Useful applications of omega-3 fatty acids part 2: behavioural problems, learning difficulties, immunomodulation

Parents bringing up children with behavioural problems or learning difficulties will be well aware of the fact. It is difficult to ascertain what precisely is going wrong! After all, ADHD, dyslexia, dyspraxia or autism are developmental disorders with overlapping characteristics. Although classic medicine is making frantic efforts to attribute the 'right' clinical picture to these children according to their treatment, it is also worthwhile dwelling for a moment on possible common factors. One of these is undoubtedly an impaired fatty acid metabolism.

The overview in figure 1 serves as a guide for giving the fatty acids under discussion their rightful place in the conversion blueprint of fatty acids from the omega-3 and omega-6 family.

Omega-6 fatty acids	Omega-3 fatty acids
Linoleic acid (LA)	α-linolenic acid (ALA)
↓	⇣
γ-linolenic acid (GLA)	Eicosapentaenoic acid (EPA)
↓	⇣
Dihomo-γ-linolenic acid (DGLA)	Docosahexaenoic acid (DHA)
↓	
Arachidonic acid (AA)	

Figure 1. Conversion of the basic omega-6 (LA) and basic omega-3 (ALA) fatty acid into their respective longer-chain versions or HUFAs (highly unsaturated fatty acids). This conversion takes place in the body, but not always with equal efficiency. (Solid arrows point to the direct conversion product, broken arrows indicate that there are still interim products.)

Developmental disorders under the magnifying glass

It is not easy to apply the gold standard for clinical investigation, namely double-blind, placebo-controlled studies, to disorders of such a complex and multifactorial nature as ADHD, dyslexia, dyspraxia or autism. It seems there is no chance of obtaining any effect with a monotherapy such as omega-3 fatty acids. And yet such controlled studies point to the benefit of supplementation. Persons with developmental disorders suffer from an inadequate conversion efficiency (from ALA to EPA/DHA and from LA to GLA/DGLA/AA) and/or display a higher decomposition of these HUFAs through on the one hand oxidation and on the

other through an overactive PLA2 enzyme (phospholipase A2) that releases these HUFAs from the cell membranes.

Figure 2 visualises the vision of Prof. Richardson, Senior Research Fellow at Mansfield College and the university laboratory of physiology at Oxford. Although the primary characteristics of the various developmental disorders have been defined (dyslexia = difficulties in learning to read and write; dyspraxia = difficulties in planning and co-ordinating movements; ADHD = attention problems and/or hyperactive/impulsive behaviour; autism = pronounced social and communicative disorders), Prof. Richardson advocates a total and individual approach because the so-called 'pure cases' are the exception rather than the rule (figure 2).

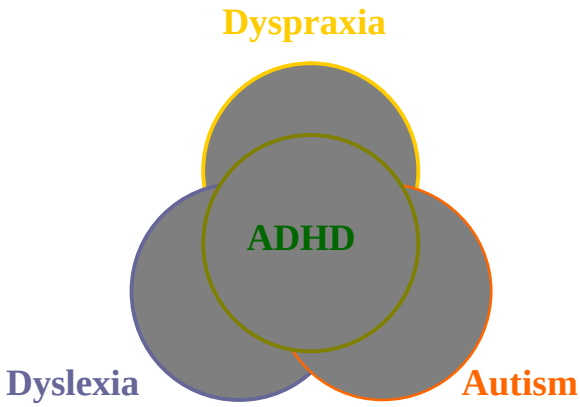

Figure 2. Only occasionally can the various developmental disorders be traced back to a single affliction. Normally there are several overlaps between symptoms. Overlap between ADHD/dyspraxia and dyslexia/dyspraxia is estimated at 50%. Dyslexia and ADHD occur jointly in 30-50% of cases, although the association with dyslexia mainly occurs with ADHD with attention problems. The association of ADHD, dyspraxia and dyslexia with autism is run-of-the-mill, although the main autistic characteristics generally have the upper hand.

ADHD

- Two studies in (31 and 18) ADHD patients who took evening primrose oil (270 mg GLA and ≈ 2 g LA) for 4 weeks did not produce any noteworthy improvements. Only in children with a low zinc status were a slight improvement in short-term memory and a reduced hyperactivity noted. It is therefore no surprise that zinc supplementation currently heads the list of recommended supplements for persons with ADHD. Meanwhile, after taking zinc sulphate (150 mg/day), older ADHD patients with a high BMI value achieved a better score in hyperactive/impulsive behaviour, but no solution was found for the attention problems. There may well be something in the fact that zinc is a major co-factor of the enzymes responsible for converting the basic omega-3/6 fatty acids into their HUFAs.

