PUFA with omega-3 fatty acids – essential for clever heads

Claudia Reinke

It is now generally accepted that long chain polyunsaturated omega-3 fatty acids (n-3 polyunsaturated fatty acids = n-3 PUFAs) play an essential role in the development and function of the brain. This does not only apply to the development of the brain during pregnancy and breast feeding, but also to the cognitive functions of the adult and aging brain. As a consequence of their neuroprotective properties, n-3 PUFAs also are evidently capable of counteracting mental and neurological disorders, such as depression or Alzheimer's disease. It is therefore by no means surprising that children with the attention deficit/hyperactivity syndrome (ADS, ADHS), who suffer from problems in learning and behaviour, benefit from therapy with PUFA. This was demonstrated by current studies, presented at a satellite symposium («Fish for the Brain») during the Trinational Meeting of the societies for clinical nutrition of Austria (AKE), Germany (DGEM) and Switzerland (GESKES) in June 2009 in Zürich.

The introductory lecture was given by Professor Berthold Koletzko of the Dr. von Hauner Children's Hospital, Ludwig Maximilian-University of Munich. He emphasised that it was essential for the course of the pregnancy and the health of the child that the mother should be optimally supplied with long chain PUFAs during pregnancy and breastfeeding. The polyunsaturated fatty acids alpha-linolenic acid (C18:3) and linoleic acid (C18:2) are essential nutrients. Secundary PUFAs are formed from these acids in the body by the introduction of additional double bonds and chain elongation, in a multiple step synthesis. While n-6 linoleic acid (LA) is converted in this way to the omega-6 fatty acid arachidonic acid (AA; C20:4), the n-3 alpha-linolenic (ALA) acid is converted to the omega-3 fatty acids eicosapentaenoic acid (EPA; C20:5) and docosahexaenoic acid (DHA; C22:6). However, only about 0.5% of the supply of alpha-linolenic acid is converted into DHA and, as unborn children and breastfed babies need increased levels of n-3-fatty acids, this must be compensated by supplying DHA and EPA in the mother's food. The main sources of DHA and EPA are fatty cold water fish, such as salmon, herring, mackerel and halibut, as well as marine algae. These are part of the food chain and are essential for ensuring that fish are well supplied with n-3 fatty acids. Numerous randomised controlled studies in recent years have investigated the effects of the n-3 PUFAs on the course of pregnancy and on child development. Three recently published meta-analyses have evaluated some of these studies. These showed, for example, that, if the mother is well supplied with n-3 PUFAs from fish oil, this increases the length of the pregnancy and the birth weight of the child. Moreover, the rate of premature births was significantly reduced - by more than 30% – and diseases of pregnancy were prevented.

In particular, the long chain n-3 fatty acid DHA has a major effect on the early development and function of the brain and the central nervous system (CNS), as well as the retina and thus on the child's visual function. It is mainly during the second half of pregnancy that DHA is stored in cerebral membrane lipids in nerve cells and in the retinal photoreceptors. As a consequence, the DHA requirement is increased to 30 to 45 mg/day during the last three months of pregnancy. Evidently the DHA taken by the mother is preferentially transported to the foetus through the placenta by means of specific transport systems. If the mother regularly takes enough DHA during pregnancy and breastfeeding in the form of fish or n-3-PUFA supplements, numerous favourable effects are observed on child development, extending up to school age – as has been demonstrated in many controlled studies. Thus there are significant improvements in the development of visual

acuity in the child, as well as in cognitive function and consequently in IQ development, attention and social development. There is also a favourable effect on the development of the sleeping pattern and on spontaneous motor activities, as Koletzko explained.

On the basis of the available data and with the support of the European Commission and many international professional societies, consensus recommendations have been developed for fat intake during pregnancy and breastfeeding. These state that pregnant and breastfeeding women are to be recommended to take a mean of 200 mg DHA per day. This can usually be achieved with two portions of fatty sea fish per week. Women who do not regularly eat fish should consider using special supplements. Koletzko considered that this was justified by the proven biological significance of a good perinatal intake of n-3 PUFAs for development in early childhood.

Possible effects of a diet rich in n-3 PUFAs on the adult and aging brain

Anne Eckert, Professor for Experimental Psychiatry in the Neurobiology Laboratory for Brain Aging and Mental Health in the Psychiatry University Clinic in Basle University, reported that 50 to 60% of the dry mass of the human brain consists of lipid. Neuronal tissue has a particularly high content of long chain polyunsaturated fatty acids – particularly DHA. The adult brain is evidently sensitive to diet, as has been shown in animal experiments. In other words, the brain can take up dietary long chain fatty acids from serum and incorporate them.

