Focus Issue.
The Management of ADHD in Children, Young People and Adults

Guest Editor: Dr Chinnaiah Yemula.
Consulting Editors: Professor Eric Taylor and Professor Peter Hill.
Editor-in-Chief: Professor Frank M.C. Besag.
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Foreword

Clinical and basic research on ADHD has increased dramatically over the past decade with more than 3,000 articles being published in English in scientific journals alone during the past 6 years. Capturing and briefly summarizing what is known about ADHD given so vast an archive of research is a difficult undertaking but it is one that I believe has been quite successfully accomplished in this volume entirely dedicated to the topic. This is a remarkable collection of papers on ADHD ranging from genetics to forensics, from ethics to therapeutics, from epidemiology to parent support and from neuroimaging to classroom teaching strategies, with much more as well. The range of authorships includes many of the international leaders in the field and the wide array of topics clearly reflects how vibrant the field of research and clinical practice remains. It is a pleasure to endorse such a representative and cutting edge volume such as this that will help to not only bring the reader up to date on trends within this field but also dispel many of the myths about ADHD and even improve both professional and public understanding of such a complex condition. Although the journal is aimed at general practitioners and trainees, a wide range of people, including parents, teachers, nurses, psychologists and consultant psychiatrists, are likely to find it of interest, not only because of the broad range of topics covered but also because of the succinct approach and clarity of expression that characterise so many of the papers.

It is both a great honour and a privilege for me to welcome you to the wealth of knowledge and wisdom in these pages.

Russell A. Barkley, Ph.D.
Clinical Professor of Psychiatry and Pediatrics
Medical University of South Carolina, Charleston, USA.
Editorial

It has been tremendously exciting to have the opportunity of editing this focus issue on ADHD. Although, between us, we have several hundred patient years of experience in managing ADHD, reading these papers has taught us so much.

ADHD is a complex condition. We have endeavoured to cover as wide a range as we could, both in terms of the authorship and in terms of the subject matter. As well as having papers from some of the leading international doctors in the field we have excellent contributions representing parents, teachers, psychologists, support workers and others. It would be impossible, in a brief editorial, to summarise the wonderful content in all of the 30 papers but there are certain themes that have arisen consistently.

First, the diagnosis of ADHD still leaves much to be desired. On one hand, some children are inappropriately labelled with the condition whereas on the other hand, many are left undiagnosed and untreated. In adults, the condition is often not even considered. In some cases the consequences of undiagnosed ADHD may be devastating. Academic and employment abilities may fail to be realised. The untreated impulsivity of ADHD may result in encounters with the law or even imprisonment. The rate of substance misuse is high in people with ADHD but is almost certainly lower if the condition is properly treated. Because girls with ADHD generally present with less obvious behavioural disturbance than boys with the condition, there seems to be a reluctance to diagnose girls, despite the fact that they might have major academic and other problems.

In the past, ADHD has been considered as a childhood condition and sometimes treatment has been stopped in the teenage years, despite the fact that it has been clear the ADHD has been ongoing from childhood. One of the striking findings that has become clear is that 30% to 70% of children with ADHD continue to have this condition into adulthood and reliable epidemiological studies estimate that around 3% of adults have ADHD, although most remain untreated. Adult ADHD clinics were previously a rarity but the need for adult ADHD services has now been specified clearly in the NICE guideline. This need remains largely unmet. Setting up these services remains a major challenge.

Although lip-service has been paid to the need for behavioural interventions and family support, these are often not provided. Recent research evidence indicates that for milder forms of ADHD behavioural intervention might be as effective as medication, although for severe ADHD medication should not be withheld.

Another key theme that has been emphasised in these papers is the importance of recognising and treating comorbidity. There are several conditions that are frequently comorbid with ADHD. In many cases both the ADHD and the comorbidity require treatment if the individual and family are to have a satisfactory quality of life.

Because ADHD is a complex condition, close cooperation between the key professionals and the families is essential. Clear ADHD Care pathways can help to ensure that all the appropriate issues are addressed. For children, the parent support group, parent training and the involvement of the teacher all play an important part. Family support groups can also be of value in the management of adults with ADHD.

In addition to being a highly educational experience for us, it has been a great privilege and pleasure to work with such a wonderful group of authors, including international leaders in the field. We hope that you will also derive enormous pleasure from having access to the wealth of information, insight and common sense that they have shared. The challenge for us all is to put this knowledge and wisdom into practice so as to provide better services for people with ADHD, who have so often been poorly served by professionals in the past.

Professor Frank M.C. Besag FRCP FRCPsych FRCPCH, Editor-in-Chief.
Dr Chinnaiah Yemula, Guest Editor.
Epidemiology of ADHD

Luis A Rohde, Rachel E. Verin, Guilherme V. Polanczyk

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Abstract

In this selective review of the literature, we present recent data on the epidemiology of Attention Deficit Hyperactivity Disorder (ADHD) across the life-cycle. The worldwide ADHD prevalence rates are around 5.3% in children and adolescents and 2.5% in adults. The literature suggests that 40 – 60% of affected children continue having the disorder during adulthood, depending on the criteria for persistence applied. Demographic correlates such as gender, socio-economic stratum and ethnicity impact on prevalence rates in the community. There are clear barriers for treatment access even in developed countries.

Key-words: ADHD, Hyperkinetic Disorder, prevalence, epidemiology.

Introduction

An understanding of the epidemiological aspects of ADHD may provide insights into its distribution and aetiology, as well as information for planning the allocation of funds in mental health services to deal with the disorder. ADHD is a neurobiological disorder with a pattern of persistent and impairing symptoms of inattention, hyperactivity and impulsivity affecting individuals across the life cycle (1).

First, it is important to note that our two main classification systems used for diagnosing mental disorders, the International Classification of Diseases, tenth revision (ICD-10) and Diagnostic and Statistical Manual of Mental Diseases, fourth edition, text revision (DSM-IV-TR) (2,3), employ different nomenclature and criteria to define the disorder. Although the list of symptoms and the evaluated constructs are very similar between DSM-IV-TR and ICD-10, differences emerge in the way the diagnosis is constructed. The ICD-10 uses the nomenclature of Hyperkinetic Disorder (HD) and requires both a minimum number of symptoms in all three dimensions (inattention, overactivity, and impulsivity) and presence of each symptom in at least two different settings. Furthermore, the ICD-10 has mood, anxiety and developmental disorders as exclusion diagnoses. DSM-IV-TR allows the establishment of ADHD diagnosis in the presence of mood and anxiety disorders, but not of pervasive developmental disorders (4).

Prevalence

Numerous cross-sectional, clinical and longitudinal studies have been conducted globally in attempts to determine the prevalence of ADHD in the community for both children and adults. Studies have found rates ranging from as low as 0.9% to as high as 20% (5). In an effort to gain a better understanding of the prevalence of ADHD and the reasons for this variability, Polanczyk et al. (6) conducted a comprehensive systematic review and meta-analyses including 102 investigations with non-referred samples of children and adolescents from all continents and documented a worldwide pooled prevalence of ADHD of 5.29% (CI95% = 5.01 – 5.51%). However, a significant heterogeneity among rates emerged. Through a meta-regression approach, the authors demonstrated that the three main reasons for the variability in prevalence rates were: information source used, presence or not of a definition of impairment and diagnostic system utilised (the largest differences were detected among studies using DSM-IV and ICD-10). Thus, general practitioners, paediatricians and child psychiatrists in the United Kingdom should expect to find fewer cases using ICD-10 criteria for HD than their North-
American colleagues using DSM-IV criteria for ADHD. However, the findings from the study from Polanczyk et al. (6) suggest that when methodological differences are adjusted among investigations, no significant differences are detected in prevalence rates among Europe and North America. After this extensive review, two very relevant studies were published on the prevalence of ADHD in children and adolescents in the US. Merikangas et al. (7) found a 12-month prevalence of ADHD around 8.6% (±0.7) in a nationally representative probability sample of non–institutionalised children and adolescents (8–15 years of age) from the National Health and Nutrition Examination Survey. Interestingly, Merikangas et al. (8) conducted another nationally representative survey with 10,123 adolescents aged 13 to 18 years from the National Comorbidity Survey – Adolescent Supplement, documenting a very similar ADHD prevalence of 8.7% (±0.7). However, lifetime prevalence was assessed in this study.

There is a strong and growing interest in the diagnosis of ADHD in adults. While the WHO World Mental Health survey that included 10 countries produced a global adult ADHD prevalence rate of 3.4%, the range varied between 1.2% (Spain) to 7.3% (France) (9). Simon et al. (10) conducted surveys of ADHD in adults using a similar approach to the one developed by Polanczyk et al. (6) in children and adolescents. They found a pooled ADHD prevalence rate of 2.5% (CI95% = 2.1 – 3.1%). However, it is important to note that authors were able to find only 6 studies to include in this meta-analysis.

**Persistence across development**

ADHD was first conceptualised as a disorder restricted to childhood and adolescence. Longitudinal studies showed that although there is a clear decline of symptoms with age, they tend to persist in a variable proportion of people who are more frequently impaired than controls in several major life activities (11). Longitudinal studies available are limited by the relatively short periods of follow up (only one study evaluated subjects in their early thirties) and by the historical changes in classificatory systems. Similarly to prevalence estimates of the disorder in childhood, estimates of persistence of the diagnosis vary substantially across studies, from 4% to 80%. This is probably due to methodological artefacts, such as the definition chosen for persistence in adult life (syndromic versus symptomatic), origin of the sample (non-referred or clinical), attrition rates and age of individuals at follow-up (5, 12). One of the major difficulties in determining the persistence of ADHD in adults is the difficulty in establishing which criteria best capture the latent construct of this diagnosis in adulthood, since the current DSM/ICD ADHD criteria were developed only in samples of children and adolescents. There are clinically-relevant doubts about whether DSM/ICD criteria adequately describe the phenotype in adults or whether broader conceptualisations, including executive function deficits and emotional impulsivity are better for adults (4). In addition, there is a clear decline of hyperactive symptoms across development (13), making motor hyperactivity less relevant for diagnosing ADHD in adults.

In a 15 year follow-up study of a referred sample of hyperactive children, Weiss et al. (14) tracked the lives of 63 subjects with the disorder and 41 controls. Of the 63 hyperactive subjects, 66% continued to have disabling symptoms of ADHD and 23% had an antisocial personality disorder. In general, it is expected that 40 – 60% of affected children from clinical samples continue to have the disorder during adulthood.

An important piece of data lacking in the literature is what the predictors of persistence of ADHD during the life cycle are. Although the presence of symptoms in both dimensions (inattention and hyperactivity/impulsivity) during childhood and childhood treatment of ADHD have been suggested as potential predictors (15), it is not clear whether they might not only be mediators of severity. More data from non-referred longitudinal studies are definitely needed.

**Demographic Correlates**

Studies in children consistently suggest that the ADHD prevalence is higher in boys than in girls. In our systematic review and meta-regression, the pooled ADHD prevalence for boys was 2.45 times higher than that for detected girls (only non-referred samples were included) (6). The prevalence among girls seems to be higher in community samples than in clinical samples, probably because there is a barrier to diagnosis and treatment referral for females. The male preponderance even in non-referred samples clearly decreases with age with the result that females are overrepresented in some adult samples (10).
The impact of ethnic and socio-economic issues on the prevalence rates of ADHD is much more controversial and deserves much more research. Although some studies suggest no effect of ethnicity on prevalence rates of ADHD, others suggest a higher prevalence of ADHD symptoms in African-American children (16). Regarding socio-economic stratum (SES), the issue is even more complicated. Positive and negative associations between SES and ADHD appear in the literature. Even in investigations reporting an association, it is impossible to disentangle the direction of the association. Parental ADHD diagnosis is frequent in families of ADHD children and ADHD has been correlated with lack of financial independence, lower SES and lower educational attainment levels later in life.

**Treatment access**

Although there is a clear increase in the rates of methylphenidate consumption worldwide (17), the vast majority of subjects affected by ADHD are not receiving treatment in health systems either in developed or in developing countries. The situation is even worse for adults and minorities both in the US (16) and for subjects at all ages worldwide (18).

The study of barriers for treatment access is extremely context dependent. A recent study in Great Britain suggested that child factors (e.g., severity of ADHD and a comorbid emotional or behavioural disorder) were the main determinants of service use. Moreover, the authors did not identify an excess of ADHD medication use (19).

**GP Comment**

**What have I learned from this paper?**

1. The overall prevalence of ADHD is about 5% but the rate depends on the assessment criteria used; more stringent criteria (ICD10) are used in the UK, resulting in a lower apparent prevalence.
2. In community samples, the rate in boys is about 2½ times that in girls; clinic samples might show a much higher preponderance of boys because males are more likely to present with difficult behaviour.
3. About 40-60% of children with ADHD will continue to have the condition into adulthood and many of those with ADHD, both children and adults, will have additional psychiatric disorders or other problems.
4. Knowing that the rates of ADHD are so high in both children and adults will make me very aware of the possibility of this diagnosis, emphasising the importance of referring for specialist assessment for treatment, although the secondary care services for adult ADHD are less well provided.

**Dr John Kedward, GP, Bedford.**

**References**


Potential conflict of interests: Dr Luis Augusto Rohde was on the speakers’ bureau and/or acted as consultant for Eli-Lilly, Janssen-Cilag, Novartis and Shire in the last 3 years (less than U$ 10,000 per year and reflecting less than 5% of his gross income per year). He also received travel support (air tickets and hotel) for attending two Child Psychiatric Meetings from Novartis and Janssen-Cilag in 2010. The ADHD and Juvenile Bipolar Disorder Outpatient Programs chaired by him received unrestricted educational and research support from the following pharmaceutical companies in the last three years: Abbott, Bristol-Myers Squibb, Eli-Lilly, Janssen-Cilag, Novartis, and Shire. He also receives research support from Brazilian government institutions (CNPQ, FAPERGS, HCPA and CAPES). Ms Rachel Verin has no conflict of interests. Dr Guilherme Polanczyk has served as a speaker and/or consultant to Eli-Lilly, Novartis, and Shire Pharmaceuticals, developed educational material for Janssen-Cilag, and received unrestricted research support from Novartis and from the National Council for Scientific and Technological Development (CNPq, Brazil).
The Genetics of ADHD

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Abstract

Results from family studies, adoption studies and, in particular, twin studies have indicated that there is a strong genetic predisposition to ADHD. However, environmental factors also appear to be important. No single gene is associated with a high risk of ADHD. Among the candidate genes that have been studied, the increased risk of ADHD associated with each gene is small; it is highest for the dopamine receptor gene DRD4 (odds ratio 1.33, 95%, confidence interval 1.15-1.54). Although genetic studies offer great promise and there have been significant advances in the technology, the translation of genetics research into clinical practice for the management of ADHD remains a challenge.

Introduction

Attention deficit hyperactivity disorder (ADHD), comprised of the triad of inattention, hyperactivity and impulsivity, is one of the most common childhood-onset neurodevelopmental disorders, with a prevalence of around 5% in children (1) and 3% in adults (2). While the onset is usually before the age of 7 years, a majority (up to 65% of cases) have persistent, impairing symptoms into adulthood (3) and therefore it is associated with significant academic, behavioural and social impairment throughout the life span (4,5). Consistent evidence for the importance of genetic factors in the aetiology of ADHD has come from both behavioural genetic studies and molecular genetic studies.

Behavioural genetic studies

Traditional behavioural genetic research, including family, twin and adoption designs have been used to examine if ADHD runs in families and how important genetic factors are in its expression.

Family studies evaluate the relative risk for other members of the family if one member of the family has been diagnosed with ADHD. These have consistently reported that parents and siblings of children with ADHD are 4-6 times more likely to have ADHD than the parents and siblings of children who do not have ADHD, the risk being even higher for those with persistent ADHD (6). However, traits and disorders can cluster in families because in addition to genes, they share much of their environment; twin and adoption studies are needed in addition to family studies to separate the effects of genes from common environment.

Adoption studies are difficult to carry out due to difficulty with accruing adequate numbers; however, there has been support for the importance of genetic factors in ADHD using this method in that adopted children with ADHD are more similar to their biological parents on ADHD measures, than to their adoptive parents (7).

Twin studies can be used to examine the presence or absence of a categorical diagnosis of ADHD (concordance or discordance) or the correlation between dimensional ratings of ADHD traits in monozygotic (MZ) and dizygotic (DZ). The higher the concordance/correlation in MZ twins (share ~100% of their genes) compared to DZ twins (share ~50% of their genes), the greater the genetic contribution and the higher the heritability (h^2) estimate. Concordance rates for ADHD have been found to be significantly higher for MZ than DZ and even recent, improved, systematic analyses taking into account possible biases of twin studies (such as lack of power to detect sibling interaction and the correction used for contrast effects), have estimated that genetic factors explained 60% of the phenotypic variance of ADHD (8). Furthermore, it appears that whether ADHD is defined categorically by diagnostic algorithms or dimensionally by rating scales the genetic component is strong and there is genetic overlap between these two constructs (9). Criticisms of twin studies have included the use...
of the “equal environment assumption” (EEA) in mathematical modelling of the data in that the environment of MZ and DZ twins with ADHD may not be the same, however two studies of ADHD have demonstrated that biases introduced by possible violation of the EEA do not significantly affect the heritability estimates (10;11) and therefore twin studies can be interpreted reliably as supplying evidence for the importance of genetic factors in ADHD (8).

a) In addition to simply answering the question about the size of the genetic component of ADHD, behavioural genetic studies have been used to examine a variety of hypotheses e.g. (i) the homogeneity of DSM-IV subtypes of ADHD (combined, inattentive, hyperactive-impulsive), (ii) if the genetic component is different for males and females, or (iii) if there is an effect on co-morbidity.

b) Results to date provide conflicting evidence in favour of genetically distinct subtypes (12), although it is likely that while genes associated with the hyperactivity-impulsivity dimension will also be associated with the inattentive dimension, there is some support for some symptom-specific genes also (13).

c) Despite the higher prevalence of ADHD in males (~3:1) (1), twin studies have not shown a substantive quantitative or qualitative sex difference for ADHD combined subtype (14;15). However for the inattentive subtype, a second genetic factor has been described more commonly in girls that was not present in boys and may account for the genetic correlation between anxiety disorder and inattentive symptoms observed in girls and not boys (16;15;17). The lower overall prevalence of ADHD in girls might be explained by a higher liability threshold model and that girls may have some protective factor(s) (e.g. oestrogen) that is neuroprotective (18;19).

d) Comorbidity of ADHD with conduct disorder has been found to index a phenotype with a higher genetic load (6;20;21) and longitudinal twin data suggest that common genetic factors substantially underlie the comorbidity of ADHD with conduct disorder (15). ADHD also co-occurs with reading disability and autism spectrum disorders (ASDs). Most studies show a stronger genetic overlap between reading disability and inattentive problems rather than with hyperactive/impulsive symptoms (22). Likewise, evidence suggests that shared genetic risk factors are responsible for the co-occurrence of ADHD with ASD (23;24).

Molecular Genetic Studies

Since the 1990s, candidate gene association studies of ADHD have been carried out. These studies test if there is a statistical difference between the presence of a genetic variant in people with ADHD compared to unaffected controls. These studies are based on a priori hypotheses and have focussed on common genetic variation (>/> =5% of population) in a limited number of genes (mainly involved in neurotransmitter pathways) that have been implicated in the aetiology of ADHD.

A meta-analysis of candidate association studies reported significant associations between ADHD and common variants in the following 6 genes; dopamine transporter (DAT1 or SLC6A3), dopamine receptor 4 (DRD4), dopamine receptor 5 (DRD5), serotonin transporter (5HTT), serotonin receptor 1B (HTR1B), and synaptosomal-associated protein 25 (SNAP25) (25). The odds ratio for each of these genes individually was very small, the highest being for DRD4 at 1.33 (CI 95% 1.15-1.54). It is likely that multiple risk genes of small effect combine additively, interactively or with the environment to produce ADHD symptoms (26) . Structural and functional brain imaging studies have lent further support for the aetiological importance of some of these implicated genes (e.g. SLC6A5 and DRD4) (8).

A whole genome systematic approach has been to look for genetic linkage in families with multiple affected individuals (usually affected sibling pairs) and aim to identify broad regions in the genome that could harbour susceptibility genes. This approach is based on the premise that if there is a risk variant in a region of the genome, there will be a region of the chromosome extending for some distance beyond it that will be shared more often than expected by siblings who are both affected compared to siblings where one is unaffected. A meta-analysis of seven independent linkage scans in ADHD has identified genome-wide significant linkage on chromosome 16 between 64 and 83 Mb
in which lies the CDH13 gene, which has been implicated in substance use disorders (27). However, it has been difficult for individual groups to achieve independent replication of linkage findings. The reasons for this may be that large enough numbers have not been achieved, that the common susceptibility genes for ADHD are of small effect size and that this approach is not most suited to finding risk genes for ADHD (28).

