Managing attention deficit/hyperactivity disorder: unmet needs and future directions

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Arch Dis Child 2005;90(Suppl 1):i19–i25. doi: 10.1136/adc.2004.059352

The management of attention deficit/hyperactivity disorder (ADHD) requires a multimodal approach. Although shared-care protocols are suggested, uptake by general practice has been tentative. Behavioural management, both on its own and in combination with pharmacotherapy, reduces core symptoms and associated behaviours, such as oppositional defiant disorder (ODD). Links with education and social support are also important for helping children and their families. Psychostimulants have shown to be effective in the treatment of ADHD, however, their short duration of action highlights potential limitations. Other drugs used in the management of ADHD and comorbid disorders include antidepressants, clonidine and its analogues, newer atypical neuroleptics, and atomoxetine, a novel, non-stimulant therapy that has potential to fulfil some unmet treatment needs. Further research is needed in preschool children, girls, those with epilepsy, young adults, and in those with associated sleep disturbance. Selected rating scales and careful history taking, allied to close links with schools, are vital for the initial and ongoing assessment of ADHD and its comorbidities.

- Psychological and behavioural strategies.
- Social support, such as parent support groups, financial assistance, and respite care.
- Appropriate educational strategies and support in school, including help for children with coordination difficulties.
- Discussion and consideration of pharmacotherapy.

Clinicians responsible for the diagnosis and management of ADHD are therefore responsible for multidisciplinary liaison and contact with a number of other professionals and agencies. Because of the considerable ADHD caseload and the need for long term treatment, clear communication and regular contact with general practice is mandatory. Consequently, shared-care protocols are suggested by the Scottish Intercollegiate Guidelines Network (SIGN) and the National Institute for Clinical Excellence (NICE), an example of which is shown in box 1.^{3,4} Anecdotal evidence suggests that the uptake of such shared arrangements has been slow, and limited published studies from the UK indicate that many in general practice remain reluctant to refer to, or become involved in, joint management. Reports suggest that many primary care teams lack confidence in this area and in supervising follow up care; understandably they feel that further education and training are important before taking on these responsibilities.^{5–8} Despite the high prevalence and long term implications of ADHD and comorbid disorders, commitment by GPs to training in this area and contribution to shared care remain disappointing, as judged from experience in the UK.

BEHAVIOURAL MANAGEMENT

Behavioural management of ADHD, using contingency measures both at home and at school, has been shown to be effective, resulting in reduced symptoms, defiance, and conduct problems, with enhanced self esteem and academic improvements. Such management must be sustained over time in order to be effective. It should include strategies to simplify, shorten, and highlight tasks, positive and negative reinforcement, proper use of “time out”, token economies, and home/school diaries. Appropriate support for associated learning difficulties as part of an individualised learning package is also essential. Behavioural techniques have a reasonably

This article aims to provide an overview of current treatments for attention deficit/hyperactivity disorder (ADHD) and comorbid disorders from the perspective of a UK based clinician who, in common with many colleagues, sees and manages large numbers of children and young people with this challenging condition. The evidence base is discussed where relevant, highlighting gaps in knowledge, treatment provision, and research. The paper is not intended as an in-depth review of evidence based technologies, but seeks to complement other articles in this supplement.

ADHD represents a common developmental disorder of children and young people, often persisting into adulthood. Comorbid problems are common,^{1,2} therefore long term management invites a so called “multimodal” approach that helps to reduce ADHD symptoms, but also allows treatment of these associated areas of difficulty (figs 1 and 2).

The cornerstones of long term multimodal management³ are:

- “Psychoeducation”—information, explanation, and counselling about ADHD for children, parents, and others.

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Abbreviations: NICE, National Institute for Clinical Excellence; ODD, oppositional defiant disorder; SIGN, Scottish Intercollegiate Guidelines Network; SSRI, selective serotonin reuptake inhibitor.

Figure 1 ADHD comorbidities in the MTA study.¹ ODD, oppositional defiant disorder.

strong evidence base, and can be taught for home and school use.^{9–11} In comparison, individualised cognitive behavioural therapy does not appear to be as effective.^{3, 12}

Following the Multimodal Treatment study of ADHD (MTA)¹ there was a risk that behavioural treatments for ADHD would be downgraded in importance, or even abandoned.^{13–15} However, there were significant improvements in the behavioural treatment arm of this study, and when used alongside pharmacotherapy, “combined” treatment was more acceptable to parents and allowed lower doses of medication. Other social, behavioural, and educational gains were also seen, emphasising the importance of “multimodal” management. Adherence to “combined” treatment, avoiding the temptation for parents to neglect

Figure 2 Child's exercise book with adverse teacher comments.

Box 1 Sample shared-care protocol for the management of ADHD

Aspects of care for which the paediatrician and/or psychiatrist is responsible

- Assessment and diagnosis of children with ADHD.
- Initiation of psychostimulant therapy and supply of the medicines for one further month after the dose has been stabilised.
- Patient monitoring—initially every three months, then every six months in the longer term. This includes height, weight, and blood pressure.
- Discontinuation—advising the GP when psychostimulants should be discontinued in children receiving long term drug therapy. The specialist will provide necessary supervision and support during the drug discontinuation phase.
- Updating the patient held monitoring sheet.
- Continuing supply of psychostimulant medication for children under 6 years.

Aspects of care for which the general practitioner is responsible

- Prescribing psychostimulants once the patient is stabilised.
- Liaising with the paediatrician/psychiatrist regarding any complications in treatment.

