The Oxford-Durham Study: A Randomized, Controlled Trial of Dietary Supplementation With Fatty Acids in Children With Developmental Coordination Disorder
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ABSTRACT. Background. Developmental coordination disorder (DCD) affects ~5% of school-aged children. In addition to the core deficits in motor function, this condition is associated commonly with difficulties in learning, behavior, and psychosocial adjustment that persist into adulthood. Mounting evidence suggests that a relative lack of certain polyunsaturated fatty acids may contribute to related neurodevelopmental and psychiatric disorders such as dyslexia and attention-deficit/hyperactivity disorder. Given the current lack of effective, evidence-based treatment options for DCD, the use of fatty acid supplements merits investigation.

Methods. A randomized, controlled trial of dietary supplementation with ω-3 and ω-6 fatty acids, compared with placebo, was conducted with 117 children with DCD (5–12 years of age). Treatment for 3 months in parallel groups was followed by a 1-way crossover from placebo to active treatment for an additional 3 months.

Results. No effect of treatment on motor skills was apparent, but significant improvements for active treatment versus placebo were found in reading, spelling, and behavior over 3 months of treatment in parallel groups. After the crossover, similar changes were seen in the placebo-active group, whereas children continuing with active treatment maintained or improved their progress.

Conclusions. Fatty acid supplementation may offer a safe efficacious treatment option for educational and behavioral problems among children with DCD. Additional work is needed to investigate whether our inability to detect any improvement in motor skills reflects the measures used and to assess the durability of treatment effects on behavior and academic progress.


From the *University Laboratory of Physiology, Oxford, United Kingdom; and Departments of Psychiatry and Social Policy and Social Work, University of Oxford, United Kingdom. Accepted for publication Jan 13, 2005. doi:10.1342/peds.2004-2164 Conflict of interest: Dr Richardson works as a consultant to companies that make fatty acid supplements. Address correspondence to Alexandra J. Richardson, DPhil(Oxon), University Laboratory of Physiology, Parks Road, Oxford OX1 3PT, United Kingdom. E-mail: alex.richardson@physiol.ox.ac.uk PEDIATRICS (ISSN 0031 4005). Copyright © 2005 by the American Academy of Pediatrics.
an acceptable safe intervention if found to be effective. We therefore assessed the effects of dietary supplementation with \( \omega-3 \) and \( \omega-6 \) fatty acids among children with DCD, between 5 and 12 years of age, who were identified from a geographically defined, general school population. The primary outcome measures were standardized, age-adjusted measures of motor skills, literacy skills (word reading and spelling), and teacher-rated behavioral and learning difficulties usually associated with ADHD. The hypothesis was that treatment for 3 months with a fatty acid supplement would lead to significant improvements, compared with placebo, in these key areas of functioning.

METHODS

Study Design

This was a randomized, double-blind, placebo-controlled trial involving treatment in parallel groups for 3 months, followed by a 1-way crossover (placebo to active treatment) for an additional 3 months. Active treatment was a food supplement containing \( \omega-3 \) and \( \omega-6 \) fatty acids, whereas the placebo was a similar supplement containing olive oil. All primary outcome measures were obtained at pretreatment baseline and 3- and 6-month follow-up points.

Comparison of the effects of parallel treatments for 3 months was the primary focus of the study. This treatment period is the minimum suitable for this kind of intervention, because of the slow turnover of these fatty acids in neuronal membranes. A full crossover design would be inappropriate, for similar reasons.

Participants

Eligibility Criteria

The study was approved by the local research ethics committee and was open to mainstream schoolchildren, 5 to 12 years of age, who met DSM-IV criteria for DCD but were not receiving any treatment for this condition. DCD diagnoses were confirmed with age-standardized measures (full-scale IQ\(^7\) of >70 and motor skills below the 15th percentile with objective testing\(^18\)) and case histories from teachers and parents, which verified that the children’s impairments interfered with academic achievement and activities of daily living. Other eligibility criteria included provision of baseline data for any of the key outcome measures, permission from the primary caregiver, who provided written informed consent, and confirmation that the child was not under medical supervision for any major physical or mental health condition (eg, epilepsy, diabetes mellitus, depression, or chronic fatigue syndrome), as confirmed by the child’s physician.