- In the Purdue study of 50 children with ADHD symptoms, supplementation with a combined formula (80 mg EPA, 480 mg DHA, 96 mg GLA and 40 mg AA/day) over 4 months produced significant increases in AA, EPA, DHA and vitamin E in the cell membranes of the red blood cells. This change in fatty acid composition of the cell membranes was linked to positive changes in behaviour.
- Two other studies in which (for 4 and 2 months) only DHA (345 mg/day and 500 mg/day) was administered to (63 and 40) children with ADHD did not give any indications of an improvement in the symptoms. On the contrary, the placebo group displayed better results.

Because supplementation with EPA+DHA does produce improvements while supplementing with DHA does not, current research is focusing mainly on EPA as a therapy for ADHD.

Dyslexia and dyspraxia

- In 41 dyslexic children with characteristics of ADHD a combined supplementation (186 mg EPA, 480 mg DHA, 96 mg GLA, 60 IU vitamin E, 864 mg LA, 42 mg AA and 8 mg thyme oil) over 12 weeks led to an improvement in the severity of the following symptoms: attention problems, impaired memory function and anxiety in social contacts. A second study with the same fatty acid formulation, but in 120 dyslexic children, investigated problems in reading. The higher the children scored on signs of fatty acid deficiency (see below) or visual problems at the start of this 6-month intervention, the better they reacted to the fatty acid supplementation.
- For the same parameters (ADHD symptoms, problems reading and writing), a 12-week supplementation with 80% fish oil (558 mg EPA and 174 mg DHA/day), 20% evening primrose oil (60 mg GLA/day) and 9.6 mg vitamin E (α-tocopherol) in 116 children with predominantly dyspraxia produced even better results than the dyslexia study.

The investigators attribute the better results of the second study to the higher EPA/DHA ratio.

Autism

A randomised, double-blind study is still being carried out, but preliminary positive results also point in the direction of EPA supplementation.

Recommendations

Table 1 shows the advice unveiled by Prof. Richardson at the 6th nutrition and health conference held on 7 November 2003 in Brussels Exhibition Centre (Heizel).

Fish oil supplements with an excess of EPA compared to DHA form the current basis of a supporting therapy for developmental disorders	
Decisive characteristic	**Recommended daily dose**
dyslexia and dyspraxia	500 mg EPA/day
ADHD and autism	1 g EPA/day
▪ Current research uses supplements with an EPA/DHA ratio of at least 7/1. ▪ The importance of a combined omega-3/omega-6 fatty acid supplementation cannot currently be precluded. The addition of a daily dose of 50-100 mg GLA is a further option, especially if the patients are also suffering from eczema. ▪ The Belgian Health Council advises taking 0.4 mg α-tocopherol equivalents (αTE - vitamin E) per gram PUFA to minimise peroxidation. Good fish oil supplements already contain vitamin E. ▪ Fish liver supplements are not suitable because they are rich in vitamin A. To obtain high doses of EPA from fish liver supplements, you would be simultaneously consuming high doses of vitamin A.	

Table 1: Recommended fatty acid supplementation.

Who benefits most from treatment with EPA?

There are a number of external characteristics that help determine the chance of success (table 2). Symptoms generally improve after 2 weeks to 3 months of supplementation. If there is no discernible improvement after three months, the patient is most likely not deficient in omega-3 fatty acids. Never forget that developmental disorders require a multidisciplinary approach!

External characteristics of fatty acid deficiency
▪ excessive thirst ▪ frequent urination ▪ very dry skin and dry hair ▪ anxiety and/or fits of anger ▪ sleep problems (problems falling asleep and waking up) ▪ eczema, asthma and other allergies

Table 2. Parameters that increase the chance of success of omega-3 supplementation.

Immunomodulation in a nutshell

- EPA makes the immune system more alert to UVB skin damage.
- EPA reduces the activity of NK cells. NK cells are responsible for rejecting transplanted bone marrow cells or organs. Taking EPA temporarily (shortly before and just after the transplant) may therefore prove beneficial.
- Many chronic disorders such as psoriasis, autoimmune diseases (rheumatoid arthritis, Crohn's disease, ulcerative colitis, multiple sclerosis, lupus erythematosus) and asthma are associated with an increased production of one or more of the following factors: thromboxane A2 (TXA_2), leukotriene B_4 (LTB_4), IL1β, IL6, TNFα and "C-reactive protein" (CRP). All these factors occur less frequently in the body with an increased consumption of omega-3 fatty acids (ALA and in particular EPA).

References

- Richardson AJ. Prostaglandins Leukot Essent Fatty Acids 2004; 70:383-90.
- Hirayama S et al. Eur J Clin Nutr 2004; 58(3):467-73.
- Bilici M et al. Prog Neuropsychopharmacol Biol Psychiatry 2004; 28(1):181-90.
- Johnson SM et al. J Clin Psychiatry 2003; 64(7):848-9.
- Richardson AJ et al. Prog Neuropsychopharmacol Biol Psychiatry 2002; 26(2):233-9.
- Ward PE. Prostaglandins Leukot Essent Fatty Acids 2000; 63(1-2):65-8.

Dr. Apr. Geert Vergote