The potential role of fatty acids in developmental dyspraxia – can dietary supplementation help?

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Summary

1. Dyspraxia or developmental coordination disorder (DCD) shows substantial overlap with other developmental and psychiatric conditions both within individuals and within families – notably dyslexia, ADHD and autistic spectrum disorders, but also mood disorders and schizophrenia spectrum disorders. This indicates some common predisposing factors at the biological level. The proposal considered here is that these could involve aspects of fatty acid metabolism.

2. Certain HUFA of the omega-3 and omega-6 series are essential for normal brain development and function. Together they should make up around 20% of the dry mass of the brain, and adequate supplies are also crucial for efficient information processing within the brain and nervous system, as well as for many aspects of general health.

3. These key HUFA are often lacking from modern diets and must therefore be manufactured within the body from simpler essential fatty acids (EFA). However, this process is inefficient in humans, and can also be blocked by dietary and lifestyle factors. Furthermore, dietary intake of the necessary omega-3 EFA in particular is often low.

4. The predisposition to dyspraxia and related conditions may involve mild constitutional inefficiencies of fatty acid metabolism that increase the usual dietary requirements for HUFA. These could include (a) poor EFA-HUFA conversion, (b) difficulties in incorporating HUFA into brain cell membranes and/or (c) unusually high rates of HUFA breakdown and loss, although there are other possible mechanisms.

5. Many features associated with dyspraxia are consistent with HUFA deficiencies or imbalances. These include the core difficulties with motor coordination, attention and sensory processing, as well as the excess of males affected, proneness to allergic or autoimmune conditions, disturbances in temperature regulation and sleep, and irregularities of mood.

6. There is already some experimental evidence for fatty acid abnormalities in ADHD, dyslexia and the autistic spectrum. Although dyspraxia has never been 'factored out' in studies of these related conditions, no studies of dyspraxia per se have yet been reported although these are now underway.

7. If fatty acid deficiencies were a contributory factor in these developmental conditions then dietary supplementation with HUFA might be of benefit. In ADHD, a few controlled treatment studies have been reported, with mixed results; and in dyslexia, the first controlled trial has shown that treatment with omega-3 and omega-6 HUFA can reduce attentional problems, anxiety, and disruptive behaviour.

8. In dyspraxia, no properly controlled trials of HUFA supplementation have yet been reported. One small open study indicated possible benefits, but without a placebo control group these cannot be attributed to the treatment itself. A large-scale randomised controlled trial of HUFA treatment in dyspraxic children is now underway.

9. As yet there is therefore no firm evidence of benefits from HUFA supplementation in dyspraxia, although many people are already trying this approach. HUFA are generally safe and have many general health benefits, but medical advice is recommended before taking any food supplement. Furthermore, fatty acid supplements vary widely in their composition and quality. Available evidence indicates that omega-3 fatty acids – and particularly EPA – may be most effective, but this still requires confirmation.

10. Other aspects of diet may also merit attention, but nutritional intervention is obviously only one aspect to consider in the management of dyspraxia, and cannot be expected to benefit more a subset of affected individuals. Some features that may indicate a good response to HUFA supplementation have already been identified, but further research is needed to verify their predictive power.

Introduction

Dyspraxia or developmental co-ordination disorder (DCD)[1] remains one of the least studied of a range of common and interrelated developmental disorders of childhood. Conditions showing substantial overlap include dyslexia, attention-deficit / hyperactivity disorder (ADHD) and autistic spectrum disorders (ASD). Dyslexia refers to specific difficulties in the acquisition of written language skills, but these are part of a developmental syndrome involving a much broader range of features (Miles, 1994). The ADHD diagnosis involves hyperactive and impulsive behaviours, attentional difficulties, or both; but controversy still surrounds this diagnosis and its treatment (NIH Consensus Statement 1998). In autistic spectrum disorders, the central features are specific difficulties in social interaction and communication and a restricted range of behaviours, but again, diagnosis is fraught with difficulties and the clinical picture includes many other features (Jones, 2000). In practice, therefore, there is substantial variability within each of these diagnostic categories, and most affected individuals show features of more than one of these conditions, i.e. 'pure' cases are the exception, not the rule.

Between them these developmental conditions affect more than 10% of the school-age population; and as they all have a dimensional aspect, milder difficulties are even more common. Although they often go unrecognised, the earlier these kinds of behavioural and learning difficulties can be identified, the better are the chances of successful management and remediation. However, because the formal diagnoses of dyspraxia, dyslexia, ADHD, and ASD all involve different sets of operational criteria, each tends to involve specialists from different professional disciplines and therefore different management approaches. Unfortunately, practitioners dealing with any one of these conditions may be unfamiliar with at least some of the others, and thus unaware of co-morbidity issues and their implications.

In none of these conditions is the possible role of nutrition considered as part of standard evaluation and management, despite its obvious and fundamental importance for optimal functioning of the brain. A whole range of micronutrients is essential in this respect, but in particular, there is mounting evidence – summarised here - that deficiencies or imbalances in certain highly unsaturated fatty acids (HUFA) of the omega-3 and omega-6 series may contribute to both the predisposition and the developmental expression of dyspraxia and related conditions (Richardson and Ross, 2000). This raises the possibility that dietary supplementation with the relevant HUFA might help in their management, but further research is needed to investigate this. Very few properly controlled treatment trials have yet been carried out, and these have involved children with a primary diagnosis of either ADHD or dyslexia, although a trial involving dyspraxic children is now in progress (Richardson and Portwood, in preparation). What evidence there is from trials of fatty acid treatment in related conditions is therefore considered here, followed by a discussion of the potential practical implications.

[1] In neuropsychology, dyspraxia refers to specific problems in the planning and execution of complex, sequenced actions - the most obvious of which involve motor co-ordination difficulties. The DCD diagnosis adopted by the DSM-IV (American Psychiatic Association, 1994) is much broader, but developmental dyspraxia has come to be used by many in a similarly general way, as it will be here for convenience.