Neurones make up 22% of the cerebral cortex and their membrane phospholipids are particularly rich in DHA. According to Eckert, there had not yet been sufficient research on the precise physiological role of n-3 PUFAs in the CNS – particularly in the adult and in the aging brain. Animal studies had shown that long chain n-3 fatty acids play a decisive role in the modulation of signal transduction cascades (e.g. serotonin or acetylcholine). PUFAs are precursors for the formation of eicosanoids, making them essential control elements for cell functions. Thus rats fed for several weeks with a low n-3 PUFA diet exhibit marked changes in the expression of essential enzymes in the AA and DHA cascade, accompanied by bipolar disorders. A recently published study of the effect of a n-3 PUFA-rich diet on the brain, using an aging mouse model, showed that dietary DHA is incorporated into the membranes of the CNS. This was particularly marked in the structures of the hippocampus and amygdala, which had a positive effect on the animals' learning and memory.

Membrane fluidity and consequently the plasticity of the human brain decrease with age and this is accompanied by a gradual decrease in cognitive performance. If insufficient quantities of n-3 PUFAs are taken up over an extended period of time, there are disturbances in intracellular signal transmission, so that the decrease in mental performance is enhanced and progresses more rapidly. However, if n-3 PUFAs are taken specifically and as regularly as possible, this has been shown to increase the proportion of phospholipids in the CNS. This also increases the release of neurotransmitters such as serotonin and dopamine in the frontal cortex, enhancing the neuronal functions of the CNS and consequently the retention of learning and memory. Some recent studies indicate that intake of n-3 fatty acids may protect from Alzheimer's disease and may be successfully used in the therapy of depression. This positive neuroprotective effect is thought to be mediated by DHA and by neuroprotectin D1 (NPD1), a metabolite formed from DHA. NPD1 evidently possesses potent anti-inflammatory and anti-apoptotic properties and provides protection from inflammatory changes and premature neuronal cell death – processes which play a decisive role in neurodegenerative diseases such as Alzheimer's disease.

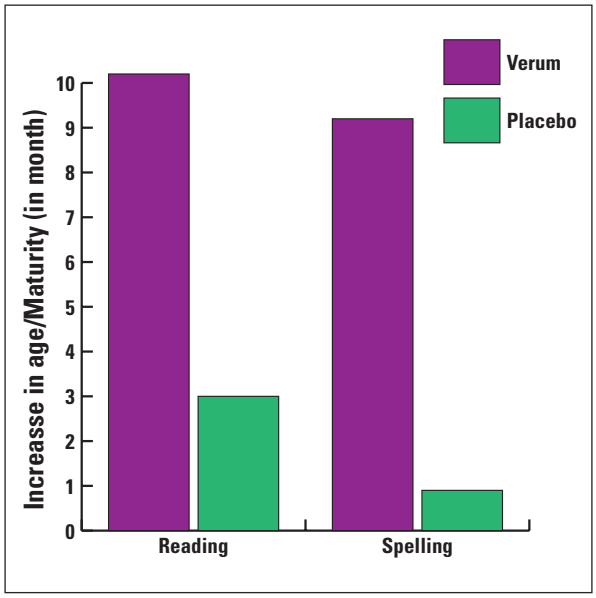
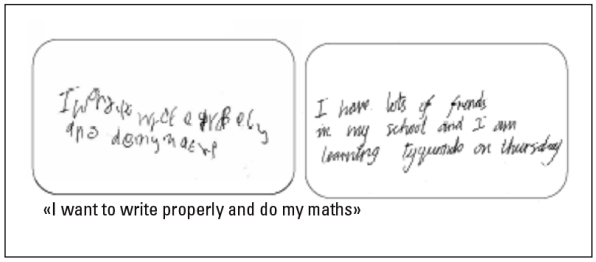


Figure 1: Significant improvements in reading (9.5 vs. 3.3) and writing ability (6.6 vs. 1.2) in comparison with placebo ($p < 0.004$ and $p < 0.001$) after administration of supplement (Equazen®) for three months (1)



«I want to write properly and do my maths»