More recently, with the progress that has been made through the Human Genome Project and improved technologies, a number of genome-wide association studies (GWASs) also known as whole genome association study (WGA study or WGAS), have been carried out for ADHD. This method systematically examines genetic variation in most/all genes across the entire genome in a single experiment using a glass microarray. In order to have enough power to detect signal it is important to have large sample sizes of cases and controls. This has been a problem for ADHD, as a meta-analysis of all published studies to date revealed that despite the emergence of several novel genes for ADHD using this method, the combined total of all samples collected to date from around the world is still underpowered (29). Other psychiatric disorders with similarly complex genetic architectures to ADHD have been successful, but only with sample sizes of tens of thousands of cases. However, the data from GWAS studies has been useful in that it is possible to pull out genes that rank highly in terms of significance (even if not reaching a stringent genome-wide significance of \( p = 10^{-8} \)) and use these in bioinformatic pathway analyses to determine which neural pathways may be disrupted in ADHD. Approximately half of the proteins coded for by the ~100 highly ranked genes so far, are involved in neurite outgrowth (neurotrophins) and point towards the importance of the antenatal period of brain development for ADHD (30).

In addition to common genetic risk variants, there are rare family/individual-specific genetic variants that can affect genes involved in neurodevelopment. A class of rare variants that have recently aroused interest are referred to as copy number variants (CNVs). These are segments of DNA of at least 1kb (but can be much larger) that vary in number between individuals. Copies of these segments can be increased from the normal two copies (duplications or insertions, where there are three or more copies) or decreased (deletions, where there is one copy). Recent studies of autism, schizophrenia, epilepsy and intellectual disability have implicated these CNVs as being potentially pathogenic (31). CNVs are part of normal variation in the human genome and not all of them are thought to be pathogenic (32). Even those that are putatively pathogenic have variable penetrance (33). Advances in technology (e.g. array CGH is offered now by many cytogenetics laboratories) have made CNV detection more cost and time effective. There have been few studies of CNVs in ADHD to date. An initial study did not report an excess of duplications or deletions in ADHD compared to controls; however, the CNVs found in the ADHD sample were significantly enriched for genes reported as candidates in other neuropsychiatric disorders and neurodevelopmental pathways (34). A second study in a sample with severely affected individuals with ADHD and controls found an excess of putatively pathogenic CNVs in the ADHD sample (35). This study reported a duplication of a chromosomal region that includes the gene encoding neuropeptide Y (NPY) and this was associated with increased NPY plasma concentrations, and impairments on functional neuro-imaging tasks related to reward and emotion processing. Finally, a third study reported an increased rate of CNVs in ADHD compared to controls (0·156 vs 0·075), especially in individuals with intellectual disability (ID), though there was also a significant excess in cases without ID (36). CNVs identified this ADHD cohort were significantly enriched for loci previously reported in both autism and schizophrenia, suggesting pleiotropy (when a single gene can influence multiple traits).

Other rare genetic phenomena comprised of a number of different chromosomal anomalies including abnormalities in the number of chromosomes (aneuploidies) and single gene disorders have been recognised for many years to be associated with higher rates of ADHD (37). Fragile X syndrome, tuberous sclerosis and several microdeletion syndromes including Smith Magenis and Velocardiofacial (VCFS; 22q11 microdeletion) syndromes are associated with ADHD. Again these abnormalities are also associated with other neuropsychiatric disorders (e.g. autism spectrum disorders and psychoses).

In summary, several lines of converging evidence support a strong genetic component in the aetiology of ADHD. However, this does not negate the importance of environmental factors. Genetic
risk and environmental factors can affect ADHD through gene-environment correlation or gene-environment interaction (see Stergiakouli and Thapar (28) for review). It is not easy to identify or measure environmental risk; however, although several factors have been individually investigated for a link to ADHD, the best evidence to date relates to relatively rare extreme adversities such as extreme prematurity, very low birth weight, foetal alcohol syndrome and a pattern of behaviours associated with institutional deprivation in the early years (38). Molecular genetics is seen as an important tool with which to unravel gene-environment interplay in ADHD and early findings suggest that this line of enquiry promises to yield important insights in the future (39).

Molecular genetic approaches have recently been used to identify genetic contributors to clinical response to pharmacological agents as well as to adverse drug reactions (ADRs), in the rapidly advancing field of pharmacogenomics (often used interchangeably with pharmacogenetics). This approach is particularly important for paediatric cases as there is significant inter-individual variability between young people in the clinical response (i.e. improvement of symptoms, dose-response relationship, and occurrence of side effects and adverse events) to the same pharmacological agent and furthermore the same child may respond to the same agent in different ways through time, because the affinity, functional capacity, and expression of the targets (e.g. enzymes and transporters) of medications vary along development (40). Pharmacogenomic studies in ADHD have typically taken variants in candidate genes found to be associated with ADHD and examined clinical response to methylphenidate (31 studies) or atomoxetine (2 studies) (41), though systematic GWAS approaches are being undertaken (42). There are some interesting initial findings relating to pharmacodynamic variants and methylphenidate response as well as pharmacokinetic variants (in the cytochrome P450 system, CYP2D6) and atomoxetine response and adverse events. This approach could have enormous clinical relevance in the short to medium term.

Translation of genetic studies into clinical practice will be a major focus of future research investment. Identifying specific genetic risk factors will improve diagnosis and classification as well as stratify patient groups for specific treatments. It is likely that the clinical genetics laboratories will universally substitute routine comparative genome hybridisation array technology (array CGH) for light microscopy and therefore increase the yield of detected structural genetic variants in neurodevelopmental disorders such as ADHD (43). Personalised medicine will be the goal of modern practitioners. Rapid advances in stem cell technology, specifically induced pluripotent stem cell (iPSC) technology, where an individual’s somatic cells (e.g. blood, hair, skin cells) can be grown in a dish, transformed into stem cells and differentiated along neuronal lines and tested using several different drugs, could significantly advance the process of finding individualised therapies (44).

GP Comment.

What have I learned from this paper?

1. ADHD has a tendency to run in families.

2. Because of this I shall be very aware of the possibility of the same diagnosis in other family members of a patient with ADHD.

3. Although there is a genetic predisposition to ADHD, no single gene has been identified as being responsible for the condition.

Dr John Kedward, GP, Bedford.


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ADHD: What have we learned from Neuroimaging?

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Abstract

The last two decades of modern imaging techniques applied to research into attention deficit hyperactivity disorder (ADHD) have substantially expanded our knowledge of the underlying neural substrates of this condition and have shed light on the mechanism of action of the most common treatment of the disorder, stimulant medication. Studies have shown that ADHD is a multisystem disorder affecting several late developing fronto-cortical and fronto-subcortical pathways that mediate mature adult behaviour and cognition. Psychostimulants appear to modulate brain catecholamines and to have a normalising impact on some of the brain deficits in ADHD. The challenge lies in finding avenues to use neuroimaging techniques in clinical practice to aid diagnosis, treatment and prediction of response to treatment of ADHD.

Key words: ADHD, fMRI, MRI, methylphenidate, psychostimulant medication, frontal lobes, basal ganglia, cerebellum, parieto-temporal regions.

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is characterised by age-inappropriate symptoms of inattention, impulsiveness and hyperactivity (DSM IV) (1). It disrupts academic and social development, and is associated with significant psychiatric comorbidities and mental health problems in adult life (2). ADHD affects 5% of school-aged children worldwide (3) and persists into adulthood in 65% of cases affecting 4% of the adult population (4).

Impairment of Executive Functions

Both children and adults with ADHD have been found to be impaired in executive functions (EF) which develop late in life and are necessary for mature adult goal-directed behaviour, such as inhibitory control, cognitive flexibility, attention, working memory, planning, decision making and temporal foresight (5). These functions are mediated by neural networks comprising the frontal lobes, the basal ganglia and parieto-temporal regions that develop late in their structure and function (6, 7).

Neuroimaging and brain abnormalities

ADHD was originally considered a mild disorder, labelled “minimal brain disorder” in the seventies. Given that impulsivity, inattention and hyperactivity naturally diminish with age, it was observed that children with ADHD behave like younger children and it was hypothesised that ADHD might therefore be a delay of normal brain development. It was also hypothesised that ADHD patients suffer from deficits in prefrontal brain regions, based on the observation that patients or animals with frontal brain lesions can develop impulsiveness and/or ADHD-like symptoms. Furthermore, the chance discovery that methylphenidate (MPH) and other psychostimulants are effective in reducing the clinical symptoms of the disorder led to the suggestion that the basal ganglia must be affected too, given that MPH manipulates dopamine levels in the basal ganglia.

The last two decades of application of modern neuroimaging techniques such as positron emission tomography (PET) and magnetic resonance imaging (MRI) to ADHD research has substantially revolutionised our knowledge of the underlying neural substrates of ADHD. Neuroimaging of ADHD has proved direct evidence for these early theories of fronto-striatal deficits but, most importantly, has substantially widened our knowledge on the underlying brain abnormalities, revealing that ADHD is...
more than a problem of frontal and striatal deficits.

Structural imaging studies have shown that children and adults with ADHD, relative to healthy controls, have abnormalities not only in several late-developing fronto-striatal networks but also in temporo-parietal and fronto-cerebellar neural networks which mediate the above-mentioned cognitive control functions that are impaired in this disorder. Thus, reduced volume and cortical thickness have been observed in several frontal brain regions, parieto-temporal areas, the basal ganglia, the cerebellum and the splenium of the corpus callosum (for review see (8); for meta-analysis of region of interest studies see (9)). Two subsequent meta-analyses of whole-brain morphometry studies in children and adults with ADHD found that the most consistent regional grey matter reduction in ADHD patients compared to controls were in the basal ganglia (10, 11). Most interestingly, both age and psychostimulant medication were associated with the structural deficits, so that older adult patients were no longer impaired in their basal ganglia volumes, and equally, studies that included a high proportion of patients who had been chronically medicated, also no longer showed any structural abnormalities (11). These findings suggest that basal ganglia deficits normalise both with age and with chronic psychostimulant medication. Longitudinal imaging studies have furthermore provided evidence that the structural abnormalities observed in children with ADHD compared to healthy peers in frontal, striatal, parietal and cerebellar regions may be due to a delay in structural brain maturation (12, 13). This finding was seminal, given that it provided the very first scientific evidence for the 40 year old observation-based hypothesis of a delay in brain maturation.

Diffusion tensor imaging studies measure the integrity of white matter tracts, thus providing a measure of structural interconnectivity. These studies have shown global deficits in patients with ADHD in late-developing white matter tracts connecting fronto-striatal, fronto-parietal, fronto-cerebellar and parieto-occipital regions, assumed to reflect late brain maturation. These studies provide evidence for widespread abnormalities at the neural network level, and not only in isolated brain regions (14).

Underactivation of regions of the brain

Functional MRI (fMRI) studies investigate the brain while in action, e.g. while patients perform cognitive tasks in which they are known to be compromised. fMRI studies have provided evidence that these fronto-striatal, as well as parieto-temporal and cerebellar regions are not only structurally abnormal but also under-functioning in ADHD patients relative to controls. Children and adults with ADHD have shown underactivation relative to controls in several prefrontal regions, most prominently the dorsolateral and the inferior frontal cortex, but also in the anterior cingulate, the basal ganglia, the supplementary motor area, the cerebellum and temporo-parietal cortices during compromised functions, such as inhibition, attention and timing functions (for reviews see (8, 15, 16)). More recent studies have also provided evidence for functional deficits in ADHD patients in the orbitofrontal and limbic brain regions during tasks of motivation, suggesting deficits in fronto-limbic areas that mediate the control of motivation and affect (8, 15, 16). Recently developed functional connectivity fMRI analyses allow the investigation of the extent to which brain regions work together functionally. These studies have shown that brain regions are less functionally interconnected in ADHD, both during the resting state and when they perform cognitive tasks (14). Together with the DTI studies that show underdeveloped white matter tracts, these studies suggest that both the “software” and the “hardware” are wired less effectively in ADHD patients relative to controls (14).

In conclusion, MRI neuroimaging has substantially widened our horizon with respect to the underlying neurobiological deficits in ADHD. We have moved from the notion of a disorder of fronto-striatal deficits to the notion of a disorder with relatively widespread neural deficits in multiple interconnected systems of the brain that are important for adult mature behaviour including inhibitory (fronto-striatal deficits), attention (parieto-temporal regions), and motivation control (fronto-limbic networks) as well as timing functions (fronto-striato-cerebellar networks).
How do the psychostimulants work?

Another important contribution of modern neuroimaging has been the understanding of the brain mechanisms of the action of psychostimulants. Psychostimulant therapy is the most effective pharmacological treatment for ADHD, improving clinical symptoms in 70% of patients (17). PET studies have shown that methylphenidate, the most commonly used psychostimulant, blocks up to 70% of striatal dopamine transporters in both those with ADHD and healthy adults, enhancing striatal dopamine availability, with additional catecholamine-enhancing effects in the frontal regions (17). PET studies have provided further evidence that ADHD patients suffer from abnormal striatal dopamine transporter levels, that are important for cognitive and motivation functions, although findings have been inconsistent with respect to whether these are elevated or reduced (17).

A recent meta-analysis of PET studies showed that dopamine transporter levels in ADHD patients are elevated, but this is associated with psychostimulant effects, so that patients who have been long-term medicated have elevated dopamine transporter levels, while medication-naive patients have reduced levels (18). This suggests that the brain undergoes plastic changes in neurotransmitter transporter density in response to long-term medication. This is parallel to the above-mentioned findings of more normal structure in the basal ganglia in long-term medicated ADHD patients, suggesting that long-term medication has a neuroplastic effect on both brain structure and brain chemistry. While the functional significance of the elevation of dopamine transporter levels after long-term medication is unclear, the more normal brain structure after long-term medication needs to be seen as a positive development. It suggests that fears by parents, patients and practitioners of a negative impact of medication on normal brain development may be unjustified, with medication appearing to have positive rather than negative effects on the structural brain development of ADHD. This is also hinted at by other individual studies that show that long-term medicated ADHD patients have more normal brain structure than medication-naive patients in other brain regions, such as the frontal and parietal lobes (19), cerebellum (20) and anterior cingulate (21). See Figure 1.

Functional imaging studies also show that both the short–term as well as the long-term administration with MPH upregulates and even normalises fronto-striatal, cerebellar and parietal brain function in ADHD patients (22-26). Longitudinal randomised controlled studies, however, are needed to corroborate these findings from cross-sectional studies that are confounded by selection bias.
What have we learned so far?

In conclusion, neuroimaging has substantially expanded our knowledge on the underlying substrates of ADHD, showing that the disorder is characterised by relatively widespread and presumably immature changes in fronto-striatal but also other fronto-subcortical and fronto-cortical neural networks that mediate the behavioural and cognitive abnormalities that characterise the disorder. Neuroimaging has also provided us with some insights into the underlying abnormalities of the dopamine system of the disorder and the mechanism of action of the most commonly used dopamine-agonist treatment of ADHD. Important tasks, however, still lie ahead. For neuroimaging to be clinically useful, it needs to help with diagnosis, prognosis and treatment.

Looking into the future

Future neuroimaging studies need to investigate the disorder-specificity of these structural and functional deficits in order to establish objective disorder-specific biomarkers that can classify individual patients and potentially aid in clinical diagnosis. PET studies will be needed to investigate abnormalities in other neurotransmitters such as the serotonin, noradrenaline, glutamate and GABA in order to develop novel and more targeted pharmacological treatment. Gene-imaging interaction studies could potentially establish the genetic risk for brain abnormalities, for disorder trajectory or for treatment response. Finally, functional neuroimaging techniques in combination with neuro-feedback or brain stimulation techniques such as transcranial magnetic stimulation (TMS) could potentially be used directly as non-pharmacological treatment for ADHD to upregulate those brain regions that neuroimaging has found to be under-functioning in ADHD.

GP Comment.

What have I learned from this paper?

1. The whole concept of mental disorder may be considered controversial as there are often no physical signs to establish a diagnosis. However, this article describes our advancing knowledge in brain structure and functioning to aid diagnosis, prognosis and treatment.

2. It is interesting and also of great concern that neuro-imaging has revealed much more extensive structural and functional brain abnormalities in ADHD than originally suspected.

3. I am reassured that neuro-imaging appears to show that long-term stimulant medication may improve brain function and structure. GPs are expected to continue prescribing medication when stabilised by a specialist and this offers hope that we are acting in the best interests of the patient and their families. However, I agree with the author that there is still much to learn! I wonder if ‘normal’ brain structure equates to ‘normal’ behaviour and how is ‘normal’ defined?

4. Does drug treatment result in improved long-term health outcome?
The real challenge for researchers is to establish a causal relationship between long-term health outcome and the process of care - i.e. psychological, social, educational or pharmaceutical. Assuming a bio-social-psychological model of health, how do researchers ensure results are not confounded by a myriad of unknown external variables outside their control?

5. As ultimate health outcome is influenced by patient experience and their subjective perception of care received, it might be suggested that qualitative research methods as well as quantitative tools are required.

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References


Diagnosis of ADHD

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Abstract

ADHD is a descriptive term covering a heterogeneous condition characterised by hyperactivity, impulsivity and inattention that is enduring, pervasive (occurring across different situations) and impairs function. It begins early in life, under seven years of age. It is often associated with comorbidity, including disturbed behaviour, anxiety, autism spectrum disorders, learning disability and other problems. The diagnosis should be made by an experienced, trained specialist, based on information gathered from a number of sources; it cannot be made on the basis of behavioural scales alone. Referral pathways can facilitate diagnosis and management by clarifying professional roles and responsibilities.

The diagnostic criteria

Making a diagnosis of ADHD is, at first sight, relatively straightforward. There are slightly different criteria for the diagnosis in the American DSM-IV-TR system (1) and the International Classification of Diseases (2) but general UK practice seems to be a blend of the two and recognises a pattern of six items from each of the two lists in Box 1. These must be:

- more severe than is normal for (mental) age
- evident in at least two types of situation in the individual's life, such as home and school or the workplace
- not explained by any other pathology or general developmental delay
- associated with impaired functioning.

They must also have been consistently present from the first few years of life (before age 7).

In other words there should be an enduring, pervasive, impairing pattern of severe hyperactivity, impatient, impulsive behaviour with poor concentration and self-organisation, not explained by anything else.

One can quibble endlessly about the fine detail of diagnostic criteria and variations in how they are applied. That need not concern us beyond noting a couple of issues. American practice is to recognise subtypes such as inattentive or hyperactive-impulsive, indicated by a minimum of six items on either of the lists in Box 1 but this appears to be a practice little used in the UK. The WHO term 'hyperkinetic disorder' is less used than previously. It refers to a subgroup of ADHD which is more severe than 'American' ADHD. Many UK specialists will effectively use the criteria for hyperkinetic disorder (which are a little more stringent than those used in the USA) yet still refer to the diagnosis as ADHD, using the American term. This is what NICE (3) referred to as severe combined ADHD which has a prevalence rate of about 2% in childhood (4). On the other hand, American diagnostic practice recognises a milder condition with about 5-6% prevalence (5) in childhood, and about 3% in adulthood using current criteria (6).

The current diagnostic criteria are heavily orientated towards children and it is felt that the criteria for ADHD in adults should be somewhat different when DSM-IV-TR is revised. No final decision has been reached but it is widely recognised that problems with inattention and impulsivity are more evident in adult ADHD and some phenomena, such as emotional lability, become more of a concern with increasing age, while hyperactivity lessens.
Conceptual issues

NICE (3) examined the scientific evidence and concluded that ADHD is a valid concept and a ‘real’ disorder. Apparent controversy, particularly in the mass media, about the ‘reality’ of ADHD usually arises because some conceptual issues are misunderstood. There are four crucial concepts relevant to the diagnosis.

First, that it is a descriptive diagnosis, a pattern of behaviours and difficulties that is based on observation and not determined by any objective test.

Second, this pattern is at the extreme end of a distribution of behaviours present in the general population, especially among males. Put differently, ADHD is a ‘spectrum’ condition. The items in Box 1, which, if sufficiently numerous, pervasive enduring and impairing will lead to a diagnosis of ADHD, can readily be identified in milder form among normal people, especially boys. There is a difference in medical and social culture as far as identifying the cut-off between normal range and pathology; Europeans recognising a narrower and more severe disorder than Americans, Australians or South Africans.

<table>
<thead>
<tr>
<th>Hyperactivity/impulsivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Fidgets</td>
</tr>
<tr>
<td>• Leaves seat when should remain seated</td>
</tr>
<tr>
<td>• Runs/climbs excessively and inappropriately</td>
</tr>
<tr>
<td>• Noisy in play</td>
</tr>
<tr>
<td>• Persistent motor overactivity unmodified by social context</td>
</tr>
<tr>
<td>• Blurts out answers before question completed</td>
</tr>
<tr>
<td>• Fails to wait turn or queue</td>
</tr>
<tr>
<td>• Interrupts others’ conversations or games</td>
</tr>
<tr>
<td>• Talks excessively for social context</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inattention</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Careless with detail</td>
</tr>
<tr>
<td>• Fails to maintain attention</td>
</tr>
<tr>
<td>• Appears not to listen</td>
</tr>
<tr>
<td>• Does not finish instructed tasks</td>
</tr>
<tr>
<td>• Poor self-organisation</td>
</tr>
<tr>
<td>• Avoids tasks requiring sustained mental effort</td>
</tr>
<tr>
<td>• Loses things</td>
</tr>
<tr>
<td>• Easily distracted</td>
</tr>
<tr>
<td>• Seems forgetful</td>
</tr>
</tbody>
</table>

Items must be frequently manifest, excessive for mental age and clinically significant to be included

Need 6/9 from each list for combined type ADHD

Pervasiveness across situations, onset before age 7 and impaired functioning also necessary.