Recruitment

Participants were drawn from the first 12 schools in County Durham, United Kingdom, that were willing to assist with the study. Potential volunteers were identified by teachers at those schools, from all children whom they suspected of having DCD-type difficulties, and all data were collected from those school sites. The recruitment process yielded 117 eligible participants, who were randomized as shown in Fig 1.

Interventions

The active treatment was a supplement containing 80% fish oil and 20% evening primrose oil (a ratio similar to that used in previous studies\(^23\)) in gelatin capsules. The daily dose of 6 capsules provided \( \omega-3 \) fatty acids (558 mg of eicosapentaenoic acid and 174 mg of docosahexaenoic acid) and the \( \omega-6 \) fatty acid \( \gamma \)-linoleic acid (60 mg) plus 9.6 mg of vitamin E (natural form, \( \alpha \)-tocopherol). Placebo treatment consisted of olive oil capsules, which were carefully matched with the active treatment with respect to both appearance and flavor.

On weekdays, treatments were administered at the schools, by coordinating teachers, in 3 divided doses of 2 capsules each (early morning, lunchtime, and late afternoon). For weekend use, children were given capsules to take at home on a similar schedule, under parental supervision. At the end of each 3-month treatment period, compliance was assessed through counts of capsules remaining, cross-checked against the daily logbooks kept by teachers who administered and supervised the ingestion of supplements on weekdays and who also checked for any adverse events. A percentage figure for treatment compliance was calculated from a combination of teacher logbooks and counts of capsules returned from supplies provided to parents for use during weekends and holidays.

Randomization and Allocation

A computer-generated random sequence was used to prepare the treatments in sequentially numbered containers. Two registrants, one revealing only the treatment group (coded A or B) and the other noting the actual identity of the treatments (active or placebo), were kept in a remote secure location by an independent third party until all study data had been collected, collated, checked, and verified. Treatments were assigned to each participating school in sequentially numbered blocks matching the number of children taking part. The allocation sequence was concealed completely from all staff members involved in data collection or analysis. Participants, those administering the interventions, and those assessing the outcomes were all blinded with respect to group assignments.

Outcomes

The primary outcome measures were the changes observed during 3 months of treatment, in parallel groups, on age-standardized tests of (1) motor function (assessed with the Movement Assessment Battery for Children\(^19\)), (2) reading and spelling achievement (assessed with the Wechsler Objective Reading Dimensions\(^20\)), and (3) teacher-rated ADHD-related symptoms (assessed with Conners’ Teacher Rating Scales, Long Version [CTRS-L\(^21\)]).

Analyses

All data were analyzed by the authors.

Power Calculations

Because this was the first study of its kind, power calculations were based on the nearest comparable study\(^22\) involving children with specific reading difficulties assessed with the parent-rated version of the Conners’ ADHD rating scales used here. Scores on the DSM-IV total ADHD scale showed a treatment effect of 0.6 SD. Power calculations indicated that group sizes of 42 would give >80% power at the .05 level. A target sample size of 50 subjects per group was therefore chosen for this study.

Planned Comparisons

Planned group comparisons were performed on the primary outcome measures. Data distributions were not normal; therefore, nonparametric tests (Mann-Whitney, 2-tailed tests) were used for all analyses. Missing data (see flowchart in Fig 1) were imputed by using the last observation carried forward.

Multiple Comparisons

In the case of our behavioral change measures, it was recognized that, in comparisons of the 2 treatment groups with respect to changes in all 13 of the age-standardized CTRS-I scales, some group differences could reach conventional significance levels simply by chance. However, statistical correction for multiple comparisons would be inappropriate, because scores on many of these scales are intercorrelated (because they are derived from different but overlapping combinations of the 59 items in the inventory). Group comparisons were therefore performed by using the total raw scores obtained by summing across all items. To allow comparisons with other studies, however, results from the age-standardized scales were also computed.