Associations between dyspraxia and other behavioural and learning difficulties

The overlap between dyspraxia and dyslexia is between 30-50% in both directions, depending on the exact criteria and 'cut-off' points used in each diagnosis. Individuals with both conditions often show more difficulties with spelling, handwriting and written expression than they do with reading per se, and other common features include directional confusions, weaknesses in working memory and the sequential organisation of ideas, and inefficient automatisation of skills. It seems likely that dyspraxia may involve the same kinds of difficulties in rapid visual processing that have already been well-documented in dyslexia (Stein and Walsh, 1997), although this has not yet been formally investigated. Within dyslexia, poor motor coordination has also been particularly associated with attentional difficulties (Denckla et al, 1985), suggesting that the interface between dyslexia and dyspraxia also overlaps into the broad territory of ADHD. However, motor abnormalities in early development appear to be fundamental to dyslexia (Haslum,1989), as are general difficulties in the automatisation of skills; hence the cerebellum has become a focus of recent study. This brain region is crucially involved in motor control, but also plays a key role in cognition; it is especially important for the acquisition of any new skills (including language) as well as the smooth performance of previously mastered skills. Cerebellar activation in dyslexic adults was found to be dramatically lower than that of non-dyslexic adults during both acquisition of new skills and the performance of previously learned skills (Nicolson et al, 1999), and metabolic differences in cerebellar activity in dyslexia have also been reported (Rae et al, 1998). Dyspraxia has not usually been considered in studies of dyslexia, but this – as well as separate studies of dyspraxia - is clearly long overdue; and anomalies of cerebellar function seem more than likely in this condition (Nicolson, 2000).

The mutual overlap between dyspraxia and ADHD can also be as high as 50%. Population studies indicate that this combination syndrome, involving deficits in attention, motor control and perception (DAMP), may actually identify a much more homogeneous group than does the ADHD diagnosis. Furthermore, long-term follow-up studies indicate that these children – who meet criteria for both DCD and ADHD at primary school entry - have a particularly poor prognosis in terms of later achievement and social adjustment (Hellgren et al, 1994; Rasmussen and Gillberg, 2000). Within ADHD, different underlying factors probably contribute to the two dimensions of attentional difficulties and hyperactivity-impulsivity, and the former seem more fundamentally associated with dyspraxia. Such attentional problems are often associated with emotional sensitivity, mood swings and anxiety, which may be 'internalised' and thus not always obvious to others. By contrast, hyperactive and impulsive behaviour is more 'externalised' and overtly disruptive, but this can be associated either with apparent 'carelessness' and a remarkable *lack* of anxiety, or with powerful emotional frustration and a tendency to cycle between a tense, overaroused state and periods of apparent apathy and fatigue. There is mounting evidence that in many cases, apparent 'ADHD' symptoms of either variety may actually reflect an underlying mood disorder – either depression, or even bipolar (manic-depressive) traits. This issue is emphasised by Papolos and Papolos (1999) in their excellent book on bipolar disorders in children; and it has very important implications for management, because the stimulant medications typically used to control ADHD symptoms can have disastrous consequences for children with a bipolar temperament. The fact that omega-3 fatty acids have been found to stabilise mood swings in adult bipolar disorder (Stoll et al, 1999) make this an approach well worth exploring in either children or adults with an 'ADHD'/bipolar profile.

The overlap between dyspraxia and autistic spectrum disorders is also substantial, particularly for milder forms of the latter such as Asperger's syndrome. Early difficulties with feeding are common in both cases, often associated with digestive problems that may reflect food allergies or intolerances. These - together with the so-called 'leaky gut' syndrome - still remain a source of

controversy that will only be resolved by further investigation, but sensitivity to cow's milk appears to be a real issue for some individuals, and the predisposition to dyspraxia and related conditions may well involve overactive immune responses, as discussed later. Other features common to dyspraxia and the autistic spectrum include sleep problems, poor temperature regulation, physical anhedonia and/or hypersensitivity to touch, and excitability or instability of mood. These physical features are well known to both clinicians and those directly affected by these conditions, but unfortunately most research to date has largely neglected these kinds of physiological aspects, focusing rather on the behavioural or cognitive features of each condition.

In summary, diagnostic criteria for the four conditions considered here are completely different, and yet the evidence shows that boundaries between them are far from clear-cut. This is not surprising when we remember that the diagnostic labels used to classify developmental disorders simply describe patterns of behaviour. They do not provide any explanation of the *causes* of that behaviour – which are almost always multifactorial, and may differ substantially between individuals with exactly the same clinical diagnosis. When it comes to management, it therefore makes sense for practitioners to focus on treating the individual concerned, and to attempt to identify any factors that may be relevant to their particular difficulties. An excellent case study of a boy with 'dyslexia' exemplifies this approach (Baker, 1985). Biochemical investigations of this child revealed fatty acid deficiencies as well as other imbalances that were easily corrected via nutritional management, and improvements in schoolwork followed. As the author acknowledges, single case studies of this kind cannot provide definitive evidence, and this approach is likely to help only a subset of children with the 'dyslexia' label. However, it is hard to disagree with his statement that *'when the stakes are high, and the risk or cost is low, it makes sense to consider any factor that has reasonable odds of playing a role'*.

The perspective taken here is that dyspraxia, dyslexia, ADHD and autistic spectrum disorders are all highly complex developmental syndromes with a constitutional basis. As readers of this journal will already be aware, the developmental dyspraxia label itself can encompass a very broad and varied range of features. However, some of this variation undoubtedly reflects the high clinical overlap with these other developmental conditions, and the many associated features they share point to some common underlying factors at the level of biological predisposition. These could plausibly include anomalies of fatty acid metabolism, acting to increase the usual dietary requirement for certain highly unsaturated fatty acids that are essential for optimal brain development and function, but are unfortunately lacking from many modern diets.

Familial associations and genetic factors

Dyspraxia, dyslexia, ADHD and autistic spectrum disorders not only overlap within the same individuals, but also cluster within the same families, as do many of the associated physical features (such as elevated rates of non-right-handedness, and an apparent increased susceptibility to allergic or autoimmune disorders). Some psychiatric conditions also appear to be associated with these developmental ones, including depression, bipolar (manic-depressive) disorder, substance abuse, antisocial or other personality disorders and schizophrenia. It has been proposed that 'phospholipid spectrum disorders' might better describe this diverse range of interrelated conditions than do the current diagnostic labels (Peet, Glen and Horrobin, 1999), because there is now mounting evidence that abnormalities of fatty acid and phospholipid metabolism play at least some part in each case, and could perhaps help to explain some of their overlap.

In all these conditions there is a clear genetic component, but the evidence indicates several if not many different genes acting together to increase or reduce risk; and the very high prevalence of dyspraxia and related developmental conditions indicates that the predisposing genes for these are

widely distributed in the general population. No specific genes have yet been identified, but it seems likely that some will be found to play a part in more than one of these conditions.[2] A review of proposed sites of genetic linkage to this range of developmental and psychiatric conditions shows many commonalities, and many of these sites also contain genes known to be important in phospholipid and fatty acid metabolism (Bennett and Horrobin, 2000).