Box 1. Diagnostic item list for ADHD
Third, that it is heterogeneous, necessarily so, since it is arrived at by a minimal number of observable items drawn from a larger list. Selecting six, seven, eight or nine out of a list of nine elements in each of the two lists in Box 1 yields a possible 130 combinations for each list i.e. 16,900 (130^2) different combinations of items. This exaggerates the issue, of course, since the items overlap somewhat in their interpretation of behaviour.

Fourth, that it is a syndrome; a profile that has various causes, usually a combination of risk factors: genetic, toxic and environmental, although the balance between these varies between individuals.

Nevertheless it is remarkable how well identification of the syndrome predicts a treatment response to specific medications and, to a lesser degree, neurological findings, prognosis and likely comorbidity.

**Impairment**

ADHD is necessarily associated with impaired functioning in various domains:

- life within the family as sibling, child or parent,
- work at school or place of employment
- self-control and resistance to temptation
- relationships
- self-organisation and achievement

Failure in such domains can be a source of considerable distress to parents, partners or the patients themselves. This may be because of a subjective perception of failure but there is also an obvious risk that the reasons for difficulties can be wrongly attributed by others to personal weaknesses or motivational problems which should be overcome by willpower or moral backbone. Individuals afflicted by ADHD commonly experience a stream of criticism and pointless exhortation to ‘try harder’.

**Commonly associated symptoms**

Certain symptoms very often occur alongside ADHD without being core criteria. The most obvious is a fierce temper but others include aggressive behaviour, difficulty in learning from mistakes or ordinary discipline, poor sleep, general untidiness, poor quality relationships with others and low self-esteem.

**Comorbidity**

(Also see paper on ADHD comorbidity by Dr Thomas Brown in this issue.)

It is more likely than not that other conditions exist alongside ADHD. Indeed ADHD in pure form is uncommon.

These conditions include patterns of angry, aggressive behaviour. In childhood, Oppositional-defiant disorder (extreme, persistent, negative opposition to authority, often excitable, provocative and aggressive) and Conduct disorder (extreme antisocial behaviour that violates the rights of others) are very frequently associated and are often wrongly thought to be part of ADHD. If these antisocial patterns of behaviour exist alongside ADHD, referral to a specialist service is much more likely to be made, especially to a child and adolescent mental health service. In adult life, antisocial personality disorder is the equivalent association.

In childhood a range of developmental disorders are quite closely associated with ADHD. These include dyslexia, dyspraxia, dysgraphia (specific physical difficulties with handwriting), autism spectrum disorders, specific language impairment and tic disorders, including Tourette syndrome.
Anxiety is not uncommon among children with ADHD and by the late teenage years and in adult life emotional disorders such as depression or generalised anxiety disorder are increasingly evident but the strongest association in that age group is between ADHD and substance misuse: alcohol, cannabis and nicotine being very commonly abused with dependency emerging. This has not a consequence of previous or concurrent medical treatment of ADHD which may indeed be preventative.

Differential diagnosis

The pattern of inattentive, impatient restlessness seen in ADHD is not specific to it. At any age, assessment needs to exclude

- normal population variability
- immature development associated with varying degrees of intellectual disability

In childhood, those who have had

- poor quality institutional care or
- weak emotional attachment to caregivers

can show a picture hard to differentiate from ADHD symptomatology but with a rather less straightforward response to medication.

A more difficult diagnostic problem arises when there is overactive, impulsive behaviour with a refusal to comply with parental demands or school discipline which is the result of poor quality parenting or family conflict. A detailed history and observational reports can distinguish this from ADHD but it has to be remembered that disruption of parenting and family harmony can also be caused by ADHD as a primary problem, establishing a vicious circle or vicious spiral.

ADHD is quite often associated with poor quality sleep but it is also the case that poor sleep can give rise to an ADHD pattern, usually with relatively recent onset. The same is true for anxiety which may result from family tensions. Less commonly, attentional problems can be caused by short-term memory difficulties, informational processing difficulties or autism spectrum disorders.

In the classroom, inattentive restlessness can result from general or specific academic difficulties, hearing difficulty, preoccupation with family stress or bullying and disciplinary failure at home or school.

In adult life, recent onset symptoms can result from hypomania or agitated depression or from substance misuse. In none of these will there be an enduring pattern from early childhood.

Assessment

The corollary of all this is that it takes judgement and information to make a diagnosis. This particularly applies to establishing

- whether the behaviours are extreme and beyond normal variation in cultural context
- the extent of impairment
- the antecedents in early childhood
- co-existing problems
- co-existing disorder (comorbidity)
- differential diagnosis.
As part of this, questionnaires and scales completed by the patient or others are helpful but rating scales alone are not a sufficient basis for a diagnosis to be made.

Although there are a number of specific neuropsychological, neuroanatomical and neurophysiological findings that are associated with ADHD, none of these is yet sufficiently specific or practicable to form a diagnostic test in clinical practice. Descriptive or functional brain scans and EEG studies indicate positive findings (mainly understandable in terms of immature and insufficient brain development or poor frontal lobe functioning) in research studies. Yet they are not yet sufficiently well developed to be able to differentiate ADHD from normal variation or inattentive restlessness arising from other causes. No objective test can confirm or deny the existence of ADHD as things stand, although findings from psychological assessments, tests of reaction time and accuracy, and measures of mobility can contribute to a diagnostic decision.

This is an argument for specialist assessment within which information should be gathered from various sources: general practitioner, teachers or employers, parents or partners, and be supplemented by a physical and developmental assessment where appropriate. Often this is best carried out on a multidisciplinary basis, although this is not mandatory when good information from a variety of sources can be evaluated by a trained, experienced specialist.

**Referral**

Local referral pathways to specialists vary. In childhood and adolescence, different areas place different emphasis upon general or specialist services, paediatric or child and adolescent mental health service (CAMHS), although there will nearly always be an agreed referral pathway available from local CAMHS or child development centres. Services for adult ADHD are currently poor, but NICE has made a specific recommendation that they should be developed within adult community mental health services. Most children with suspected ADHD are referred to specialist services through educational channels and primary healthcare makes few referrals. This is seen by some (7) as a barrier to adequate service provision for children and families and thought to be because of low levels of awareness of ADHD in primary care.

**GP Comment**

**What have I learned from this paper?**

1. ADHD is a heterogeneous condition characterised by enduring, pervasive hyperactivity, impulsivity and inattention, beginning under seven years of age and not explained by another diagnosis.

2. GPs need to be aware of the importance of referring children with these characteristics to specialist services for diagnosis and treatment.

3. Most referrals for the diagnosis of possible ADHD come from parents who have been told the possibility by either pre-school or primary school teachers and request further referral to the local Child and Adolescent Mental Health Services.

4. Referral pathways can help to facilitate the process of referral and clarify the roles of professionals.

5. The transition from adolescent to Adult diagnosis ADHD requires further referral to another service which in our particular area is to the adult ADHD service at the Maudsley Hospital in London.

6. Development and resources are required to make ADHD services less of a lottery; this could be developed via new Commissioning Groups.

Dr Peter Cliffe, GP, Surrey.
References


ADHD – NICE guidelines and standard treatments

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Declarations of Interest

Chris Hollis was a member of the NICE ADHD Guideline Development Group.

Abstract

The NICE Guideline on ADHD published in 2008 represents a major advance in evidence-based healthcare for children, young people and adults with ADHD. It draws together systematic reviews and expert opinion to produce clinical practice recommendations covering diagnosis, behavioural and pharmacological treatment and organisation of services for children and adults. This article summarises the key practice recommendations, highlights where gaps remain in the evidence base and describes some of the challenges for implementing the guideline in routine clinical practice. Some of the key recommendations of the NICE guideline are that ADHD should only be diagnosed by specialists in secondary care, that parent training/education should be used as first-line management in those with moderate ADHD but medication may be offered as first-line line treatment for severe ADHD, alongside other management strategies. The recommended medications are methylphenidate, atomoxetine and dexamfetamine. Attention is drawn to the fact that ADHD can occur in the presence of co-existing conditions such as learning disability and autism spectrum disorder.

Introduction

ADHD (attention deficit hyperactivity disorder) is a heterogeneous behavioural syndrome characterised by maladaptive levels of hyperactivity, impulsivity and inattention. ADHD (as defined by DSM-IV-TR) is a common disorder affecting 3.6% of boys and 0.85% of girls between ages 5 to 15 years in the U.K (1). DSM-IV describes three subtypes of ADHD according to the mix of symptoms: predominantly inattentive (ADHD-I), predominantly hyperactive-impulsive (ADHD-HI) and combined type (ADHD-C). The ICD-10 definition of hyperkinetic disorder (HKD) represents a severe sub-group of the DSM-IV combined type ADHD and affects about 1.5% of primary school age boys. In recent years there has been an increase in the clinical recognition of ADHD/HKD with a corresponding rise in the numbers diagnosed and treated: from an estimate of 0.5 per 1,000 children diagnosed in the UK 30 years ago (2), to more than 3 per 1,000 receiving medication for ADHD in the late 1990s (3). This article summarises the main recommendations from the ADHD guideline produced in 2008 by the National Institute of Health and Clinical Excellence (NICE). Readers should refer to the full guideline for the complete set of recommendations and supporting evidence (4) (www.nice.org.uk/CG072).

What the guideline covers

• The diagnosis of ADHD in children, young people and adults.
• The treatment of children aged 3 years and older, young people (12-18 years) and adults with a diagnosis of ADHD and HKD.
• Specific treatments considered include: pharmacological and psychological interventions including family interventions, cognitive-behavioural treatments and parent training. Other physical treatments are considered such as dietary elimination and supplementation.
• The management of ADHD in the presence of comorbid conditions in children, young people and adults, including conduct problems, anxiety, ASD, learning disability, neurological disorders and substance misuse.
• The organisation of care and services for children, young people and adults with ADHD.
Methodology

The guideline was developed by the National Collaborating Centre For Mental Health using standard NICE methodology the details of which are given in the Guidelines Manual (5). Essentially, this process involved a detailed systematic review and evidence synthesis by an expert Guideline Development Group (GDG) made up of clinicians, academics and service users/carers. The GDG produced recommendations for clinician management and service organisation based on the best available evidence, and where evidence was lacking by expert consensus.

NICE has published two technology appraisals relevant to the management of ADHD on drug treatment (www.nice.org.uk/TA098) and parent training/education programmes (www.nice.org.uk/TA102). The 2008 NICE ADHD Guideline incorporates recommendations from both technology appraisals. The full guideline is over 600 pages and covers all aspects of ADHD from epidemiology and aetiology to treatment and organisation of services. It provides a detailed review of the literature for those wishing to learn more about specific aspects of aetiology, diagnosis and management.

Recommendations

Diagnosis

• Diagnosis should only be made by a psychiatrist, paediatrician or other healthcare professional with specialist training and expertise in the diagnosis of ADHD.

• ADHD should be considered in all age groups. Adjust symptom criteria for age-appropriate changes in behaviour. Diagnosis should be based on:
  – a full clinical and psychosocial assessment. Discuss symptoms and impairment in the different domains and settings of the person’s everyday life
  – a full developmental and psychiatric history, and
  – observer reports (e.g. from parents, teachers, spouse/partner) and an assessment of mental state.

• Diagnosis should be made when symptoms of hyperactivity, impulsivity and inattention:
  – meet the criteria in DSM-IV or ICD-10 (HKD) and
  – are associated with at least moderate psychological, social and/or educational or occupational impairment based on interview and/or observation in multiple settings, and
  – are persistent and trait-like (i.e. not episodic).

• As part of the diagnostic process, include an assessment of coexisting conditions, social, familial and educational or occupational circumstances and physical health. For children and young people also include an assessment of the parents’ or carer’s mental health.

• Do not diagnose ADHD based on rating scales or observational data alone. However, rating scales are valuable adjuncts, and observations (for example, at school) are useful if there is doubt about the presence of symptoms and impairment in different settings.

• Take into account children or young people’s views when determining the clinical significance of impairment.

Identification and referral to secondary care

Primary care

• Determine the severity of symptoms and impairment suggestive of ADHD and how they affect the child or young person and their parents or carers in different domains and settings.

• Where impairment is at least moderate severity such that impairment attributable to ADHD occurs across multiple domains and settings (e.g. adverse impact on development, family life, friendships and education), consider:
• watchful waiting for up to 10 weeks
• offering referral to a parent-training/education programme; this should not wait for a formal diagnosis of ADHD.

• If the problems persist with at least moderate impairment, refer to secondary care (paediatrician, child psychiatrist or specialist ADHD child and mental health services [CAMHS]).

• If the problems are associated with severe impairment (corresponding to a diagnosis of HKD with impairment affecting multiple domains in multiple settings), refer directly to secondary care.

It can be seen from the recommendations above that those children identified in primary care with moderate impairment may be observed with watchful waiting for up to 10 weeks or referred to a group-based parent training programme without a formal diagnosis of ADHD.

School

• Universal screening for ADHD should not be undertaken in schools or nurseries.

• On referral to a special educational needs coordinator (SENCO), the SENCO should:
  – advise teachers on classroom strategies to help children or young people with suspected ADHD.
  – inform the parents about local group-based parent training/education programmes.

Treatment and Management

Pre-school children

• Drug treatment is not recommended.

• Offer parents or carers referral to a group-based parent training/education programme as first-line treatment if they have not attended one, or if it has been only partially effective.

• If treatment is effective, before discharge from secondary care:
  – review the child with their parents or carers and siblings for residual coexisting conditions and develop a treatment plan for these if necessary.
  – monitor for recurrence of ADHD symptoms and associated impairment after the child starts school.

• If treatment is ineffective consider referral to tertiary services.

School-age children and young people with moderate ADHD

• Drug treatment is not indicated as first-line treatment.

• Offer parents or carers referral to a group-based parent training/education programme or other group-based psychological treatments (cognitive behavioural therapy [CBT] and/or social skills training) for the child or young person.

• Consider individual psychological interventions (such as CBT or social skills training) for older adolescents.

• If treatment is effective, before discharge from secondary care, review the child or young person with their parents or carers and siblings for residual problems such as anxiety, aggression or learning difficulties. Develop a treatment plan for these if necessary.

• Reserve drug treatment for children and young people with:
  – moderate impairment where non-drug interventions have been refused
  – persisting symptoms and impairment following a parent-training/education programme or group psychological treatment.

School-age children and young people with severe ADHD (hyperkinetic disorder)

• Offer drug treatment as first-line treatment (see below). Also offer the parents a group-based parent-training/education programme.

• If drug treatment is not accepted, advise parents or carers and the child or young person of the
benefits and superiority of drug treatment. If drug treatment is still not accepted offer a group parent-training/education programme.

- If group parent-training/education is effective for those who refused drug treatment:
  - assess for coexisting conditions
  - develop a longer-term care plan.
- If group parent-training/education is ineffective for those who refused drug treatment:
  - discuss drug treatment again, or other psychological treatment (group CBT and/or social skills training)
  - highlight the benefits and superiority of drug treatment in severe ADHD.

The guideline contains detailed recommendations for drug treatment and monitoring.

- Drug treatment should:
  - Only be started by a healthcare professional with expertise in ADHD
  - Always form part of a comprehensive treatment plan that includes psychological, behavioural and educational interventions.
- A pre-drug treatment assessment should be carried out as shown in Figure 1.
  - Cardiovascular examination; pulse and blood pressure (BP) plotted on centile chart
  - Height and weight plotted on centile chart
  - Routine blood tests and/or ECG not recommended

![Figure 1](image.png)

- Monitoring for adverse effects
  - Adverse effects should be routinely monitored and recorded during treatment
  - Pulse and blood pressure should be measured at each dose change and thereafter every 3 months.
  - Weight should be measured at 3 months and 6 monthly thereafter. Height should be measured every six months.
- Management plan for those who fail to respond to treatment. Consider:
  - Is drug adherence adequate?
  - Is diagnosis correct?
  - Has adequate dose been given?
  - If adequate dose has been given – consider switching to a) a different methylphenidate formulation, or b) a different drug: atomoxetine or dexamfetamine.
Choice of drug treatment

• Methylphenidate, atomoxetine and dexamfetamine are recommended, within their licensed indications, as options for the management of ADHD.

• Decide which drug treatment to use based on:
  - comorbidities (for example, tics, Tourette syndrome, epilepsy)
  - their different adverse effects
  - potential problems with compliance (for example, modified release/once daily formulations to avoid taking medication at school),
  - potential for drug diversion and misuse
  - preferences of the child or young person and their parent or carer.

• Consider:
  - methylphenidate for ADHD without significant comorbidity
  - methylphenidate for ADHD with comorbid conduct disorder
  - methylphenidate or atomoxetine in the presence of tics, Tourette syndrome, anxiety disorder, stimulant misuse or risk of stimulant diversion
  - atomoxetine if methylphenidate has been tried and has been ineffective at the maximum tolerated dose, or the child or young person is intolerant to low or moderate doses of methylphenidate.

Initiation and titration of medication

- Initial treatment should begin with low doses
- Titration with methylphenidate may be with either immediate- or modified-release preparations.

Modified-release methylphenidate may be preferred to increase adherence and if there are concerns about diversion or substance misuse.
  - Dose should be titrated against symptoms and adverse effects for 4-6 weeks for methylphenidate and dexamfetamine.
  - Titration may require 8 to 10 weeks to obtain optimal effects on atomoxetine

Duration, discontinuation and long term drug treatment

- Following an adequate treatment response, drug treatment should be continued for as long as clinically effective and reviewed annually.
- Drug holidays are not routinely recommended

Transition to adult services

• Reassess a young person treated in CAMHS or paediatric services at school-leaving age to determine if treatment needs to be continued. If it does, arrange for transition to adult services (usually by age 18), giving details of the anticipated treatment and services required.

• Consider a formal meeting involving CAMHS and/or paediatrics and adult psychiatric services.

• Give the young person information about adult services and involve them, and their parent or carer, in the planning. Use the care programme approach for young people aged 16 years and older.

• After transition, carry out an assessment of personal, educational, occupational and social functioning, and coexisting conditions, especially drug misuse, personality disorders, emotional problems and learning difficulties.

Commentary

The guideline represents an important advance in the evidence-based management of ADHD. A number of new and clinically relevant issues are addressed by the guideline.

• The diagnosis and treatment of ADHD in adults and the transition of young people with ADHD into adult services.
• The recognition that ADHD can occur alongside co-existing conditions such as autism/ASD and learning disability.
• The guideline distinguishes between ‘moderate’ and ‘severe’ ADHD, where severe ADHD corresponds approximately to the ICD-10 diagnosis of hyperkinetic disorder (HKD) with severe impairment affecting multiple domains in multiple settings.
• The proposal of a ‘stepped-care’ model for management where the degree of impairment is a key factor in determining the level of intervention, with psychological interventions generally considered prior to, or alongside, drug treatment.
• The recommendation that psychological treatments, predominantly group-based parent training, should be offered as first-line treatment in all pre-school children with ADHD and to older children with moderate ADHD.

While the guideline is based on the best available evidence, important gaps in the evidence base should also be recognised and affect some key recommendations. The evidence supporting group-based parent training programmes comes almost entirely from pre-school children with ADHD and school-age children with conduct disorder (6). Although drug treatments are often used for many years, there is little evidence regarding the long-term risks and benefits of drug treatment for ADHD. While the model of “stepped-care” i.e. recommending psychological treatments first-line for less severe cases is similar to the approach advocated in other NICE guidelines for mental disorders (e.g. depression) this model of care is not evidence-based.

The guideline also raises considerable challenges both for front-line clinicians and those organising and planning services. The onus is on primary care practitioners and schools to recognise possible ADHD and make referrals to secondary care for diagnostic assessment. The guideline requires practitioners in primary care to make an important distinction between moderate and severe impairment, which may be difficult for busy clinicians with limited training and experience. For the “stepped-care” model to work a clinician (typically a primary care practitioner) needs to monitor and review the outcome in a parent training programme so that children with moderate ADHD who fail to respond adequately are referred for more intensive treatments. The recommendation to monitor pulse and blood pressure three-monthly for those receiving drug treatment may be difficult to implement for many clinicians as it will represent an increase in the frequency of routine physical monitoring.

The recommendation of group-based parent training programmes aimed at parents of children with conduct problems may not adequately address the needs of parents for specific psychoeducation and advice on ADHD management. In secondary care, there is a lack of availability of psychological treatments for children with ADHD. Finally, it is likely that increasing numbers of young people will require transition to adult services and this, together with more adults being referred with suspected ADHD will have major implications for training and service delivery within adult mental health services.

