

## **Dyslexia in adults is associated with clinical signs of fatty acid deficiency**

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### **Summary**

Developmental dyslexia is a complex syndrome whose exact cause remains unknown. It has been suggested (1) that a problem with fatty acid metabolism may play a role, particularly in the more visual symptoms exhibited by many dyslexics. We explored this possibility using two self-rated questionnaires, designed on the basis of clinical experience, to assess symptomatology and signs of fatty acid deficiency in known dyslexic and non-dyslexic subjects. Dyslexics=signs and symptoms included the phonological problems traditionally associated with the disorder, as well as visual problems (both with reading and more generally) and motor problems. We found that the severity of the signs and symptoms correlated positively with the severity of clinical signs of fatty acid deficiency. Sex differences were observed. Our findings are consistent with the hypothesis that fatty acid metabolism may be abnormal in developmental dyslexia.

## Introduction

It has been proposed (1) that developmental dyslexia may involve deficiencies in certain highly unsaturated fatty acids (HUFA). Although as yet relatively little research has been done on the biochemistry of dyslexia, there is suggestive evidence to support this hypothesis. Baker (2) noted clinical signs of fatty acid deficiency in a dyslexic child and confirmed this with biochemical testing, reporting that fatty acid treatment was followed by improvements in the child's schoolwork. Stordy (3) found visual deficits in dyslexic adults that normalized after supplementation with omega-3 fatty acids, and brain imaging has shown abnormalities of membrane lipid turnover in dyslexic adults consistent with HUFA deficiency (4). Deficiencies of HUFA are also found in related conditions such as attention deficit hyperactivity disorder (ADHD), where they have been shown to relate to various clinical soft signs of fatty acid deficiency including polydipsia, polyuria, and dull, dry skin and hair (5).

Existing evidence thus suggests a mild abnormality of fatty acid metabolism in dyslexia that may be amenable to correction through diet. To investigate this, a large randomised double-blind trial of dietary supplementation with HUFA is approaching completion, involving dyslexic and non-dyslexic adults. We used baseline data available from this clinical trial to address the primary question of whether fatty acid deficiency is associated with dyslexia. Our aims were to compare dyslexic and non-dyslexic adults on clinical signs of fatty acid deficiency using the scale employed by Stevens et al (5) in studies of ADHD, and to examine relationships between fatty acid deficiency signs and other features associated with dyslexia. Possible sex differences were also explored, as there is evidence from animal studies that males may be more vulnerable than females to fatty acid deficiency (6, 7).

Dyslexia - like many other neurodevelopmental disorders - is more common in males, and there are some indications that the etiology of this condition may differ somewhat by sex (8).

## **Methods**

Subjects were 135 dyslexic adults (74 male, 61 female) and 71 controls (31 male, 40 female).

They were matched as closely as possible for age and general ability: there were no significant differences between groups on sex, age, WAIS Similarities or WAIS Block Design (all group comparisons were two-tailed t-test except for sex, in which Fisher's Exact test was

used). The psychometric measures used were: the Wechsler Adult Intelligence Scale (9): WAIS Similarities, Block Design, Digit Span and Digit Symbol; Wide Range Achievement Test (10): WRAT Word Reading, Spelling; Gray Oral Reading Test (11): GORT Passage Reading. These are all widely-used in the classification of the dyslexic phenotype.

Dyslexic subjects were selected according to the following criteria: (1) previous history / assessment; (2) a discrepancy between verbal ability and reading of at least 1.5 standard deviations; (3) positive indicators including particular impairments in auditory working memory (Digit Span), or a score of 10 or more on an adult dyslexia screening checklist (12). Controls were selected for no history of reading difficulties, reading and spelling within the normal range, and a score of less than 10 on the adult dyslexia screening checklist.

Differences between groups on WRAT and GORT reading measures, WRAT spelling, WAIS Digit Span and Digit Symbol were all significant at the  $p < 0.00001$  level. Exclusion criteria for all subjects were low general ability (IQ pro-rated from WAIS Similarities and Block design  $< 80$ ), any significant neurological, psychiatric or other major medical disorder, a high

reported consumption of oily fish (regularly more than twice a week) or any use of fatty acid supplements within the last six months.

Interview / checklist ratings were used to assess clinical signs of fatty acid deficiency. The rating scale has 7 items (excessive thirst, frequent urination, dry skin, dry hair, soft or brittle nails, dandruff and follicular keratosis), each scored 0-3 according to the degree of endorsement, giving a maximum possible score of 21. Total scores on this scale have been shown to relate to blood biochemical measures of HUFA deficiency (5).

In addition, the Dyslexic Symptom Questionnaire (DSQ) (13) was used to assess a variety of other signs and symptoms often associated with dyslexia. The DSQ comprises 61 questions grouped into sections. These include self-rated assessments of difficulties with reading, spelling, speech processing and other well known features of dyslexia, as well as visual symptoms and related complaints, organisational difficulties and motor coordination problems. For the study, we assessed dyslexic symptomatology using global scores on the five major sections of the DSQ: visual problems when reading, general visual or visuo-motor problems, auditory-language confusions, spoken language problems, and motor problems.