In discussing genetic factors it is crucial to emphasise that 'genetic' does not mean 'fixed' or 'pre-determined'. Environmental factors (both physical and social) are constantly acting to regulate gene expression, such that genes are actually being switched on and off every millisecond in response to a whole array of 'environmental' stimuli. These include what we experience through our senses as well as what we take in through our skin, via the air that we breathe, and also – most relevant to the topic under discussion here – from the food that we eat. Thus genetic and environmental influences are inextricably linked, and the tedious 'nature *versus* nurture' issue so beloved of journalists is largely meaningless. Environmental factors (including other genes) influence gene expression; and conversely, genetic factors can lead individuals to select certain aspects of their environments. It is also worth emphasising that most environmental factors can usually be modified rather more easily than can genes.

Fatty acid metabolism actually lies at the interface of gene-environment interactions, because individual differences exist for many genes that influence the absorption, transport and utilisation of fatty acids; and the expression of individual genetic differences of all kinds depends heavily on dietary intake of fatty acids, both during development and throughout life. These points are discussed further in a recent book containing a wealth of accessible information on the importance of lipids in the evolution of the modern human brain, and the relevance of this for developmental and psychiatric conditions, particularly schizophrenia (Horrobin, 2001). The central proposal is that the individual differences underlying these conditions are actually as old as humanity, but that their developmental expression will depend crucially on dietary fatty acid intake.

The role of fatty acids in adult psychiatric conditions has now started to receive considerable attention, not least because omega-3 fatty acids (found naturally in fish oil, but often seriously lacking from modern diets) appear to be a very promising new line of treatment. Benefits from omega-3 supplementation – and particularly the fatty acid EPA - have now been demonstrated in controlled trials of schizophrenia (Peet et al 2001; Peet and Horrobin, 2002a) bipolar (manic-depressive) disorder (Stoll et al, 1999), and most recently, treatment-resistant depression (Nemets et al, 2002; Peet and Horrobin, 2002b). Similar research concerning the developmental conditions is still in its early stages, but the evidence from these studies will be discussed later. Meanwhile, an overview of the nature and importance of highly unsaturated fatty acids is first provided, followed by the background evidence for fatty acid deficiencies or imbalances in dyspraxia and related conditions.

Fats and the brain – essential fatty acids (EFA) and highly unsaturated fatty acids (HUFA)

It is not widely appreciated (particularly by those who choose to adopt 'low-fat' or even 'no-fat' diets) that 60% of the non-water content of the human brain is actually fat. Moreover, just four highly unsaturated fatty acids should make up around 20% of the brain's dry mass: EPA and DHA

[2] It is important to make clear that there are not - and never will be - any genes *'for'* behaviourally-defined conditions such as dyspraxia, dyslexia, ADHD, or autism – because genes simply do not operate at that level. Genes provide coded information for making different kinds of proteins - the basic building blocks for bodies and brains, and for the enzymes that constantly regulate the innumerable complex biological processes involved in living. Therefore genes cannot possibly account directly for any complex, socially-learned behaviours, although they can certainly help to shape the *predisposition* to such behaviours.

from the omega-3 series, and DGLA and AA from the omega-6 series. What makes these fats so special is the number of 'double-bonds' in their long carbon chains, which give them unique biological properties. By contrast, saturated fats have no such double bonds (the carbon atoms are literally 'saturated' with hydrogen atoms) while 'monounsaturated' fats such as oleic acid, found in olive oil, have just one double-bond.

Table 1: Omega-6 and omega-3 fatty acids

The truly essential fatty acids (EFA) that cannot be synthesised within the body are linoleic acid (LA) of the omega-6 series and alpha-linolenic acid (ALA) of the omega-3 series.

The longer-chain, highly unsaturated fatty acids (HUFA) that the brain needs can in theory be synthesised from these EFA precursors - via processes of desaturation (insertion of a double-bond) and elongation (adding two carbon atoms to the fatty acid chain).

However: the conversion of EFA to HUFA is relatively slow and inefficient in humans, so pre-formed HUFA from dietary sources may be needed to ensure an adequate supply of these vital nutrients**.**

OMEGA-6 series		Enzymes involved in HUFA synthesis	OMEGA-3 series	
Linoleic Acid (LA)	18:2		Alpha-linolenic Acid (ALA)	18:3
↓		*Delta 6- desaturase*	↓	
Gamma-linolenic Acid (GLA)	18:3		Octadecatetraenoic Acid	18:4
↓		*Elongase*	↓	
Dihomogamma-linolenic Acid (DGLA)	**20:3**		Eicosatetraenoic Acid	20:4
↓		*Delta 5-desaturase*	↓	
Arachidonic Acid(AA)	**20:4**		**Eicosapentaenoic Acid (EPA)**	**20:5**
↓		*Elongase*	↓	
Adrenic Acid	22:4		Docosapentaenoic Acid (DPA)	22:5
↓		*Elongase, Delta 6-desaturase, Beta-oxidation*	↓	
Docosapentaenoic Acid (DPA)	22:5		**Docosahexaenoic Acid (DHA)**	**22:6**

Four HUFA are particularly important for brain development and function: DGLA and AA from the omega-6 series, and EPA and DHA from the omega-3 series.

- AA and DHA are major structural components of neuronal membranes (making up 20% of the dry mass of the brain and more than 30% of the retina).
- EPA and DGLA are also crucial, but they play functional rather than structural roles.
- EPA, DGLA and AA (but not DHA) are needed to manufacture *eicosanoids* - hormone-like substances including prostaglandins, leukotrienes, and thromboxanes - that play a critical role in the moment-by-moment regulation of a very wide range of brain and body functions.

Fatty acids from one series cannot be converted into the other within the body. However, both are essential, and the balance of omega-3 and omega-6 fatty acids is very important, as they play complementary roles in many biological functions.

For example, derivatives of AA include the 'pro-inflammatory' series 2 prostaglandins, while DGLA and EPA give rise to 'anti-inflammatory' prostaglandins (series 1 and series 3 respectively). Similarly, thromboxanes derived from AA act to constrict blood vessels while those derived from EPA act to relax blood vessels and improve blood flow.