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behavioural approaches and become too reliant on medication (“Doctor, your pills aren’t working!”), is less likely if adequate time is invested in psychoeducation.¹⁶ Recent research does, however, add fuel to the debate regarding the relative importance of pharmacotherapy versus behavioural and other supports for ADHD. A two year, dual centre, randomised study of 7–9 year old children with methylphenidate responsive ADHD found no “extra” improvement in behavioural, academic, social and emotional adjustment, or parental practices following intensive add-on multimodal psychosocial treatments.^{17–21}

Further studies of similar design would be of considerable interest to examine these important questions further. Behavioural support for ADHD is expensive, time consuming, and potentially burdensome for many children and families and, in practice, compliance and adherence are often poor. The evidence base for effectiveness remains significantly weaker than for medication approaches.

SOCIAL SUPPORT AND COMMUNITY INTERVENTION

On a day to day basis, the families of children and young people affected by ADHD are subjected to considerable stress and pressure associated with the disorder, particularly when ODD or conduct disorder are also present.²² Families show differing capacities to cope and this often changes over time. Provision of support beyond both the extended family and friends frequently forms an important part of multimodal management. The need for social support must be considered on an individual basis and may include befriending, self help groups, respite, and financial help. All too often in clinical practice in the UK we witness a shortfall in such provision; we need to continue to press for and advocate increased

Figure 3 Caricatures of ADHD, particularly in girls, are not supported by objective research. Reproduced by kind permission of *Private Eye* magazine.

recognition, planning, and resources for ADHD care within social services.

LINKS WITH EDUCATION

Dialogue and regular contact with schools is pivotal, avoiding potential disconnection²³ between health and education, and to ensure that performance and behaviour in school are optimised. Teams that include clinicians able to contribute personally to school review meetings are in a strong position not only to exchange views and information, but also to inform and educate about ADHD. Furthermore, where necessary they can advocate on behalf of individual children. Within the school setting, particular attention may need to be paid to girls (fig 3). Reports suggest that the pattern of ADHD in girls is associated with intellectual impairment, lower levels of hyperactivity and less challenging behaviour; thus there is a risk of these children being ignored or overlooked because they are not causing trouble in classes.^{24–25} Lastly, children and young people should be afforded adequate privacy within the school environment for receiving their medication. Anecdotal evidence suggests that this is not always the case, with potential for embarrassment, increased anxiety, and reduced compliance.

PHARMACOTHERAPY

Psychostimulants

Research into the effectiveness and safety of psychostimulants is distinguished overall by quantity²⁶ rather than quality.^{27–28} Over time, however, a sufficient number of studies of adequate design have provided strong evidence that short acting stimulants are effective in reducing core ADHD symptoms and that side effects are predictable and seldom serious.^{3–29–30} Although long term, placebo controlled studies are not feasible, there is some evidence that behavioural and cognitive gains are sustained over the longer term.^{18–19–31–32} Accordingly, at the time of writing, NICE (2000) and SIGN (2001) guidelines recommend stimulants as “first line” treatment for core ADHD symptoms in children and young people.^{3–4} This approach is also supported by the recently upgraded European Guidelines for the management of Hyperkinetic Disorder.³³

The limitations of currently available short acting stimulant preparations are well documented.^{3–34–35} These include appetite suppression, potential long term growth concerns,³⁶ insomnia, headache, dizziness, and abdominal pain. Less frequent side effects include anxiety, irritability, proneness to

crying, and emergence of, or increase in, motor tics. Stimulant side effects are generally predictable and often relatively minor. If present, they can be tolerated by some children over a number of years.³¹ However, in other children (probably up to around 30%) medication will prove to be ineffective, or side effects will lead to withdrawal of treatment.

Compliance with short acting stimulants may be adversely affected by the requirement for multiple dosing through the day;³⁷ additionally, observed “acute tolerance” results in potential loss of effectiveness and a need to give larger doses (for example, at lunchtime and late afternoon).³⁸ Practical problems with regard to storage and administration of medication in school, concerns about diversion of medication supplies, and pupil embarrassment all contribute to a risk of medication being missed. Other relevant and potentially important treatment gaps occur in the early morning before medication is given or can take effect, and in the evening, when the re-emergence of ADHD behaviours has a particular impact on life and relationships at home.

Abuse potential with stimulants looms large in the media, but it is infrequent, and has been overstated. Indeed, evidence strongly suggests that long term stimulant treatment may be a protective factor against substance abuse in adolescence and early adulthood.³⁹ Unfortunately, parental, public, and professional concern regarding stimulant use remain, as does the dismissal of ADHD as a valid diagnosis.⁴⁰ Consequently, the so called “Ritalin Wars” continue.⁴¹ Robust media skills are important if clinicians are to convey the importance of early recognition and proper management of ADHD, backed by reasoned scientific argument.^{42–44}

Sustained release methylphenidate preparations available in the UK include an osmotic controlled release formulation (OROS-methylphenidate (Concerta XL)), and beaded release system (Equasym XL; currently only available on a special license basis). These products offer advantages over their short acting equivalent, with evidence of equal efficacy and tolerability in clinical trials.^{38–45–47} The pharmacokinetic profiles of the two preparations differ,⁴⁸ with more methylphenidate released early in the day with the beaded release preparation and more available later in the day with the osmotic preparation. Once-daily dosing removes the requirement to seek and receive medication in school, removing much potential embarrassment and stigma;⁴⁹ it is also likely to improve compliance. Moreover, issues surrounding storage, safety, and diversion in school are also removed. Unfortunately, the efficacy and advantages of these medications do not extend beyond a maximum of 8–12 hours. Thus, treatment gaps remain in the early morning and evening, and the risk of disrupted sleep persists.

