# Fatty Acids in the Management of ADHD

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Attention-deficit hyperactivity disorder (ADHD) is a debilitating behavioural disorder affecting school work, family relationships and social interactions with peers. Although the causes are multi-faceted and can, in part, be inherited there is an abundance of studies indicating that omega-3 fatty acids, especially eicosapentaenoic acid, may have a role to play in the management of ADHD. This article will review evidence from key studies in this area.

## Introduction

ADHD is a common behavioural disorder, affecting eight to 12 per cent children worldwide.[1] Common symptoms are shown in **Table One** but the condition is typically characterised by short attention spans, impulsivity and hyperactivity, with at least half of children with ADHD retaining some of these symptoms in adulthood.[1]

### Table One: Common Problems Associated with ADHD in Children

| |
|---|
| Aggression |
| Clumsiness |
| Immature language |
| Literacy problems |
| Mood swings |
| Non-compliant behaviour |
| Sleep disturbances |
| Temper tantrums |
| Unpopularity with peers |

Source: Adapted from NICE (2009)

The causes are multi-faceted and involve complex interplay between genetic and environmental factors.[2] One recent case-control study found that children with ADHD were more likely to have small segments of their DNA duplicated or missing than other children, suggesting a genetic aetiology.[3] Other work suggests that dietary factors, including the long-chain polyunsaturated fatty acids (PUFAs) omega-6 (n-6) and omega-3 (n-3), play a central role in normal functioning of the brain and central nervous system.[4] In particular, the n-6 fatty acid arachidonic acid (AA) and the n-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), can alter neuronal processes, with effects ranging from changes in membrane fluidity to gene expression.[4] Long-chain n-3 fatty acids are also known to have anti-inflammatory properties, and their ability to alter cell membrane fluidity and phospholipid composition can modulate serotonin and dopamine secretion; effects which may explain their role in improving mood disorders.[5]

In terms of prevalence, self-reported data from the UK Millennium Cohort Study suggest that around 1.4 per cent of children (mean age 7.2 years) have ADHD.[6]

A number of studies have also shown that children and teens with lower levels of plasma and blood PUFAs, especially n-3 PUFAs, are more likely to exhibit behavioural problems and symptoms of ADHD.[7] For example, a case-control study found that while children with ADHD consumed similar amounts and types of fatty acids to controls, they had lower blood levels of total n-3 fatty acids and DHA, indicating that children with ADHD may have differences in their fatty acid metabolism.[8] This article will look at the latest evidence evaluating the role of fatty acids in the management of ADHD. Particular focus will be given to the role(s) of n-3 fatty acids in relation to their biological effects on ADHD symptoms.

## Intervention studies

A PubMed search identified 11 randomised controlled trials (RCTs) published over the last 10 years investigating the effects of fatty acid supplementation on symptoms of ADHD (see **Table Two**). Of these, most assessed changes in ADHD using different combinations of reading, drawing, spelling, memory and behaviour tests, typically evaluated by teachers, parents or psychiatrists. Other studies measured plasma and blood levels of fatty acids biomarkers, correlating these with cognitive or behaviour tests/scores. It should, however, be noted that the methods used to assess changes in ADHD vary broadly between studies limiting the comparison of results.

The Oxford-Durham Study was one of the first studies to identify links between fatty acid supplementation and behaviour, reading and spelling performance.[9] Children aged five to 12 years (n=117) were randomised to take a supplement providing 558mg EPA, 174mg DHA and 60mg gamma-linoleic acid (GLA) daily, with vitamin E to protect the fatty acids from oxidation, or an olive oil placebo. After three months, the placebo group switched to the active treatment. The results showed that the n3/n6 fatty acid supplement significantly improved reading and spelling age, suggesting that this could be an effective treatment for children experiencing educational and behavioural problems.[10]

Since then, several other studies have been published. In one of the largest studies, 409 children were randomised to take an n-3/n-6 supplement (as described above) or a placebo containing palm oil.[11] While benefits were not seen for reading and spelling, drawing skills significantly improved in the n-3 intervention compared with the placebo group (P=0.029), especially amongst indigenous seven to 12 year olds (P=0.008). In this study, it was also reported that around 35 per cent of children never consumed fish or ate it once a week or less, indicating that natural dietary sources of n-3 PUFAs are in short supply.[11]

Other studies have used either single doses or different combinations of fatty acids. For example, Gustafsson *et al.* (2010) found that children with low EPA levels at baseline were more likely to respond to EPA treatment.[12] EPA (500mg taken daily) was also found to improve Conner's Teacher Rating Scores for inattention (P=0.04).[12] Similarly, in another study, children with ADHD showing signs of inattention were more likely to respond to n-3/n-6 supplements containing high EPA levels.[13]

Recently, Johnson *et al.* (2012) found that n-3/n-6 supplements significantly improved blood levels of n-3 fatty acids in children classified as responders (defined as having a ≥25% reduction in ADHD symptoms).[14] Similarly, a smaller pilot study of nine children with ADHD found that ingestion of a high-dose liquid supplement providing 10.8g EPA and 5.4g DHA also significantly improved plasma phospholipid levels of EPA and DHA (P<0.01) and markers of behaviour, as assessed by a qualified psychiatrist.[15] Another study found that EPA and DHA supplementation helped to reduce the severity of tics in children with autism,[16] although these findings need to be replicated.