If these four key HUFA are not directly available in the diet, they can in theory be manufactured within the body from simpler 'essential' fatty acids (EFA), as shown in Figure 1. However, it has only recently become clear that this EFA-HUFA conversion process is actually very slow and inefficient in humans (Salem et al, 1999; Pawloski et al, 2001; Brenna, 2002), probably reflecting the fact that we evolved on a 'hunter-gatherer' diet that was very rich in pre-formed HUFA. To make matters worse, this pathway for HUFA synthesis is further impeded by a wide range of dietary, lifestyle or chance factors that can act to block the enzymes required (Brenner, 1981).

These inhibiting factors include:

- a high dietary intake of saturated fats, hydrogenated or 'trans' fatty acids (the artificial fats found in most margarines and processed foods),
- lack of the necessary vitamin and mineral co-factors (particularly zinc, magnesium and vitamins B3, B6 and C)
- heavy use of caffeine (found not only in coffee and tea, but in a wide range of soft drinks including coca-cola)
- viral infections
- high levels of the hormones released in response to stress.

Other relevant lifestyle factors include heavy consumption of alcohol, and smoking, although these primarily appear to act by destroying HUFA rather than preventing their synthesis. Their effects in depleting HUFA levels are so reliable and pronounced that these factors need to be carefully controlled whenever HUFA status is under experimental investigation.

Why HUFA are essential for normal brain development and function

Structurally, AA and DHA are key components of brain cell membranes, making up 15-20% of the brain's dry mass and more than 30% of the retina. Adequate supplies of these HUFA are therefore essential during prenatal development, and the placenta has been shown to double the levels circulating in maternal plasma in order to meet the needs of the growing baby's brain (Crawford et al, 2000). Severe HUFA deficiencies can have permanent effects if they occur during critical periods of neural development, but milder deficiencies are likely to give rise to more subtle developmental difficulties (Crawford, 1992). The omega-6 fatty acid AA is crucial to brain growth, and mild deficiencies are associated with low birth weight and reduced head circumference, while the structural omega-3 fatty acid DHA is particularly concentrated in highly active sites such as synapses and photoreceptors, and is essential for normal visual and cognitive development (Neuringer et al, 1994).

In early life, HUFA are essential in supporting further brain growth and maturation and are therefore found in breast milk, although they are still not present in many formula feeds. Carefully controlled studies comparing the effects of infant formula with and without pre-formed HUFA have shown clear advantages for both visual and cognitive development from their addition (Makrides et al, 1995; Willatts and Forsyth, 2000)

Throughout life, adequate supplies of HUFA remain crucial for optimal brain function. They are essential for maintaining the fluidity or elasticity of neuronal membranes (while saturated, hydrogenated or trans fats and cholesterol act to reduce this). This fluidity is key to the proper functioning of the membrane-bound and membrane-associated proteins that carry the chemical or electrical signals underlying all information processing in the brain. Certain HUFA – notably AA and EPA - also play key roles as 'second messengers' in chemical neurotransmitter systems, as well as contributing to many other aspects of cell signalling (Nunez, 1993).

Functionally, three HUFA are particularly important in the brain: the omega-6 fatty acids DGLA and AA and the omega-3 fatty acid EPA. In the body these give rise to a very wide range of substances collectively known as the 'eicosanoids', highly bioactive hormone-like substances including prostaglandins, leukotrienes and thromboxanes. These HUFA derivatives can exert profound influences on brain development and function, as they play key roles in regulating blood flow, hormonal systems and immune function. Their effects on the immune system may be particularly relevant to dyspraxia and related conditions, and it is therefore worth noting that while AA's derivatives tend to be pro-inflammatory, the substances produced from both DGLA and EPA have powerful natural anti-inflammatory effects.

In summary, adequate supplies of all four key HUFA (the omega-3 fats EPA and DHA and the omega-6 fats DGLA and AA) are required for normal brain development, and for efficient information processing within the brain and nervous system throughout life. Unfortunately, there are many possible reasons why their availability may be less than optimal, and these will briefly be considered next.

Possible reasons for HUFA deficiencies or imbalances

a) Inadequate dietary intake of HUFA (and/or the relevant EFA)

Oily fish and seafood provide the only significant direct dietary source of the crucial omega-3 fatty acids that the brain needs (EPA and DHA), and this fact supports the traditional wisdom that 'fish is good for the brain'. The 'parent' essential fatty acid of the omega-3 series (ALA) is found in dark green leafy vegetables and certain nuts and seeds (walnuts, pumpkin seeds and linseed (flax) are particularly rich sources), but levels of both ALA and the more important omega-3 HUFA tend to be very low in many modern diets. The dramatic increase in the ratio of omega-6 to omega-3 fats in our diet over the last century (from around 3:1 to over 100:1 by some estimates) is believed by many experts to present serious health problems, although in reality, it is likely to be the HUFA ratio that matters most. Together with the increase in total fat (particularly from saturated and artificial fats), abundant evidence suggests that a relative lack of omega-3 HUFA may underlie the equally dramatic increase in many 'modern' disorders of physical and mental health, including heart disease and stroke, inflammatory and other immune system disorders (including cancer) and depression (Holman, 1998; Alexander, 1998; Hibbeln, 1998; Horrobin and Bennett, 1999).

The 'parent' omega-6 fatty acid (LA) is very unlikely to be lacking from the diet, as this is found in most vegetable oils. However, as noted above, conversion of EFA to HUFA appears to be inefficient in many people. One of the key omega-6 HUFA, AA, is found in meat and dairy products, so this is also fairly abundant in modern diets (although vegetarians and vegans may need to take steps to ensure an adequate intake). However, an excess of AA in relation to EPA and DGLA - which by contrast are often lacking from the diet - can increase tendencies to inflammation. The only food known to contain significant quantities of the other crucial omega-6 fatty acid, DGLA, is human breast milk; but this fatty acid is very easily synthesised from its immediate precursor, GLA, which is found in some seed oils such as evening primrose, blackcurrant and borage oils. Supplementation with GLA can therefore bypass the initial 'delta-6-desaturase' enzyme step in EFA-HUFA conversion, which is usually the limiting factor.