Role of the Funding Source

The study was funded by the Dyslexia Research Trust and the Durham Local Education Authority, neither of which had any involvement in study design, analysis and interpretation of data; writing of the report; or the decision to submit the article for publication.
RESULTS

Study Sample

The flow of participants through the study is shown in Fig 1. The sample consisted of 78 boys and 39 girls, with a mean age of 105.8 months (SD: 16.3 months; range: 70–147 months). The mean Wechsler Intelligence Scale for Children full-scale IQ was 90.3 (SD: 8.1; range: 71–110), ie, −0.67 SD below the general population average. The verbal IQ mean was 94.0 (SD: 7.8; range: 76–116) and the nonverbal IQ mean was 88.4 (SD: 8.3; range: 71–110). Attrition rates were low, and attrition was entirely attributable to refusal to take part in additional assessments. Seven children dropped out before the 3-month point (5 in the active treatment group and 2 in the placebo group), and a total of 17 children dropped out by 6 months (10 in the active treatment group and 7 in the placebo group). In all such cases, the children first stopped taking the capsules; therefore, data on the capsule intake of these children were not included in the figures for treatment compliance during each study phase, as given below.

Parallel-Group, 3-Month Treatment Phase

Compliance Rates

The mean treatment compliance rate at 3 months for all children who completed this phase of the study (n = 110) was 88.7% (SD: 7.1%), and rates did

Assessments used at each study time point:
(1) Motor skills: Movement ABC
(2) Reading and Spelling
(3) Teacher-rated ADHD-related symptoms

Fig 1. Flow of participants through the study. Although these data show the numbers of participants at each stage of the trial, all analyses were performed on an intention-to-treat basis, with the last observation carried forward, for all randomized children provided that baseline data for that measure were available. Therefore, the numbers of participants (n) reported in our analyses (see Tables 1–3) differ slightly among the 3 main outcome measures (motor skills analyses, n = 117; reading and spelling, n = 112; ADHD-related symptoms, n = 102). ABC indicates Assessment Battery for Children; GP, general.
not differ between the treatment groups. No adverse effects were reported.

**Motor Skills**

Age-standardized scores from the Movement Assessment Battery for Children are shown in Table 1. At baseline, mean percentile scores were below the 6th percentile. The scores improved to the 12th percentile during the 3-month parallel-group treatment phase, but the mean changes did not differ between the 2 treatment groups.

**Reading and Spelling**

Reading and spelling ages are shown in Table 2. Before treatment, mean achievement scores for these measures were ~1 year below chronologic age. During the 3-month, parallel-group phase, the mean increases in reading age were 9.5 months (SD: 13.9 months) for active treatment and 3.3 months (SD: 6.7 months) for placebo, a highly significant difference ($z = 2.87, P < .004$). The mean increases in spelling age were 6.6 months (SD: 11.4 months) for active treatment and 1.2 months (SD: 5.0 months) for placebo; again, the group difference was highly significant ($z = 3.36, P < .001$).

**ADHD-Related Symptoms**

Age-standardized scores on the CTRS-L, assessing ADHD-related symptoms, are shown in Table 3. At baseline, mean scores for both groups were on average slightly more than 1 SD above population means. To the best of our knowledge, no child had a formal ADHD diagnosis. However, 32 of the 102 children with CTRS-L scores at baseline (17 boys and 15 girls), ie, 31% of this sample, had scores ≥2 SD above the general population average on the DSM-IV total scale of the CTRS-L. Very similar proportions were within the same range for the DSM-IV hyperactivity and DSM-IV inattention scales. Scores at this level would place these children within the usual clinical range for a DSM-IV ADHD diagnosis, although this could be confirmed only with a full psychiatric assessment, which was not feasible in this study.

After 3 months of treatment in parallel groups, reductions on all CTRS-L global scales were significantly greater for active treatment than for placebo. Results for the subscales were similar, with only perfectionism and social problems scales failing to show a significant advantage for active treatment.