Figure 2: Comparison of writing before (left) and after (right) six months of supplement treatment (1)

n-3 PUFA supplements – efficient and active in children with ADS/ADHS syndrome

One of the issues discussed in the last lecture was whether food supplements containing omega-3 fatty acids of unspecified composition were as active for the brain as PUFA supplements of specific composition. Dr. Madeleine Portwood is a British scientist and Senior Educational school Psychologist, Durham County Council. She gave an interesting lecture on the influence and effects of long chain PUFAs on the behaviour of children with developmental disorders (dyspraxia),

characterised by restrictions in motor functions. This affects about 5% of school age children and is tending to increase. This is frequently accompanied by learning difficulties, abnormal behaviour and psychosocial disorders, which may extend to the early adolescence. Observation over several years of the normal school day in County Durham led to the insight that these difficulties are often accompanied by the development of neurological and psychological disorders, such as dyslexia, autism, attention deficit and hyperactivity (ADS/ADHS). There is now increasing evidence that the affected children suffer from nutritional deficiency of long chain PUFAs. There is increasing evidence from supplementation studies that this hypothesis is correct. Administration of a specific combination of the n-3 PUFAs EPA and DHA and the n-6 fatty acid gamma-linoleic acid (evening primrose oil) was found to be particularly effective. It was also shown that EPA is more important than DHA in the treatment of this symptom complex; the efficacy was demonstrated for an EPA to DHA ratio of 3:1. As an example, Dr. Portwood presented the Oxford-Durham study. This was the first randomised placebo-controlled double blind study and included 117 children, aged from 5 to 12 years and with developmental coordination disorders, school problems and behavioural disorders (1). The active treatment group were given 3 x 2 capsules of a food supplement daily for three months. The supplement consisted of 80% fish oil (EPA: 558 mg, DHA: 174 mg), 20% evening primrose oil, as well as vitamin E (Equazen®). This was followed by a one way crossover from placebo to active treatment for a further three months. The study found clear and significant improvements in reading and writing ability in comparison to placebo, as well as in the behavioural disorders typical of ADHS. The children initially treated with placebo for 3 months caught up after switch to active treatment and showed similar improvements compared to the group given active treatment in the first half of the study. Portwood has also performed an open label study with 12- to 15-year old secondary school children with mild to severe ADS/ADHS symptoms (Greenfield study [2]). This study found that the administration of that fish oil supplement caused significant improvements in all behavioural abnormalities typical of ADHS after only three months. The behaviour of small children with developmental problems could also be clearly improved by the administration of this fish oil supplement, as shown by the Sure Start study. This study included 65 infants aged between 18 and 30 months, of whom 80% exhibited developmental delays in their abilities to speak, communicate or concentrate. After five months of treatment with the food supplement, 79% of these children exhibited good or very good ability to concentrate. Their ability to communicate and speak improved, as did their social behaviour. According to Portwood, «Some of the children had a vocabulary of only 25 words before starting the study. After five months, they were capable of constructing complete sentences.» To investigate whether the administration of the fish oil supplement is advantageous for all children, a study is currently being performed with healthy children without developmental or concentration problems (Middlesbrough study). This study has been completed and is now being prepared for publication.

On the basis of epidemiological data and the available study results, it may be concluded that some children and young adults suffer from deficient supply with essential fatty acids, leading to abnormal behaviour and learning and concentration disorders, which can thus harm the child's self-esteem. Portwood concluded that it is important that parents, teachers, school psychologists and doctors should be aware how important it is that children should be regularly supplied with appropriate levels of n-3 PUFAs, as this guarantees long-term healthy development.

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Source:
«Fish for the Brain: Essential Fatty Acids and Their Significance for the CNS»; Vifor Satellite Symposium during the Trinational Meeting on Nutrition 2009 of the AKE, DGEM and GESKES in Zurich, 4 June 2009; based on the lectures given by Prof. Berthold Koletzko, Munich («EPA and DHA in the Development of the Brain and Recommendations for Supply»), Prof. Anne Eckert, Basle («PUFA and Metabolites: Implications for the Adult and Aging Brain»), Dr. Madeleine Portwood, Durham, UK («The role of EFAs in children's behaviour and learning»).

Literature:
1. Richardson AJ, Montgomery P: The Oxford Durham study: a randomized controlled trial of dietary supplementation with fatty acids in children with developmental coordination disorder. Pediatrics. 2005; 115 (5): 1360–1366.
2. Portwood M.M.: The role of dietary fatty acids in children's behaviour and learning. Nutrition and Health 2006; 18: 219–232.

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