b) Difficulties in EFA-HUFA conversion

Various dietary and lifestyle factors that can impair the (already limited) synthesis of HUFA from EFA have already been noted earlier, but difficulties in EFA-HUFA conversion can also occur for constitutional reasons. Atopic conditions such as eczema are associated with impaired HUFA

synthesis (Manku et al, 1984; Wright and Bolton, 1989), and the same appears to be true in diabetes (Arisaka et al, 1986; Horrobin, 1988). Of particular interest in relation to the excess of males affected by dyspraxia and related conditions is the fact that males are particularly vulnerable to HUFA deficiency, because oestrogen helps to conserve HUFA under conditions of dietary deprivation, while testosterone can inhibit HUFA synthesis (Huang and Horrobin, 1978; Marra and de Alaniz, 1989).

c) *Difficulties in recycling HUFA*

Other possible constitutional reasons for HUFA deficiencies or imbalances include inefficiencies in the enzymes responsible for recycling them within the brain and body. HUFA are constantly replaced and recycled, both during the normal turnover and remodelling of cell membranes, and in the chemical cascades triggered by normal cell signalling processes. Particular enzymes from the phospholipase A2 (PLA2) group act to remove HUFA from membrane phospholipids, and this creates free fatty acids and other products that are highly vulnerable to destruction by oxidation, and therefore have to be rapidly recycled in at least two further enzyme steps. The efficiency of these processes will differ between individuals, and there is some evidence for both excessive HUFA breakdown and recycling problems in developmental conditions related to dyspraxia, as discussed below.

Features of dyspraxia consistent with fatty acid deficiencies

Difficulties in motor coordination are obviously the fundamental issue in dyspraxia, and evidence from other areas indicates that these are often associated with fatty acid deficiencies. The movement disorders that develop in many elderly people were found to be robustly associated with HUFA deficiencies in a carefully controlled general population study (Nilsson et al, 1996). The same appears to be true of the movement abnormalities in Huntington's disease and those that can result from antipsychotic drug treatment in schizophrenia (Vaddadi, 1996). Furthermore, preliminary evidence shows that treatment with fatty acids may be beneficial in both of these conditions (Peet et al, 2001; Peet and Horrobin, 2002b; Puri et al, 2002), and recent studies have also shown that DHA – one of the key omega-3 HUFA - is particularly concentrated in brain regions involved in motor control.

HUFA deficiencies could also contribute to some of the developmental difficulties in visual processing that are characteristic of dyspraxia. The omega-3 fatty acids are likely to be most relevant here: DHA makes up 30-50% of the retina and when omega-3 fatty acids are lacking from the diet this is replaced by 22:5 omega-6. However, despite the fact that this fatty acid differs from DHA by only one double bond, the effect of this substitution is a dramatic reduction in the efficiency of signal transduction in the retina – the very first stage of visual information processing (Litman et al, 2001). An enormous research literature now testifies to the essentiality of omega-3 fatty acids for other aspects of visual development and function, (Neuringer et al, 1994; Uauy et al, 2001), and deficits in visual selective attention and spatial learning are among the classic consequences of omega-3 deficiency.

With respect to the more general difficulties with attention and arousal that are common in many dyspraxic individuals, the existing evidence for fatty acid deficiencies in ADHD is obviously relevant, and this is considered in the following section. However, in terms of possible mechanisms, it is noteworthy that chronic omega-3 deficiency is associated with reduced levels of dopamine (and its binding to D2 receptors) in frontal cortex (Delion et al, 1994), and this is of course the main neurotransmitter boosted by the stimulant medications used to treat ADHD. Moreover, detailed studies indicate that the reduced storage of dopamine in these regions following omega-3 deficiency

may be insufficient to maintain the high release needed during 'stimulated cognitive processes' such as sustained attention to a demanding task (Zimmer et al, 1998). Animal studies have also shown that the behavioural effects of n-3 HUFA deficiency include changes in attention, motivation, and reactivity to stimuli and rewards, but not necessarily locomotion (Francàs et al, 1995). This is interesting in view of our own clinical impressions that omega-3 supplements may perhaps have more effect on the 'attentional' aspects of ADHD than on hyperactivity per se, although this still awaits confirmation.

Many other features associated with dyspraxia are also consistent with HUFA deficiencies, including:

- *The excess of males affected.* Sex hormones appear to increase vulnerability to HUFA deficiency in males, as noted above.
- *An apparent susceptibility to allergic or autoimmune disorders.* This may reflect constitutional inefficiencies of EFA-HUFA conversion, and would be exacerbated by an excess of AA relative to EPA and DGLA, both of which have anti-inflammatory effects.
- *Disturbances in temperature regulation and sleep.* These are also consistent with a less than optimal balance of eicosanoids (produced from AA, DGLA and EPA), as these help to regulate the hormonal and other systems involved in these functions.
- *Irregularities of mood and arousal.* HUFA can have profound effects on the neural systems governing arousal, and as noted earlier, recent evidence shows that the omega-3 fatty acids – particularly EPA – can help to stabilise mood swings and counteract depression.

Experimental evidence for fatty acid abnormalities in related conditions

Unfortunately, no studies of fatty acid metabolism in dyspraxia per se have yet been reported, although research of this kind is now underway. However, there is already experimental evidence for fatty acid abnormalities in related conditions including ADHD, dyslexia and the autistic spectrum. It is also worth noting that dyspraxia has never yet been 'factored out' in these studies, hence many of the participants may have had dyspraxic-type difficulties in addition to their primary diagnosis.

Physical signs of fatty acid deficiency

Mild physical signs consistent with fatty acid deficiency were first reported in connection with ADHD (Colquhoun and Bunday, 1981; Stevens et al, 1995, 1996). These include excessive thirst, frequent urination, rough, dull or dry skin and hair, dandruff, soft or brittle nails, and 'follicular keratosis' (a build-up of hard skin around the hair follicles that gives the skin a 'bumpy' appearance and feel). Although each of these signs can have other possible causes, their association with fatty acid deficiency has been well-studied in animals; and in children with ADHD, when scored on a simple questionnaire scale their presence and severity has been shown to relate to HUFA status as assessed via blood biochemical measures (Stevens et al, 1995).

These fatty acid deficiency signs were very marked in the dyslexic boy studied by Baker (1985), and their association with dyslexia has been confirmed in subsequent studies. Ratings of these signs were significantly higher in dyslexic than non-dyslexic adults (Taylor et al, 2000); and within the dyslexic group they were associated with visual symptoms when reading, other visual problems, auditory and language confusions and motor problems. Their occurrence and severity was also found to correlate with the severity of difficulties with reading, spelling and working memory in dyslexic children (Richardson et al, 2000).