Other drugs used in the management of ADHD and comorbid disorders

In the UK, tricyclic antidepressants (TCAs) are presently recommended as a second line treatment for the reduction of ADHD symptoms in patients where stimulants are ineffective or poorly tolerated.⁵⁰ Extensive use has possibly been limited because of concern about side effects and potential cardiotoxicity, reflecting the narrow therapeutic index of this class of drugs.³

A number of alternative medications have been investigated for effectiveness in ADHD management; those most frequently used in clinical practice are summarised in table 1. Comorbid disorders, such as anxiety, depression, tics, and/or poor response to stimulants or TCAs, support consideration of these drugs, albeit mostly “off license” either as monotherapy or as part of rational combined treatment under relevant specialist supervision.³ The use of

Table 1 Alternative medications for ADHD and comorbid disorders in children and young people

Medication	Putative mechanism	Comments
Clonidine, guanfacine, and lofexadine	Alpha-noradrenergic agonists (Guanfacine and lofexadine are less sedating)	Limited studies, some when in combination with methylphenidate. May be useful for tics, aggression, and sleep problems. ⁹⁸⁻¹⁰⁵
Bupropion	Dopamine/noradrenaline agonist	Very limited studies. Antidepressant effects; risk of seizure exacerbation. ¹⁰⁶⁻¹⁰⁷
SSRIs	Serotonin reuptake inhibition	Limited studies in ADHD with comorbid depression. Now limited to fluoxetine in the UK (see text). ¹⁰⁸⁻¹⁰⁹ Beware of increased agitation with fluoxetine.
Venlafaxine	Serotonin/noradrenaline reuptake inhibition	Very limited studies. Possible indication for comorbid mood and anxiety. ¹¹⁰
Risperidone	Dopamine receptor blocker	No studies in ADHD, but supported by RCPCH's <i>Medicines for Children</i> . Emergent literature supports effectiveness for control of aggression, tics, and in autism (see text). Appetite stimulation and weight gain common.
Atomoxetine	Long acting selective noradrenergic reuptake inhibition with parallel effects on prefrontal cortex dopamine pathways	Recent placebo controlled studies (see text). Positive effects on mood, anxiety, and sleep possible. Slow onset of action but 24 hour effect.

SSRI, selective serotonin reuptake inhibitor.

Please note that all medications noted above are currently unlicensed for use in ADHD, although a UK license for atomoxetine was granted in May 2004.

selective serotonin reuptake inhibitors (SSRIs), risperidone, and atomoxetine deserves special mention.

The paediatric use of SSRIs in the UK is now restricted to the prescription of fluoxetine, at a time when the evidence base and role of this class of medication for the treatment of depression (often comorbid with ADHD) is being questioned.⁵¹⁻⁵³

Although there are no systematic studies of the atypical neuroleptic risperidone for the treatment of ADHD, anecdotal evidence suggests that it is used by clinicians in many specialist centres, particularly for treating aggression in ADHD, Tourette's Syndrome, and for children with autism. Such use is supported by an increasing number of controlled trials.⁵⁴⁻⁵⁹

The use of atomoxetine, a novel, non-stimulant, noradrenaline reuptake inhibitor is discussed more fully elsewhere in this supplement. Trial evidence and clinical experience in the USA supports the effectiveness of atomoxetine in reducing ADHD symptoms in children and adolescents, with benefits that include once-daily dosing, "whole day" action, and positive effects on mood, anxiety, and sleep. Recent studies have shown that a once-daily dose of atomoxetine can offer symptom relief late into the evening and the following morning.⁶⁰ This continuous symptom relief promises to close some of the treatment gaps referred to earlier in the discussion of neurostimulant therapy. Furthermore, this broader efficacy may have an associated positive impact on self esteem, and social and family functioning, without a requirement for *combined* treatments.⁶¹⁻⁶² Atomoxetine was approved by the US Food and Drug Administration in November 2002 for treatment of children, adolescents and adults with ADHD, and was licensed for use in the UK in May 2004.

NUTRITIONAL APPROACHES

Advocates of dietary modification for the management of behavioural problems in children, including ADHD, have been remarkably persistent, despite a lack of scientific evidence of acceptable quality.²³⁻³³⁻⁶³ A very limited number of adequately designed studies describe behavioural or cognitive improvements with additive-free diets in a small percentage of children, particularly preschoolers, with changes significantly less than those reported (and experienced) with neurostimulant treatment.⁶⁴⁻⁶⁶

Studies of dietary effects on behaviour pose significant methodological challenges and at the present time it would be inappropriate, for example, to extrapolate results obtained in preschool children and apply them to the general older population of children and young people with ADHD.⁶⁷ The same scientific rigour applied to research into medications needs to be applied to dietary research.

The prospect of long term medication, however, continues to make many patients uneasy and results in a search for treatments perceived as "natural", or "safer" than drugs.⁶⁸ Special diets require extra work and often expense for a family who may already be hard pressed on account of their child's behaviour. Taking into account the present paucity of evidence and the difficulty often experienced in persuading children and adolescents to comply with restricted diets, dietary management is not recommended, except possibly in a relatively small number of preschool children; in some of this age group, a diagnosis of ADHD may not in any event have been definitely confirmed. If so persuaded, for example, in response to parental pressure, and in some cases motivated by a need to maintain trust and a "therapeutic alliance", a food diary approach allied to regular review can be helpful to identify those children in whom continuing dietary manipulation is justified.³³ This is an area where fads abound, but where further large scale unbiased study is necessary to inform future practice.

