EDITORIAL

"Nutrition & Mental Health"

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Abstract

Mounting evidence suggests that a relative lack of certain polyunsaturated fatty acids (PUFAs) may contribute to related neurodevelopmental and psychiatric disorders such as dyslexia and attention-deficit/hyperactivity disorder. Fatty acid supplementation may offer a safe efficacious treatment option for educational and behavioural problems among children with developmental coordination disorder. There is increasing evidence that fatty acid deficiencies or imbalances may contribute to childhood neurodevelopmental disorders. There is preliminary evidence that omega-3 fatty acids may be an effective treatment for children with autism. Bioactive lipids, in particular arachidonic acid, are vital for monoaminergic neurotransmission, brain development and synaptic plasticity. Recent supplementation trials suggest that purified ethyl-eicosapentaenoic acid (E-EPA) is a modestly effective augmentation treatment resulting in reduced doses of antipsychotic medication in acutely ill patients with schizophrenia. EPA may be an effective and well-tolerated add-on treatment in schizophrenia. E-EPA might accelerate treatment response and improved the tolerability of antipsychotic medications in first-episode psychosis. Given that omega-3 PUFAs are generally beneficial to health and without clinically relevant adverse effects, their preventive use in psychosis merits investigation. Long-chain omega-3 PUFAs reduce the risk of progression to psychotic disorder and may offer a safe and efficacious strategy for indicated prevention in young people with subthreshold psychotic states.

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The theme of the 37th Annual Conference of Indian Psychiatric Society, Eastern Zonal Branch (CEZIPS 2011) held on 22nd & 23rd October 2011 at Agartalla, Tripura was "Nutrition & Mental Health."

Developmental coordination disorder (DCD) affects approximately five percent of school-aged children.[1] In addition to the core deficits in motor function, this condition is associated commonly with difficulties in learning, behaviour and psychosocial adjustment that persist into adulthood.[1] Mounting evidence suggests that a relative lack of certain polyunsaturated fatty acids (PUFAs) may contribute to related neurodevelopmental and psychiatric disorders such as dyslexia and attention-deficit/hyperactivity disorder.[1] Given the current lack of effective, evidence-based treatment options for DCD, the use of fatty acid supplements merits investigation.[1] Richardson & Montgomery[1] conducted a randomised, controlled trial of dietary supplementation with omega-3 and omega-6 fatty acids, compared with placebo, with 117 children with DCD (five to 12 years of age). Treatment for three months in parallel groups was followed by a one-way crossover from placebo to active treatment for an additional three months. No effect of treatment on motor skills was apparent but significant improvements for active treatment versus placebo were found in reading, spelling and behaviour over three 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. Fatty acid supplementation may offer a safe efficacious treatment option for educational and behavioural problems among children with DCD. Additional work is needed to investigate whether inability to detect any improvement in motor skills reflects the measures used and to assess the durability of treatment effects on behaviour and academic progress.

There is increasing evidence that fatty acid deficiencies or imbalances may contribute to childhood neurodevelopmental disorders.[2] Amminger *et al*.[2] conducted a randomised, double-blind, placebo-controlled six-week pilot trial investigating the effects of 1.5 g/d of omega-3 fatty acids (.84 g/d eicosapentaenoic acid, .7 g/d docosahexaenoic acid) supplementation in 13 children (aged five to 17 years) with autistic disorders accompanied by severe tantrums, aggression or self-injurious behaviour. The outcome measure was the Aberrant Behavior Checklist (ABC) at six weeks. They observed an advantage of omega-3 fatty acids compared with placebo for hyperactivity and stereotypy, each with a large effect size. Repeated-measures analysis of variance

indicated a trend toward superiority of omega-3 fatty acids over placebo for hyperactivity. No clinically relevant adverse effects were elicited in either group. The results of this study provide preliminary evidence that omega-3 fatty acids may be an effective treatment for children with autism.

Bioactive lipids, in particular arachidonic acid (AA), are vital for monoaminergic neurotransmission, brain development and synaptic plasticity.[3] Phospholipases A2 (PLA2) are key-enzymes in AA metabolism and are activated during monoaminergic neurotransmission.[3] Reduced membrane AA levels and an altered activity of PLA2 have been found in peripheral membranes of drug-naïve patients with schizophrenia with some conflicting results in more chronic patient populations.[3] Furthermore in vivo brain phosphorus-31 magnetic resonance spectroscopy suggests reduced lipid membrane precursors (phosphomonoesters) and increased membrane breakdown products (phosphodiesters) in drug-naïve or early treated first-episode schizophrenia patients compared to age-matched controls or chronic populations and these changes were correlated with peripheral red blood cell membrane AA levels.[3] Berger *et al*.[3] postulated that processes modulating membrane lipid metabolism were associated with psychotic illnesses and might partially explain the mechanism of action of antipsychotic agents as well as experimental agents such as purified ethyl-eicosapentaenoic acid (E-EPA). Recent supplementation trials suggest that E-EPA is a modestly effective augmentation treatment resulting in reduced doses of antipsychotic medication in acutely ill patients with schizophrenia (but not in residual-type schizophrenia). They investigated the role of bioactive lipids in schizophrenia and its treatment as well as its potential use in prevention.

Emsley *et al*.[4] investigated the efficacy and tolerability of E-EPA as add-on treatment in chronic, severe schizophrenia. A randomised, parallel-group, double-blind, placebo-controlled, fixed-dose, add-on study was conducted over 12 weeks. Forty patients with persistent symptoms after at least six months of stable antipsychotic treatment received E-EPA or placebo in addition to their existing treatment. At 12 weeks, the E-EPA group had significantly greater reduction of Positive and Negative Syndrome Scale total scores and of dyskinesia scores than the placebo group. They concluded that EPA may be an effective and well-tolerated add-on treatment in schizophrenia.

