key role as a 'secondary messenger' in neurotransmitter systems, as well as contributing to many other aspects of cell signalling. It is also the substrate for anti-inflammatory eicosanoids, a highly bioactive group of hormone-like substances including prostaglandins, leukotrienes and thromboxanes. It is through the regulatory influences on endocrine, cardiovascular and immune systems, that these EPA derivatives exert profound influences on brain development and function. [15] 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. [16, 17] Circulating levels of inflammatory cytokines are directly correlated to behaviour problems in children with ADHD. [18, 19] Omega-3 supplementation decreases plasma inflammatory mediators and oxidative stress in children with ADHD.[20]

Micronutrients: zinc, magnesium and vitamin B6 and neurodevelopmental disorders

Several controlled trials using omega-3 combined with micronutrients show considerable reductions in aggressive, antisocial and violent behaviour in youth and young adult prisoners.[21]

Breakdown of several neurotransmitter pathways is commonly observed in neurodevelopmental disorders, particularly for dopamine, and is thought to occur due to differences in receptor subtypes and transporter pathways, [22, 23] imbalances in excitatory and inhibitory receptors (as in the case of GABA) [24] or through genetic variations that impede normal neurotransmitter function. [25, 26]

Zinc is not only required for neurotransmitter synthesis, but also directly interacts with neurotransmitter transporter proteins, thereby playing a direct role in regulating the rate at which neurotransmitters are deposited into the synapse, [27, 28] Low levels of zinc can impede normal neurotransmitter function and deficiencies are common in neurodevelopmental disorders, [29] with zinc supplementation leading to improvement in symptoms, [30]

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, [31] which is associated with disturbances in neurotransmission. [32] Vitamin B6 supplementation improves speech and language in some children, but use of the active form, pyridoxal-5-phosphate (PLP) is necessary due to poor conversion rates of other forms of B6 in children with autistic spectrum disorders. [33] Supplementation with vitamin B6 combined with magnesium has been shown to improve symptoms relating to ASD and ADHD, [8-10] which is increased when used in combination with omega-6 (GLA) and omega-3 fatty acids (EPA ± DHA). [34]

Ubiquinol and neurodevelopmental disorders

There is emerging evidence that the 'active' form of CoQ10, ubiquinol, may be helpful in the management

of neurodevelopmental disorders, specifically autism, and one study has shown that 100mg of ubiquinol given daily resulted in significant improvements in autism symptoms. [35] Ubiquinol appears to be helpful because of its role in reducing high oxidative stress levels and subsequent lipid peroxidation, both of which are heavily associated with autism. Ubiquinol is a potent antioxidant and so can help alleviate the damage associated with poor antioxidant function and status seen in ASD children. [36] In addition, studies

Have also linked the importance of CoQ10 in mitochondrial function to improved brain and neuron function, as well as enhanced ATP production in the brain. Further, CoQ10 is necessary to the activity of the voltage-dependent anion channel (VDAC), an important trans-membrane channel that facilitates the exchange of ions and molecules between the mitochondria and the cytosol and heavily involved in cellular redox reactions. Antibodies to 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.[37]

Recommended protocol for neurodevelopmental disorders:

Mechanisms of action:

Vegepa

- ✓ Restores optimal long-chain omega-3 status
- ✓ Restores optimal omega-6 to omega-3 ratio
- ✓ Protects neurotransmitter synthesis and function
- ✓ Reduces inflammation
- ✓ Restores BDNF signalling

Neurobalance

- ✓ Provides zinc, magnesium and B6 for neurotransmitter synthesis and function
- ✓ Reduces kynurenine accumulation
- ✓ Promotes tryptophan conversion to serotonin

VESIsorb Ubiquinol-QH

- ✓ Reduces high oxidative stress levels and subsequent lipid peroxidation
- ✓ Helps alleviate the damage associated with poor antioxidant function
- ✓ Helps restore VDAC function

Notes:

- Capsules and tablets should be taken as a split-dose **and with food** for optimum absorption and to improve bioavailability.
- At six months, if client is happy with level of improvement, the doses can be reduced where relevant.
- Should symptoms show signs of recurrence, the client should be advised to increase dosage.
- Clients should be encouraged to continue with long-term maintenance dose to avoid remission.

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