OTHER CHALLENGES IN ADHD MANAGEMENT IN CHILDREN AND YOUNG PEOPLE

ADHD typically begins in early childhood, but unfortunately it has not been widely studied in preschool children. Increased attention to accurate and early diagnosis may improve long term outcome. There is also increasing evidence for effectiveness of neurostimulants in ameliorating core symptoms in this age group, at a time when medication remains off license for children under 6 years of age.⁶⁹⁻⁷⁰ Further research and treatment guidance for this age group is needed.

In addition to showing a complex association with behavioural and learning difficulties, children and young people with epilepsy also show increased rates of reported ADHD symptoms.⁷¹ Potential contributions include psychological adjustment to epilepsy, learning difficulty, anti-epileptic drug effects, and the type of underlying epilepsy or

brain disorder. This is an area of clinical practice that would benefit considerably from more research and treatment guidance. Present evidence does not indicate that neurostimulants should be withheld from patients with epilepsy and confirmed ADHD.⁷²

For adolescents and young adults who outgrow paediatric clinics, there is a national shortage of adequate diagnostic and treatment facilities for ADHD, in spite of strong evidence for the persistence of this disorder into adulthood and the value of ongoing treatment, including medication.^{73–74} It is incumbent on our colleagues in adult services to make good this shortfall as a matter of urgency. Previously, there were no licensed medications for the management of adult ADHD. However, atomoxetine is licensed for adults, as well as children and adolescents, and offers treatment across the lifespan.

Sleep disturbance, although not a diagnostic requirement, is common in ADHD, with a prevalence of up to 50%.⁷⁵ Recent studies stress the variability and instability of sleep in ADHD, noting that reported difficulties are multifactorial, resulting from behavioural and psychological effects, such as ODD, anxiety, mood disorders, and potential medication effects associated with prescribed neurostimulants.^{76–80} In practice, neurostimulants may need to be reduced or discontinued in the face of persistent insomnia. It is important to take time to identify the pattern and causes of sleep problems in individual cases to allow the most appropriate and effective treatment.^{81–84} Evidence based treatment guidelines for the management of sleep in ADHD are lacking at present.

HOW ADHD IMPROVEMENTS ARE MONITORED AND ASSESSED

At initial outpatient review, any changes in ADHD and associated behaviours as a result of treatment are often very clear (one way or the other) by observing general appearance, demeanour, and interaction—particularly between child and parents.²⁹ Further careful history taking is, however, necessary for clarification, supplemented by selective use of appropriate rating scales. When time allows, these can be useful for patient monitoring, audit, and accountability, but they are not a substitute for clinical intuition, experience, or history taking.⁸⁵

Although there are many to choose from,⁸⁶ frequently used rating scales based on DSM-IV criteria include the ADHD Rating Scale (ADHD-RS),^{87–88} and Conners' Parent and Teacher Rating Scales revised versions.^{89–90} Conners' Scales also allow exploration of other domains including oppositionality, learning difficulties, somatic symptoms, socialisation, and anxiety. A similar range of extended difficulties can be identified using the "Strengths and Difficulties Questionnaire", popular in the UK.⁹¹

Other diagnostic and monitoring questionnaires are increasingly used in research to examine broader issues such as physical, emotional, and social wellbeing, including self esteem and family function. The use of devices that attempt to address these questions promises to significantly increase our insight into the overall impact of ADHD and its management on the quality of life for both children and their families. Examples include the Child Health Questionnaire,⁹² Child Health and Illness Profile-Child Edition (CHIP-CE),⁹³ Harter Self Esteem scale,⁹⁴ and a new rating scale under evaluation, the Daily Parent Rating of Evening and Morning Behaviours-Revised (DPREMB-R), which addresses specific behaviours in the evenings and early mornings.⁹⁵

Successful completion of ongoing trials, such as the multicentre Attention Deficit hyperactivity disorder Observational Research in Europe (ADORE) study, and an open label study of the potential broader effectiveness of

Box 2 Summary

- Pivotal importance of "psychoeducation" regarding ADHD for child, family, and professionals.
- Requirement for a clear multimodal and therefore multidisciplinary approach to ADHD management, incorporating comorbidities.
- Seek wider acceptance and use of "shared care" protocols; increase knowledge and awareness of ADHD in primary care.
- Maintain and augment liaison and contact with schools.
- Seek improvements in diagnostic, treatment, and follow up services for preschool children and young adults, including respite care and social support.
- Avoid "over medicalisation" of ADHD and its treatment. Avoid over reliance on medication at the expense of behavioural strategies.
- Important "treatment gaps" remain with current medication approaches (for example, mornings, evenings, sleep, comorbid aggression, anxiety, self esteem, family relationships, and quality of life). "Broader" sustained treatment effectiveness is needed to provide longer term amelioration of symptoms, with minimum side effects.
- Clearer representation and advocacy about ADHD and its treatment to the public and media.
- Research and audit in the UK and Europe (for example, on childhood epilepsy and ADHD; ADHD in girls; sleep; dietary effects; wider impact on family and society) are essential.

atomoxetine, which includes examples of these scales, seem likely to significantly improve our understanding of this challenging disorder.