As noted earlier, correction for multiple comparisons would be inappropriate, because scores on many of these age-standardized scales involve some of the same items and are thus intercorrelated. To avoid this potential confounding, CTRS-L total raw scores were also examined.

For active treatment, scores decreased from a mean of 74.7 (SD: 26.7) to 58.1 (SD: 27.7), a reduction of >0.5 SD during the 0- to 3-month parallel-group treatment phase. In contrast, almost no change was seen in the placebo group (pretreatment mean: 69.5; SD: 33.1; posttreatment mean: 67.9; SD: 34.8). This group difference was highly significant ($z = 5.48, P < .001$).

At 3 months after treatment, only 24 children (23.5%) still had CTRS-L scores that placed them in the clinical range for ADHD. Among those receiving active treatment, 7 of the initial 16 no longer fell into this category; in the placebo group, only 1 of 16 improved in this way.

**Follow-Up Phase, Months 3 to 6 (1-Way Treatment Crossover)**

The mean treatment compliance rate during the 3- to 6-month follow-up phase with 1-way treatment crossover was 85.5% (SD: 8.6%) for all children who completed this phase of the study ($n = 100$), and rates did not differ between groups. The mean increase in motor skills during this period did not differ between groups, as shown in Table 1. With respect to reading and spelling, however, children

| TABLE 1. Movement Assessment Battery for Children (Motor Skills) for Active Treatment and Placebo-Crossover Groups at Pretreatment Baseline, 3 Months, and 6 Months |
|---|---|---|---|
| | Mean Score (SD) | 0- to 3-mo Group Comparisons, Mann-Whitney 2-Tailed Test | Mean Score (SD), 6 mo |
| | Baseline | 3 mo | Placebo LOCF (n = 2) | Placebo LOCF (n = 2) | Z | P |
| | Active (n = 60) | | Placebo (n = 57) | | Active LOCF (n = 10) | Crossover LOCF (n = 7) |
| Manual dexterity | 10.0 (2.5) | 8.7 (2.8) | 8.7 (1.9) | 0.96 | .4 | 7.4 (2.3) | 7.6 (2.1) |
| Ball skills | 2.1 (2.5) | 1.7 (2.3) | 1.6 (2.2) | 0.57 | .6 | 1.1 (1.8) | 1.1 (1.8) |
| Static and dynamic balance | 3.5 (3.6) | 2.5 (3.3) | 1.8 (2.5) | 1.03 | .3 | 1.9 (2.8) | 1.3 (2.2) |
| Total impairment | 15.6 (5.7) | 13.1 (5.9) | 12.1 (5.1) | 0.42 | .7 | 10.4 (4.9) | 10.0 (5.0) |
| Percentile | 5.9 (4.6) | 12.3 (11.2) | 12.9 (10.1) | 0.58 | .6 | 19.5 (14.7) | 20.0 (12.6) |

The scores shown are derived from 8 different subtests of the Movement Assessment Battery for Children, which are grouped into 3 categories, manual dexterity (3 subtests), ball skills (2 subtests), and static and dynamic balance (3 subtests). Each subtest yields a crudely age-standardized impairment score, ranging from 0 (no impairment) to 5 (severe impairment). For the manual dexterity and static and dynamic balance categories, the maximal possible impairment score is 15; for ball skills, the maximal possible impairment score is 10. The total impairment score represents the sum of these 3 categories (maximum of 40). For any of these impairment scores, reductions correspond to improved performance. Percentile scores (relative to general population normative values) are derived from the total impairment scores, with higher percentiles representing better overall motor performance. Because analyses were conducted on an intent-to-treat basis, the total number of participants ($n$) remained constant throughout the duration of the study, but data for children who had dropped out at each time point were imputed as the last observation carried forward (LOCF), and their numbers are shown.
TABLE 2. Reading and Spelling Ages for Active Treatment and Placebo-Crossover Groups at Pretreatment Baseline, 3 Months, and 6 Months

