

Editorial

Role of dietary supplementation
in attention-deficit hyperactivity disorder

Priya Rajyaguru and Miriam Cooper

**Summary**

Dietary constituents have been increasingly researched as both potential aetiological factors and interventions for attention-deficit hyperactivity disorder (ADHD) symptoms. Although the involvement of dietary factors in ADHD is biologically plausible, the literature to date does not indicate

causality and there are no grounds yet for the routine recommendation of dietary manipulation in ADHD.

Declaration of interest

None.

Priya Rajyaguru (pictured) was, at the time of writing this editorial, a Cardiff University School of Medicine medical student affiliated to the Child & Adolescent Psychiatry Section, Institute of Psychological Medicine and Clinical Neurosciences. Miriam Cooper is a clinical lecturer in the Child & Adolescent Psychiatry Section, Institute of Psychological Medicine and Clinical Neurosciences, MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University School of Medicine.

What do we know about the role of dietary supplementation in ADHD?

Dietary deficiency as a potential aetiological factor in ADHD

The dietary constituents that have been investigated most widely as supplements in ADHD are iron (e.g. Konofal *et al*⁶), zinc (e.g. Bilici *et al*⁷) and omega-3 and/or -6 polyunsaturated fatty acids (PUFAs, e.g. Johnson *et al*⁸). Does deficiency of such nutrients contribute to risk for ADHD? The rationale for investigating supplementation has usually been the premise that there may be an insufficiency of the nutrient in question. Although the adverse effects of gross nutritional deficiencies of such substances on neurodevelopment are established, the effects of less pronounced insufficiencies are not so clear.⁴ Evidence from animal studies lends biological plausibility to the hypothesis that subtle alterations in these nutrients could have an impact on aspects of neurotransmission and cognition that may be altered in ADHD. There is also a limited background of cross-sectional research in children with diagnosed ADHD identifying possible deficiency states or correlations between lower serum levels and enhanced symptom severity,⁴ but consistent evidence for baseline nutritional insufficiencies in ADHD is lacking.

Using supplementation as an intervention

Such studies have provided the rationale to investigate nutritional supplementation as an intervention. However, deficiency states have not necessarily been tested for in the context of supplementation research, with some studies effectively using supplements more as dietary enhancers, and treating regardless of potential deficiency. Some supplementation studies have examined the effect of nutrients in isolation, whereas in recent years research has emerged assessing supplementation with nutrients as part of a complex (e.g. Huss *et al*⁹). However, it is difficult to delineate the effect of each when the impact of each in isolation has yet to be fully understood. Considering research examining each of these dietary components (iron, zinc and PUFAs) in isolation, some beneficial effects of supplementation have been found on measures of ADHD symptomatology, but interpretation of results overall is hindered by methodological heterogeneity, meaning interpretation of findings can only be made tentatively. Study designs vary from case studies to randomised placebo-controlled trials, giving widely varying strength of evidence. Although there is relative consistency across main study inclusion and exclusion criteria, not all studies make standardised diagnoses of ADHD.

What is attention-deficit hyperactivity disorder?

Attention-deficit hyperactivity disorder (ADHD) is the most common childhood-onset neurodevelopmental disorder and has a complex aetiology. Currently approved treatments for ADHD in children and young people are behavioural and educational interventions and/or stimulant or noradrenergic medication.¹

What is the background of research into diet and ADHD?

With rising prescription rates and side-effects of current ADHD medication contributing to negative public perception and concern, potentially more acceptable effective alternatives are now being increasingly searched for. Although such statements as 'you are what you eat' are perhaps too sweeping and controversial for serious consideration, the importance of healthy eating is of recognised relevance for child and adult health. Dietary factors have also been investigated in relation to general aspects of child cognition and behaviour (e.g. Black,² White & Wolraich³) and to ADHD itself for several decades now. Dietary constituents have been explored as both risk factors for ADHD symptoms in terms of nutritional deficiencies/surpluses and as interventions for the disorder in terms of restriction/elimination and supplementation (both reviewed by Sinn⁴). Intervention studies in particular have had a recent resurgence with both dietary restriction (e.g. Pelsser *et al*⁵) and supplementation increasingly being researched as potential alternative avenues for treatment. The pragmatism and safety of restriction diets in young children is potentially difficult to address, but although it is easier to foresee the practicality and immediate appeal of nutritional supplements as treatments, caution should be exercised in considering their utility. Here, we will focus on the evidence for the potential role of nutritional supplementation as an intervention for children and young people with ADHD and what the clinician should advise in this regard.

Stimulant medication status is an important confounder in the evaluation of some results, with children having variable past and current stimulant medication histories that cloud the interpretation of observed effects. Much of the literature is limited by small sample sizes, reducing the power to detect effects and hindering subgroup analysis. Studies that do not ascertain serum levels of the nutrient in question pre- and post-intervention are limited in their ability to infer a definite association in the magnitude of effect between the nutrient consumed and any observed cognitive or behavioural improvements. Heterogeneity in the mode of intervention delivery and use of potentially 'active' placebos are particular issues in PUFA research.