In members of the autistic spectrum, recent studies indicate that these physical signs of fatty acid deficiency are even more prevalent than they appear to be in ADHD or dyslexia (Bell et al 2000, 2002). In dyspraxia, no studies have yet been reported but these are now underway, and clinical experience and anecdotal evidence suggest that the same physical signs will also be associated with this condition. Given that the checklist first developed by Stevens et al. (1995) for rating these signs is a very simple instrument that could potentially be used with minimal guidance by parents, teachers or other professionals, further studies to validate this against objective biochemical measures of fatty acid status are also in progress.

Evidence from biochemical and brain imaging studies.

In ADHD, several biochemical studies have now shown reduced concentrations of HUFA in the blood of ADHD children compared with matched controls (Mitchell et al, 1987; Bekaroglu et al, 1996; Arnold et al, 1994; Stevens et al, 1995, 1996; Burgess et al, 2000).
The most detailed studies (Stevens et al, 1995, 1996) revealed no deficiencies of the 'parent' EFA – either in the blood samples or in these children's diets. This observation is consistent with difficulties in EFA-HUFA conversion, as first suggested by Colquhoun and Bunday (1981), but it would also be explicable in terms of an unusually rapid rate of HUFA breakdown and loss in children with ADHD.

Further analyses of the combined sample of ADHD boys and controls revealed that irrespective of clinical diagnosis, HUFA deficiencies were significantly associated with a range of behavioural, learning and health problems (Stevens et al, 1996). These findings are in keeping with a dimensional view of ADHD, at least with respect to fatty acid deficiencies as a possible contributory factor. Of particular note is that low levels of omega-6 fatty acids were related only to some physical health measures (such as dry skin and hair, frequency of colds, and antibiotic use), but not to parental ratings of behaviour or learning. By contrast, low omega-3 fatty acid status was associated not only with physical signs of fatty acid deficiency (particularly excessive thirst, frequent urination and dry skin) but also with both behavioural problems (including conduct disorder, hyperactivity-impulsivity, anxiety, temper tantrums and sleep problems) as well as learning difficulties in these children. This is consistent with substantial evidence from other sources that the omega-3 fatty acids play a particularly key role in brain function.

Blood biochemical studies of individuals with autistic spectrum disorders have also shown reductions in HUFA concentrations relative to controls in both plasma (Vancassel et al, 2001) and red cell membranes (Bell et al, 2000, 2002). In the latter case, differences did not reach significance in the small number of subjects studied to date, as wide individual variation was observed even within ASD groups separated into 'classical' or 'regressive' autism (according to whether symptoms were present from birth, or developed after the age of 18 months). However, a significant elevation in both groups relative to controls was found in the ratio of AA to EPA, a potential index of 'pro-inflammatory' tendencies. The studies by Bell and colleagues have also revealed that red cell membrane HUFA of individuals with a regressive form of autism are unusually vulnerable to further breakdown during storage unless the blood samples are kept at extremely low temperatures. Possible explanations for this include an excess of a PLA2 enzyme that removes HUFA from membrane phospholipids, as very low storage temperatures are required to inactivate this enzyme. High levels of PLA2 have previously been reported in both schizophrenia and dyslexia (Macdonell et al, 2000), consistent with an unusually rapid rate of breakdown and potential loss of HUFA via oxidation.

In dyslexia, blood biochemical evidence confirmed the clinical picture of fatty acid deficiency in the case study reported by Baker (1985), but further blood biochemical evidence in this condition is

still awaited, as is also the case with dyspraxia. However, in dyslexic adults, brain imaging with cerebral 31-phosphorus magnetic resonance spectroscopy (a non-invasive method of assessing the chemical composition of brain tissue) has revealed anomalies of membrane lipid turnover that would be consistent with HUFA deficiency (Richardson et al, 1997).

Can dietary supplementation with highly unsaturated fatty acids help?

The suggestive evidence for HUFA deficiencies or imbalances in dyspraxia and related conditions has raised the possibility that dietary supplementation with HUFA might be of some benefit. Anecdotal evidence suggests that this is true in at least some cases, but carefully designed and properly controlled studies are needed to establish whether or not this is really the case. Randomised, double-blind, placebo-controlled trials are regarded as the 'gold standard' in this respect: participants are allocated at random to either the treatment under study or a placebo, and no-one is permitted to know which treatment any individual is receiving until all study data have been collected and verified. While controlled trials of this kind remain the only reliable way to eliminate the influence of expectations, they do have their limitations (Slade and Priebe, 2001). They are most suited to evaluating single treatments for physical medical conditions involving clear diagnostic criteria and homogeneous study populations. They are much less suited to behaviourally-defined developmental conditions such as dyspraxia, dyslexia, ADHD or the autistic spectrum (or any psychiatric conditions), where the causes are likely to be complex and multifactorial, and standard diagnostic criteria will identify a very heterogeneous population.

In ADHD, several controlled treatment trials have been reported to date, with somewhat mixed results. The first such studies involved supplementation with evening primrose oil, supplying the omega-6 fatty acid GLA, and these indicated only marginal if any clear benefits (Aman et al, 1987; Arnold et al, 1989). However, mounting evidence now indicates that omega-3 fatty acids are likely to be more important than omega-6 in their effects on behaviour and learning, and these are also more likely to be lacking from modern diets.

In another randomised controlled trial of fatty acid treatment in ADHD children, a supplement of fish oil and evening primrose oil was therefore used, supplying mainly the omega-3 fatty acids (EPA and DHA) as well as a little omega-6 (GLA and AA). An early report of this study indicated blood fatty acid changes in the treated children that were associated with reduced ADHD symptoms (Burgess, 1998), but a full publication of the results has not yet appeared at the time of writing. Meanwhile, supplementation with DHA alone was recently found to be completely ineffective in ADHD (Voigt et al, 2001). These findings are consistent with other evidence that EPA, not DHA, is the important omega-3 fatty acid for improving attention and mood and reducing perceptual or cognitive disturbances, as discussed further below.

In dyslexia, several randomised controlled trials have now been carried out involving both children and adults, although only one of these has so far reached full publication (Richardson and Puri, 2002). This was a small pilot study involving dyslexic children from a special school who also showed features of ADHD, although none of them had a formal ADHD diagnosis. Results showed that compared with placebo treatment, HUFA supplementation for three months led to significant reductions in attentional problems, anxiety, and disruptive behaviour as assessed by the Conners' Parent Rating Scales (CPRS-L). When the placebo group were then given HUFA supplementation (without the children or their parents and teachers being aware of the switch) they showed a similar reduction in ADHD-related symptoms over the next three months, in stark contrast to their earlier lack of improvement on placebo (Richardson et al, in preparation). In a different, larger study of clinic-referred dyslexic children, preliminary results suggest that HUFA treatment may also improve reading progress (Richardson et al, in preparation). Full analyses of the data from this trial

are still in progress, but treatment effects seem to be particularly pronounced in children showing either physical signs of fatty acid deficiency or visual symptoms before treatment.