**Key Clinical Messages**

- ADHD should only be diagnosed by specialists in secondary care.
- ADHD can be diagnosed in adults and in children with co-existing learning disability and/or autism spectrum disorder (ASD). (Also see paper in this issue on ADHD and autism.)
- Drug treatment is not recommended in pre-school children.
- Parent training/education programmes should be used as first line treatment for pre-school children and older children with moderate ADHD.
- Drug treatment should be offered as a first-line treatment to school-age children and young people with severe ADHD, and to adults. Parents should also be offered a group-based parent-training/education programme.
GP Comment.

What have I learned from this paper?

Excellent paper with clear guidelines.

1. Although GPs play an important role in identifying children, young people or adults with suspected ADHD, the diagnosis should only be made by an experienced specialist in secondary care; this implies that I shall have no hesitation in referring patients who appear to have ADHD to secondary care for assessment and initial management.

2. I shall suspect the diagnosis of ADHD in a patient of any age who has the three key symptoms of hyperactivity, impulsivity and inattention that are significantly affecting their quality of life in the psychological, social, occupational or educational areas.

3. Development of Specialist Mental Health Nurses who are trained in the diagnosis of the various levels of ADHD attached to CAMHS or in Adult Services could be our first referral point and reduce waiting times. They could possibly be based in the community as part of community-based mental health services. They would be able to see the children with parents in the surgery setting or even in their homes to achieve a more all-round understanding of the family setting. This would reduce the referrals to expensive secondary care centres initially and speed up the referral. Many parents are at their wits end at the point of presentation.

4. Parent training/education is an integral component of the comprehensive management of the child with ADHD; although medication can be used as first-line treatment for severe ADHD, it should only form part of this comprehensive management and should only be initiated by a specialist.

5. Shared care guidelines are already in use in most areas following NICE Guidelines between specialists and GPs over prescribing in ADHD.

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How is standard ADHD medication used in clinical practice and how is this supported by research?

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Abstract

ADHD is a common neurodevelopmental disorder. It is important for the clinician to keep up-to-date with the new developments in using ADHD medications effectively, while empowering patients and parents to make informed choices. The aim of this paper is to assist the clinician in deciding which medication or formulation to recommend in different circumstances. Ten simple principles of administering ADHD medication are outlined, along with comprehensive tables and a flow chart. An up-to-date summary of the research supporting current practice is presented.

How is standard ADHD medication used in clinical practice?

1. When should ADHD medication be considered?
   • The NICE guideline (1) recommends that medication is used as a first-line treatment in children and young people with severe ADHD and also for those with moderate ADHD and persisting significant impairment following a parent-training/education programme or group psychological treatment.
   • Medication should always be a part of a comprehensive treatment plan that includes psychological, behavioural and educational advice and interventions.
   • The decision to start medication should be made by a specialist in paediatrics, child and adolescent psychiatry or learning disability.
   • Drug treatment is not recommended for pre-school children (1).

2. What medications are available to treat ADHD in the UK?
   • Currently methylphenidate, dexamfetamine (stimulants), and atomoxetine (non-stimulant) are available as standard ADHD medications. Methylphenidate and atomoxetine are licensed for use from 6 years of age. Dexamfetamine is licensed from 3 years of age but the BNF (7) only recommends its use from the age of 6 years.
   • See table 1 for standard medications, available strengths, frequency of administration, titration and maximum recommended doses.

3. Identifying goals of treatment with parent and/or patient
   • Identify the goals/targets to be achieved with ADHD medication; this needs to be agreed with the parent/carer and the child/young person, where applicable. It is also important to involve the school teacher.
• The primary goal is to control the symptoms of ADHD. As a result of this, secondary effects may be improvements in academic performance, social skills, challenging behaviour and family relations but these may depend very much on a comprehensive approach, involving far more than the medication alone.

4. Choosing the right treatment – Methylphenidate or Atomoxetine?

The choice of medication should take into consideration the different properties of the available drugs and preparations, co-morbid conditions (for example, sleep disorders), the adverse-effect profile, potential for drug misuse or diversion, and the preferences of the patient and carers.

**Methylphenidate**

• Consider Immediate Release (IR) methylphenidate (generic methylphenidate, Ritalin® or Medikinet®) in the following circumstances.
  
  • During initial titration to determine correct dosing level
  
  • If more flexible dosing is required.
  
  • Modified-release methylphenidate might achieve the following (1).
    
    a. Improved compliance.
    
    b. Reduced stigma by avoiding the necessity for medication at school.
    
    c. Avoiding the problems of medication storage and administration at school.
    
    d. A more even, consistent and longer-duration response.

• Use Equasym XL or Medikinet XL once a day in the morning if there is a need to cover the school day. IR methylphenidate can be tried after the school day to cover the evening period.

• Use Concerta® XL to cover the school day and evening at home.

• Always use brand names when prescribing modified-release preparations of methylphenidate because different brands have different profiles/durations of action (see Table 1). Follow the guidelines for prescribing controlled drugs (see paper on Shared Care Guidelines in this journal).

• The child/young person can have drug holidays during weekends/school holidays, if their behaviour at home is manageable and there is no interference with achieving agreed goals/targets. However, drug holidays are not routinely recommended.

**Atomoxetine**

• Consider atomoxetine in the following circumstances.
  
  a. When all-day cover is needed and if there are significant ADHD symptoms during early morning and/or late evening.
  
  b. When there are unacceptable adverse effects with methylphenidate.
  
  c. If there is inadequate response to the maximum tolerated dose of methylphenidate.
  
  d. A strong family preference for a non-stimulant (3).
  
  e. Risk of drug “diversion”.

Other indications include tics, substance abuse or comorbid anxiety.

• The child/young person cannot have drug holidays: atomoxetine should be taken every day.

**Dexamfetamine**

Dexamfetamine can be used as an alternative in children who do not respond to methylphenidate or atomoxetine (7).

• If there is a choice of more than one drug, use the drug of lowest overall cost (1).

5. Titration of medications

• Titration is best carried out by using a ‘start low and go slow’ regime. Start with a small dose and build up gradually over a period of 4 weeks, whilst monitoring for both clinical response and adverse effects (see table 1).
• Regarding methylphenidate: warn parents that doses that are too high may lead to a withdrawn, depressed, tearful state which can be reversed immediately by reducing the dose. It is not usually necessary to stop the drug.

• Regarding atomoxetine: explain to parent/carer and young person, when applicable, that it may take 6 weeks or longer to achieve the full effect of the medication (3). It would be wise to continue treatment up to 12 weeks before deciding to discontinue because of lack of response.

6. Provide appropriate and relevant written information to the parent/carer and child/young person, when applicable

• Leaflets/books
  - Provide parents/carers with basic information leaflets about ADHD, e.g. The Royal College of Psychiatrists parent information sheets.
  - There are several self-help guide books for parents, children and young people.

• Websites and support groups
  - Parents/carers can access reliable information from local/national support groups. ADDISS, a national support group, is a useful resource and can be accessed at www.addiss.co.uk
  - It is important to warn parents/carers about websites propagating negative information about ADHD and medications. Reputable websites include www.addiss.co.uk and www.rcpsych.ac.uk/mentalhealthinfo

• Travel advice about controlled drugs
  - Methylphenidate and dexamfetamine are controlled drugs. Parents/carers and young people should receive advice when travelling abroad with these medications.
  - A doctor’s letter stating that the individual has ADHD and needs to have the medication regularly should be carried; it is advisable to take a simple leaflet or a booklet about the condition, just in case.

7. Initiating and monitoring treatment: response and adverse effects

• Carry out a pre-treatment check before commencing medication. Check for cardiovascular conditions in the child and family (see papers on NICE guidelines & standard treatments, and the paper on CVS adverse effects in this issue).

• Follow the NICE guidelines; check weight and height (plot on growth chart), blood pressure and pulse rate (plot on centile chart).

• Inform parent/carer of adverse effects of medication and monitor for adverse effects.

• Use well-established instruments/questionnaires to monitor progress
  - ‘Dundee Difficult Times of the Day Scale’ (D-DTODS) is completed by parent and teacher to assess difficult behaviour and monitor pattern of response to treatment throughout the day.
  - Conners Parent and Teacher Rating Scales and Clinical Global Impression – Improvement scale (CGI-I), to monitor response.
  - ADHD-Rating Scale (ADHD-RS)

8. Liaison with school regarding progress

• School teacher/SENCo (Special Educational Needs Coordinator); telephone discussion as and when needed.
• Consider using SKAMP rating scale to measure classroom behaviour and response to medication.
• Professionals meetings at school as required.

9. Shared care with an expert paediatrician/child and adolescent psychiatrist

• Follow the local shared-care guidelines.
10. Review of medication regularly and manage comorbid conditions, if present

- Review at least 6 monthly/yearly once the treatment response is established.
- If stimulant medication is used, ask whether there is a marked change in the morning after the medication is given; if not, then question whether the medication should be continued.
- Drug treatment should be continued as long as it is clinically effective and this should be reviewed at least annually (1).
- Discontinue methylphenidate if there is no response after one month.
- Always ensure associated comorbid conditions are managed appropriately.
<table>
<thead>
<tr>
<th>Medication</th>
<th>Stimulant</th>
<th>Non-stimulant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short acting Dexamphetamine</td>
<td></td>
<td>Long acting MPH*</td>
</tr>
<tr>
<td>Long acting MPH*</td>
<td></td>
<td>Long acting Atomoxetine</td>
</tr>
<tr>
<td>Formulation</td>
<td>Tablet</td>
<td>Tablet</td>
</tr>
<tr>
<td>IR:ER ratio of MPH**</td>
<td>IR 100%</td>
<td>IR 50%</td>
</tr>
<tr>
<td>See table 2</td>
<td></td>
<td>ER 50%</td>
</tr>
<tr>
<td>Duration of action</td>
<td>Up to 4 hrs (2)</td>
<td>Up to 4 hrs (2)</td>
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<tr>
<td>Up to 24 hrs (5, 6)</td>
<td></td>
<td></td>
</tr>
<tr>
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<td>5mg, 10mg, 20mg, 30mg, 40mg</td>
<td></td>
</tr>
<tr>
<td>XL</td>
<td>10mg 30mg 30mg 36mg</td>
<td></td>
</tr>
<tr>
<td>**Can be sprinkled (7)</td>
<td></td>
<td></td>
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<td>IR 30%</td>
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<td>Equivalent daily doses of MPH (1)</td>
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<td>10mg</td>
</tr>
<tr>
<td>(Not equivalent in profile/duration of action)</td>
<td>5mg</td>
<td>10mg</td>
</tr>
<tr>
<td>of dexamphetamine</td>
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<td>is equivalent to</td>
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</tr>
<tr>
<td>10mg of IR MPH (2)</td>
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<td>40mg</td>
</tr>
<tr>
<td></td>
<td>60mg</td>
<td>60mg</td>
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<tr>
<td>Titration</td>
<td>2.5mg 2 to 3 times a day and increase by 5mg per day at weekly intervals (7)</td>
<td>Start with 5mg 1-2 times daily, increase by 5-10mg/day at weekly intervals (7)</td>
</tr>
<tr>
<td>Start low and go slow</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age: 6-18 years</td>
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<tr>
<td>Frequency of doses/day</td>
<td>2 or 3 times a day</td>
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<td>Once a day in the morning with or without food</td>
<td>Once a day in 2 divided doses/day</td>
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<td>Maximum dose per day***</td>
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<td>Licensed maximum 60mg/day</td>
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<td>20mg/day (1, 7)</td>
<td></td>
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<td>Up to 40mg/day may occasionally be required (1)</td>
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<tr>
<td>18mg</td>
<td>27mg</td>
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<tr>
<td></td>
<td>36mg</td>
<td></td>
</tr>
<tr>
<td>40mg</td>
<td>45mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>54mg</td>
<td></td>
</tr>
<tr>
<td>72mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MPH** – methylphenidate; **IR: ER ratio** – proportion of Immediate Release and Extended Release components of methylphenidate in the long-acting preparations.

***Sprinkle** – this means the content of the capsule can be opened onto tablespoon full of apple sauce, then swallowed immediately without chewing, for children with swallowing difficulties.

***Maximum dose per day** - Take advice from a specialist while using maximum dose per day, when it is unlicensed.
Table 2  Modified-release methylphenidate: Strengths of tablets/capsules and proportion of immediate release (IR) to extended release (ER)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Medikinet® XL (capsule) IR:ER 50:50</th>
<th>Equasym® XL (capsule) IR:ER 30:70</th>
<th>Concerta® XL (tablet) IR:ER 22:78</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet/capsule strength</td>
<td>5mg 10mg 20mg 30mg 40mg</td>
<td>10mg 20mg 30mg</td>
<td>18mg 27mg 36mg</td>
</tr>
<tr>
<td>IR proportion (Immediate Release) MPH</td>
<td>2.5mg 5mg 10mg 15mg 20mg</td>
<td>3mg 6mg 9mg</td>
<td>4mg 6mg 8mg</td>
</tr>
<tr>
<td>ER Proportion (Extended Release) MPH</td>
<td>2.5mg 5mg 10mg 15mg 20mg</td>
<td>7mg 14mg 21mg</td>
<td>14mg 21mg 28mg</td>
</tr>
</tbody>
</table>
Flow chart on how standard ADHD medication is used in clinical practice

ADHD

Severe ADHD

Moderate ADHD

Parent training and Behavioural treatments

No response

Consider medication
- Always as part of comprehensive treatment plan which includes behavioural, psychological and educational interventions.
- The decision to start medication should be made by a specialist in paediatrics, child and adolescent psychiatry or learning disability.

Educate parent/carer and child/young person
- Discuss ADHD and medications
- Provide written information
- Refer to parent training, if not already done

Identify and agree goals of treatment
- ADHD symptoms
- Behaviour, social skills
- Family relations
- School performance

Pre-treatment check
- Family history of CVS problems
- CVS examination
- Weight, height (Growth chart)
- Pulse rate and blood pressure (Centiles)

Choice of medication
- Methylphenidate, usually first line
- Atomoxetine, typically second line
- See text for indications

Treat with medication
- Gradual titration of medication
- Achieve maintenance dose
- See table 1

Monitor progress
- Adverse effects of medication
- Response
  - Conners rating scales
  - D-DTODS, CGI-I, ADHD-RS

Follow local shared-care guidelines

Regular review
- Medication
- Weight, height, pulse and BP
- Follow NICE guidelines

School support
- Liaison
- Educational support and interventions

Other support
- Refer to local/national support groups

Further management
- Manage any comorbid conditions
- Consider referral for family work (e.g. parent training) if not already provided
- Consider referral for social skills training (e.g. via school) if available

No response

- Check compliance
- Ensure dose is right
- Consider other medication

Identify and manage Comorbid conditions
Re-check diagnosis of ADHD
References for Part 1: How is standard ADHD medication used in clinical practice?

1. Attention Deficit Hyperactivity Disorder – diagnosis and management in children, young people and adults, NICE clinical guideline 72, Developed by the National Collaborating Centre for Mental Health, Sep 2008

2. ADHD - the facts by Mark Selikowitz and published by Oxford University Press, 2nd edition 2009


5. 100 Questions and Answers about ADHD in Women and Girls by Patricia O. Quinn and published by Jones & Bartlett Learning, 2011

6. Once daily Atomoxetine for treating Pediatric Attention Deficit/Hyperactivity Disorder: Comparison of morning and evening dosing. Block SL et al Clinical Pediatrics Sep 2009; Vol 48: no7; 723-733

7. BNF (British National Formulary) for Children, 2011-12

Part 2: How are these recommendations supported by research on treatment outcomes. (This section is by Dr Dave Coghill.)

Notwithstanding the fact that there has been a significant interest in the treatment of ADHD over the past few years, few of the recently published papers have had a major impact on treatment protocols. There are, however, some exceptions. One of the most influential and widely-quoted studies is the Multimodal Treatment of ADHD study (MTA study) in which four treatment arms were compared (medication, behavioural, combined and treatment as usual in the community). Comparison of the medication arm, in which the medication was carefully titrated and monitored, and the community arm, in which medication was often given but not as carefully titrated or monitored, demonstrated just how important it is to have a carefully crafted approach to prescribing in ADHD (1). Comparison of the three active treatment arms was initially interpreted as demonstrating the superiority of medication over behavioural treatment (2). However, a reanalysis of the MTA data demonstrated that for those children and young people who met the criteria for hyperkinetic disorder (severe pervasive impairing ADHD) medication treatment was clearly superior to behavioural treatment, whereas for those with less severe forms of ADHD the two treatment approaches were similar in effectiveness (3).

When thinking about which order the different medications should be considered it would be good to be able to use data from direct head-to-head comparisons of the different medications. Unfortunately there are few such studies and it is therefore necessary to use indirect comparisons of standardised data from different studies. The most common method of making such comparisons is to use effect sizes. These are a standardised measure of the strength of action of a treatment (also see paper on “ADHD and Other Medications” in this issue, in which effect sizes are defined and discussed). In clinical trials of medications for ADHD, both stimulants (short and long acting) and atomoxetine have been associated with moderate to large effect sizes. The effect sizes for stimulants are generally larger (mean ranges between 0.8 and 1.0) than those for atomoxetine (0.7) (4). However recent clinical trials with atomoxetine that have been longer in duration (up to 12 weeks) have reported effect sizes up to 1.3 (5). It is important to put these effect sizes into context as they are considerably greater than those seen with other psychiatric drugs (e.g. SSRI antidepressants 0.5, antipsychotics 0.25).

When using long-acting methylphenidate preparations it is essential to acknowledge that the three licensed long-acting methylphenidate preparations; Equasym XL, Medikinet XL and Concerta® XL each have different proportions of immediate-release and extended-release methylphenidate and the extended-release component also differs with respect duration of action (see Table 1). Studies have demonstrated that these differences translate into different profiles of action across the day and that these are very closely related to the pharmacokinetic profiles of each preparation (6, 7). It is therefore very important that clinicians familiarise themselves with these different profiles and make use of them to tailor treatment to individual needs.
For patients who have problems in the evening it may be helpful to consider atomoxetine, as studies have suggested that, even when given once daily, the effects of atomoxetine can continue throughout the evening and into the morning (8). Recent evidence suggests that the effects of atomoxetine continue to develop over the first few months of treatment. It is therefore sensible to continue with treatment for at least 12 weeks before conceding a lack of effect (5, 9). Evidence is also starting to emerge to support the notion that atomoxetine impacts positively on quality of life as well as reducing symptoms (10). Unfortunately similar studies for stimulants are still to appear.

Where methylphenidate has been tried but resulted in an inadequate response at the maximum tolerated dose, it has become fairly routine to consider atomoxetine. It is worth noting however that only around 40% of methylphenidate non-responders respond to atomoxetine (11) compared to around 66% who will respond to dexamfetamine (12).

In this context it is interesting to speculate why dexamfetamine, which has been available for many years, is used so infrequently in the UK, whilst in the United States amphetamine products are much more widely used. Even though NICE excluded almost all of the clinical trials of dexamfetamine in ADHD because of their crossover design, there is considerable evidence to support the use of dexamfetamine as an alternative in children who do not respond to methylphenidate or experience significant adverse effects from this drug. The main drawback of dexamfetamine is that it is only available as an immediate-release preparation in Europe. This is particularly pertinent in view of the concerns about abuse potential. Studies do, however, suggest that the amphetamines are equally effective as methylphenidate with no additional safety or tolerability issues (13). In general 70% of patients will respond to methylphenidate, 70% will respond to amphetamines and between 90 and 95% will respond to one or the other (12). As noted above it is therefore more likely that a methylphenidate non-responder will respond to dexamfetamine than to atomoxetine. These findings may become more relevant in Europe in the near future if lisdexamfetamine, an amphetamine prodrug that is already marketed in North America, is licensed for use in Europe. Several published studies have supported the efficacy, tolerability and safety of lisdexamfetamine in the treatment of ADHD (14, 15) and studies in Europe are ongoing.

Two other treatments for ADHD that have been used off-label for many years have now been approved by the FDA for use in the United States (also see paper on “ADHD and Other Medications” in this issue). These are the two alpha-2 agonists, clonidine and guanfacine (both preparations are extended release). Randomised controlled trials have demonstrated both to be safe and effective in treating ADHD, although only the results of the guanfacine studies have been published (16, 17). The effect sizes for the alpha-2-agonists are smaller than those for stimulants. The adverse-effect profile of these drugs suggests that they may be particularly beneficial as adjunctive rather than stand-alone treatments. Again European studies of extended-release guanfacine are ongoing.

GP Comment.

What have I learned from this paper?

1. These are clear useful medicines-management guidelines on drugs for treating ADHD.

2. This practical guide should be very useful for the GP in the day-to-day management of patients with ADHD by offering a quick reference to the issues that matter, supported by reputable publications.

3. The large amount of information and the increasing numbers of medications/formulations used to treat ADHD can be very confusing; the flow sheets and table in this paper offer clear guidance and information.

4. A community-based mental health nurse would be able to liaise with the GP, schoolteachers and family during the ongoing treatment phase of medication.
5. It is reassuring to know that current practice in treating ADHD is supported by published research.