<table>
<thead>
<tr>
<th>Subscales</th>
<th>Mean Age (SD) 0- to 3-mo Group Comparisons, Mann-Whitney 2-Tailed Test</th>
<th>Mean Age (SD), 6 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opposition</td>
<td></td>
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<tr>
<td>Cognitive problems</td>
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<td>Hyperactivity</td>
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<tr>
<td>Anxious/shy</td>
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<tr>
<td>Perfectionism</td>
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<td>Social problems</td>
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<tr>
<td>Global scales</td>
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<tr>
<td>Conners’ index</td>
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<td>Conners’ global restless-impulsive</td>
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<td>Conners’ global emotional lability</td>
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<td>Conners’ global index</td>
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<td>DSM-IV inattention</td>
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<td>DSM-IV hyperactivity</td>
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<tr>
<td>DSM-IV Total ADHD</td>
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</table>

The CTRS-L20 consists of 59 items describing different aspects of child behavior, each endorsed with a 4-point scale. Item scores are combined in different ways to yield raw scores for the 6 subscales and 7 global scales shown, each of which then yields an age-standardized score for comparability with general population normative values. Because analyses were conducted on an intent-to-treat basis, the total number of participants (n) remained constant throughout the duration of the study, but data for children who had dropped out at each time point were imputed as the last observation carried forward (LOCF), and their numbers are shown.

Reading and spelling ages indicate the level of achievement that would be expected by a normal child of a given chronologic age. These scores were derived from single-word reading and spelling tests from the Wechsler Objective Reading Dimensions19 battery. Because analyses were conducted on an intent-to-treat basis, the total number of participants (n) remained constant throughout the duration of the study, but data for children who had dropped out at each time point were imputed as the last observation carried forward (LOCF), and their numbers are shown.

In terms of behavior, the placebo-active treatment crossover group showed reductions in CTRS-L scale scores similar to those of the active group in the 0- to 3-month period (Table 3). Their mean total raw score decreased to 57.8 (SD: 38.0), whereas children continuing with active treatment showed some additional improvement, with their mean total raw score decreasing to 52.6 (SD: 32.8).

DISCUSSION

To our knowledge, this is the first randomized, controlled trial of this kind among children with DCD. Our hypothesis was that treatment for 3 months with a fatty acid supplement would lead to significant improvements over placebo, as assessed with changes in motor skills, reading and spelling ages, and teacher ratings of behavioral and learning difficulties usually associated with ADHD.

Results showed no effect of treatment on motor skills but significant improvements in reading, spelling, and behavior for active treatment versus placebo during 3 months of treatment in parallel groups.

crossing over from placebo to active treatment showed improvements similar to those shown earlier by children receiving active treatment (Table 2). Their mean reading age improved by 13.5 months (SD: 11.9 months), and their spelling age improved by 6.2 months (SD: 6.8 months). Children continuing on active treatment also showed improvements above chronologic age (mean reading age gain: 10.9 months; SD: 11.8 months; mean spelling age gain: 5.3 months; SD: 6.9 months).

In terms of behavior, the placebo-active treatment crossover group showed reductions in CTRS-L scale scores similar to those of the active group in the 0- to 3-month period (Table 3). Their mean total raw score decreased to 57.8 (SD: 38.0), whereas children continuing with active treatment showed some additional improvement, with their mean total raw score decreasing to 52.6 (SD: 32.8).
After a 1-way treatment crossover (placebo to active), similar changes were seen in the placebo crossover group, whereas children continuing with active treatment maintained or improved their progress.

This study involved 117 children, between 5 and 12 years of age, from mainstream schools in 1 United Kingdom county, all of whom met DCD criteria but were otherwise normal and not receiving any other treatment for their specific learning difficulties. Although it seems unlikely that these children would differ significantly from general population samples in other developed countries, generalizability to other age groups and cultures cannot be assumed. The low rate of dropout and high rate of compliance with treatment indicated that the researchers and teaching staff members provided very strong motivation, which might not be the case in other circumstances. No adverse events were reported, and the high compliance rate also suggests good acceptability of fatty acid supplements.