CONCLUSIONS

A summary of the key points from this paper is shown in box 2. Briefly, proper "psychoeducation", allied to properly resourced multiagency and "multimodal" management remain pivotal if long term outcomes in ADHD are to improve.³ It is also important to avoid regarding currently available pharmacological approaches as a single or satisfactory solution to complex difficulties, focusing on the relief of daytime core ADHD symptoms, particularly in school. Significant treatment gaps persist, even with adequately applied multimodal approaches. In the future, a broader approach to symptom control (for example, through advances in psychopharmacology) to provide extended treatment effects, alongside consistent behavioural approaches may prove more effective and lead to further improvements in self esteem, social relationships, family functioning, sleep patterns, and overall quality of life. Continuing audit and good quality research will help to make this happen.^{3–96} There is a huge need for more UK based research into ADHD, at a time when recommendations for the management of hyperkinetic disorder in Europe are beginning to resemble more closely approaches to ADHD management in North America.³³ Increased networking and collaboration between centres and clinicians with an interest and expertise in ADHD, from child and adolescent mental health services and paediatrics, would help to generate research of adequate power and quality in the future. Enhanced training opportunities, such as the recent popular

and successful European Quality Training initiative (EINAQ),⁹⁷ should also help to maintain the quality of ADHD care based on sound and well researched practice.