Dr. Peter Cliffe, GP, Surrey.

References for Part 2.


Other Medications of Use in ADHD

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Abstract

Perhaps as many as 20% of individuals with ADHD will not respond adequately to the three medications recommended in the current NICE guideline. This paper considers treatments that are not recommended in the guideline but appear to be useful in the treatment of ADHD. The “effect size” and “common language effect size” (CLES) are defined and are quoted where data is available, as a guide to choosing effective alternatives. The alternative medications considered include clonidine, atypical antipsychotics, antidepressants, modafinil, and amantadine.

Introduction

The NICE guideline recommends only methylphenidate, atomoxetine and dexamfetamine as pharmaceutical treatments for ADHD. However, as the effect sizes suggest, as many as 20% of children needing treatment for ADHD will not respond sufficiently to these alone. This paper covers other drugs which have shown promise in the treatment of ADHD.

“Effect Size” and “Common Language Effect Size” (CLES) are standard measures used to evaluate the efficacy of drugs and will be quoted in this paper where the data is available. These terms are defined in the Appendix. However, effect sizes are not sufficient in themselves. The literature that generates them needs to be combined with professional skill in order to choose the best alternative or addition. Below are some rules of thumb, which should ensure that a clinician is able to employ both professional skill and the literature available in the most effective manner.

1. Ensure that the prescribed medications are actually being taken.

2. Prescribe guideline drugs at sufficient dosage and for sufficient duration. This is particularly important for atomoxetine, which can take several weeks to become fully effective.

3. Hunt for comorbidity. Psychiatric comorbidity is common in people with ADHD (1). (See other papers on comorbidity in this issue.) Adding a drug to treat a comorbid condition, or changing to a drug or dosage which treats it, might improve effectiveness.

4. Consider “trailing edge” technology. Older drugs often have better understood adverse-effect profiles; the commercial pressures to gain a return on investment will be less, and there will be a longer period for evidence to accumulate.

5. Unless comorbidity suggests otherwise, try switching drugs before combining drugs. Both on empirical and theoretical grounds, adverse effects are more likely with multiple drugs, and there is no empirical evidence to prefer combinations.

6. Do not disregard adding further psychological interventions if initial physical interventions are insufficient; empirical evidence suggests they can add effectiveness, particularly in the presence of comorbidity (2,3).

7. Guidance is expensive and time-consuming to produce, and so is updated infrequently. Therefore, it is reasonable to investigate drugs which have been approved for use in other jurisdictions. The American FDA have stringent and transparent approval processes, enabling reasonable assessment of efficacy.
Alternative drugs approved elsewhere

The alpha-2 adrenergic agonists, clonidine and guanfacine, have both been licensed for ADHD by the American FDA. Clonidine has been used for some time as an adjuvant to stimulants, particularly when the symptoms of ADHD have been associated with severe temper outbursts or tics (4), although the use of this combination waned when safety concerns emerged (5). The concern about cardiovascular safety has been challenged (6) and it would appear that there is no basis for this in individuals who do not have pre-existing cardiac problems. Some practitioners recommend an ECG before treating with a combination of methylphenidate and clonidine or even before treating with clonidine without methylphenidate. Subsequently, clonidine began to be used alone for sleep disorders (7) and was suggested as a first-line treatment for ADHD in the presence of tics (8). It has been evaluated, in a new long-acting form, for treatment of ADHD, where the estimated effect size for dosage up to 0.4mg/day was between .7 and .8 (CLES .69 – .71) (9). Patches have been trialled for tic therapy, and no additional safety issues have emerged (10). The long-acting versions are not available as part of the British formulary but the half-life of clonidine is typically 12-16 or more hours in adults and, in practice, twice daily administration appears to be satisfactory in children. There is a theoretical risk of rebound hypertension if doses are missed; this has not been formally evaluated but the usual advice is to avoid stopping clonidine suddenly because of the potential risk of a sudden rise in blood pressure. The drug has “orphan” status in relation to Fragile X syndrome. Guanfacine is similar to clonidine, except that its half-life is 18 hours, giving it a longer duration of action and possibly less susceptibility to rebound hypertension, though the risk theoretically remains. A long-acting preparation is now available to provide 24 hour cover and has been trialled for ADHD. It demonstrated an effect size of between .62 and .89 (CLES .66 – .74) (11,12), with insignificant adverse effects reported so far.

A second rational choice would be drugs shown to be useful in other disorders, which have been found to have efficacy in ADHD. Table details the effect sizes of the major classes of these drugs.

Table: Effect sizes and Common Language Effect Sizes on ADHD for medications used in other disorders (13)

<table>
<thead>
<tr>
<th>Medication class</th>
<th>EFFECT SIZE</th>
<th>CLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRIS FOR OBSESSIVE-COMPULSIVE DISORDER OR DEPRESSION</td>
<td>.5</td>
<td>.64</td>
</tr>
<tr>
<td>ANTIDEPRESSANTS FOR GENERALIZED ANXIETY DISORDER</td>
<td>.39</td>
<td>.61</td>
</tr>
<tr>
<td>ATYPICAL ANTIPSYCHOTIC DRUGS* FOR SCHIZOPHRENIA</td>
<td>.25</td>
<td>.57</td>
</tr>
</tbody>
</table>

*OLANZAPINE, QUETIAPINE, RISPERIDONE, AND SERTINDOLE

19% of children with ADHD are reported as having comorbid anxiety and 14% comorbid depression (14); given that inattention is an important symptom for both these disorders, the effect sizes quoted above may underestimate the impact of effective treatment of these comorbidities.

Antipsychotics are valuable for mood dysregulation, aggression and irritability, which are frequently comorbid with, but not diagnostic of, ADHD, implying that these drugs are likely to be valuable for augmenting first-line treatments in the presence of comorbidity. Risperidone appears to be particularly valuable in reducing anxiety and behavioural problems in children with learning disability and autism spectrum disorder; as a result, it may also decrease some of the characteristics associated with ADHD in these children. McCracken et al., in a randomised, double-blind, placebo-controlled trial demonstrated reductions in irritability (p<0.001), tantrums, aggression and self-injurious behaviour in children with autistic disorder treated with risperidone. Aripiprazole is also being used for this indication, although the evidence is relatively sparse.

1 A drug is said to be “orphaned” when a possible indication for a rare disorder exists, but the likely returns on investment are deemed too small to allow a commercial development programme.
Tricyclic antidepressants and buspirone have an anti-hyperactivity effect; however, the adverse effects associated with these drugs have resulted in very limited current use. They might be considered if licensed medications have failed or have been unacceptable.

Modafinil is not related to any of the drugs already discussed. It is used to treat narcolepsy but several studies found it to be effective in ADHD, with an effect size of 0.69 – 1.08 (CLES 0.69 – 0.76). There has been concern about reports of skin rashes, with the unconfirmed possibility of Stevens-Johnson syndrome. However, all the skin rashes reported resolved without sequela, and not all were unequivocally related to modafinil. Aggression has also been reported as being a problem in around 2%. The decision not to develop modafinil further as a treatment for ADHD was taken by the drug company, rather than regulatory agencies, who had merely asked for more data. It may remain a possibility for difficult-to-treat ADHD, although it might be advisable to escalate the dose slowly and to monitor the patient closely because of the possible risk of skin rash (15).

Finally, amantadine has the advantages of a long history and a well-understood adverse-effect profile; it is better known for its use in post-traumatic attentional states (16) but may also be of benefit in ADHD (17). The single randomised controlled trial undertaken, an equivalence study with methylphenidate, does not allow estimate of effect size.

Alternative formulations approved elsewhere

Though not licensed in the UK, methylphenidate is also available as a transdermal patch; it has shown good acceptability, equivalent effectiveness to oral delivery methods (18) and possibly some advantages for the child’s quality of life (19). It is clearly of use for children who have difficulty swallowing tablets.

Though amphetamine is of equivalent efficacy to methylphenidate, and with a slightly worse adverse effect profile overall (20), nonetheless individuals may respond differently to amphetamine from methylphenidate, allowing a switch within the most effective class of medication for treating ADHD. While long-acting amphetamine preparations are not licensed in the UK, oral long-acting preparations have received FDA approval (21), and offer a potential alternative without requiring frequent dosage. Lisdexamfetamine is an interesting formulation of dexamfetamine because it is said to be active only when taken by mouth; this avoids the likelihood of “diversion” into intravenous or inhaled use. It has been approved by the FDA and there has been some recent activity to obtain European approval.

Conclusion

There is evidence that some drugs not recommended in the NICE guideline may nevertheless be effective and these should be considered if the child with ADHD has not responded to the standard drugs. However, before changing medication, the whole situation, including issues such as social factors, compliance and appropriate dosage, should be re-assessed carefully.

Appendix.

Definitions of “Effect Size” and “Common Language Effect Size” (CLES).

Effect size is the difference between two means (generally of the treatment group and placebo group) divided by the standard deviation of what is being measured. Effect sizes of around 0.2 are considered “small”; 0.5 “moderate” and 0.8 “large” (3). However, this figure disguises the proportion of cases in the treatment group which have not improved relative to the control group. The equivalent “Common Language Effect Size” (CLES) is defined as the probability that a person selected at random from the treatment group will have a higher score than that of the control group (4). It can be thought of as the likelihood that a “typical” patient who is treated will be better than a “typical” patient remaining untreated. A CLES of .5 means that treated and untreated groups will have a similar proportion of patients getting better (Definition adapted from Wikipedia.)
GP Comment.

What have I learned from this paper?

1. Methylphenidate, dexamfetamine and atomoxetine are recommended by the NICE ADHD guideline but are not always effective or may have unacceptable adverse effects, implying that other medication may be required.

2. There is reasonable evidence for a positive effect of clonidine in ADHD and it can be particularly helpful in individuals who have sleep disturbance; however, it should not be stopped suddenly because of the theoretical risk of rebound high blood pressure.

3. There is good evidence for reduction of irritability, anxiety and behavioural disturbance with risperidone, particularly in young people with autism spectrum disorder, although this drug might not directly treat the core symptoms of ADHD.

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References.


Adverse effects of medication

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No financial competing interests. The author was a member of a NICE guidelines development group and a European Guidelines Group review of adverse effects and has published books and papers on the treatment of ADHD.

Abstract

The commonest adverse effects of methylphenidate and dexamfetamine are appetite suppression, weight loss and sleep disturbance, although sometimes sleep is improved. There can be a modest effect of stimulant medication on decreasing growth velocity, but even this can be avoided by regular monitoring and adjustment of dosage or preparation when needed. Tics are not a contraindication to stimulant medication but exacerbation of tics may warrant dose reduction or change of medication. Both stimulant medication and atomoxetine can increase blood pressure, but any increases are usually small. The risk of sudden death does not appear to be increased by stimulant medication. Routine ECGs are not recommended. Specialist opinion should, however, be sought before medication is commenced for patients with a relevant personal or family cardiac history. Baseline measurement and regular follow-up monitoring of blood pressure, pulse, height (in children) and weight are recommended for patients taking stimulant medication or atomoxetine. The potential for substance misuse is probably not increased by prescribing medication for ADHD. Psychotic symptoms are only rarely associated with ADHD treatment. Most of the adverse effects of licensed medication for ADHD are mild and/or easily reversible.

Introduction

Because millions of patients have been treated with stimulant medication, which has been prescribed for several decades, the adverse effects are well known. Methylphenidate, dexamfetamine and atomoxetine are licensed and widely used in the UK for the treatment of ADHD in children. They are also useful and authoritatively recommended for treating adults even though no marketing licences are in place (except for atomoxetine, provided treatment was started in childhood).

Adverse effects need to be prevented and managed. This article considers their prevalence and recommends actions for prescribers.

Neurological effects

Most adverse neurological effects are mild and/or temporary: headache and dizziness in the early stages of treatment will often disappear without any particular action or simply by dosage reduction for a period.

Insomnia is quite common in children with ADHD who are not medicated (1). Studies comparing medicated and un-medicated children describe inconsistent outcomes, both for polysomnographic measures and for parental reports (2). It is only to be expected that stimulants will stimulate, but the short action of most stimulants means that most of the effect has disappeared by bedtime. Furthermore, for some children falling asleep may be a problem in self-regulation that stimulant drugs may actually help.

The initial management will probably be by advising sleep hygiene, behaviour therapy techniques based on stimulus control, and appropriate bed-time scheduling. Adjusting the timing of doses is often effective; eg switching from a long-acting drug (such as Concerta XL) to a shorter-acting preparation of medication (such as Equasym XL, Ritalin LA, Medikinet or immediate-release methylphenidate).
The next step will be to consider a change of medication. Atomoxetine does not usually disturb sleep, and in one study (2) was shown to be more helpful for sleep than methylphenidate. Clonidine, which has both sedative and anti-hyperactivity actions, can be effective in ADHD with associated sleep problems (3). Melatonin has trial evidence to support its use in reducing sleep-onset problems in ADHD children (4), and is probably the most widely used add-on for this purpose in the UK.

Tics are quite common in un-medicated people with ADHD (5). Some formularies still present a contraindication for the use of stimulants in patients with Tourette Disorder (5,6), and even for people who only have a family history of tics, but this is outdated. Recent reviews (7,8,9) indicate that stimulants do not cause de novo Tourette, and “should not be disregarded” when planning treatment for ADHD in the presence of tics.

On the other hand, a few people with established tics (about 5-10%) may show an exacerbation with stimulants. The natural history of tics is to fluctuate, so a rapid reaction by the prescriber is not usually the best way to go. An increase due to stimulants will be reversible with withdrawal or dose reduction of the drug and in any case may be seen as a price worth paying for good ADHD control. Atomoxetine does not worsen tics and may even improve them, so it can be a useful add-on medication (10,11,12). Clonidine has some action in reducing tics, and has some anti-hyperactivity action when in combination with methylphenidate; so it can be a useful add-on medication (13).

Epilepsy is not a contraindication to anti-hyperactivity medication. There are occasionally concerns that, as with other psychotropics, ADHD medications may lower the seizure threshold so as to cause seizures in previously seizure-free individuals. However, in prospective trials, retrospective cohort studies and postmarketing surveillance in ADHD patients without epilepsies, the incidence of seizures did not differ between ADHD pharmacotherapy and placebo (relative risk for current vs non-use for methylphenidate: 0.8; for atomoxetine: 1.1) (14,15).

**Cardiovascular adverse events**

CNS Stimulants can increase both blood pressure (average increases 1 to 4 mm Hg systolic and 1 to 2 mm Hg diastolic) (16) and heart rate (1-2 beats per minute) (17,16). While such small changes seem trivial, they can imply an increase in the number of children at the extreme end of the scale. The risk from hypertension is considered to need intervention when the blood pressure exceeds the 95th centile. The initial evaluation and monitoring of blood pressure should therefore be recorded on centile charts. Normative charts are available for several countries (18,19,20), so local norms should be used wherever possible. Monitoring of blood pressure and heart rate should be at least 6-monthly; and in any case after dose increases. If the first recording is elevated, then it should be repeated at least twice and if still elevated, and above the 95th centile, then a dose reduction or drug holiday should clarify whether the drug is responsible. If the blood pressure remains high, then referral to a paediatric hypertension specialist is required, for 24-hour ambulatory blood pressure recordings to confirm the diagnosis and to initiate any investigations for end organ damage. If the blood pressure has come down to normal, implying that the drug is responsible, then the options available include reverting to non-pharmacological management of hyperactivity, which is not always successful, or switching medication. However, other drugs may well have the same effect. Specialist paediatric consultation is advised; the outcome may include continuing medication with the addition of an antihypertensive (clonidine being an obvious choice).

Routine ECG monitoring is not required for children on stimulant medication or atomoxetine. The biggest fear has been that there might be a risk for sudden death. Epidemiological surveillance, however, has indicated that otherwise unexplained sudden death is extremely rare in the medicated population – so rare, indeed, that it is very hard to tell whether it is any commoner than in the general population of children (where the rate is approximately 1.2 to 1.3/100,000/yr) (21,22,23,24,25) 25 sudden deaths were identified by the FDA in individuals prescribed ADHD medications, corresponding to a low figure of 0.2-0.5/100,000/year (21). This does not, of course, mean that the anti-hyperactivity drugs are protective against sudden death. It is very possible that there is under-reporting – a rule of thumb is that about 50% of major adverse effects are not reported, but there is much room for uncertainty.
The average QTc interval is not changed significantly by methylphenidate, amphetamine salts or atomoxetine. If there is a risk in the individual case (e.g. in a patient known to show the congenital long-QT syndrome), then detailed discussion and a cardiological opinion should guide practice. In summary, pre-treatment cardiovascular screening should include any known cardiac problem, a history of cardiac symptoms (e.g. arrhythmias, or undue breathlessness, or syncope on exercise), a positive family history of sudden death below the age of 40 years, and measurement of blood pressure and heart rate.

Self-injury

Suicidal thinking was found to be a little more common among children and adolescents treated with atomoxetine (5/1357) compared to those treated with placebo (0/851) in clinical trials. This implied a number needed to harm (NNH) of 227, compared to the number needed to treat (NNT) of 5, to achieve remission of ADHD symptoms (26). The evidence for stimulants is less clear, so, as a precaution, they too should be seen as carrying a small risk. Families and caregivers should be advised of the need to recognize any emergence of emotional change or self-injurious thinking; and to communicate well with the prescriber (27).

Adverse effects on growth

On average, the reduction in height amounts to approximately 1 cm/year during the first 1-3 years of treatment (28). The reduction in weight gain appears to be somewhat more pronounced than that for height (over a 3-year period about 3 kg less than predicted) (29,30).

Small effects were seen for atomoxetine during the first 2 years of treatment; but in those who received prolonged treatment for up to 5 years, no long-term effects on growth were apparent, apart from an overweight subgroup (31,32).

Patients and their parents should therefore be told about the potential for growth suppression. A 1-year height velocity >2 SDs below the mean, or a 2-year height velocity >1.5 SDs below the mean would trigger particular concern. Nevertheless, the use of a growth chart (e.g 6-monthly) should detect any early signs of growth slowing (33). Symptomatic measures would include adjusting the timing of doses (e.g. taking the first dose after breakfast) and meals (e.g., late evening meal) and encouraging the use of high-energy, nutritious snacks. Drug holidays usually seem to allow children to return to their normal growth trajectory.

Substance abuse and psychotic symptoms

Stimulants can be misused to achieve a ‘high’ (by injection or inhalation, not ordinarily by the oral route) or for other reasons, such as to aid weight loss, improve studying, or manage without sleep (34,35).

Whether stimulant medication adds to the risk for substance abuse is not clear; several studies suggest it does not. A meta-analytic review of six studies suggested that stimulant therapy in childhood may be associated with a reduction in risk, compared to un-medicated ADHD subjects, for subsequent drug and alcohol use disorders (36). The reduction in risk might be attributable to treatment rather than stimulant medication in particular: the follow-up of a large clinical trial found a reduction in risk for those patients treated with behaviour therapy; medication had no effect one way or the other (37). Euphoric properties and reinforcing effects of methylphenidate are associated only with intravenous injection or nasal inhalation and not with oral administration (38). Misuse or diversion of stimulants has been reported in adolescents and young adults in North America, usually in order to improve academic performance (studying, staying awake, improved alertness) (39,40,41).

Depending on the specific situation, current or previous substance abuse in the family should be seen as either a relative contraindication for stimulant prescription, (especially in the immediate
release preparation), or as a reason for particularly close monitoring of a patient’s stimulant use. The extended-release formulations of stimulants are less prone to diversion because these preparations cannot easily be crushed into powder for injection or snorting, and also because the once-a-day administration makes parental supervision easier to enforce. On the evidence of preclinical data and short-term clinical and abuse liability studies, atomoxetine does not appear to be associated with risk for substance use disorders, and may well be preferred in high-risk cases (42).

Use of cannabis is not necessarily a contraindication to prescribing stimulant medication, and a pragmatic approach will be required. The other dangers of cannabis, however, should not be ignored and patients will need to be warned of these. Cocaine, however, is likely to be a real hazard in view of its sharing neurochemical effects with dopaminergic drugs, and the two should not be combined. Psychotic symptoms are only rarely associated with ADHD drug treatment. The United States Food and Drugs Administration reviewed 49 RCTs of ADHD drugs in children and found a total of 11 psychosis/mania events during 743 person years of exposure with ADHD drug treatment, compared to no psychosis events reported with placebo (43). If psychotic symptoms occur, the medication should be stopped and an urgent referral to the specialist should be made.

Conclusions

The licensed medications for ADHD should be considered as low-risk, and safer than other psychotropic drugs. For most cases, monitoring of blood pressure, pulse rate, and growth in height and weight, will be sufficient in primary care. Shared care with a specialist service should be developed for the regulation of dose and psychological effects, and for management of any of the uncommon adverse events described in this paper. A recent, full review of adverse events has been published by a European Guidelines Group (44), and is recommended for further reading. The author, who was a member of the group, has drawn on his colleagues’ work, and gratefully acknowledges their systematic research.

GP Comment.

What have I learned from this paper?