Berger *et al*.[5] investigated if E-EPA augmentation improved antipsychotic efficacy and tolerability in first-episode psychosis (FEP). They performed a 12-week, randomised, double-blind, placebo-controlled trial of two-g E-EPA augmentation in 80 FEP patients. Sixty-nine patients were eligible for analysis; a post hoc analysis was computed for a subgroup of nonaffective FEP patients (N=53). The first participant was included in November 2000 and the last participant completed the trial in August 2003. Primary outcome measures were symptom change scores and time to first response while tolerability measures and cumulative antipsychotic dose were secondary outcome measures. Analysis of covariance controlling for baseline symptoms found no significant mean difference between E-EPA and placebo at week 12 for symptom change scores. Cox regression analysis revealed a significant treatment by diagnosis interaction (p=.024) for time to first response favouring E-EPA in nonaffective psychosis. Post hoc analysis for cumulative response rates further confirmed a higher response rate at week six (42.9% [15/35] vs. 17.6% [6/34] for all participants, p=.036; 54.2% [13/24] vs. 17.2% [5/29] for the nonaffective psychosis subset, p=.008); however, the difference at week 12 was no longer significant. Analysis of secondary outcome measures revealed that E-EPA-augmented participants needed 20% less antipsychotic medication between weeks four through six (p=.03), had less extrapyramidal side effects in the initial nine weeks (p<.05 for all participants and for all timepoints) and reported less constipation (p=.011) and fewer sexual side effects (p=.016) than those treated with antipsychotic medication alone. The findings suggested that E-EPA might accelerate treatment response and improved the tolerability of antipsychotic medications. However it was not possible to demonstrate a sustained symptomatic benefit of E-EPA in early psychosis, possibly due to a ceiling effect since a high proportion of first-episode patients already achieve symptomatic remission with antipsychotic medication alone. Further controlled trials in nonaffective early psychosis seemed warranted.

The use of antipsychotic medication for the prevention of psychotic disorders is controversial.[6] Long-chain omega-3 PUFAs may be beneficial in a range of psychiatric conditions including schizophrenia.[6] Given that omega-3 PUFAs are generally beneficial to health and without clinically relevant adverse effects, their preventive use in psychosis merits investigation.[6] Objective of Amminger *et al*.[6] was to determine whether omega-3 PUFAs reduce the rate of progression to first-episode psychotic disorder in adolescents and young adults aged 13 to 25 years with subthreshold psychosis. Design was randomised, double-blind, placebo-controlled trial conducted between 2004 and 2007. Setting was psychosis detection unit of a large public hospital in Vienna, Austria. Participants were eighty-one individuals at ultra-high risk of psychotic disorder. A 12-week intervention period of 1.2-g/d omega-3 PUFA or placebo was followed by a 40-week monitoring period; the total study period was 12 months. The primary outcome measure was transition to psychotic disorder. Secondary outcomes included symptomatic and functional changes.

The ratio of omega-6 to omega-3 fatty acids in erythrocytes was used to index pretreatment vs posttreatment fatty acid composition. Seventy-six of 81 participants (93.8%) completed the intervention. By study's end (12 months), two of 41 individuals (4.9%) in the omega-3 group and 11 of 40 (27.5%) in the placebo group had transitioned to psychotic disorder (p=.007). The difference between the groups in the cumulative risk of progression to full-threshold psychosis was 22.6% (95% confidence interval, 4.8-40.4). Omega-3 PUFAs also significantly reduced positive symptoms (p=.01), negative symptoms (p=.02) and general symptoms (p=.01) and improved functioning (p=.002) compared with placebo. The incidence of adverse effects did not differ between the treatment groups. Their conclusion was that long-chain omega-3 PUFAs reduce the risk of progression to psychotic disorder and may offer a safe and efficacious strategy for indicated prevention in young people with subthreshold psychotic states.

References

1. Richardson AJ, Montgomery P. The Oxford-Durham study: a randomized, controlled trial of dietary supplementation with fatty acids in children with developmental coordination disorder. Pediatrics. 2005;115:1360-6.

2. Amminger GP, Berger GE, Schäfer MR, Klier C, Friedrich MH, Feucht M. Omega-3 fatty acids supplementation in children with autism: a double-blind randomized, placebo-controlled pilot study. Biol Psychiatry. 2007;61:551-3.

3. Berger GE, Smesny S, Amminger GP. Bioactive lipids in schizophrenia. Int Rev Psychiatry. 2006;18:85-98.

4. Emsley R, Myburgh C, Oosthuizen P, van Rensburg SJ. Randomized, placebo-controlled study of ethyl-eicosapentaenoic acid as supplemental treatment in schizophrenia. Am J Psychiatry. 2002;159:1596-8.

5. Berger GE, Proffitt TM, McConchie M, Yuen H, Wood SJ, Amminger GP, *et al*. Ethyl-eicosapentaenoic acid in first-episode psychosis: a randomized, placebo-controlled trial. J Clin Psychiatry. 2007;68:1867-75.

6. Amminger GP, Schäfer MR, Papageorgiou K, Klier CM, Cotton SM, Harrigan SM, *et al*. Long-chain omega-3 fatty acids for indicated prevention of psychotic disorders: a randomized, placebo-controlled trial. Arch Gen Psychiatry. 2010;67:146-54.