The improvements in literacy skills and behavior found here are consistent with other reports of benefits from fatty acid supplementation among children selected for dyslexia or ADHD,5,6 but it is noteworthy that no group effect of treatment on motor skills was apparent. The similarity in the effect sizes for ADHD-related symptoms between this DCD sample and one selected with standard criteria for dyslexia5 suggests that these results may be more widely generalizable. Although the focus of this investigation was DCD, the high level of comorbidity typically found between these conditions and the heterogeneity within each of them suggest that a symptom-based approach may be more fruitful than an exclusive focus on current diagnostic categories.

In this kind of population, delays in literacy development usually increase over time, indicating the value of early intervention. Children in the placebo group fell even more behind with spelling during the 0- to 3-month parallel-group phase, although they did show average progress in reading. In contrast, children receiving active treatment improved by 0.5 SD in the 0- to 3-month parallel-group phase, with some additional improvements in the follow-up phase. In the placebo group, no changes were observed until the children crossed over to active treatment. The first-line treatment for ADHD symptoms in most developed countries is methylphenidate, for which a recent meta-analysis21 found an overall effect size of 0.78 with the Conners’ index but little or no evidence of durability beyond 4 weeks of treatment. By comparison, in this study the effect sizes with this measure were 0.55 for the first 3 months and 0.70 over 6 months for children receiving fatty acid treatment throughout.

The problems faced by this kind of population are enduring. Follow-up studies indicate that, without specific intervention, children with DCD and ADHD at 7 years of age have unusually poor academic, social, and health outcomes in adolescence and young adulthood.13,22,23 Studies with older populations are therefore required, in addition to replication of the current findings. Although our data suggest that continuing treatment from 3 to 6 months may produce additional benefits, issues of both durability and maintenance of treatment effects also require attention in future studies.

The optimal dosage and combination of fatty acids are at present unknown. An ω-3/ω-6 ratio of 4:1 was selected for this study on the basis of previous work indicating benefits in dyslexia and ADHD,5,6 although in this case the marine oil contained a higher eicosapentaenoic acid/docosahexaenoic acid ratio. Additional studies are needed to establish both the optimal composition of fatty acid treatments and dose-response relationships.

This study was a pragmatic one designed to investigate the efficacy of fatty acid treatment and can therefore shed no light on the possible mechanisms at work. The findings do suggest, however, that fatty acid supplements of this type may be a safe, tolerable, effective treatment for improving academic progress and behavior among children with DCD.

ACKNOWLEDGMENTS

Thanks are due to the many staff of Durham Local Education Authority, who assisted with recruitment and data collection for this study. Particular thanks are also due to all the pupils and parents involved for their participation.

REFERENCES


E-MAIL—THE FUTURE?

“Doctors may no longer make house calls, but they are answering patient e-mail messages, and being paid for it. In a move to improve efficiency and control costs, health plans and medical groups around the country are now beginning to pay doctors to reply by e-mail, just as they pay for office visits. While some computer-literate doctors have been using e-mail to communicate informally with patients for years, most have never been paid for the service. . . . Blue Shield of California pays [one patient’s] doctor $25 for each online exchange, the same as it pays for an office visit. Some insurers pay a bit less for e-mailing, and patients in some health plans are charged a $5 or $10 co-payment that is billed to their credit card and relayed to the doctor. For doctors, the convenience of online exchanges can be considerable. They say they can offer advice about post-surgical care, diet, changing a medication and other topics that can be handled safely and promptly without an office visit or a frustrating round of telephone tag. And, surveys have shown that e-mail, by reducing the number of daily office visits, gives physicians more time to spend with patients who need to be seen face to face. For patients, e-mail allows them to send their medical questions from home in the evening, without missing work and spending time in a doctor’s waiting room. In fact, many say exchanges in the more relaxed, conversational realm of e-mail make them feel closer to their doctors.”


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