REFERENCES

- 1 The MTA Cooperative Group. A 14-month randomised clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 1999;**56**:1073–86.
- 2 Pliszka SR. Psychiatric comorbidities in children with attention deficit hyperactivity disorder: implications for management. *Pediatr Drugs* 2003;**5**:741–50.
- 3 Scottish Intercollegiate Guidelines Network SIGN. No 52. *Attention deficit and hyperkinetic disorders in children and young people*. A National Clinical Guideline, June, 2001.
- 4 National Institute of Clinical Excellence (NICE). Technology Appraisal Guidance No 13. Guidance on the use of methylphenidate (Ritalin, Equasym) for attention deficit/hyperactivity disorder (ADHD) in childhood, October, 2000.
- 5 Klasen H, Goodman R. Parents and GPs at cross purposes over hyperactivity: a qualitative study of possible barriers to treatment. *Br J Gen Pract* 2000;**50**:199–202.
- 6 Ball C. Attention deficit hyperactivity disorder (ADHD) and the use of methylphenidate: a survey of the views of general practitioners. *Psychiatric Bull* 2001;**25**:301–4.
- 7 Sayal K, Taylor E, Beecham J, et al. Pathways to care in children at risk of attention deficit hyperactivity disorder. *Br J Psychiatry* 2002;**181**:43–8.
- 8 Thapar A, Thapar A. Is primary care ready to take on attention deficit hyperactivity disorder? *BMC Fam Pract* 2002;**3**:7.
- 9 Anastopoulos AD, Shelton TL, DuPaul GJ, et al. Parent training for attention-deficit hyperactivity disorder: its impact on parent functioning. *J Abnormal Child Psychol* 1993;**21**:581–96.
- 10 Pelham WE Jr, Wheeler T, Chronis A. Empirically supported psychosocial treatments for attention deficit hyperactivity disorder. *J Clin Child Psychol* 1998;**27**:190–205.
- 11 Barkley RA. Psychosocial treatments for attention-deficit/hyperactivity disorder in children. *J Clin Psychiatry* 2002;**63**(Suppl.12):36–43.
- 12 Abikoff H. Cognitive training in ADHD children: less to it than meets the eye. *J Learn Disabil* 1991;**24**:205–9.
- 13 Jensen PS. Fact versus fancy concerning the multimodal treatment study for attention deficit hyperactivity disorder. *Can J Psychiatry* 1999;**44**:975–80.
- 14 Pelham WE. The NIMH multimodal treatment study for attention deficit hyperactivity disorder: just say yes to drugs alone? *Can J Psychiatry* 1999;**44**:981–90.
- 15 Taylor E. Development of clinical services for attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 1999;**56**:1097–9.
- 16 Corkum P, Rimer P, Schachar R. Parental knowledge of attention deficit hyperactivity disorder and opinions of treatment options: impact on enrolment and adherence to a 12-month trial. *Can J Psychiatry* 1999;**44**:1043–8.
- 17 Klein RG, Abikoff H, Hechtman L, et al. Design and rationale of controlled study of long-term methylphenidate and multimodal psychosocial treatment in children with ADHD. *J Am Acad Child Adolesc Psychiatry* 2004;**43**:792–801.
- 18 Abikoff H, Hechtman L, Klein RG, et al. Symptomatic improvement in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *J Am Acad Child Adolesc Psychiatry* 2004;**43**:802–11.
- 19 Hechtman L, Abikoff H, Klein RG, et al. Academic achievement and emotional status of children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *J Am Acad Child Adolesc Psychiatry* 2004;**43**:812–19.
- 20 Abikoff H, Hechtman L, Klein RG, et al. Social functioning in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *J Am Acad Child Adolesc Psychiatry* 2004;**43**:820–9.
- 21 Hechtman L, Abikoff H, Klein RG, et al. Children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment: impact on parental practices. *J Am Acad Child Adolesc Psychiatry* 2004;**43**:830–8.
- 22 Johnston C, Mash EJ. Families of children with ADHD: review and recommendations for future research. *Clin Child Fam Psychol Rev* 2001;**4**:183–207.
- 23 National Institutes of Health Consensus Statement. *Diagnosis and treatment of attention deficit hyperactivity disorder*, November 16–18, 1998.
- 24 Gaub M, Carlson CL. Gender differences in ADHD: a meta-analysis and critical review. *J Am Acad Child Adolesc Psychiatry* 1997;**36**:1036–45.
- 25 Hinshaw SP. Preadolescent girls with attention-deficit/hyperactivity disorder: I. Background characteristics, comorbidity, cognitive and social functioning, and parenting practices. *J Consult Clin Psychol* 2002;**70**:1086–98.
- 26 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.
- 27 Miller A, et al. A review of therapies for attention deficit hyperactivity disorder. Ottawa: Canadian Coordinating Office for Health Technology Assessment, (CCOHTA), 1999.
- 28 McMaster University. *The treatment of attention deficit hyperactivity disorder*, Agency for Healthcare Research and Quality. Evidence Based report/Technology Assessment No 11. AHRQ. Pub No 00-E005. Rockville, MD, 1999.
- 29 Barkley RA. Hyperactive boys: stimulant effects on mother-child interactions. *J Child Psychol Psychiatry* 1989;**30**:379–90.
- 30 Gadow KD, Nolan EE, Sverd J, et al. Methylphenidate in aggressive-hyperactive boys: 1. Effects on peer aggression in public school settings. *J Am Acad Child Adolesc Psychiatry* 1990;**29**:710–18.
- 31 Charach A, Ickowicz A, Schachar R. Stimulant treatment over 5 years: adherence, effectiveness and adverse effects. *J Am Acad Child Adolesc Psychiatry* 2004;**43**:559–67.