As yet, there have been no properly controlled trials concerning either dyspraxia or the autistic spectrum. One small open study of dyspraxic children has been reported, involving supplementation for three months with both omega-3 and omega-6 HUFA from a combination of fish oil and evening primrose oil (Stordy 2000). Reductions were found in both motor difficulties (as assessed via parental report and the Movement ABC) and ADHD symptoms (as assessed by the Conners Parent Rating Scales). However, without a placebo control group it is not possible to ascribe these changes to the treatment itself, as expectations can obviously play a significant role.

The first randomised, double-blind, placebo-controlled trial of HUFA treatment in dyspraxic children is now underway, involving 120 children aged 8-12 years. Measures of motor function, visuomotor skills and ratings of ADHD-related features are being assessed before and after treatment with either a HUFA supplement (containing 80% high-EPA fish oil and 20% evening primrose oil, supplying mainly omega-3 but some omega-6 HUFA) or a placebo (containing olive oil, and carefully matched for both appearance and flavour with the active treatment). This study also includes a new biochemical measure in the form of a 'breath test' designed to measure levels of ethane, the final breakdown product of omega-3 fatty acids (Ross, 2002). High levels of expired ethane would suggest that these fatty acids are being lost more rapidly than usual (rather than being recycled), and the breath test may therefore help to identify those individuals who may need a higher dietary intake of these key fatty acids.

In summary, only a few properly controlled trials of HUFA supplementation in ADHD and dyslexia have yet been carried out. The balance of evidence suggests that this may have benefits in at least some cases, but differences in the populations studied, the supplements used, and the outcome measures as well as the trial designs make clear interpretation difficult. Many of these early studies have involved only small numbers of participants – and while this obviously makes generalisation difficult, it also means that much larger treatment effects are required in order to show statistically significant group differences. Further studies are therefore needed, but given the heterogeneity within dyspraxia and related conditions, a focus on subsets of individuals defined by specific features - rather than these broad diagnostic labels - may be the most fruitful approach.

Practical guidance

As noted above, there is not yet any firm evidence that dietary supplementation with HUFA is beneficial for dyspraxia. However, as a result of increasing public awareness and the many positive anecdotal reports that have been circulating both within support groups and via the media, many people are already trying this approach for themselves. Unfortunately, accurate information on how to go about this is often lacking, and there are actually many important factors to consider.

First, prior consultation with a medical practitioner is always advisable before taking any food supplement, and this is clearly essential for anyone undergoing medical treatment or supervision. If possible, guidance from a well-qualified nutrition practitioner is also recommended, as there may well be other aspects of diet that require attention. Dietary and lifestyle changes alone can substantially increase the availability of HUFA, although if individual needs are unusually high then supplements may be the only practicable option. It must also be firmly emphasised that this approach cannot be expected to help every individual with the 'dyspraxic' label. However, provided that some basic precautions are taken, HUFA supplements are very unlikely to do any harm, and furthermore, they are already known to have a wide range of general health benefits. The only known negative effects involve mild digestive upset, although this is relatively uncommon and can

usually be minimised with attention to other aspects of the diet. Allergies to any food substance are of course possible in some individuals, and if this possibility is suspected, medical advice and/or supervision should always be sought in advance.

Choosing Supplements

It is crucial to recognise that although many different fatty acid supplements are available, these vary widely in both their composition and their quality. With respect to quality, it is an unfortunate fact that some fish and fish oils may contain pollutants such as mercury, PCBs or dioxins. Although EU regulations set strict limits on this, food supplements are unfortunately not monitored as strictly as pharmaceutical products. However, information on this – and on quality control procedures – should be available from reputable suppliers on request. The quality (and therefore the efficacy) of both omega-3 and omega-6 oils is also affected by the methods of manufacturing, processing and storage used. In brief, they are destroyed by exposure to light, heat or air,[3] so the packaging and storage conditions should minimise any such exposure, and consumers should take every care both to keep this to a minimum and to abide by the 'use by' dates, which should be clearly marked.

Ideally, information on quality and safety issues should be obtained from an independent source (such as a suitably qualified practitioner) before choosing any supplement. At the very least, it should definitely not be assumed that the cheapest supplements provide the 'best value'; but equally, a high price should not be taken as a guarantee that the product is of high quality, as sadly there are many cases when this may instead reflect expensive packaging and marketing and/or high profit margins. With respect to the composition of supplements, several points are relevant:

1. **Omega-3 HUFA appear more relevant than omega-6 to these developmental conditions, and these are also the ones more likely to be lacking from modern diets.** The 'parent' omega-6 EFA (LA) is plentiful in most vegetable oils, and the important omega-6 HUFA arachidonic acid (AA) is supplied directly by most meat and dairy products. However, if EFA-HUFA conversion is inefficient there might still be a relative lack of the omega-6 fatty acid DGLA. If so, additional evening primrose oil to supply GLA (easily converted to DGLA) may be helpful.
2. **Within the omega-3 HUFA, the latest research indicates that it is EPA, not DHA, that is likely to be most effective.** Both are essential for optimal brain function, but while DHA is important in brain *structure* (hence adequate supplies are particularly needed during early brain development), EPA plays important roles in the moment-by-moment regulation of brain *function*. Substances produced within the body from EPA are crucial for regulating immune function, hormonal balance and blood flow, which can all affect brain function as well as many other aspects of health. Pure DHA has been found ineffective in treating both depression and schizophrenia, while pure EPA has shown significant benefits in these conditions (Peet et al, 2001; Peet and Horrobin 2002a,b). Pure DHA was also found to be completely ineffective in reducing ADHD symptoms (Voigt et al, 2001), while preliminary evidence suggests that supplements containing both EPA and DHA may help to do this (Burgess, 1998; Richardson and Puri, 2002). Standard fish oils contain both EPA and DHA in ratio of around 3:2, but supplements containing higher proportions of EPA are now available.
3. **Fish liver oils are not generally suitable for these purposes** owing to their high Vitamin A content, because this vitamin is stored by the body and can be toxic in excess. As noted above, any HUFA supplements for which premium quality cannot be guaranteed should also

[3] See Erasmus (1993) for a full and extremely readable explanation of the implications of this for the manufacturing of all fats and oils, as well as the importance of omega-3 and omega-6 oils for general health.

be avoided. These may not only be ineffective, but could contain harmful residues (from environmental pollution or from extraction and processing methods), as noted above.

