

# Equivalent response to methylphenidate in children with ADHD plus anxiety and those with ADHD only

Diamond IR, Tannock R, Schachar RJ. *Response to methylphenidate in children with ADHD and comorbid anxiety. J Am Acad Child Adolesc Psychiatry* 1999 Apr;38:402-9.

## Question

Does comorbid anxiety moderate the response to methylphenidate in children with attention deficit hyperactivity disorder (ADHD)?

## Design

Randomised, double blind, placebo controlled, trial with 4 months follow up.

## Setting

An outpatient, referral based, assessment and treatment programme for ADHD in a university clinic at The Hospital for Sick Children, Toronto, Ontario, Canada.

## Patients

91 children between 6 and 12 years of age (mean age 8 y, 81% boys) with a confirmed diagnosis of ADHD beginning before 7 years of age were included. Exclusion criteria were: attended a full time residential or day treatment programme, received regular medication for a medical problem, had a primary anxiety or affective disorder (ie, the child required treatment for these disorders first), or had a chronic medical condition including a tic disorder or Tourette's syndrome. 38 children had comorbid anxiety disorder.

## Intervention

Children and their families were assigned to 1 of 4 treatment conditions: (1) methylphenidate plus parent training, (2) methylphenidate plus parent support, (3) placebo plus parent training, or (4) placebo plus parent support. Methylphenidate was titrated

to a dose of 0.7 mg/kg twice daily. The 2 methylphenidate groups (n=46) and the 2 placebo groups (n=45) were combined because drug effect was evaluated at the end of 4 months whereas the parent groups lasted for 12 months.

## Main outcome measures

Aggressiveness and hyperactivity measured using the IOWA Conners rating scale (IOWA-C); quality of child behaviour measured using the Telephone Interview Probe (TIP); and side effects. All measures were collected over the telephone.

## Main results

No differential response to methylphenidate or placebo existed between children with ADHD plus comorbid anxiety disorder and children with ADHD only on any side effect (affective, over-focusing, physiological, or tics) or behavioural measures (aggression, hyperactivity, inattention, impulsive, oppositional, or situations). The study had a power of 80% to detect an effect size of 1 (a 1 SD difference between any of the study groups in their response over time).

## Conclusion

Comorbid anxiety disorder did not influence development of side effects or behavioural response to methylphenidate in attention deficit hyperactivity disorder.

Source of funding: Medical Research Council of Canada.

For correspondence: Dr R J Schachar, Department of Psychiatry, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario M5G 1X8, Canada. Fax +1 416 813 6565.

## Commentary

The study by Diamond *et al* refutes a commonly held notion that comorbid anxiety disorder moderates the response of ADHD to stimulants. Methodological issues, however, may have produced a type 2 error.

Two components of this study need to be addressed for relevance to clinical practice. Firstly, the children had problems with anxiety as detected either by self report (Revised Children's Manifest Anxiety Scale) or by parental diagnosis (Parent Interview for Child Symptoms). Only 2 children were positive on both reports. Children with primary anxiety disorders were not included, which may affect the generalisability of the findings. Moreover, the authors do not report what diagnosable anxiety disorders (impairing conditions) the children showed (separation anxiety disorder or overanxious disorder). If all the children failed to meet minimum criteria for a disorder (meaning they were

not impaired by their anxiety), then failure to find a moderating effect could be a type 2 error.

Secondly, the authors only report no difference for mean scores between the 2 groups. They do not provide the response rates to placebo and methylphenidate for children with ADHD compared with those with ADHD plus comorbid anxiety disorder which would have been helpful in clinical interpretation. With effect sizes for methylphenidate reported to be 0.5 for parents and 1.0 for teachers,<sup>1</sup> it would have been simple to report whether response rates were similar. In this study, calculations suggest much lower effect sizes for ADHD plus comorbid anxiety. Clinicians might view this report with more caution if the response rates to the drug were low or the response rates to placebo were high—2 problems that have been raised by other investigators working with

children with ADHD plus comorbid anxiety.

The clinical application of these study results is for clinicians to measure physiological symptoms before initiation of pharmacological treatment to avoid incorrectly attributing them to treatment. In light of subsequent studies that show that *DSM-IV* diagnosed anxiety disorder moderates the treatment response of children with ADHD (ie, improves response to behavioural treatments), it may influence the choice of treatment modalities.<sup>2</sup>

Laurence Greenhill, MD  
New York State Psychiatric Institute  
New York, New York, USA

- 1 Spencer T, Biederman J, Wilens T, *et al*. Pharmacotherapy of attention-deficit hyperactivity disorder across the life cycle. *J Am Acad Child Adolesc Psychiatry* 1996;35:409-32.
- 2 The MTA Cooperative Group. Moderators and mediators of treatment response for children with ADHD: the MTA Study. *Arch Gen Psychiatry*; in press.