Total fatty acid deficiency signs (FADS) scores were first compared between dyslexic and control groups, and comparisons were repeated for each sex separately. Mann-Whitney two-tailed non-parametric statistics were used for comparisons unless stated otherwise. FADS scores were then examined in relation to scores on the adult dyslexia screening checklist (12), and scores on the five sections of the DSQ. Spearman nonparametric correlations were used to assess relationships between these measures, both in the sample as a whole, and separately for subdivisions by dyslexic status and sex.

## Results

### *Fatty acid deficiency signs by dyslexic status:*

Total fatty acid deficiency signs (FADS) were found to be significantly higher in the dyslexic group ( $p < 0.05$ ). However, subdivision of the sample by sex revealed that within females there were no differences between total FADS scores for dyslexic and control subjects, whereas within males the group difference was highly significant ( $p < 0.0005$ ). Figure 1 shows the mean values, with error bars of  $\pm 1$  standard error, for the dyslexic and control groups subdivided by sex.

Figure 1 about here

We found an overall sex difference in FADS in the whole group ( $p < 0.001$ ). Control males and females also differed significantly on FADS ( $p < 0.001$ ). Dyslexic males and females also differed, but to a lesser degree ( $p = 0.03$ ). As Figure 1 shows, control females show an elevated mean FADS score.

### *Fatty acid deficiency signs by dyslexia screening test scores:*

FADS were very strongly associated with higher scores on the adult dyslexia screening checklist ( $r_s = 0.28$ ,  $p < 0.0001$ ). This relationship held within both dyslexic ( $r_s = 0.24$ ,  $p < 0.007$ ) and control groups ( $r_s = 0.38$ ,  $p < 0.002$ ), as illustrated in Figure 2.

Figure 2 about here

*Fatty acid deficiency signs by features associated with dyslexia:*

In the whole sample, FADS were also associated with a wide range of self-reported features associated with dyslexia, as assessed using the DSQ. Significant correlations were found between FADS and all DSQ global scales. The strongest of these were for general visual problems ( $p < 0.000001$ ), motor problems ( $p < 0.0001$ ) and visual symptoms when reading ( $p < 0.0001$ ). Table 1 shows the correlation coefficients and significance levels for the whole sample and subgroups by dyslexic status and sex.

Table 1 about here

Scatterplots showing the correlations between FADS and the visual DSQ scales are shown in Figures 3 (visual problems when reading) and 4 (other visual problems). We note that dyslexics and controls are much more clearly differentiated by their scores on the first category than the second.

In dyslexics, but not in controls, correlations with FADS were significant for spoken language problems and motor problems, and at trend level for auditory and language problems.

There were interesting sex differences. Male controls showed no significant correlations between fatty acid deficiency signs and any of our DSQ measures. In female controls significant correlations were found between FADS and both visual scales but not other DSQ measures. Dyslexic males=scores on FADS were significantly correlated with visual reading problems and with spoken language problems. In dyslexic females, FADS correlated only

with the motor and visual other-categories of the DSQ.

## **Discussion**

Our data show clearly that clinical signs of fatty acid deficiency are higher in dyslexic than non-dyslexic adults. Interestingly, the differences found here were highly significant in males but not in females. This was owing to an unexpected elevation in female controls, which could reflect sampling bias. There is evidence from animal studies that the sex hormones exert differential effects on fatty acid metabolism (14). However, more work is needed to explore this issue further.

In both dyslexic and non-dyslexic subjects, we found that the severity of fatty acid deficiency signs correlated positively with scores on a widely-used adult dyslexia screening checklist. In addition, fatty acid deficiency signs are associated with a range of other features characteristic of dyslexia, as assessed using the DSQ, including visual symptoms when reading, other visual problems, auditory and language confusions and motor problems. Within the dyslexic group, all the associations were significant except for that with auditory and language problems which was at trend level. Within the control group, only the visual symptoms were significantly correlated with fatty acid deficiency signs.

These results support the hypothesis that fatty acid metabolism is abnormal in dyslexia. They are also consistent with suggestions that a high dietary intake of HUFAs may be beneficial in dyslexia. The associations found in controls between fatty acid deficiency signs and visual symptoms suggest that HUFA supplementation might also help some non-dyslexic individuals. Clinical treatment trials to evaluate this, involving both dyslexic and non-dyslexic adults, are now approaching completion.

We propose that further investigation of the relationship between fatty acid metabolism and dyslexia is clearly warranted by these results. Further investigations of fatty acid metabolism in dyslexia are underway using more objective measures, which we hope to be able to compare with the checklists used in the study. These measures include assessment of blood fatty acid composition, skin flushing responses to niacin (a marker of levels of free arachidonic acid) and <sup>31</sup>-phosphorus MRS (providing indices of brain lipid turnover). They should help to increase further our growing understanding of the relationship between fatty acid deficiency and developmental dyslexia.

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