- 32 National Institutes of Mental Health. Multimodal treatment study of attention deficit hyperactivity disorder. Follow up at 24 month outcomes of treatment strategies for attention deficit hyperactivity disorder. *Pediatrics* 2004;**113**:754–62.
- 33 Taylor E, Dopfner M, Sergeant J, et al. European clinical guidelines for hyperkinetic disorder—first upgrade. *Eur Child Adolesc Psychiatry* 2004;**13**(Suppl 1):17–30.
- 34 Barkley RA, McMurray MB, Edelbrock CS, et al. Side effects of methylphenidate in children with attention deficit hyperactivity disorder: a systematic placebo-controlled evaluation. *Pediatrics* 1990;**86**:184–92.
- 35 Campbell Daley K. Update on attention deficit hyperactivity disorder. *Curr Opin Pediatrics* 2004;**16**:217–26.
- 36 Joshi SV. Attention deficit hyperactivity disorder, growth deficits, and relationships to psychostimulant use. *Pediatr Rev* 2002;**23**:67–8.
- 37 Swanson J. Compliance with stimulants for attention-deficit/hyperactivity disorder. Issues and approaches for improvement. *CNS Drugs* 2003;**17**:117–31.
- 38 Swanson J, Gupta S, Lam A, et al. Development of a new once-a-day formulation of methylphenidate for the treatment of attention-deficit/hyperactivity disorder. Proof of concept and proof of product studies. *Arch Gen Psychiatry* 2003;**60**:204–11.
- 39 Wilens TE, Faraone SV, Biederman J, et al. Does stimulant treatment of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature. *Pediatrics* 2003;**111**:179–85.
- 40 BBC News. Public inquiry call over drug. 2 July 2001. Available at: <http://news.bbc.co.uk/1/hi/Scotland/1417080.stm>.
- 41 Diller LH. The Ritalin Wars continue. *West J Med* 2000;**173**:366–7.
- 42 Barkley RA. International Consensus Statement on attention deficit hyperactivity disorder. *Clin Child Fam Psychol Rev* 2002;**5**:89–111.
- 43 Timimi S, Taylor E. ADHD is best understood as a cultural construct. *Br J Psychiatry* 2004;**184**:8–9.
- 44 Double DB, Taylor E. Meanings and causes in ADHD. *Br J Psychiatry* 2004;**184**:453–4.
- 45 Pelham WE, Gnagy EM, Burrows-Maclean L, et al. Once-a-day Concerta methylphenidate versus three-times daily methylphenidate in laboratory and natural settings. *Pediatrics* 2001;**107**:e105.
- 46 Wolraich ML, Greenhill LL, Pelham W, et al. Randomised, controlled trial of OROS methylphenidate once a day in children with attention-deficit/hyperactivity disorder. *Pediatrics* 2001;**108**:883–92.
- 47 Greenhill LL, Findling RL, Swanson JM, the ADHD Study Group. A double-blind, placebo-controlled study of modified-release methylphenidate in children with attention-deficit hyperactivity disorder. *Pediatrics* 2002;**109**:e39.
- 48 Swanson JM, Wigal SB, Wigal T, et al. A comparison of once-daily extended-release methylphenidate formulations in children with attention-deficit/hyperactivity disorder in the laboratory school (the Comacs Study). *Pediatrics* 2004;**113**:e206–16.
- 49 Sleator EK, Ullmann RK, von Neumann A. How do hyperactive children feel about taking stimulants and will they tell the doctor? *Clin Pediatr* 1982;**21**:474–9.
- 50 Pliszka SR. Non-stimulant treatment of attention-deficit/hyperactivity disorder. *CNS Spectr* 2003;**8**:253–8.
- 51 Coghill D. Evidence-based psychopharmacology for children and adolescents. *Curr Opin Psychiatry* 2002;**15**:361–8.
- 52 Jureidini JN, Doecke CJ, Mansfield PR, et al. Efficacy and safety of antidepressants for children and adolescents. Clinical Review. *BMJ* 2004;**328**:879–83.
- 53 Vitiello B, Swedo S. Antidepressant medications in children. *N Engl J Med* 2004;**350**:1489–91.
- 54 McCracken JT, McGough J, Shah B. Risperidone in children with autism and serious behaviour problems. *N Engl J Med* 2002;**347**:314–21.
- 55 Pappadopoulos E, Macintyre IJ, Crismon ML, et al. Treatment recommendations for the use of antipsychotics for aggressive youth (TRAA). Part II. *J Am Acad Child Adolesc Psychiatry* 2003;**42**:145–61.
- 56 Scathill L, Leckman JF, Schultz RT, et al. A placebo-controlled trial of risperidone in Tourette Syndrome. *Neurology* 2003;**60**:1130–5.
- 57 King B, Zwi K, Nunn K, et al. Use of risperidone in a paediatric population: an observational study. *J Paediatr Child Health* 2003;**39**:523–7.
- 58 Gilbert DL, Batterson JR, Sethuraman G, et al. Tic reduction with risperidone versus pimozide in a randomised, double-blind, crossover trial. *J Am Acad Child Adolesc Psychiatry* 2004;**43**:206–14.
- 59 Findling RL, McNamara NK, Branicky LA, et al. A double-blind pilot study of risperidone in the treatment of conduct disorder. *J Am Acad Child Adolesc Psychiatry* 2000;**39**:509–16.
- 60 Kelsey D, Summer C, Casat C, et al. Once-daily atomoxetine in childhood ADHD: continuous symptom relief. Poster presented at the 50th American Academy of Child and Adolescent Psychiatry meeting, Miami, Florida, 14–19 October, 2003.
- 61 Kratochvil CJ, Vaughan BS, Harrington MJ, et al. Atomoxetine: A selective noradrenaline reuptake inhibitor for the treatment of attention-deficit/hyperactivity disorder. *Expert Opin Pharmacother* 2003;**4**:1165–74.
- 62 Michelson D, Faries D, Wernicke J, et al. & the Atomoxetine ADHD Study Group. Atomoxetine in the treatment of children and adolescents with