1. Appetite suppression, weight loss, sleep disturbance, small increases in blood pressure and pulse, and some effects on growth can occur with medication used to treat ADHD but these adverse effects are usually mild and/or easily reversible.

2. In keeping with NICE guidelines, height, weight, blood pressure and pulse should be monitored regularly.

3. The “side effects” of some medications may be helpful; for example, clonidine used to treat ADHD may also assist with sleep disturbance.

4. Previous concerns about risk of sudden death with ADHD treatment have not been confirmed.

5. The evidence suggests that the risk of substance misuse is not increased by medications for ADHD.

6. Overall, it would appear that the recommended medication used to treat ADHD is associated with a low risk of any serious adverse effects.

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References


Cardiovascular effects of ADHD medications in children

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Abstract

While methylphenidate, amphetamines and atomoxetine play a significant role in the pharmacological management of ADHD, there have been some safety concerns raised over the last few years with respect to cardiovascular morbidity. The literature has been reviewed, exploring the effects of ADHD medications with respect to sudden death and alterations of heart rate (HR), blood pressure and QT interval. There is some evidence of increased HR and BP using these medications but there is no evidence of a clinically-significant impact. However, most of the published data is on average results and might mask individual cases in which there is a clinically significant change. Regular monitoring of BP and pulse, using the same procedure on each occasion, is recommended. There is no convincing evidence of an association with QT interval prolongation or sudden death. Routine ECGs before starting these medications are not considered to be necessary. However, for each child a careful personal and family history of cardiovascular problems should be taken and a cardiovascular examination should be performed before medication is commenced.

Introduction

Attention deficit hyperactivity disorder (ADHD) is one of the commonest neurobehavioural conditions in children with a worldwide mean prevalence of approximately 5% (1). The figures for prevalence depend on the criteria used. In the UK, a survey of 5-15 year old children revealed that 3.62% of boys and 0.85% of girls had ADHD (2).

The management of ADHD is predominantly a combination of behavioural strategies and pharmacological agents, commonly methylphenidate, amphetamines and atomoxetine. There is good evidence that these measures have a beneficial effect. As these drugs are so widely used it is important to ensure that they are safe. In recent years concerns about the cardiovascular safety of drugs used in the treatment of ADHD have been raised and this culminated in the suspension of a mixed amphetamine salt in Canada (2005) and a “black box” warning by the US FDA Drug Safety and Risk Management Advisory Committee (2006) about possible cardiovascular risks associated with stimulant medication (3).

This article will explore the cardiovascular effects of the main ADHD medications, namely methylphenidate, amphetamines and atomoxetine in relation to sudden death and, alterations in heart rate, blood pressure and QT interval.

Sudden Death

In the general paediatric population, sudden death is a very rare event with a rate ranging from 0.8 to 8.5/100000 patient-years (4). In comparison, the reported rates were 0.2 to 0.5 per 100000 patient-years associated with methylphenidate, amphetamine products and atomoxetine (5). The risk of methylphenidate causing sudden death to patients has been estimated to be 0.22 deaths per 1 million prescriptions (6). The USA the Food and Drugs Administration (FDA) combined with Health Canada, have identified 12 cases of children aged 1 to 18 years taking ADHD medications between 1999-2003 who fulfilled the criteria for sudden death (4). This data must be interpreted with caution as only an estimated 1-10% of serious adverse effects are actually reported and an association does not necessarily imply causation. In the UK a similar system is led by the Medicines and Healthcare Products Regulatory Agency (MHRA). With respect to methylphenidate only 12 reports of fatalities have been reported for all ages from 1964 to 2010 (7). Many of these deaths were placed in categories unrelated
to sudden death. Finally the analysis of 10 year adverse event reporting in Denmark revealed no sudden deaths in children taking ADHD medications (8).

A recent matched case-control study compared stimulant use in 564 children who had sudden unexplained death in one group and passengers dying in motor vehicle accidents in the other group (9). There were ten (1.8%) children in the former group compared to 2 (0.4%) children who in the latter were on stimulant medications. The authors stated that this provided support for the association of stimulant use and sudden unexplained death. The FDA expressed reservations about this study: a retrospective cohort study of over 1.2 million children and young adults (2-24 years old) has not shown an increased risk of serious cardiovascular events (sudden cardiac death, acute myocardial infarction, and stroke). However, the authors stated that the upper limit of the 95% confidence interval indicated that a doubling of the risk of a serious cardiovascular event could not be ruled out.

Although it is difficult to interpret and compare data directly, it would appear that sudden death remains an extremely rare event. At present there is no convincing data suggesting that ADHD medications increase the risk of sudden death.

**Heart rate & blood pressure**

Both heart rate (HR) and blood pressure (BP) are dynamic variables influenced by several factors. Studies assessing the effects of ADHD medications on HR and BP need to take these factors into account and should attempt to standardise these measurements as much as possible (39). There should be a clear protocol for measuring BP and HR and this should include serial measurements. Because there are various formulations of methylphenidate, including immediate-release and extended-release varieties, comparing BP and HR at a set time after the drug dose may not be appropriate in view of the different pharmacodynamics. Further confounding factors for long-term studies (over several months to years) attempting to assess the impact of ADHD medications on HR and BP are the normal decrease in HR and increase in BP which occur with increasing age (39). It should also be noted that average data are presented in most publications; such data may conceal individual cases in which large, clinically important, changes might occur.

Studies examining the effects of methylphenidate treatment over a few weeks either reported that methylphenidate did not result in a statistically significant increase in HR and BP or, in circumstances where there was a statistically significant increase, that the effects were not considered to be clinically significant (10-17). One long-term study over several months indicated that methylphenidate might increase HR and systolic BP by up to 3.9 beats per minute (bpm) and 3.3mmHg respectively, although another study demonstrated no effect on HR and a 3.4mmHg rise in systolic BP (18, 19).

Amphetamines in the short-term (within 12 weeks of commencing treatment) caused statistically significant increased HR of up to 5 bpm in some studies compared to placebo, (3,20) whereas others showed no significant difference in HR (21-23). None of these studies showed significant changes in BP. Long-term treatment with amphetamines did cause statistically significant increases in HR (up to 4.4 bpm) and BP (up to 1.7mmHg for systolic BP) but these were judged by the authors of the studies not to be clinically significant (20, 22, 24-26).

Atomoxetine does appear to cause statistically significant increases in HR in the short-term and long-term (27-32). The mean increase in HR was up to 9 bpm in these studies. Diastolic BP increased by up to 3mmHg while systolic BP was not affected in some studies and in others it rose by up to 9mmHg. These figures did not take into account the changes that occur to HR and BP with increasing age (up to 4 years in some studies) and the authors did not consider that these changes were clinically significant. It should also be noted that these measurements were not the primary outcome of the studies.

Although there are significant methodological limitations, some studies demonstrate statistically significant effects on BP and HR, while others demonstrate no effect. Therefore, it is very important to consider whether these have clinically significant effects on children and more important whether any associated morbidity arises from these effects. At present there is no strong evidence demonstrating
a clinically significant effect of increased HR and BP or cardiovascular morbidity associated with ADHD medications (39).

**QT interval prolongation**

A prolonged QT interval may be associated with fatal cardiac arrhythmia and has therefore become a surrogate marker for a potential increased risk of sudden cardiac death (45). Data on ECG changes with methylphenidate is lacking, although there is no evidence supporting prolonged QTc interval with this drug. Methylphenidate may cause other ECG changes but these appear to be very rare. Furthermore, current National Institute for Health and Clinical Excellence (NICE) and American Academy of Pediatrics (AAP) guidelines state that children commencing methylphenidate do not routinely require an ECG (33, 34).

Amphetamines and atomoxetine have been studied in more detail. The majority of evidence suggests that amphetamines do not cause a statistically significant increase in QTc interval; in a couple of studies there was a significant change in QTc, but this was considered to be clinically insignificant by the authors (40-44). Case reports to the MHRA have suggested that atomoxetine might increase the QTc interval when used at the correct doses in the majority of studies (27, 35-37). However, in a recent long-term study, although there was no overall significant change in QTc interval, as many as 30% of children had an increase in QTc ≥ 30msecs. This depended on the formula used to measure the QTc but suggests that in individual cases atomoxetine may indeed increase the QTc (31). The authors regarded the increases seen as clinically insignificant.

**Conclusions**

Methylphenidate, amphetamines and atomoxetine are the commonest medications used to treat ADHD. Although there is some evidence of increased HR and BP with these medications, there is no evidence of any clinically significant impact. Similarly, there is no convincing evidence of QT interval prolongation or sudden death and therefore, a routine ECG in children with ADHD is not recommended (34). The recent European guidelines on managing the adverse effects of ADHD medications suggest the checking of BP and HR prior to treatment with monitoring every 3 to 6 months, although it states this may vary with individual cases (4). Further research and continued reporting of suspected cardiovascular adverse effects are recommended, to identify potential rare adverse effects. However, at present, these ADHD medications appear safe and they play an important role in the comprehensive management of ADHD in children.

**GP Comment.**

What have I learned from this paper?

1. Provided there is no personal or family history of cardiovascular problems and if the cardiovascular examination is normal, I can reassure families that there is no evidence showing an increased rate of heart problems or sudden death associated with methylphenidate, dexamfetamine or atomoxetine.

2. There is some evidence for increased heart rate and blood pressure with ADHD medication; regular monitoring of heart rate and blood pressure is recommended.

3. Despite the reassuring lack of strong evidence that these drugs have a significant impact on cardiovascular health, the paper still acknowledges potential risks; it cautions clinicians to monitor HR and BP prior to treatment and at 3-6 monthly intervals, even if there is no personal or family history of cardiovascular problems and if cardiovascular examination is normal.

4. I would suggest there is a need to investigate the long-term health outcome of these drugs, arguably over many years into adulthood.
5. In contrast psychological help to re-inforce the natural support system of family plus educational support has no adverse effects or risks to health- to my knowledge! In addition these simple measures support independence rather than encouraging reliance on drugs and professionals.

6. Without doubt, drug therapy is needed for some children and this article offers some reassurance.

7. As a GP with no expert knowledge of these drugs, I have witnessed the benefits of early psycho-social support.

8. I wonder in times of limited resources, if targeting vulnerable children and families to improve coping skills before crises develop might prevent escalation to ill-health and be more beneficial for long term health outcome and for the public purse?

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References


Abstract

Although both the diagnosis and treatment of ADHD are well-established, controversy continues to surround the prescription of medication. This article considers the ethical and legal basis for such prescriptions, indicating how other professional and family concerns and values may be explicitly included in giving appropriate advice about the appropriateness of drug prescriptions.

Introduction

The diagnosis and treatment of ADHD remains controversial. There is continuing negative media coverage, especially over the prescription of medication (1). Recent American data suggests that 3.5% of children there are taking medication to treat ADHD (2), which is much higher than the rate in UK children (3). Specialists have to defend their decisions, but much concern is also likely to be expressed to GPs, who often share responsibility for medication management of ADHD; some GP opinion-formers have strongly sceptical views about the prescription of medication for ADHD (4). This may pose considerable problems for GPs when discussing matters with patients, particularly as the initial decision to medicate is usually not their own. The anti-medication argument has two strands. The first, regarding the reliability and validity of the ADHD diagnosis and treatment effectiveness, is discussed in the context of applying the model proposed here. The second involves the value placed upon behaviour of children, particularly in relation to ownership of responsibility for that behaviour.

This strand cannot be answered by a simple appeal to the literature; a different approach is required, which directly addresses the ethical questions it raises.

Medication or Moral Responsibility in ADHD: a false choice

The essence of the moral objection to the use of medication for ADHD is that it implies that the diagnosis may be used to excuse morally repugnant actions by those with it, and those actions may be recruited as evidence for the diagnosis. Impulsive antisocial behaviour, if repeated enough times, may attract an ADHD diagnosis, which then excuses those actions, and the provision of medication confirms that excuse. If the medication is successful in suppressing the behaviour, then the ADHD sufferer obtains full rehabilitation without any apparent mental effort or requirement for remorse. Central to this argument is the ancient concept of “Mens Rea”, or evil intent, which is deemed an essential part of establishing criminal responsibility (5), and the lack of which is understood to be a consequence of mental illnesses and disabilities of all kinds. Arguments may be developed to recruit psychological treatments to programmes of moral improvement (6) but it is hard to see how drugs, which produce behaviour change irrespective of the willed choice of the user, can be deemed to improve morality without undercutting one of the basic tenets of ethical behaviour; freedom of moral choice.

To manage these moral issues, we should begin with who we are in this context: medical practitioners. This implies, as it always has, that our moral judgements should be limited to our own behaviour, not those of our patients. So, irrespective of whether we agree or disagree with the moral position just set out, we have no professional justification to apply our conclusions to our patient. Instead, our duty is to apply ordinary medical ethical principles, and show to our patients and our families we are following them honestly in making our recommendations.
An ethical model for ADHD diagnosis and medication management

If we are to apply ordinary medical ethics, it follows that in the diagnosis of ADHD, and subsequent prescription of medication, ethical medical practice must be consistent with respect to four principles: respect for autonomy, beneficence, non-maleficence (which is better known as “primum non nocere” – first do no harm) and justice (7). Ethical concerns lead to legal processes, the task of which is to ensure ethical practice. So, legal processes should be interpreted—with respect to doctors and as far as possible—as applications of the ethical principles just mentioned, and should be followed accordingly. Finally, we should work to the interests of our patients. Combining these three components allows the development of a working ethical model to provide useful, reliable guidance in ordinary clinical practice (8).

Consider an ordinary referral for a hyperactive child, who is assessed, diagnosed and treated. We begin by meeting our legal duty to manage the referral to ensure it is treated optimally. We seek consent, aware that assessment or treatment without consent, normally constitutes the legal offence of battery (9). Usually, we seek consent from the parents but try to take the child's views and wishes into account. Despite concerns about whether this offers children, particularly teenagers, sufficient autonomy, the overwhelming weight of law and guidance is on our side. We undertake a thorough assessment and treat on its basis, ensuring both assessment and treatment are consistent with current professional guidelines (11,12), meeting the legal requirement that our practice should be both reasonable and agreed with peers (13). This process clearly involves respect for autonomy in obtaining appropriate consent, beneficence and non-maleficence in providing appropriate care. Justice is also involved, though less obviously. For example, we consider it just (fair) to be expected to manage the assessment and medical treatment of these cases well, while the legal framework and guidance just outlined tells us what 'well' means. Our model tells us that, if we approach ordinary cases of hyperactivity in an ordinary way, we are acting both ethically and legally. There is more to this than reassurance. Despite the controversy surrounding it, the diagnosis of hyperactivity is at least as well established as other medical diagnoses (14,15). So, our model both permits us to use the diagnosis despite doubt, while philosophical or theoretical objections are not sufficient grounds to refuse to make the diagnosis – any objections must be specified in terms of the model e.g., a valid objection would be that the methods used to achieve diagnosis have insufficient validity or reliability to trust it sufficiently. The model similarly makes clear that we should not be swayed by prejudice in treatment. For example, being ‘against medication’ must be justifiable in terms of the individual patient, against the standards set by the model. In both cases, the alternative is to risk ethical criticism or even legal sanction.

Given the safety of the treatments available for hyperactivity (16) and the significant disability the condition imposes (17), beneficence and non-maleficence rarely conflict. Respect for autonomy presents few challenges at initial assessment, as the children are usually so young that one may place the overwhelming responsibility for consent on the parents who have brought the child and still respect the child’s autonomy. As the treatment is over several years, the model suggests that the child’s appreciation of the treatment should be reviewed as time passes, to ensure that the practitioner appreciates how the balance of autonomy is shifting, and can respond to it as necessary. ‘Gillick competence’ i.e., to understand the treatment and its benefits sufficiently to give informed consent, which a child must possess in order to give consent independently without parents, is based on an assessment of the child’s competencies, not age (18). Though a child’s wishes may be overruled until aged eighteen, assessment of autonomy is essential to ensure that sufficient weight is given to the child’s views, as in the case of an older child, they may not be overset lightly (19,20). Only those with parental responsibility can give consent for more than immediate or emergency treatment, though only one parent is needed to consent (21). People who cannot give full consent include teachers at boarding schools, foster-carers, unmarried fathers or stepfathers who have not been granted parental rights by a court, and social workers, unless the child is under a care order – being ‘accommodated’ or under a supervision order will not do. So, practitioners must be careful that the adult with the child is actually able to give consent, if the child (as is usually the case in hyperactivity) is not ‘Gillick’ competent.
Incorporating the model in everyday practice

Previous descriptions of the application of this model (8) referred largely to circumstances (incorporating the view of agencies bound by different ethical and legal principles) more appropriate to a specialist than a GP. However, the model may be readily incorporated into more medical decision-making systems that explicitly include values e.g., Huninks PROACTIVE model (22). PROACTIVE is an acronym which describes nine stages of good medical decision-making (identify the Problem, Reframe in soluble form, define Objectives, consider Alternative routes to them, reflect on the Consequences of the alternatives, and the Trade-offs between them, then Integrate the evidence with values, maximise the Value obtained, and Experiment to check the best decision has been achieved). The last three stages allow direct engagement of the moral strand of opposition to medication for ADHD-related symptoms, by requiring those holding that position to integrate their views with the ethical practitioner model just detailed, so that the benefit to the child is maximised, and then review the outcome of the resulting course of action in comparison to the alternatives, to ensure that the choice is correct from the perspective of the child. These three stages are examples of, respectively, dialectic, specification and balancing, which Beauchamp and Childress identified as essential to the effective application of ethical principles to practical situations, resolving the conflicts which their application inevitably generates (8).

Conclusion

Despite the ongoing controversy about prescribing medication for ADHD, by ensuring that the process of decision making is based on a firmly grounded ethical framework, it should be possible for the clinician to justify the decision reached for each individual patient.

GP Comment.

What have I learned from this paper?

1. It was useful to be reminded of what we already know, namely that we should do what is in the best interests of our patients and that our moral judgements should be limited to our own behaviour, not those of our patients.

2. Controversy about the medical treatment of ADHD and even about the validity of the diagnosis of ADHD underlines the importance of applying ethical principles to the management of this condition. This was nicely summarised in the statement that ethical practice must be consistent with four principles: respect for autonomy, beneficence, non-maleficence (first do no harm) and justice.

3. There is a considerable body of evidence about the efficacy of treatment of ADHD; we should not be swayed by prejudice but should be guided by the evidence.

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Non-drug Management

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Abstract

The words “inattentive” or “hyperactive” are often applied when a young person seems to lack concentration, or is overly boisterous, disorganised or consistently acting in a manner that is at odds with the demands of their environment. For some, these difficulties will be sufficiently chronic, pervasive and impairing that a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) may be warranted. At present, ADHD is recognised to be a biologically-based neurodevelopmental disorder that can be effectively treated through medication. However, there is also a wide range of non-drug approaches that can be used on their own or in conjunction with medication to treat, support, and empower affected individuals and their families. This paper discusses the value of psychoeducation, behavioural therapy, social skills training and cognitive behaviour therapy (CBT) in the management of ADHD and signposts the reader to additional relevant sources.

Introduction

Almost everyone exhibits overactive, inattentive or impulsive behaviour on occasions. Indeed, there are some situations and environments where behaving in a disinhibited or hyperactive manner may be the most adaptive style of responding. Expectations for behavioural control differ across situations and cultures, yet the vast majority of children and young people will, through the course of normal development and experience, acquire the capacity to ascertain what is required in a given setting, to control and execute their behaviour accordingly, and to modify their behaviour as needed when demands in the environment change. For these children, the ability to manage themselves in relation to what is expected and what is likely to lead to the most desired or useful outcome will become second nature and relatively automatic. For a small minority of others, however, effective self-regulation and behavioural control will remain elusive. When this happens, when such capacities fail to emerge in a timely manner, the young person is at considerable risk of encountering a range of difficulties. They will almost certainly present parents and teachers with a host of challenges. For a subset of these children, young people and adults, their struggles with overactivity, inattention, and impulsiveness will be sufficiently impairing, pervasively present, and chronic that a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) will be warranted.

Longitudinal research leaves little doubt that hyperactivity has the potential to compromise long-term educational, social and behavioural functioning significantly (1). Clear guidelines and best practice protocols are available to help guide professionals in evaluating, diagnosing, and treating hyperactive behaviour (2). This paper presents the issues associated with managing ADHD through non-drug means, highlighting key concepts and strategies. As an exhaustive review of options is available elsewhere (3), the current discussion is meant to introduce what is available and provide a platform for thinking how to access, apply, and evaluate these options in clinical practice.

What is “non-drug management”?

Treatment approaches in general can take many forms but, broadly speaking, it can be useful to categorise them into two general types: "pharmacological" and "non-drug". Terms that are often used synonymously with pharmacological approaches to ADHD include: "psychopharmacology," "drug therapy," "physical treatments," and "medical interventions." In the "non-drug intervention" category, the words "psychological," "psychosocial," "environmental," or "non-medical approaches" are used interchangeably. These terms can lead to confusion. For example, the authors of “What works
for whom," state, "Psychosocial treatment is arguably the most rigorously evaluated of all medical interventions, and certainly this is the case for mental health interventions." (4, p19) (emphasis added). Whilst this compliments the robustness of the evidence base, the phrase also exemplifies that psychosocial approaches can be considered “medical” in certain contexts.

