Cognitive effects of immediate-release methylphenidate in children with attention-deficit/hyperactivity disorder

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CRD summary
This review assessed the cognitive effects of immediate-release methylphenidate in children with attention-deficit/hyperactivity disorder. The authors conclude that variability in outcomes across studies may be explained by a number of clinical and methodological factors. The review has several methodological weaknesses and it is unclear whether the results of the included studies and their subsequent synthesis can be relied upon.

Authors' objectives
To evaluate the nature, magnitude and types of cognitive effects of immediate-release methylphenidate in children with attention-deficit/hyperactivity disorder (ADHD).

Searching
MEDLINE and PsycINFO were searched; the search terms were provided but not the search dates. The aim was to identify studies published since a 1993 review, so presumably the searches were from 1992/1993 onwards. The contents tables of at least five journals that commonly publish articles on the pharmacotherapy of ADHD were also reviewed.

Study selection

Study designs of evaluations included in the review
Comparative studies with at least 10 children in the intervention and control group were eligible for inclusion.

Specific interventions included in the review
Studies comparing immediate-release methylphenidate with placebo were eligible for inclusion. The majority of the included studies used a single dose immediate-release methylphenidate that was not varied based on patient characteristics.

Participants included in the review
Studies of children who met formal diagnostic criteria for ADHD or attention-deficit disorder, or who were described as hyperactive or hyperkinetic, were eligible for inclusion. Studies were excluded if all the participants had a single co-morbid disorder. The age range of the children in most of the included studies was 6 to 12 years, though some studies included older children. The clinical population appeared to vary between studies. Participants had ADHD, ADHD combined type or ADHD inattentive type. The prevalence of co-morbid disorders ranged from 40 to 90% and included conditions associated with cognitive impairment independent of ADHD.

Outcomes assessed in the review
Studies assessing performance on cognitive tasks were eligible for inclusion. A wide variety of cognitive measures were used across the included studies.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Studies were defined as having a positive treatment response where there was a statistically significant improvement in performance on any of the cognitive measures.

**Methods of synthesis**

How were the studies combined?
The studies were discussed in a narrative synthesis. Cognitive tests were grouped into one of ten cognitive domains and the proportion of studies reporting a positive medication effect was calculated.

How were differences between studies investigated?
Differences between the studies were tabulated.

**Results of the review**

Forty studies (n=1,684) were included; 30 were described as double-blind randomised controlled trials (RCTs), 25 of which were crossover trials. Two further studies were RCTs but it was unclear whether the remaining controlled studies were randomised.

Following treatment with methylphenidate, 63.5% of studies found improvement in some aspect of cognitive function, whereas 36.5% found no change or decline in function. The highest rates of positive response (in at least two-thirds of studies) were on tasks assessing saccadic eye movements, planning/cognitive flexibility, attention/vigilance and inhibitory control. Fifty-eight per cent and 50% of studies that evaluated tasks of memory and working memory/divided attention, respectively, noted improvement.

**Authors’ conclusions**
The variability in outcomes across studies may be explained by the differential effects of methylphenidate on brain function, individual variability in treatment response, methodological limitations and problems with aspects of the cognitive assessment.

**CRD commentary**

There was a clearly stated review question. Relevant sources were searched for studies though specific attempts were not made to identify unpublished studies, thus introducing the risk that studies not reporting a positive effect were missed. Study quality was not assessed and the authors did not report using standard review methods to minimise error and bias in the study selection and data extraction processes.

Relevant details of the included studies were provided. However, in relation to the outcomes, the authors only reported whether or not there was a statistically significant improvement. It is unclear whether this was in relation to between-group or within-group comparisons. As the authors acknowledged, failure to find a positive effect may simply have reflected low statistical power. The authors’ conclusions, which mainly relate to the variability between studies, seem reasonable given the evidence presented. However, due to methodological weaknesses it is unclear whether the results of the included studies and their subsequent synthesis can be relied upon.

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

Practice: The authors did not state any implications for practice.

Research: The authors stated that further research is required to assess the effects on cognition of extended-release methylphenidate and other stimulants such as dextroamphetamine and non-stimulant medications. Reliable and valid cognitive tests suitable for repeat testing in children should be used.
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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.