- attention-deficit/hyperactivity disorder: a randomised, placebo-controlled, dose response study. *Pediatrics* 2001;**108**:1–9.
- 63 **Dulcan M.** Practice Parameters for the assessment and treatment of children, adolescents and adults with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 1997;**36**(Suppl 10):85S–121S.
 - 64 **Wender EH.** The food additive-free diet in the treatment of behavior disorders: a review. *J Dev Behav Pediatr* 1986;**7**:35–42.
 - 65 **Mattes JA.** The Feingold Diet: a current reappraisal. *J Learn Disabil* 1983;**16**:319–23.
 - 66 **Bateman B, Warner JO, Hutchinson E, et al.** The effects of a double blind placebo controlled artificial food colourings and benzoate preservative challenge on hyperactivity in a general population sample of pre-school children. *Arch Dis Child* 2004;**89**:506–11.
 - 67 **Eigenmann PA, Haenggeli CA.** Food colourings and preservatives—allergy and hyperactivity. *Lancet* 2004;**364**:823–4.
 - 68 **Chan E, Rappaport LA, Kemper KJ.** Complementary and alternative therapies in childhood attention and hyperactivity problems. *J Dev Behav Ped* 2003;**24**:4–8.
 - 69 **DuPaul GJ, McGoey KE, Eckert TL, et al.** Preschool children with attention-deficit/hyperactivity disorder: impairments in behavioural, social and school functioning. *J Am Acad Child Adolesc Psychiatry* 2001;**40**:508–15.
 - 70 **Short EJ, Manos MJ, Findling RL, et al.** A prospective study of stimulant response in preschool children: insights from ROC analyses. *J Am Acad Child Adolesc Psychiatry* 2004;**43**:251–9.
 - 71 **Dunn DW, Austin JK, Caffrey HM, et al.** A prospective study of teachers' ratings of behavior problems in children with new-onset seizures. *Epilepsy Behav* 2003;**4**:26–35.
 - 72 **Scottish Intercollegiate Guidelines Network.** Diagnosis and management of epilepsies in children and young people. SIGN, 2005 (in press).
 - 73 **Barkley RA.** Diagnosis and treatment of attention deficit hyperactivity disorder. Long-term course, adult outcome and comorbid disorders. In: NIH Consensus Development Conference, Bethesda, MD, 16–18 November, 1998:57–60.
 - 74 **Vollmer S.** ADHD: it's not just in children. *Family Practice Recertification* 1998;**20**:45–68.
 - 75 **Corkum P, Tannock R, Moldofsky H.** Sleep disturbances in children with attention deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 1998;**37**:637–46.
 - 76 **Mick E, Biederman J, Jetton J, et al.** Sleep disturbances associated with attention-deficit hyperactivity disorder: the impact of psychiatric comorbidity and pharmacotherapy. *J Child Adolesc Pharmacol* 2000;**10**:223–31.
 - 77 **Gruber R, Sadeh A, Raviv A.** Instability of sleep patterns in children with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2000;**39**:495–501.
 - 78 **Owens JA, Maxim R, Nobile C, et al.** Parental and self report of sleep in children with attention-deficit/hyperactivity disorder. *Arch Pediatr Adolesc Med* 2000;**154**:549–55.
 - 79 **O'Brien LM, Ivanenko A, Crabtree VM, et al.** Sleep disturbances in children with attention-deficit/hyperactivity disorder. *Pediatr Res* 2003;**54**:237–43.
 - 80 **O'Brien LM, Ivanenko A, Crabtree VM, et al.** The effects of stimulants on sleep characteristics in children with attention-deficit/hyperactivity disorder. *Sleep Med* 2003;**4**:309–16.
 - 81 **Reed MD, Findling RL.** Overview of current management of sleep disturbances in children: I. Pharmacotherapy. *Curr Ther Res Clin Exp* 2000;**63**(Suppl B):B18–37.
 - 82 **Stores GA.** *Clinical guide to sleep disorders in children and adolescents*. Cambridge; Cambridge University Press, 2001.
 - 83 **Stores G.** Medication for sleep-wake disorders. *Arch Dis Child* 2003;**88**:899–903.
 - 84 **Meltzer LJ, Mindell JA.** Non-pharmacological treatments for pediatric sleepiness. *Pediatr Clin North Am* 2004;**51**:135–51.
 - 85 **Conners KC.** Clinical use of rating scales in diagnosis and treatment of attention-deficit/hyperactivity disorder. *Pediatr Clin North Am* 1999;**46**:857–70.
 - 86 **Collett BR, Ohan JL, Myers KM.** Ten year review of rating scales. V: Scales assessing attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2003;**42**:1015–37.
 - 87 **DuPaul GJ.** ADHD Rating Scale: Check lists, norms, and clinical interpretation. New York: Guilford Press, 1998.
 - 88 **Faries DE, Yalcin I, Harder D, et al.** Validation of the ADHD Rating Scale as a clinician administered and scored instrument. *J Atten Dis* 2001;**5**:107–15.
 - 89 **Conners CK, Sitarenios G, Parker JD, et al.** The Revised Conners' Parent Rating Scale (CPRS-R). Factor structure, reliability and criterion validity. *J Abn Child Psychol* 1998;**26**:257–68.
 - 90 **Conners CK, Sitarenios G, Parker JD, et al.** Revision and restandardisation of the Conners' Teacher Rating Scale (CTRS): factor structure, reliability and criterion validity. *J Abn Child Psychol* 1998;**26**:279–91.
 - 91 **Goodman R.** The strengths and difficulties questionnaire: a research note. *J Child Psychol Psychiatry* 1997;**38**:581–6.
 - 92 **Landgraf JM, et al.** The Child Health Questionnaire (CHQ): A user's manual. Boston: The Health Institute, New England Medical Center, 1996.
 - 93 **Riley AW.** Child Health and Illness Profile-Child Edition (CHIP-CE). Parent reported form. Baltimore: The Johns Hopkins University Press, 2001.
 - 94 **Harter S.** *Manual for self perception profile for children*. Denver, CO: University of Denver, 1985.
 - 95 **Sutton V, Sumner C, Allen AJ, et al.** Validity, reliability, and responsiveness of the DPREMB-R scale for ADHD. Poster presented at the 50th American Academy of Child and Adolescent Psychiatry, Miami, Florida, 14–19 October, 2003.
 - 96 **Hill P, Taylor E.** An auditable protocol for treating ADHD. *Arch Dis Child* 2001;**84**:404–9.
 - 97 **Rothenberg A, Danckaerts M, Dopfner M, et al.** EINAQ—a European educational initiative on attention-deficit hyperactivity disorder and associated problems. *Eur Child Adolesc Psychiatry* 2004;**13**(Suppl 1):131–5.
 - 98 **Steingard R, Biederman J, Spencer T, et al.** Comparison of clonidine response in the treatment of attention-deficit hyperactivity disorder with and without comorbid tic disorders. *J Am Acad Child Adolesc Psychiatry* 1993;**32**:350–3.
 - 99 **Wilens TE, Biederman J, Spencer T.** Clonidine for sleep disturbances associated with attention-deficit hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 1994;**33**:424–6.
 - 100 **Singer HS, Brown J, Quaskey S, et al.** The treatment of attention-deficit hyperactivity disorder in Tourette's Syndrome: a double-blind, placebo-controlled trial with clonidine and desipramine. *Pediatrics* 1995;**95**:74–81.
 - 101 **Hunt RD, Arnsten AF, Asbell MD.** An open trial of guanfacine in the treatment of attention deficit hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 1995;**34**:50–4.
 - 102 **Horrigan JP, Barnhill LJ.** Guanfacine treatment of attention-deficit hyperactivity disorder in boys. *J Child Adolesc Psychopharmacol* 1995;**5**:215–23.
 - 103 **Connor DF, Barkley RA, Davis HT.** A pilot study of methylphenidate, clonidine, or the combination in attention deficit hyperactivity disorder comorbid with aggressive oppositional defiant disorder or conduct disorder. *Clin Pediatrics (Phila)* 2000;**39**:15–25.
 - 104 **Tourette's Syndrome Study Group.** Treatment of attention deficit hyperactivity disorder in children with tics: a randomised, controlled trial. *Neurology* 2002;**58**:527–36.
 - 105 **Niederhofer H, Staffen W, Mair A.** A placebo-controlled trial of lofexidine in the treatment of children with tic disorders and attention deficit hyperactivity disorder. *J Psychopharmacol* 2003;**17**:113–19.
 - 106 **Barrickman LL, Perry PJ, Allen AJ, et al.** Bupropion versus methylphenidate in the treatment of attention-deficit hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 1995;**34**:649–57.
 - 107 **Conners CK, Casat CD, Gualtieri CT, et al.** Bupropion hydrochloride in attention-deficit hyperactivity disorder with hyperactivity. *J Am Acad Child Adolesc Psychiatry* 1996;**35**:1314–42.
 - 108 **Barrickman L, Noyes R, Kuperman S, et al.** Treatment of attention deficit hyperactivity disorder with fluoxetine: a preliminary study. *J Am Acad Child Adolesc Psychiatry* 1991;**30**:762–7.
 - 109 **Gammon GD, Brown TE.** Fluoxetine and methylphenidate in combination for treatment of attention deficit hyperactivity disorder and comorbid depressive disorders. *J Child Adolesc Psychopharmacol* 1993;**3**:1–10.
 - 110 **Olvera RL, Pliszka SR, Luh J, et al.** An open trial of venlafaxine in the treatment of attention-deficit hyperactivity disorder in children and adolescents. *J Child Adolesc Psychopharmacol* 1996;**6**:241–50.