In this article, “non-drug management” means those approaches that do not involve pharmacological agents. The NICE guidance for ADHD (4) stipulates that “drug treatment for children with ADHD should always form part of a comprehensive treatment plan that includes psychological, behavioural, and educational advice and interventions” (p 5). Psychological, behavioural and educational aspects can all effect change by manipulating the external environment and are capable of being delivered indirectly through others. Any approach to treating ADHD must be targeted towards changing functioning at the level of observable behaviour. Treatments that improve test scores or alter brain neurochemistry are interesting. Indeed, some cognitive remediation programmes are promising in terms of improving performance on neuropsychological tests of attention (5), but reducing symptoms and improving daily functioning, especially adaptive functioning (6), remain the ultimate goal. In addition, treatment should empower patients and parents to understand, accept, and cope with the disorder and its impact. Encouraging patients and families to develop a degree of ownership and participation in intervention, communicates the message that they are an important and valued part of the “management team”.

Creating the “management team”

The medical consultant on a team will naturally lead on pharmacological intervention, but professionals from many different disciplines can be involved in the monitoring of medication effects, and contribute actively to non-drug management of hyperactivity. Parents, caregivers and the patients themselves should have a voice in describing and quantifying difficulties and treatment-associated changes. Intervention becomes something young people are collaboratively “involved in,” rather than something that is “done to” them. Management of ADHD requires a team approach and members of the team may change as treatment progresses, the young person matures, symptoms improve, or the expression of the disorder evolves.

Where to start?

In theory, decisions around treatment priorities and approaches flow directly and easily from an understanding of the key problems, the impact of these difficulties, and - to some degree – the presumed causes of the issues. In technical terms, this “understanding” is often referred to as the “case formulation”. A formulation encompasses the diagnosis, but is not synonymous with it. Formulations contain additional information that put diagnoses in context. They capture how an individual is uniquely affected by ADHD. Based upon the formulation, clinicians can create a treatment plan that offers a personalised package of patient-centred, evidence-based, principle-driven care that is appropriate for the individual’s developmental stage and social context. Ideally, such a plan also includes the manner by which treatment effectiveness will be monitored.

In practice, even when armed with a comprehensive formulation, deciding where and how to intervene can be a daunting task. The more pervasive the problems are, the greater the list of possible targets. There may be multiple and conflicting perspectives amongst the management team regarding which problems are of highest priority. This is to be expected, as other impairments often accompany ADHD, either as a result of the disorder itself, or as comorbid features (7) (also see paper on ADHD comorbidities in this issue). Clinicians must consider the extent to which issues such as aggression, oppositionality, irritability, low self-esteem, academic underachievement and peer problems are present. Agreement around how such difficulties will be handled can be established at the treatment planning stage and reviewed regularly. In choosing targets for interventions, attention must be given to what the patient wishes to prioritise. Although young people with ADHD may not be the most valid witnesses to symptoms of the disorder (8), they are often acutely aware of the negative impact upon their social functioning and other aspects of daily living. Treatment choices also need to
incorporate the level of cognitive functioning and wider developmental needs (3). Finally, determining what is realistic within the confines of time, logistics, and resource is a necessity.

The options

Features of the young person’s immediate environment, including the levels of organisation, structure, and positivity in the home and classroom, the types of behaviour management strategies used by their parents and teachers, and the way in which the young person is thinking about themselves are all important factors that can be used to improve the functioning of individuals with ADHD. Often, however, it is these very factors which add strain to the situation. In sometimes quite subtle and generally non-intentional ways, unwanted behaviours can be triggered, maladaptive ways of responding can be reinforced, negative thinking patterns can flow unchallenged, and unhelpful reputations can be perpetuated.

Non-drug approaches to management of ADHD aim to change this scene through reorganising the young person’s surroundings, (“environmental engineering”), changing the way adults think about and approach the young person’s behaviour, and modifying the way the young person thinks about and tries to control their behaviour. The strategies used to achieve these aims are varied and applied in different forms depending on the setting and child’s age.

Psychoeducation and self-help materials are an important starting point and aim to help families, patients and teachers understand the child’s condition and appreciate how the ADHD impacts upon various aspects of functioning. Countless sources of information and advice exist, creating a risk of “information overload”. Families should be encouraged to discuss their understanding of what they are reading, and supported to cope with conflicting advice and views. The goal is to help families and other caregivers to become discerning consumers of the vast amount of materials available.

Despite being over ten years old, the text “Taking Charge of ADHD: The Complete Authoritative Guide for Parents”, (9) remains a comprehensive, contemporary, and tremendously accessible resource. “Late, Lost and Unprepared: A Parent’s Guide to Helping Children with Executive Functioning” (10) is a source of useful strategies for understanding and tackling the disorganisation and planning difficulties children with ADHD often display at home and at school. Treatment teams can signpost caregivers and educators to mainstream, regularly up-dated, and adequately governed internet sites, such as those provided by the Royal College of Psychiatrists (11), the National Attention Deficit Disorder Information and Support Service (ADDIS) (12), and Young Minds (13), all of which provide immensely useful information in a variety of formats.

Behavioural therapy can be a very effective way to address issues around compliance and disruptive behaviour. Critically, this approach is also designed to foster positive adult-child interactions. For parents of children with ADHD, behavioural parenting training, usually delivered in a group format, is available throughout the UK from local agencies, such as child and adolescent mental health services (CAMHS). This training is built around social learning and operant conditioning theories. It aims to teach parents strategies for rewarding positive, adaptive behaviour with positive attention, praise and other tangibles (e.g., stickers, access to activities), as well as techniques, such as ignoring and time-out, for reducing unwanted behaviour.

Many CAMHS services offer specific parenting programmes, such as Incredible Years (14,15) and Triple P, “Positive Parenting Program” (16), which are not specific to ADHD but have been shown to be effective in reducing ADHD behaviours in younger children. Parenting training based on behaviour therapy methods are recommended as first-line approaches for mild to moderate cases of ADHD in preschool children.

General parenting advice and training is also available through voluntary agencies and charity organisations. Books including “1-2-3 Magic” (17) and “The Explosive Child: A New Approach for Understanding and Parenting Easily Frustrated, Chronically Inflexible Children” (18) offer ideas for thinking about and “reframing” the child’s problematic behaviour in ways that can encourage
compassion and increased understanding. These resources can support the acquisition of skills for managing ADHD-related behaviour and can be offered as stand-alone psychoeducation or as an adjunct to other behavioural therapy input.

One message that is unintended but frequently “heard” or inferred by parents when such books or parenting programmes are recommended, is that their current or historical parenting style is incompetent, inadequate, or even the cause of the ADHD itself. As part of the psychoeducation component, it must be emphasised that ADHD brings unique challenges to the tasks of parenting, and these challenges can make parenting a child with ADHD incredibly stressful (19). Treatment teams can help to normalise the experiences of parents and empower them with optimism that certain approaches to managing behaviour (i.e. increasing the clarity of expectations, increasing the frequency of positive consequences, increasing the levels of warmth and acceptance) should bring improvements in their child’s behaviour. These behavioural approaches are not always the most natural. Indeed, they may be slightly different from the ones used with other unaffected siblings. Yet, they are eminently teachable and, once mastered, quite easy to apply. The consistency with which they must be applied however, can surprise and overwhelm parents initially.

Structured programmes for teachers around behaviour management for ADHD are less widely available in the UK. The ability to consult with a child’s treatment team is often an essential component in helping teachers to create an optimal learning environment and to manage the child’s behaviour as proactively and positively as possible. Liaison with educational professionals to promote accurate understanding of the child’s condition and to facilitate effective home-school communication is an important component of non-drug management. The book “How to Teach and Manage Children with ADHD” (20) contains useful techniques and case studies, which bring the issues and strategies to life.

Finally, appreciating the extent to which teachers and other important figures in a patient’s life (grandparents, coaches, employers) understand and agree with the treatment team’s formulation may be important. This can have implications for levels of acceptance and general approaches to management. In some settings, diagnostic labelling (or disclosure) of an individual’s difficulties is not viewed favourably. Where conflicting views exist, the aim is not to insist on agreement with the diagnosis per se. Rather, treatment teams can work towards: (a) establishing consensus on the target problematic areas, (b) securing support for the management approaches, (c) providing a space to express alternative formulations (e.g. “this child is attention-seeking; this employee is lazy”), and (d) ensuring that the various approaches to managing behaviour or environment are not counter-productive (e.g. behaviour that is rewarded in one arena is actually being penalised in another, even though it is a reasonable way to respond).

Social skills training. Individuals with ADHD often experience difficulties with friendships and are frequently rejected by their peer group (21). Young people with ADHD frequently struggle with behaviours that underpin positive peer interactions (e.g., turn-taking, sharing, responding in a non-reactive, predictable manner). Yet the evidence for the effectiveness of stand-alone social skills training (SST) as an intervention for ADHD is limited. Part of this may be due to obstacles inherent in generalising skills learned in one setting (e.g., a social skills group) and applying them in another (e.g., the classroom) (22). NICE supports a package of care that might combine parenting training (as described above), social skills training, and cognitive behaviour therapy.

Cognitive behaviour therapy (CBT). Over the last few years, interest in CBT has increased greatly, particularly because evidence of its effectiveness as a treatment of common adult psychological problems, such as anxiety and depression, is so robust. However, the research support for CBT as a treatment of ADHD in childhood is not firmly established (3) and there are few studies examining its efficacy in adolescence. In contrast, more research has been conducted applying CBT with adults with ADHD. The book “ADHD in adults: A psychological guide to practice” (23) provides a useful overview of CBT approaches. These techniques flow from their cognitive behavioural model of ADHD in adults, which critically includes concepts of success and resilience – areas at risk of being overlooked in the management of ADHD. Individuals with ADHD often battle against low self-esteem (1), and CBT can be particularly effective in this regard.
Is treatment working?

Treatment teams can work together with patients and their families to establish whether and to what extent initiation of a particular treatment package is followed by a reduction in symptoms and an improvement in functioning. Capturing change and quantifying outcome can be complex. An organisational framework, built around the five levels of outcome differentiated by Fonagy and colleagues, (4) is presented in Table 1, and includes specific questions and possible resources one might use to gather data.
Table 1: Framework for conceptualising outcome (based upon Fonagy et al, 2002)

<table>
<thead>
<tr>
<th>Level of Outcome Measurement</th>
<th>Focuses on</th>
<th>Target of assessment</th>
<th>Questions to ask</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Symptomatic or Diagnostic</td>
<td>Core symptoms</td>
<td>Child’s behaviour</td>
<td>Has the frequency or duration of the symptoms changed? (can be considered on a continuum) Does the individual still meet criteria for diagnosis? (can be considered categorical – “yes or no”)</td>
</tr>
<tr>
<td>2 Adaptation</td>
<td>How the child functions in their environment (e.g., school, home)</td>
<td>Child’s behaviour with respect to their ability to apply their skills and knowledge This is one-way: Child ⇄ Environment</td>
<td>Is the child getting better at negotiating, compensating, overcoming, the obstacles created by/associated with the disorder? (These obstacles might be issues like making and keeping friends, or achieving in school)</td>
</tr>
<tr>
<td>3 Mechanisms</td>
<td>The cognitive and emotional capacities that are presumed to underpin symptoms and adaptation</td>
<td>Neurocognitive capacities</td>
<td>If concentration problems seemed to be getting better (Level 1), would they also do better on a psychological test designed to measure attentional skills?</td>
</tr>
<tr>
<td>4 Transactional</td>
<td>The interactions between a child and their environment</td>
<td>Interactions of child to his environment AND the reaction of the environment to the child, particularly parent-child relationships. This is two-way: Child ⇄ Environment</td>
<td>How is the behavioural disposition of the child and the way he interacts with his environment affected by how those in his environment react to him, now and over the course of time?</td>
</tr>
<tr>
<td>5 Patient satisfaction and utilisation of services</td>
<td>On how parents and patients viewed the treatment and service they received, as well as the extent to which they are in receipt of input from other services and agencies in health, education, social, justice.</td>
<td>Subjective (parent and patient perspectives on experiences and acceptability of treatments) and health economics</td>
<td>How did this intervention look and feel from the parents and patient’s perspective? Did they find the approaches acceptable? (i.e., Was the “cost” of undertaking the treatment in terms of time, effort, etc worth the “benefit” of the improvements gained?) Did their involvement with this intervention mean that they went on to require less professional input elsewhere (i.e., Did intervening now in this manner save time and money down the line?)</td>
</tr>
</tbody>
</table>
Conclusions

Supporting families affected by ADHD can take many different forms. Management approaches will be influenced by a variety of factors, including the age of the young person, the severity of the ADHD, and the presence of other problems. For some families, when ADHD is mild to moderate, advice after diagnosis, including self-instruction manuals and other materials based on positive parenting and behavioural techniques may be sufficient. For others, a more intensive treatment package that combines medication with non-drug approaches will be indicated.

The challenges associated with ADHD may change as individuals mature. The NICE (2009) guidance reminds treatment teams to anticipate major life changes and consider psychological treatment at these times. Transitioning from primary to secondary school, sitting national exams, moving away from home and ending a romantic relationship are just a few of life’s “normative events” that have the potential to bring new stressors to a young person already grappling with the symptoms of ADHD. Non-drug approaches can be instrumental in helping individuals and their families understand the ADHD, learn new repertoires of responding, sustain positive behaviour change over time, and develop a sense of resilience and self-acceptance.

GP Comment.

What have I learned from this paper?

1. Although the main role of the GP in managing ADHD is often viewed as prescribing medication, NICE guidance clearly states that drug treatment for children with ADHD should always form part of comprehensive treatment plan that includes psychological, behavioural and educational advice and interventions. The role of the GP may need to expand to making sure that these areas are covered, in addition to following any shared care protocol in regard to prescribing.

2. Key elements of ADHD management are psychoeducation and empowerment of families. There are several valuable sources of information available including well-established books, the Royal College of Psychiatrists factsheets (see website) and support organisations such as ADDISS (Attention Deficit Disorder Information and Support Service: www.addiss.co.uk).

3. Changing the way adults think and approach a child with ADHD, together with modifying the way the young person thinks and tries to control their behaviour, may be achieved through a number of valuable approaches.

Dr Tom Inskip, GP, Bedfordshire.

References


11. http://www.rcpsych.ac.uk/mentalhealthinfo

12. http://www.addis.co.uk


Teaching Children with ADHD

Fintan O’Regan
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Abstract

The three main characteristics of ADHD, namely hyperactivity, inattention and impulsivity, imply that teaching a child with this condition can be problematic. However, a number of strategies are available that can not only help to overcome some of the child’s difficulties but can also be fun. These include techniques for decreasing physical activity, increasing attention span, helping the child to focus while ignoring distractions, and overcoming impulsivity by teaching the “hesitation response.” Simple, black-and-white rules, coupled with instructions given one at a time, in language that the child will understand, can also help. Altering the classroom environment, applying some simple principles, can reduce distractions and increase the child’s engagement with the teaching process; these principles might include seating the child at the front of the class where distractions from other students will be less, surrounding the child with good role models, avoiding environmental distractions such as heaters, windows or air-conditioners, and encouraging the child to ask for help when they need it. Although teaching the child with ADHD can be challenging, applying appropriate techniques and strategies can greatly enhance their learning.

Introduction

Students with ADHD often challenge teachers in 3 main areas:

1. Activity level.
2. Attention span.
3. Impulsivity.

There are strategies for managing these challenges in the classroom.

Dealing with the activity level

Whether it is controlling their body or their mind, some children appear to leap about. It seems as if they are unable to switch their motion on and off in a controlled way, as other children do. Teaching them can be a difficult process but strategies are available that can be both effective and fun as well.

One technique for younger children to help them sit still is called “playing statues” (1). The child is asked to sit like a statue for a certain time. This game can be played using a stopwatch and recorded in terms of a visual presentation, such as a bar chart. The time can be increased in stages. The strategy helps the child to focus and to control their bodies. As a self-taught system, it is much more likely to provide a long-term solution.

Variations on this theme include other games, for example “Catch me if you Can” (1) and playing to “Beat the Clock”. These are approaches to limit extraneous movement and to help the child to focus tasks against a set of expectations in an activity set against a timed upper limit.

With older students much longer periods of sustained, controlled activity levels are expected. “Endurance training” involves lengthening the time and improving the skills in sitting still in a variety of settings.

The child will often need to have the session broken down into achievable time periods. For example, the objectives for a 40-minute lesson might be broken into stages as follows.
• To sit still during the 5 to 10 minutes introduction to the lesson. The teacher then indicates that part 1 is over.

• To focus on the task in the group discussion. The teacher then indicates that part 2 is over.

• To pay attention during the group discussion. The teacher then indicates that part 3 is over.

• To behave appropriately during clear-up time. The teacher then indicates that part 4 is over.

All of these games or techniques to harness activity level will need to be practiced. Feedback on success and failure on the initial trials will be crucial in determining long-term outcomes.

**Improving attention span**

Although being hyperactive and impulsive can be obstacles to learning, it is without a doubt the issue of poor attention span that is the most damaging feature for some children. Lengthening the attention span will be one of the most important factors in determining long-term educational success (2).

The teacher should not assume that the child understands what paying attention really is; for some children this does not come naturally. A series of role-playing activities between the teacher and child may help the child to achieve an improved attention span. For example, a taped story may be played to the child, during which the teacher role-plays a series of incidents or examples when he or she did not hear or understand what the story had been about. The child in this case would be asked to clarify examples of why the teacher did not hear the story. The child rates the teacher’s listening skills. In addition the teacher might want to demonstrate daydreaming by reading to himself or herself while the taped story is being played. The child once again rates the teacher’s performance in the style of being a detective.

Once the teacher feels that the child understands what is meant by paying attention then he or she can start to improve the attention span, timing the child’s performance against a chart or similar visual prompt. If the child is younger then the teacher may have to do the timing for them but if they are older then they should do it themselves.

Additional strategies can include devising “attention cards” that can be placed on the student’s desk or using computerised checks to “hook” the child into the overall situation by giving him or her a process to monitor self-performance on a regular basis while undertaking the work or activity required. This could be viewed as distracting the child in a proactive way.

**Impulse control**

For some children impulsivity is a major problem with significant, often negative, impact. Again, the first stage in management is to explain the concept of impulsivity to the child, who may react instinctively to situations. Other people may view the child as being “a risk taker” but in the child's own eyes their action was not taking a risk – it was a reflex action over which they had little or no control. Explaining impulsive behaviour may be easier with some students than with others. The best place to start is often to consider recent examples of their own impulsive behaviour and to ask them to express, through their own words, how these incidents might have been handled better. It may also be helpful to ask the child to consider a number of separate situations, listing an impulsive act on one hand and to contrast it with a “thought-out act” on the other.
Two examples follow.

<table>
<thead>
<tr>
<th>Impulsive Act</th>
<th>Thought-out act</th>
</tr>
</thead>
<tbody>
<tr>
<td>Running into Street.</td>
<td>Pausing at curb, checking for traffic.</td>
</tr>
</tbody>
</table>

In essence, to overcome impulsivity the child needs to be taught the “hesitation response”, to increase the length of time between thinking and acting. The way in which this is achieved will depend on the age and maturity of the child. The teacher is essentially telling the child that they can be in control of something, namely their own impulses.

Some tried and trusted strategies and suggestions for managing the child with ADHD in the classroom are listed below. In some cases these simply confirm good practice. As always, the key is to remain consistent with the overall structure but also to have some flexibility if minor distractions and incidents occur (3).

- Seat the student near the teacher but include him or her as part of the whole class.
- Place the student in front of the class with his or her back to the rest of the class, to keep other students out of view, to avoid distraction.
- Surround the student with good role models, preferably those seen as “significant others”. Encourage peer-tutoring and co-operative learning.
- Avoid distracting stimuli. Try not to place the child near heaters, air-conditioners, doors, windows or high-traffic areas.
- For those who do not handle change well, avoid transitions, changes in schedule, physical relocation and disruptions. Monitor closely on field trips.
- Be creative! Produce a “stimuli-reduced area” for all students to access.
- Maintain eye contact with the student during verbal instruction.
- Make directions clear and concise. Be consistent with daily instructions.
- Simplify complex directions. Avoid multiple commands.
- Make sure the student understands before beginning the task.
- Repeat in a calm, positive manner, if necessary.
- Help the child feel comfortable about seeking assistance, keeping in mind that most children will not readily ask for help.
- Children with ADHD need more help for a longer period of time than the average child. Gradually reduce the amount of assistance, depending on the response of the child.
- Ensure that the student has a daily assignment notebook. Make sure that the student writes down the assignment and that both parents and teachers sign daily for homework tasks.
- Give one task at a time and monitor frequently.
- Modify assignments as necessary. Develop an individualised programme.

