Could food supplements help children with common learning difficulties?

Early results from a study in which supplements of n-3 and n-6 fatty acids were given to schoolchildren with learning difficulties in County Durham were reported in many newspapers last week. What advice should pharmacists give? Pamela Mason puts the Durham study into context and summarises evidence from other research conducted so far.

EARLIER this year 120 primary schoolchildren with various types of learning difficulty were entered into a six-month trial to see whether supplements of fish oil (a source of n-3 fatty acids) and evening primrose oil (a source of n-6 fatty acids) could improve their concentration and learning ability. The children taking part in the study are aged 6 to 11 years and have various neurodevelopmental disorders such as dyspraxia, dyslexia, attention-deficit hyperactivity disorder (ADHD) and autistic spectrum disorder (see Panel, bottom p714). The study is taking place in 13 schools in County Durham.

This research is based on the idea that deficiency and/or abnormal metabolism of essential fatty acids could be a contributory factor in the development of serious learning difficulties and that supplements could therefore help.

This idea is not new. Deficiency of essential fatty acids (EFAs) in hyperactivity was first suggested over 20 years ago when a survey of hyperactive children conducted by the Hyperactive Children's Support Group (HCSG) in the UK found signs of possible EFA deficiency, including excessive thirst, frequent urination and dry skin and hair. This survey also found links between hyperactivity and eczema, asthma and other conditions with an allergic component. However, the researchers found no evidence of a dietary deficiency of the parent EFAs (see Panel, top p714) and suggested that the problem might lie with the conversion of these compounds to their longer chain derivatives. As a result of this hypothesis, they recommended supplementation with these long-chain compounds, and anecdotal evidence suggests that this was helpful in at least some cases.

ADHD AND FATTY ACIDS

Studies carried out in 1995 and 1996 at Purdue University in the US provided further confirmation that children with ADHD were more likely to exhibit signs of EFA deficiency. Moreover, these children had reduced concentrations of certain long-chain fatty acids in the blood, including arachidonic acid (AA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) despite adequate dietary intakes of the EFA precursors (linoleic acid and alpha-linolenic acid). The researchers suggested that this could be due either to a difficulty in converting the parent EFAs or to excessive breakdown of the long chain derivatives.

The Durham study is led by Dr Madeleine Portwood (senior educational psychologist at Durham County Council) in collaboration with Dr Alexandra Richardson (senior research fellow in neuroscience, Imperial College School of Medicine, MRI Unit, Hammersmith Hospital, London and University of Oxford). During the first three months of the trial, which is now complete, the children were divided into two groups and given either a supplement or placebo. During the second three months of the trial, which will be completed by the end of July, all the children are being given the supplement.

The supplement being used in the trial (eye q made by Equazen) provides 558mg of eicosapentaenoic acid (EPA), 174mg docosahexaenoic acid (DHA), 60mg gamma-linolenic acid (GLA) and 9.6mg vitamin E in a daily dose of six capsules. The placebo being used contains olive oil.

The rationale for the choice and concentration of ingredients in the supplement, particularly the relatively high ratio of EPA to DHA, which is 4:1, comes from results of previous trials with fatty acids in children with hyperactivity disorders, some of which suggest that EPA may be more effective than DPA. Indeed, a recent US intervention trial in 63 children with ADHD showed that a supplement of pure DHA had no effect. The reason for including GLA (an n-6 fatty acid) in the supplement is that fatty acids of both the n-3 and n-6 series have an important role in brain function. However, there is some evidence that n-3 fatty acids may be more beneficial than n-6 fatty acids in these conditions in that early studies with evening primrose oil (an n-6 fatty acid) alone showed hardly any benefit.

Some of the children taking part in the Durham trial have, over the first three-month period, shown improvements in measures such as reading skills and ability to concentrate. However, Dr Portwood emphasises that the study is blinded and not yet complete, so the researchers do not know which children took the supplements and which ones the placebo. Naturally, she hopes that it is the children who took the supplement who experienced benefit, but until the trial is complete she does not know that this is the case.

MISLEADING REPORTS

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Some of the reports in the media last week, which indicated that this particular study had shown that supplements could help children with learning difficulties, were therefore misleading. However, this does not mean that this study should be dismissed, but that we should wait until it is completed and the results fully analysed.

In any case, this is not the first study giving fatty acid supplements to children with learning difficulties. The team from Purdue University in the US (see above) conducted a double-blind, placebo-controlled intervention trial in children with clinically diagnosed ADHD — who also exhibited symptoms of EFA deficiency. An early report of this work indicated that supplementation with EPA, DHA, AA and gamma-linolenic acid (GLA) was associated with some reduction ADHD symptoms.

