Topics: Omega-3 fatty acids, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), long chain polyunsaturated fatty acids (LC-PUFAs), arachidonic acid (AA), attention deficit hyperactivity disorder (ADHD), learning disorders, red blood cell (RBC)

Objective: To investigate the effects of selective supplementation with EPA and DHA versus the omega-6 PUFA linoleic acid on behaviour, cognition and literacy in children with ADHD, to determine if those with lower omega-3 status were the greatest responders and to correlate changes in PUFA status with changes in behaviour and literacy/cognition.

Background: Intervention trials with omega-3 PUFAs in ADHD patients have had varying success perhaps due to methodological differences including the combination of fatty acids supplied and the subject choice. To date, the effects of EPA and DHA separately have not been compared within a single randomised, controlled, intervention trial and only a couple of studies included blood fatty acid status as biomarkers to substantiate cause and effects.

Method: This randomised, three way cross-over, triple-blind (study investigators, children and parents), placebo-controlled trial included 90 children aged 7-12 years old diagnosed with ADHD or with parent-rated symptoms >90th percentile on the Conners Parent Rating Scale (CPRS) and had parent reported learning difficulties where literacy performance was behind their level in school. Those excluded were taking any ADHD medication or had consumed omega-3 fatty acid supplements during the previous 3 months. Supplementation included 4 X 500 mg capsules per day for 4 months of either EPA-rich fish oil (1109 mg EPA & 108 mg DHA), or a DHA-rich fish oil (1032 mg DHA & 264 mg EPA) or safflower oil (1467 mg of linoleic acid as a control. The following assessments were completed:

1) RBC fatty acid profiles before and after treatment

Primary Outcomes

2) **Literacy** using the word reading and spelling subtest from the Wechsler Individual Achievement Test (WIAT-III)
3) **Vocabulary performance** using the Wechsler Intelligence Scale for Children
4) **Parent Rated ADHD Symptoms** using the long version of the CPRS.

Secondary Outcomes

5) **Various forms of attention** using the abbreviated test battery from the Test of Everyday Attention for Children
   - **Focused attention** using the Sky Search
   - **Sustained attention** using Score !
   - **Ability to switch and control attention** using Creature Counting
   - **Divided attention** by combining Sky Search and the Score! Tasks.
6) **Inhibition or ability to hold back a response** using a computerized Go/No-go task

Findings: There were no significant differences between the supplement groups in the primary outcomes after 4 mo. However, the RBC fatty acid profiles indicated that an increased proportion of DHA was associated with improved word reading (r = 0.394) and lower parent ratings of oppositional behavior (r = 0.392). These effects were more evident in a subgroup of 17 children with learning difficulties: an increased RBC DHA was associated with improved word reading (r = 0.683), improved spelling (r = 0.556), and improved ability to divide attention (r = 0.676), and lower parent ratings of oppositional behavior (r = 0.777), hyperactivity (r = 0.702), restlessness (r = 0.705), and overall ADHD symptoms (r = 0.665).

Conclusion: Increases in DHA status may improve literacy and behaviour in children with ADHD with the greatest benefits in children having comorbid learning difficulties.

Relevance to Efalex, Efalex Concentrate

Reference:
Milte CM, Sinn N, Buckley JD, Coates AM, Young RM, Howe PR. Eicosapentaenoic and docosahexaenoic acids, cognition and behavior in children with attention-deficit/hyperactivity disorder: A randomized controlled trial. Nutrition 2012 Apr 25. [Epub ahead of print].

PRESS RELEASE

New study confirms that DHA supplementation improves literacy and behaviour in children with ADHD[1].

The first study to investigate the separate effects of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in children with attention deficit disorder (ADHD) has shown that DHA works better and that there may be a subgroup of children may derive more benefit than others.

The study, completed at the Nutritional Physiology Research Centre, University of South Australia included 90 children aged 7-12 years old who were either diagnosed with ADHD or were reported by the parents to have ADHD symptoms and learning difficulties. The children were randomly allocated to take 4 X 500 mg capsules per day for 4 months of either EPA-rich fish oil (1109 mg EPA & 108 mg DHA), or a DHA-rich fish oil (1032 mg DHA & 264 mg EPA) or safflower oil (1467 mg of linoleic acid as a control. Blood samples to determine the red blood cell (RBC) fatty acid content and cognitive assessments to evaluate various forms of behaviour including attention and inhibition as well as learning skills including reading, spelling and vocabulary were completed on each child. Their RBC fatty acid profiles indicated that an increased proportion of DHA was associated with improved word reading and lower parent ratings of oppositional behavior. These effects were more evident in a subgroup of 17 children with learning difficulties: an increased RBC DHA was associated with improved word reading, improved spelling, and improved ability to divide attention, and lower parent ratings of oppositional behavior, hyperactivity, restlessness, and overall ADHD symptoms.

Results of this study help to explain results of a collaborative study between the University of Montreal and McGill University in Canada where a subgroup of 8 patients had significantly greater clinical improvements after omega-3 treatment.[2] It was the first study to report a variety of statistically significant associations implying that certain fatty acid levels correlate with specific behavioural responses. Similarly, four clinical studies reported at the 8th Meeting of the International Society for the Study of Fatty Acids & Lipids (ISSFAL 2008) in Kansas City, USA, in May 2008 also showed there may be a subcategory of people who respond more favorably to supplementation and that particular fatty acids may be required depending on the nature of the symptoms. Two of those studies assessed the effectiveness of an high EPA supplement to reduce ADHD symptoms in children and adolescents[3,4]. One study including only adolescents with high ADHD index scores and who met the ADHD criteria measured no improvement[3] while the other study including children and adolescents with ADHD and its diagnostic subtypes and comorbid conditions reported clinically meaningful improvements[4]. However, these improvements were most notable in a subgroup of patients having inattention, reading/writing difficulties, learning disorders, developmental coordination disorder and autism spectrum conditions. The first study, which reported no improvements however, reported relatively little change in blood DHA levels as a result of taking the high EPA supplement, a mixture of high eicosapentaenoic acid (EPA) fish oil and evening primrose oil. A third study supplementing ADHD diagnosed children with 0.5 g/day of EPA measured improvements only in a subgroup of children having initial low serum EPA status combined with oppositional behaviour and little hyperactive/impulsive behaviour[4]. A fourth pilot study correlated various blood fatty acid levels with responses to emotional (happy, fear, sadness) stimuli in boys with ADHD[6].

During the last two decades, many intervention trials have confirmed that fatty acid supplements such as Efalex, which are aimed at correcting deficiencies can reduced anxiety, attention difficulties and behaviour problems in dyslexics with symptoms of ADHD[7], can improve attention and behaviour[8] and reading, spelling and behaviour[9] in children with ADHD and can improve reading ability and word-brain-hand co-ordination in dyslexics[10]. Results of this latest well designed study are important because they confirm evidence from less rigorous studies showing that specific omega-3 fatty acids provide different benefits to sub-groups of people with learning disorders and that DHA is overall more effective that EPA in at least the majority of cases.

References:

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