On the whole, studies suggest that fatty acid supplementation may offer some behavioural and educational benefits for children with ADHD. Findings are generally more consistent in children that have been diagnosed with ADHD, who are underachieving or have other learning difficulties.[17] Equally, it should be considered that longer and larger studies tend to produce stronger findings, with some evidence that a high EPA content offers particular benefits for managing ADHD symptoms.

## Meta-analyses

Several meta-analyses and systematic reviews have investigated the potential roles of PUFAs on patterns of behaviour and ADHD symptoms. Most recently, Bloch and Qawasmi (2011) reviewed evidence from 10 trials comprised of 699 children, finding that n-3 supplements had a small significant effect on improving ADHD symptoms, with marginally more positive effects seen for EPA.[5]

### Table Two: Randomised Controlled Trials of Fatty Acids in ADHD Management

| Reference | Subjects | Study details | Outcomes |
|---|---|---|---|
| Milte *et al.* (2012)[17] | 90 children with ADHD symptoms, 7-12 years, Australia. | RCT. 4 months randomised to take: 1) Fish oil providing 1109mg EPA + 108mg DHA, 2) fish oil providing 264mg EPA + 1032mg DHA or 3) safflower oil providing 1467mg LA (control). | No significant differences in cognition, literacy or behaviour between groups. ↑ DHA erythrocyte levels linked to improved reading and behaviour, particularly in children with learning difficulties. |
| Richardson *et al.* (2012)[21] | 79 healthy children under-performing in reading, aged 7-9 years, Oxford. | DB RCT. 16 weeks taking 600 mg/day DHA (from algal oil), or corn/soybean oil (control). | DHA associated with reading score improvements in children whose initial reading performance was ≤20th centile (P=0.04) |
| Johnson *et al.* (2009)[13] | 75 children and teens, 8-18 years, Sweden. | RCS. 3 months randomised to: 1) 558mg EPA, 174mg DHA, 60mg GLA & 10.8mg vitamin E (Equazen eye q) or 2) olive oil (control) followed by placebo group being switched to active supplement. | Children with ADHD inattention subtype more likely to respond to n-3/6 fatty acid supplementation than those with combined symptoms of ADHD (P<0.03). |
| Johnson *et al.* (2012)[14] | As above | As above | After 6 months responders[1] had higher n-3 blood fatty acid levels and a reduced ratio of n-6/n-3 (P<0.05). |
| Gabbay *et al.* (2012)[16] | 33 children and teens, 6-18 years, New York. | RCT. 20 weeks taking combined EPA +DHA or olive oil (control). | Yale Global Tic Severity Scale Scores were significantly lower in the omega-3 vs. the placebo treated group (P=0.04). |
| Gustafsson *et al.* (2010)[12] | 92 children with ADHD, 7-12 years, Sweden. | RCT. 15 weeks randomised to take 0.5g EPA or control. | Children with lower EPA concentrations (P=0.02) were more likely to respond to EPA treatment. |
| Belanger *et al.* (2009)[24] | 26 children with ADHD, 11 months-6 years, Canada. | RCS. 16 weeks randomised to receive 20-25mg/kg/day of EPA & 8.5-10.5mg/kg/day DHA or n-6 PUFA (control) with the reverse being allocated after crossover. | Supplementation with n-3 PUFA resulted in significant ↑ EPA and DHA. Improved symptoms recorded by parents. |
| Raz *et al.* (2009)[26] | 73 children with AD/ADHD aged 7-13 years, Israel. | RCT. 7-weeks supplementation with 480 mg of LA and 120 mg of alpha-LA or 1000mg vitamin C (control). | Both treatments ameliorated symptoms, but no significant differences found between groups. |
| Sorgi *et al.* (2007)[15] | 9 children, with ADHD, 8-16 years, USA. | Pilot study, 8-weeks, open-label. Participants given 10.8g EPA + 5.4 g DHA daily for 4 weeks. Dose then adjusted for the remaining 4 weeks based on AA:EPA ratio. | Plasma phospholipid levels of EPA and DHA significantly ↑ by the end of the study (P<0.01). Significant improvements in behaviour. |
| Richardson *et al.* (2005)[10] | 117 children with DCD, 5-12 years, Oxford. | DB RCT. Treatment in parallel groups for 3 months, followed by 1-way crossover for 3 months. Active treatment was supplement containing 558mg EPA + 174mg DHA, 60mg GLA & 9.6mg vitamin E (Equazen eye q) vs. olive oil (control). | Significant improvements in reading age (P<0.004) and spelling age (P<0.001). |