Earlier this year, Dr Richardson published the results of a study of her own in which 41 dyslexic children with above average ADHD ratings were given a fatty acid supplement (supplying EPA, DHA, GLA and some AA) or a placebo for 12 weeks. Compared with the placebo group, the group treated with fatty acids showed significant reductions in cognitive and behaviour problems. However, Dr Richardson emphasises that the numbers of children in the study are small and that her results need to be confirmed by larger double-blind trials. The Durham trial will provide further information, and she does have other studies nearing completion.

The results of the Durham trial will be available by the end of September, and given the difficulties of managing severe learning difficulties, a positive outcome would be welcome because the possibility of treating sufferers with a nutritional supplement is attractive. However, even if the study does show positive results, Dr Portwood points out that not all children with learning disorders will likely benefit from supplementation. This is because these conditions are multifactorial and fatty acid abnormalities are almost certainly not the only cause.

Supplementation is most likely to help if there is already some evidence of fatty acid deficiency, she says. However, objective biochemical measures of fatty acid status are not a practical option and further research is required to identify and validate some easier methods that might be suitable for routine clinical use. To this end, Dr Portwood is also having the children's breath analysed for a range of volatile substances. Breath ethane is symptomatic of metabolic disorder, she says, and it may be possible to identify a par-

Metabolism of n-3 and n-6 polyunsaturated fatty acids

There are two essential fatty acids (EFAs), which cannot be synthesised by the body and must be provided by the diet. These are alpha-linolenic acid (ALA) of the n-3 series and linoleic acid (LA) of the n-6 series. Both are converted via enzymatic desaturation and chain elongation to longer chain polyunsaturated fatty acids (PUFAs). ALA is converted to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) while LA is converted to gamma-linolenic acid (GLA), arachidonic acid (AA) and other derivatives.

n-3 family	n-6 family
18:3 n-3 **Alpha-linolenic acid (ALA)**	**18:2 n-6** **Linoleic acid (LA)**
18:4 n-3	**18:3 n-6** **Gamma-linolenic acid (GLA)**
20:4 n-3	**20:3 n-6** **Dihomogammalinolenic acid (DGLA)**
20:5 n-3 **Eicosapentaenoic acid (EPA)**	**20:4 n-6** **Arachidonic acid (AA)**
22:5 n-3	**22:4 n-6**
22:6 n-3 **Docosahexaenoic acid (DHA)**	**22:5 n-6**

ticular breath profile in these children that is indicative of fatty acid deficiency.

PHARMACISTS' ADVICE

In conclusion, there is still much work to be done to verify the value of fatty acid supplements in dyspraxia, dyslexia and ADHD. In the meantime, what advice should pharmacists give? Dr Portwood suggests that parents and carers who want to give supplements can be advised to do so. Fatty acid supplements with doses similar to those used in the study are not harmful, and the worst that can happen is that the child's symptoms remain the same. Symptoms could improve, she says, although parents should not be given false hope.

Dyspraxia, dyslexia and attention deficit hyperactivity disorder (ADHD)

Dyspraxia, dyslexia and attention deficit hyperactivity disorder (ADHD) are developmental disorders of learning and behaviour. They affect children but usually persist into adulthood, and current estimates suggest that up to 20 per cent of the population may be affected to some degree by one or more of these conditions.

There is considerable overlap between these disorders, but sufferers of dyspraxia typically have poor motor co-ordination, which shows itself in clumsiness and difficulties in catching a ball, fastening buttons, tying shoelaces or balancing. These children have problems in planning and carrying out complex, sequenced actions and may also have difficulties with reading and writing as well as mood and behaviour problems such as impulsiveness, temper tantrums and a preference for repetitive or familiar activities.

The defining features of dyslexia are problems in learning to read and write, but problems with arithmetic and musical notation are not uncommon. Children with ADHD have problems paying attention, listening to instructions and completing tasks. In addition, they are excessively restless and may be disorganised, have poor self-discipline and low self-esteem.

Current management of these conditions varies depending on the presentation, but may include behavioural and educational interventions.

Medication (eg, dexamfetamine and methylphenidate) may also be used as part of the treatment programme but should be initiated only by specialists in these conditions. Drug treatment is quite effective but is associated with side effects. Methylphenidate may lead to growth retardation and dexamfetamine to increased irritability, restlessness and insomnia.