4. **Antioxidant intake should be considered**, because HUFA are particularly susceptible to breakdown via oxidation. Supplementation with Vitamin E in particular can help to protect them, but its efficiency in this role depends on other nutrients including Vitamin C, so a good intake of these and other antioxidants is advisable. Some specialist fatty acid supplements include a little Vitamin E, but few contain any other antioxidants.
5. **Vitamin and mineral intake is important**. Essential co-factors for the synthesis of HUFA from EFA include zinc, magnesium, and vitamins B3, B6 and C among others. These and other vitamins and minerals are required in any case for the proper functioning of the brain and body, but available evidence indicates that many individuals do not receive an adequate intake of these essential micronutrients. These should ideally be obtained from the diet, but could also be provided by a multivitamin and mineral supplement if required.
6. **Other aspects of diet may also merit attention**, and this may well be the best place to start. Advice from a well-qualified nutrition practitioner may be useful, as well as consulting with the GP (which is essential if any serious allergies or food intolerances are suspected). However, some sensible basic steps for most people would include:
    - eating plenty of fresh fruit and vegetables, nuts and seeds, fish and seafood and unrefined carbohydrates (i.e. those found in whole grains and vegetables);
    - drinking plenty of water (and avoiding too much tea, coffee, or drinks that contain caffeine or other stimulants);
    - reducing the intake of saturated fats (particularly from fried foods), and avoiding highly processed foods with artificial fats (hydrogenated and 'trans' fatty acids);
    - cutting down on sugar and refined starch (i.e. non-wholemeal bread, cakes, pastries, biscuits, sweets and soft drinks, which often have a high sugar content and/or artificial sweeteners, which may also be best avoided);
    - If food allergies or intolerances are suspected, it may also be worth exploring these, preferably with professional assistance. Some people have difficulties in properly digesting wheat and/or dairy products in particular, but many other common foods have been implicated in individual cases. Removing some foods from the diet can be very helpful in some cases, although restrictive diets should not be undertaken without specialist advice to ensure that basic nutritional needs are being met.

Dosage, duration, and monitoring of response

Dietary HUFA requirements will differ between individuals and can also differ in the same individual over time, as they will depend on other aspects of diet, stress levels or illness, among other things. Optimal dosage is therefore best determined from careful monitoring, with attention paid to any changes in other factors that may be relevant.

In our ongoing studies of dyslexia and dyspraxia, a high-EPA fish oil supplying around 500mg EPA daily is used. However, it is clear that some individuals may need more than this (particularly those with severe mood swings, emotional sensitivity and/or behavioural problems such as temper tantrums). It may be relevant that recent studies have found doses of 1g/day of EPA or more to be effective in reducing symptoms of depression (Puri et al, 2001, 2002a; Peet and Horrobin, 2002; Nemets et al, 2002), and daily doses of 2-4g pure EPA have been used successfully in disorders such as schizophrenia and bipolar (manic depressive) disorder (Puri and Richardson, 1998; Puri et al, 1999; Stoll et al, 1999; Peet et al, 2001, Peet and Horrobin, 2002).

As discussed above, supplementation with omega-3 fatty acids appears to be more important than omega-6 for these purposes, but an adequate dietary supply of both series is always needed. If an individual appears to need any additional omega-6 (e.g. there are still signs of dry skin conditions and/or possible hormonal imbalance), consultation with a suitably qualified practitioner may be helpful. For general usage, evening primrose oil supplying 50-100mg of GLA daily should be a sufficient dose, although a higher dose might be appropriate for individuals who also suffer from atopic conditions such as eczema.

It is very important to recognise that HUFA are foodstuffs and do not act as rapidly as most medications, so any effects will take time to appear. In our experience, most individuals who respond to supplementation usually report noticeable benefits within one or two weeks, but in other cases changes seem to be more gradual. The minimum trial period should be at least three months, as studies have shown that it takes 10-12 weeks for HUFA levels in brain cell membranes to return to normal levels after a long-standing deficiency (Bourre et al, 1988).

After a few months, reducing the initial dose to half or even one-third of these levels may be possible without loss of benefits, and some manufacturers advise this. Unfortunately, there is not yet any published research even comparing different doses within the same study, let alone changing the dose over time, so this remains speculative. Clinical experience suggests that many people do appear to need to maintain the initial dosage on a long-term basis in order to prevent symptoms from re-appearing, but personal experimentation is likely to be the only way to determine what may be optimal for a given individual. Any dose changes should be made as systematically as possible, and the effects of each change should be monitored carefully for at least 1-2 weeks before further changes are made.

Predicting the response to HUFA supplementation?

Given the variability that exists within dyspraxia and related conditions, fatty acid supplementation cannot be expected to benefit more a subset of affected individuals, and many people who consume a balanced and healthy diet will already be obtaining all the HUFA they need. Nonetheless, some possible indicators of a good response to HUFA supplementation have emerged from our clinical experience and research to date, and these include the following features:

- Physical signs of fatty acid deficiency (excessive thirst, frequent urination, rough or dry skin and hair, dandruff, and soft or brittle nails)
- Atopic tendencies (especially eczema)
- Visual symptoms (such as poor night vision or sensitivity to bright light, and visual disturbances when reading - e.g. letters and words move, swim or blur on the page)
- Attentional problems (including distractibility, difficulties with sustained concentration, working memory problems and feelings often described as like ‘brain fog’)
- Emotional sensitivity or lability (especially undue anxiety/tension, excessive mood swings, or temper tantrums arising from ‘low frustration tolerance’)
- Sleep problems (particularly if these involve difficulties in both falling asleep at night and waking up in the morning)

Further research is still needed to establish which of these features – if any – may respond to dietary supplementation with HUFA, but results from controlled trials in both dyspraxia and related conditions should help to elucidate this. It must also be emphasised that nutritional intervention is obviously only one aspect to consider in the management of developmental dyspraxia. Other interventions – and most important of all, understanding, appropriate support and encouragement – are likely to be needed for dyspraxic individuals to achieve their full potential.

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