**Key:** AA, arachidonic acid; AD, attention deficit; ADHD, attention-deficit hyperactivity disorder; DB, double-blind; DCD, developmental coordination disorder; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; GLA, gamma linolenic acid; LA, linolenic acid; RCS; randomised crossover study; RCT, randomised controlled trial.
**Note:** [1] responders had a reduction of more than 25% in ADHD symptoms.

Another systematic review comprised of 13 supplement trials (n=1011 children and teenagers), all lasting between four and 16 weeks found that n-3/n-6 PUFA supplements were statistically significantly more likely to improve ADHD symptoms when results were compared with placebo supplements (relative risk 2.19, 95% confidence interval 1.04-4.62). However, findings from studies using parent/teacher rankings of ADHD symptoms, in relation to supplement use were less consistent,[18] possibly because this method is somewhat subjective.

Finally, a systematic review of studies carried out prior to April 2007 concluded that n-3 PUFAs may have small benefits over placebo supplements in ADHD and related disorders and appear to be well tolerated by children. It was also stated that the benefits of n-3 PUFAs appeared greater when used in a classroom setting, rather than at home,[19] which may be due to improved compliance with supplements.

## Discussion

ADHD is a heterogenous disorder with several different sub-types resulting from various different combinations of risk factors acting together.[2] While there appears to be a genetic aetiology, dietary factors such as fatty acids do seem to have a key role in helping to improve ADHD symptoms. This is perhaps unsurprising given that n-3 PUFAs, including EPA and DHA, are known to modulate brain chemistry and are major components of neuronal membranes.[20]

As we have seen from studies discussed in this review and meta-analytical evidence,[5] combinations of long chain n-3 and n-6 PUFA, such as EPA, DHA and GLA, may be of benefit for ADHD symptoms[22] with higher doses of EPA appearing to be the most effective.[5] EPA dosages equivalent to 558mg daily have led to improvements in cognitive development,[11] attention,[12,14] reading and spelling age.[10] In contrast, a study using supplements that provided 600mg DHA daily, but no EPA, found some improvements in children's reading skills, but only in those who had lower scores at baseline.[21]

Of the studies evaluated, findings from open-label studies have tended to produce more consistent results than double-blind RCTs, perhaps because similar supplements have been used. Larger studies of three to four months duration have also provided consistent findings, while children of lower socioeconomic status and those with symptoms of ADHD and/or learning disabilities seem to benefit most from fatty acid supplementation programmes.[22] A cross-sectional study using data from the American Third National Health and Nutrition Examination study found that girls, in particular, benefited from increasing intakes of n-3 PUFAs due to higher levels of body fat stored during childhood.[23]

Considering the wider context, while children with ADHD are typically offered conventional treatments such as psychostimulants, parents often wish to consider non-drug therapies for the management of their children's ADHD symptoms.[24] Fatty acid supplementation programmes could provide a solution, when delivered in the appropriate n-3/n-6 combination and dose and over suitable periods of time. Future work is now needed to consider whether these work best when given alone, or in combination with conventional treatments.

## Conclusions

**ADHD is a chronic condition affecting educational performance and social interactions. A review of the latest scientific evidence indicates that fatty acids may have a key role to play in managing the condition by impacting positively on cognition, behaviour and learning. While oily fish is the best natural source of n3 PUFAs, many children do not eat it and fish oil supplements are a useful alternative. In particular, those high in EPA (around 560mg) balanced with DHA and GLA may be effective for ADHD symptoms if taken for at least three to four months.[5, 25]**

## Key Points

- Omega-3 and omega-6 PUFAs are central to brain function but levels of DHA and EPA are often low in Western diets.
- Randomised controlled trials show that daily supplementation with combinations of EPA, DHA and GLA over 3-4 months may help in the management of ADHD, improving levels of attention, as well as possibly benefiting school performance.
- Of these fatty acids, evidence suggests greater efficacy for higher levels of EPA (up to 558mg taken daily from supplement sources).
- EPA and DHA supplementation programmes are generally well tolerated by children.
- Further work is needed to determine whether fatty acid supplements should be given alone, or in combination with conventional treatments.

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