Considerations to be addressed in future

In summary, there are aspects of dietary supplementation that have biological plausibility and preliminary evidence of potential efficacy. But in light of the issues discussed, there are still many facets of this research to be further elucidated before nutritional supplements can be routinely recommended as efficacious treatment for ADHD. These include establishing which subgroups of children might benefit from which types of supplementation and eliciting reliable means of determining optimal nutrient levels for children with ADHD, as it is not clear whether levels considered most favourable for general health are also optimal for improving cognition in the context of altered brain function in ADHD.¹⁰ Once such issues are better understood, and if any nutritional factor is found to have consistently strong evidence for efficacy, the potential advantages of nutritional interventions could be numerous. Treatment with a dietary supplement could be seen as more acceptable to young people and their parents in terms of stigma and perceived risks. Administration of a simple supplement would be easy to implement across a range of people affected by ADHD including children with intellectual disabilities and adults. It may be that nutritional supplements have a better side-effect and tolerability profile than medication currently available for ADHD. However, there are theoretical disadvantages too. The possible physical side-effects of supplementation in the absence of a baseline general nutritional deficiency would need to be considered. The potential need to monitor blood levels could outweigh the pragmatism of a simple dietary pill. The cost–benefit balance of supplements would also need to be assessed before being recommended as routine treatments. A general issue to consider is that as substances such as iron, zinc and PUFAs are currently easily available from the health food industry, it would need to be considered how they would then be regulated, dispensed and monitored were they to become established medical treatments.

Advice for clinicians

Clinicians should be aware that although this is a growing area of research, the lack of concrete evidence for the utility and safety of dietary supplementation in ADHD is reflected in its continuing absence from treatment guidelines. The National Institute for Health and Clinical Excellence (NICE) guidance¹ highlights the general advice that a healthy balanced diet and exercise should be recommended for all with ADHD. However, it discourages removal of artificial food colourings and additives from the diet as a generally pertinent treatment for children and young people

with ADHD and also opposes fatty acid supplementation as an intervention. The only affirmative NICE guidance related to nutrition is that should an apparent link be observed between food or drink and ADHD symptomatology, a food diary should be implemented, and were this to demonstrate a link between such factors and hyperactive behaviour, then a dietetic referral should be offered. Initiation of any subsequent management such as dietary elimination should be carried out collaboratively between the dietician, ADHD clinician, patient and carers.¹ Although dietary supplementation is a plausible, interesting and exciting avenue of research with real potential benefits, conclusions drawn from research to date must acknowledge that the literature does not indicate causality. The underlying mechanisms that may be involved in potential amelioration of ADHD symptoms by nutritional intervention are yet to be conclusively identified and understood.

Priya Rajyaguru, MB BCh, BSc (Hons), **Miriam Cooper**, MSc, MRCPsych, Child & Adolescent Psychiatry Section, Institute of Psychological Medicine and Clinical Neurosciences and MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University School of Medicine, Cardiff, UK

Correspondence: Miriam Cooper, Child & Adolescent Psychiatry Section, Institute of Psychological Medicine and Clinical Neurosciences, Cardiff University School of Medicine, 4th Floor, Main Building, Heath Park, Cardiff CF14 4XN, UK. Email: cooperm1@cardiff.ac.uk

First received 24 Aug 2012, final revision 30 Oct 2012, accepted 7 Nov 2012

Acknowledgements

With many thanks to Professor Anita Thapar for her comments on this manuscript.

References

- 1 National Institute for Health and Clinical Excellence. *Attention Deficit Hyperactivity Disorder: Diagnosis and Management of ADHD in Children, Young People and Adults*. NICE Clinical Guideline 72. NICE, 2008.
- 2 Black MM. Micronutrient deficiencies and cognitive functioning. *J Nutr* 2003; **133** (suppl 2): 3927–31S.
- 3 White JW, Wolraich M. Effect of sugar on behavior and mental performance. *Am J Clin Nutr* 1995; **62** (suppl 1): 242–7S.
- 4 Sinn N. Nutritional and dietary influences on attention deficit hyperactivity disorder. *Nutr Rev* 2008; **66**: 558–68.
- 5 Pelsser L, Frankena K, Toorman J, Savelkoul H, Dubais A, Pereira RR, et al. Effects of a restricted elimination diet on the behaviour of children with attention-deficit hyperactivity disorder (INCA study): a randomised controlled trial. *Lancet* 2011; **377**: 494–503.
- 6 Konofal E, Lecendreux M, Deron J, Marchand M, Cortese S, Zaïm M, et al. Effects of iron supplementation on attention deficit hyperactivity disorder in children. *Pediatr Neurol* 2008; **38**: 20–6.
- 7 Bilici M, Yildirim F, Kandil S, Bekaroğlu M, Yildirmiş S, Değer O, et al. Double-blind, placebo-controlled study of zinc sulfate in the treatment of attention deficit hyperactivity disorder. *Prog Neuropsychopharmacol Biol Psychiatry* 2004; **28**: 181–90.
- 8 Johnson M, Ostlund S, Fransson G, Kadesjö B, Gillberg C. Omega-3/omega-6 fatty acids for attention deficit hyperactivity disorder: a randomized placebo-controlled trial in children and adolescents. *J Atten Disord* 2009; **12**: 394–401.
- 9 Huss M, Völp A, Strauss-Grabo M. Supplementation of polyunsaturated fatty acids, magnesium and zinc in children seeking medical advice for attention-deficit/hyperactivity problems – an observational cohort study. *Lipids Health Dis* 2010; **9**: 105.
- 10 Thapar A, Cooper M, Eyre E, Langley K. Practitioner review: what have we learnt about the causes of ADHD? *J Child Psychol Psychiatry* 2013; **54**: 3–16.