Nonpharmacological interventions for ADHD: systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments


CRD summary
Free fatty acid supplementation and artificial food colour exclusions appeared to have benefits for attention deficit hyperactivity disorder (ADHD); the evidence for behavioural interventions was limited. The authors’ conclusions seem reliable, but their caveat that the benefits of artificial food colour exclusions could be limited to patients with food sensitivities was not derived from the evidence presented.

Authors’ objectives
To assess the effectiveness of dietary and psychological treatments for attention deficit hyperactivity disorder (ADHD).

Searching
Twenty-one databases, including MEDLINE, PsycINFO and CINAHL, were searched for articles published up to April 2012, in peer-reviewed journals. Search terms were reported. Articles in English, German, Spanish, Dutch or Chinese were included. Published reviews were searched.

Study selection
Eligible were randomised controlled trials (RCTs) of dietary or psychological treatments, for children aged three to 18 years who had a validated diagnosis of ADHD of any subtype, or who met a validated cut-off on a recognised rating scale. Control conditions could be sham or placebo, attention or active control, treatment as usual, or waiting list. Trials in which the non-drug therapy was added to medication were excluded. Trials of children with rare comorbid conditions, such as fragile X syndrome, were excluded. The outcome of interest was the change in total ADHD symptom severity at the first assessment after treatment.

In the included trials, the dietary interventions were restrictive elimination diets (antigenic – to avoid allergic reaction, provoking or oligoantigenic – to avoid all allergic reactions), artificial food colour exclusion, or free fatty acid supplementation (Omega three or six). Behavioural interventions were cognitive training, neurofeedback, parent training, or parent and teacher training. Control groups received active treatment, placebo, waiting list, treatment as usual, or no treatment. The percentage of males ranged from 52 to 100 (where reported). ADHD measures varied widely between trials.

Two reviewers independently selected trials for inclusion. Disagreements were resolved by discussion or with the other reviewers.

Assessment of study quality
Trial quality was assessed independently by two reviewers, using the Jadad, which assessed randomisation, blinding and withdrawals (maximum score 5). Disagreements were resolved by discussion with a third reviewer.

Data extraction
The data were extracted to calculate standardised mean differences and 95% confidence intervals. Missing data were imputed.

The data were extracted by one reviewer and checked for accuracy by a second reviewer.

Methods of synthesis
Pooled standardised mean differences and 95% confidence intervals were calculated using a random-effects model. Statistical heterogeneity was assessed using $I^2$.

A “most proximal assessment” was conducted using ratings from the person who was closest to the therapeutic setting.
(often a parent, who was not blind to treatment allocation; details were reported). A “probably blinded assessment” was conducted using ratings made under clearly blind conditions (such as a placebo-controlled trial) or made by an adult unlikely to be aware of allocation (details were reported).

Sensitivity analyses were conducted to assess the impact of background ADHD medication. Meta-regression was used to assess the effects of lower quality trials on the effect sizes.

**Results of the review**

Fifty-four RCTs (3,126 participants; range 14 to 290) were included in the review. Nine trials scored 5 for quality, 12 scored 4, 14 scored 3, 13 scored 2, and six scored 1.

**Dietary interventions:** There were statistically significant effects in favour of restricted elimination diets for the most proximal assessment (SMD 1.48, 95% CI 0.35 to 2.61; seven RCTs; I²=95%), but the results were not significant, compared with controls, in the probably blinded assessment.

There were statistically significant effects in favour of artificial food colour exclusions for both the most proximal assessment (SMD 0.32, 95% CI 0.06 to 0.58; seven RCTs; I²=0) and the probably blinded assessment (SMD 0.42, 95% CI 0.13 to 0.70; seven RCTs; I²=13%). The sensitivity analysis of trials with no or low medication found no statistically significant difference between groups (four RCTs).

There were positive treatment effects for free fatty acid supplementation for both the most proximal assessment (SMD 0.21, 95% CI 0.05 to 0.36; 11 RCTs; I²=0) and the probably blinded assessment (SMD 0.16, 95% CI 0.01 to 0.31; 11 RCTs; I²=0) Sensitivity analysis of trials with no or low medication found similar effects.

**Psychological interventions:** Statistically significant treatment effects were reported for the most proximal assessment for cognitive training (SMD 0.64, 95% CI 0.33 to 0.95; six RCTs; I²=28%), neurofeedback (SMD 0.59, 95% CI 0.31 to 0.87; eight RCTs; I²=6%), and behavioural interventions (SMD 0.40, 95% CI 0.20 to 0.60; 15 RCTs; I²=54%), but not for the probably blinded assessments and not in the sensitivity analyses.

The meta-regression did not find that large effect sizes were more likely in trials with low quality scores.

**Authors’ conclusions**

Free fatty acid supplementation and artificial food colour exclusion appeared to have benefits for ADHD symptoms, but the effects of the supplementation were small and those of the exclusion might have been limited to patients with food sensitivities. The evidence for the value of behavioural interventions was only from unblinded ratings made by people likely to have an investment in treatment success.

**CRD commentary**

The review question was clear, with appropriately defined inclusion criteria. Several relevant sources were searched, with some efforts to reduce language bias. The inclusion of only published studies means that some data may have been missed. Trial quality was assessed and the results were reported for each trial, with just over half being of fair to excellent quality. Efforts were made throughout the review to reduce reviewer error and bias.

The methods of analysis appear to have been appropriate and some efforts were made to explore statistical heterogeneity. The authors highlighted a number of limitations in the evidence, including variation in ages of participant groups, some participants received medication with the intervention, differences between interventions, and a wide range of control conditions.

The authors’ conclusion on the effectiveness of the interventions reflects the evidence presented and is likely to be reliable, but their caveat that the benefits of artificial food colour exclusions could be limited to patients with food sensitivities was not derived from this evidence.

**Implications of the review for practice and research**

**Practice:** The authors stated that better evidence from blinded assessments was required for behavioural interventions, neurofeedback, cognitive training, and restricted elimination diets, before they could be supported as treatments for ADHD.
Research: The authors stated that robust randomised controlled trials, with ecologically valid outcome measures, were needed, particularly for psychological treatment. Trials should assess a broad range of child, parent and family related functional outcomes, and assess medication-naive patients, but this could introduce bias into an analysis. They recommended that psychological therapy directly targeting neuropsychological processes should be investigated.

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