The key elements in teaching rule-governed behaviour management is to limit the rules to key areas of basic health and safety, physical and verbal behaviour, uniform and timekeeping. They should be given in the form of clear, basic black-and-white instructions. All instructions should be as specific as possible, using multiple prompts to initiate the rule-training and, when possible, providing immediate feedback on outcome. The process of learning the rules should be reinforced with constant use of positive (and negative) logical consequences.

If the teacher accepts the core systems of ADHD, then the student will not necessarily be seen as
“a rule breaker” but will be viewed as someone who cannot filter out the competing demands of environmental stimuli for their attention. For example, the average child might be able to ignore a chair being scraped behind them while the teacher is talking, but the child with ADHD might find this very difficult. Another way of viewing this is to think that, for the child with ADHD, everything in their environment is equally important in terms of gaining their attention. Consequently, the first principle would be to train them to prioritise where to focus their attention in a particular situation. Putting this another way, the task of the teacher is to help the child to overcome the “distraction zapper” that take their attention away from engaging with the teaching process. Teaching the child with ADHD to overcome distractions is not an impossible task but it is a time-consuming one. Before the child can learn to ignore distractions, he or she needs to be able to identify the matter that should be holding their attention; they are then enabled to provide filtering strategies so that distractions do not take priority. A useful way of starting this process might be for the child to make a list, in each class, of the distractions that generally compete for their attention or affect their behaviour; younger children will require help from an adult in completing this exercise. As a result, it might be possible to remove physical distractions or at least to adapt them so that they are less intrusive. Identifying whether visual or auditory distractions are more important for the individual child can also be helpful. Part of this exercise will be to record how strongly each of the distractions takes the attention of the child away from engagement in the teaching process and the length of time the distraction lasts (1). One method of beating distractions is “the distraction zapper.” This is a method of turning unwanted distractions into a game of recording successful attempts to ignore them, i.e. to ignore being led away from priority tasks. The zapper can be constructed as an imaginary laser gun for younger children; a different, age-appropriate device can be constructed for older children but the principle is the same: to blow the distractions away. This can be reinforced by recording how many “hits” the child achieves in the laser-quest game. Teaching this game by role-play with a supervisor can yield the best results but each child is an individual, implying that trial and error will play a part.

**Conclusion**

Classroom success can be much more difficult to achieve for the child with ADHD. However, if the teacher has a good understanding of the condition and implements some well-tried strategies, the chances of success can be greatly enhanced.

**Editor’s note**

In our opinion there is a great unmet need with regard to professional training on non-medication interventions for ADHD. For this reason, we are pleased to state that Fintan O’Regan is available to provide training presentations to teachers, GPs and other professionals.

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**GP Comment.**

What have I learned from this paper?

1. This paper illustrates how some important approaches and strategies to teaching can make a major difference to children with ADHD, both those who are being treated with medication, as will be necessary for severe ADHD, and those who are not being treated with medication, which should be the case for milder ADHD.

2. Understanding that apparent “risk-taking” might not be wilful naughtiness on the part of the child but may be a reflection of his or her difficulty in thinking before acting is of major importance in helping the teacher or carer to adopt the right approach.

3. Some basic strategies can greatly increase the chance of success in the classroom. These include such things as putting the child in the front of the class, where other children cannot easily distract
him or her, giving instructions one at a time, keeping instructions clear and simple, and applying some basic “black-and-white” rules.

4. The teacher who understands ADHD and applies appropriate strategies to overcome the overactivity, inattention and impulsivity is much more likely to achieve success.

Dr William Hollington, GP, Bedfordshire.

References


Parent training and Support groups

Andrea Bilbow, CEO, ADDISS.

Abstract

Parents who have a child with ADHD often feel isolated. There may be delays in making the diagnosis and they may feel that they are being blamed for having a “naughty child” as a result of poor parenting. Support groups are invaluable in assisting parents through the challenges of ensuring that the needs of the child with ADHD are fulfilled. ADDISS (Attention Deficit Disorder Information and Support Service) is a national charity that provides a telephone helpline, has a website, offers training, provides resources and organises events for families of children with ADHD. It also extends to ADHD in adulthood. Although there are several parenting programmes available, 1-2-3 Magic is recommended by ADDISS, on the grounds of considerable experience and positive parental feedback. This programme is mainly non-verbal and addresses issues such as climbing, tantrums, fighting, swearing and other difficult behaviours. It is best to provide this programme for children before they reach the age of 12 years because it is less effective in older children if not started in early childhood. The younger the child the more effective the programme. Several local support groups, some of which are affiliated to ADDISS, and other parent training support programmes, for example Triple P (Positive Parenting Programme), are also available.

Parent Support Groups
National support group

ADDISS is here to help.

The national charity ADDISS (Attention Deficit Disorder Information and Support Service) has for many years worked with families who have a child with ADHD. ADDISS provides a helpline, offers training and resources, and organises events. It provides families with the best possible information, improves understanding of ADHD and highlights practical strategies that achieve positive social, health and educational results.

The work of ADDISS extends to ADHD in adulthood. It engages with professionals and practitioners across a range of disciplines, including family doctors. The GP is often the first person that a parent will approach to try and make sense of their child’s behaviour and in search of that all-important diagnosis.

Local support groups

Local support groups are usually run by volunteers who are parents themselves. If you are lucky enough to have a group in your area they can be an enormous source of support for parents. Some will be small, unconstituted groups who meet in each other’s homes or in a local church hall, offering a safe, friendly place for parents to let off steam and support each other. A few groups are better established and may have funds which enable them to have premises and admin staff. A very small number may offer holiday schemes for the children or parenting programmes. Because of the difficult nature of this complex and onerous condition, many support-group leaders burn out and the groups are unsustainable. We find groups come and go rather quickly.

The parent’s perspective.

My child’s behaviour is not really like that of his peers. I can’t quite put my finger on it, but I just know something is different.

He’s always fighting with other children and sometimes he even physically attacks me. The idea of sharing seems to be totally beyond his comprehension and so he has hardly any friends. Other people
tell me that all my naughty child needs is discipline and I know they think I’m a bad parent. Perhaps I am.

My health visitor reassured me and says not to worry, it’s just the “terrible twos”, and he’ll grow out of it - but I just know there’s more to it than that.

The local Children's Centre offered me a parenting programme but after a few sessions none of it seemed to apply to my child. I feel totally at the end of my tether. My sense of isolation is overwhelming. I can’t sleep. My marriage is in trouble and nobody seems to understand - and then someone mentions ADHD…

At ADDISS this is such a common and sad story.

**Parenting programmes**

**What is parent training?**

Parents initially feel defensive when offered parenting programmes as they feel it is an attack on them and a criticism of their skills as a parent. It is important to reassure parents and explain that they need to learn new and different skills to parent a child who has ADHD and behavioural difficulties.

Parenting programmes are crucial for families to achieve a balanced home life. There are many on offer but not all are suitable for the temperament of a child who has ADHD. Likewise many programmes are not compatible with the skill of the parents themselves, who may have undiagnosed ADHD. Parent training should be a combination of good behaviour-management skills together with a psycho-educational course on ADHD to help parents understand their child’s condition better.

<table>
<thead>
<tr>
<th>Programme</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Triple P (Positive Parenting Programme)</strong></td>
<td>A 12-week intensive course used mostly for children from age ten into their teens.</td>
</tr>
<tr>
<td><strong>The New Forest Parenting Programme</strong></td>
<td>A 12-week course which is delivered both in groups and in the home in a one-to-one setting, primarily for pre-schoolers, but also useful for older children.</td>
</tr>
<tr>
<td><strong>The Incredible Years – Webster Stratton</strong></td>
<td>A 12-week course of two hours per week for children age 3–10 years. Useful for developmental issues, changes in the family and parental mental health problems.</td>
</tr>
<tr>
<td><strong>1-2-3 Magic</strong></td>
<td>3–5 week course of up to 3 hours per session. Tackles difficult behaviour first then moves onto building family relationships.</td>
</tr>
<tr>
<td><strong>The Parent Factor in ADHD</strong></td>
<td>An 8-week course of 2 hours per session, teaching parents about ADHD and all aspects of advocating for their child.</td>
</tr>
<tr>
<td><strong>ADHD Parent Empowerment and Skills Training (PEST)</strong></td>
<td>Developed and delivered in Lancashire by ADHD Northwest. A 12-week programme delivering skills to parents to help tackle all the difficulties ADHD presents to families.</td>
</tr>
</tbody>
</table>

Each one of these programmes has its own strengths. The programme should be chosen to fit the family and their particular difficulties.

ADDISS recommends 1-2-3 Magic, a programme that really does work. ADDISS has received overwhelmingly positive feedback from parents, who say their lives have been transformed. 1-2-3 is...
a behaviour management programme designed to address the symptoms of ADHD. It fits extremely well into a psycho-educational course on ADHD.

1-2-3 Magic is designed for parents of children from the age of 2 to 12 years and is an excellent intervention for GPs to consider before making that first referral for an ADHD assessment. 1-2-3 Magic was developed by Dr Thomas Phelan in Chicago over 30 years ago. It is designed specifically for ADHD children and is delivered with ongoing support. This means that parents can face their child’s future with confidence.

Its primary appeal is that it is simple and that it appears to work almost immediately – hence the name. 1-2-3 Magic takes parents through three elements: controlling difficult and obnoxious behaviour, encouraging positive behaviour and strengthening the family relationship. Counting tactics (the 123 of the title) are used to address behaviours we want to stop and to encourage children to become better self-managers.

The programme is primarily non-verbal. Strategies address whining, tantrums, shoving, fighting, hitting, jumping, swearing and other “obnoxious” behaviours.

In practical terms 1-2-3 Magic operates through 3 to 5 sessions of up to 3 hours each. These are delivered by trained practitioners, typically on a small group or one-to-one basis. ADDISS has trained practitioners from a range of disciplines, including youth offending teams, specialist nurses, educational psychologists, local authority parent support advisors and school staff. There is an educational component that lends itself to delivery to children by teaching staff, and we have delivered training in schools.

1-2-3 Magic can be delivered in a variety of languages; ADDISS has trained practitioners in Romania, Ireland, Gibraltar and many other countries in recent years.

The recommended pattern is to deliver one session and then allow a one-week gap for parents to apply the lessons learned before embarking on the next session. In this way skills are built up and consolidated in a structured fashion, with opportunities to review successes and discuss problems along the way.

Many other parenting programmes leave parents unsupported at the end of the sessions. 1-2-3 Magic is different. Part of its strength is the monthly drop-in, which is an effective way to sustain learning when the programme is finished. ADDISS advises parents of pre-school children, in particular, to continue to attend monthly sessions for 3 to 5 years in order to gain the maximum benefit. Excellent resources are available to accompany the programme.

There are several local groups across the UK which can offer 1-2-3 Magic programmes. ADDISS can provide contact details and advice on actions that can be taken in the meantime.

1-2-3 Magic helps parents to impose a discipline that keeps the child safe, and helps them to respond and adapt to the structures of school and the wider world around them.

What about older children?

Early intervention in the pre-school years is ideal but for some families the ADHD diagnosis comes when the child is much older. However, it is not too late. The 1-2-3 Magic programme is suitable for parents of children up to the age of 12 years. However, it is less effective for a child older than this if used as a first time intervention. Catching a child before the difficult teenage years and imposing a calm and controlled structure for family life is possible; harmony in the home can be achieved even at this late stage using some of the techniques in the programme which are revisited in the follow-up programme “Surviving your Adolescents”.

In these economically difficult times, local authorities and health services are clearly mindful of the costs and benefits of parenting programmes. It is worth pointing out that this is a relatively low-
cost programme to deliver and significant savings can be achieved through investment in early intervention. In our experience, many children make such progress through the 1-2-3 Magic approach, that additional and expensive support in schools is much reduced or even no longer needed. This is a point worth remembering when commissioning services.

What is the role of the GP?

The most useful thing that family doctors can do to support families with an ADHD child is to empower the parents. A well-informed parent, equipped with skills and strategies to address their child’s needs, can achieve amazing things. Time and again we have seen families emerge from seemingly impossible situations to achieve some semblance of normal family life. Getting past the “naughty child” syndrome is one of the biggest hurdles. A listening and non-judgmental GP who can guide a family towards sources of support is priceless.

Conclusion

A child with ADHD can make great demands on the family but assistance is available through various sources, not only through professionals such as teaching and medical staff but also through parent training and parent support groups, such as the national support group ADDISS.

For more information on the service ADDISS provides and the 1-2-3 Magic programme contact Andrea Bilbow at andrea@addiss.co.uk, telephone 020 8952 2909 or take a look at the website for events and resources.

GP Comment.

What have I learned from this paper?

1. This paper confirmed my impression that ADHD is often diagnosed late, sometimes after many years of the inappropriate label “naughty child” having been applied, with no additional support having been given.

2. Support groups that offer assistance for both children and adults with ADHD, such as the national support group, ADDISS, and local support groups can be invaluable.

3. Reading this paper has made me even more aware of the importance of referring families for support and parent training.

Dr Sarah Griffith, GP, Shefford Health Centre, Bedfordshire.

ADDISS (The National Attention Deficit Disorder Information and Support Service)
Premier House
112 Station Road
Edgware
Middlesex
HA8 7BJ
Telephone helpline 0208952 2800
Email: info@addiss.co.uk
Website: www.addiss.co.uk
Other UK-based support groups

ADDISS Affiliated groups
These are independent groups who work together and have agreed to abide by a code of conduct to ensure patient and professional confidence.

London area

London Borough of Havering
Add+up
01708 454040
addup@addup.co.uk

Harrow
ADHD and Autism Support Harrow,
Tel number 020 8901 8009
Email: adhd@adhdandautismharrow.co.uk

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Recent Research into Therapeutic Outcome Measures

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Abstract

Accurate measurement of clinical outcomes forms an important part of evidence-based practice. When measuring treatment outcomes in ADHD, clinicians have tended to focus on symptoms. In the past these were generally assessed by using parent-rated or teacher-rated questionnaires. Recently, however, the focus has switched to clinician-rated measures, often using symptom questionnaires like the ADHD-IV RS and the SNAP-IV as the basis of a semi-structured interview. Helpful clinically-relevant cut-offs have been described but need further validation. Similar interviews can be used for gathering information from schools. There are also, however, several instruments, such as the SKAMP, that are specifically designed for use with teachers that can be integrated into clinic protocols. In addition, a range of disorder-specific and generic measures of impairment and quality of life can provide valuable information about broader outcomes. Recent research suggests that the relationships between symptoms and cognition in ADHD are complex. However, whilst this suggests that it may be useful to think about measuring neuropsychological performance alongside symptom scores, this is currently difficult to achieve as it is not clear which measures would be the most appropriate to use.

Integrating Recent Research on Therapeutic Outcome Measures into Clinical Practice

It is very pleasing that the publication of comprehensive evidence-based clinical guidelines for the assessment and management of attention deficit hyperactivity disorder (ADHD) (1;2) has been accompanied by increased interest in the use of standardised outcome measures in routine clinical practice. However, whilst there is now a plethora of measures available to assess a wide range of outcomes, obtaining accurate and reliable measurement of outcomes is not as simple as it may first appear. Whilst issues of validity and reliability are certainly not going to be at the top of the agenda for most clinicians it is very important to be aware that the results of instruments that either do not truly measure what they purport to measure, or do so in an unreliable way are, at the very least, clinically unsound and may, in certain situations, place patients at risk. Clinicians should therefore make sure that the instruments that they are using have been properly developed and have established validity and reliability. This brief paper will review some of the recent research findings relating to the use of various outcome measures in ADHD, highlighting some recent advances as well as some potential pitfalls. Whilst we hope that these comments will help clinicians think about how best to measure outcomes in their day-to-day clinical practice, this certainly should not be seen as a systematic review of the field. For those interested in exploring the available assessment scales in more detail, the recent book by Kollins and Sparrow provides an excellent and detailed discussion (3).

For most clinicians the main, but certainly not only, therapeutic outcome of interest when managing ADHD is the change in core symptoms. Until recently most clinicians, and indeed clinical trials, used questionnaires completed by the parent and sometimes the teacher, such as those produced by Conners (4) or DuPaul (5). However, despite these questionnaires having excellent psychometric properties, many researchers and clinicians have noted that when they ask the parent about symptom severity there are often significant discrepancies between their own clinical impressions and the scores of the self-completed questionnaires. Anecdotally, from our own clinical practice it appeared
that parents and teachers were sometimes using the questionnaires to communicate an overall message, perhaps because they were worried that if they did not take this opportunity to let the doctor know how difficult things were they might not have another opportunity. Whatever the reason, clinical trials have now almost universally started to use DSM-based symptom questionnaires, like the ADHD Rating Scale IV (ADHD RS-IV) (5) or cut-down versions of the SNAP-IV Rating Scale (6), as clinician-rated semi-structured interviews, with the clinician eliciting the symptoms from the parent and child, and then making their own judgment regarding severity. Importantly, the ADHD RS-IV, when used this way by clinicians (as opposed to experienced researchers) was found to be both valid and reliable in an observational study of ADHD in routine clinical practice that included patients from 10 European countries (7). Used this way, these instruments take between 10 and 15 minutes to complete, depending on the level of complexity of the individual case, but they allow the clinician to obtain a much clearer picture of current symptoms. We have been using the 18 ADHD symptom questions from the SNAP-IV (http://www.adhd.net/) routinely at every visit to our own clinic for several years. Whilst it was initially somewhat dispiriting to find that our patients were not doing quite as well as we had thought (in our experience using the instruments this way tends to pick up more untreated symptoms than using parent-rated questionnaires), it has allowed us to tailor treatments individually in a much better way. This has resulted in significantly improved outcomes. More recently we added in the oppositional defiant disorder questions, and now ask about these before addressing ADHD symptoms, as we feel this allows parents to vent their concerns about oppositional behaviours without those concerns spilling over into the ADHD part of the interview.

An important question to answer, when measuring outcome using one of these scales, is: “How much change is good enough?” There are two parts to this question.

1. How much does a score need to change in order for this change to be clinically relevant (i.e. has the patient improved)?

2. Below what score can I assume that the patient is within the normal range (i.e. have they improved enough)?

Using statistical techniques first devised by Jacobson and Truax (8) to evaluate psychotherapy outcomes and data from our own clinic as well as that from a European observational study we have calculated that a drop in total ADHD RS-IV (or SNAP-IV) of ≥ 11 suggests a significant treatment response whilst a total score of ≤ 24 (mean symptom score ≤ 1.3) puts a patient within the normal range (not the same as being symptom free but a useful first target for symptom reduction).

In our clinic we have recently started to use the SNAP-IV as a semi-structured telephone interview with teachers, both as a part of the assessment process and, when required, to clarify clinical response to treatment in the school setting. In general, however, we have found that, for monitoring treatment response, instruments targeted more specifically at the school situation have greater face validity with teachers and are therefore more readily accepted; they are also more sensitive to change than the generic DSM-based instruments. For this purpose we particularly like the SKAMP, a brief teacher-reported questionnaire originally designed for use in laboratory school studies. It is reliable and valid (9;10), brief, easy to score and easy to interpret.

All of the instruments described so far are focused on rating problem behaviours. As such they tend to ask the rater to choose a score somewhere between “no problems” and “extreme problems”. It is now becoming much clearer that ADHD is dimensional and to reflect the range of behaviours seen across a population properly, it is more accurate to consider rating measures such as ability to concentrate, degree of inhibitory control and ability to regulate activity levels as “well above average” through “average” to “well below average”. Swanson and colleagues correctly argue that this is an important distinction, as the use of traditional questionnaires like the SNAP-IV or ADHD-RS as a part of the assessment process will tend to over-identify those individuals at the extreme end of the continuum. They developed the Strengths and Weaknesses of ADHD-symptoms and Normal-Behaviors (SWAN http://www.adhd.net/), a questionnaire that aims to capture the full range of behaviours and results in a normal distribution of scores rather than the truncated and skewed scores one sees when a traditional symptom measure is used in a normal population (11). Whilst these are important and valid arguments, particularly if using questionnaires to identify ADHD within a population, we believe that...
the traditional measures discussed above are still currently of greater value when measuring treatment outcomes.

ADHD rarely presents in its pure form in clinical settings; most individuals have at least one comorbid problem. Even those with "pure" ADHD will, by definition, have multiple impairments across a range of settings. Clearly, limiting measurement only to symptoms and symptom change would result in a very one-dimensional picture of a patient's problems/difficulties and would be unlikely to identify areas of strength. In addition to assessing comorbid problems and using appropriate outcome scales to measure these, it can also be very helpful to consider using measures of impairment and quality of life (QoL). Tools to assess these two related but distinct concepts have been the focus of considerable research activity recently. In part, this is a response to the requirements imposed by regulators and commissioners on the pharmaceutical companies. The pharmaceutical companies are now being asked not only to demonstrate that their new product is effective, tolerable and safe but also that they are clinically effective and cost effective in the real world, both in an absolute sense and in comparison to other drug treatments (12). Whilst it is appropriate to retain a degree of scepticism about such claims, the tools that have been developed to assess both impairment and QoL can be useful in both research and clinical settings (13).

Impairment refers to an objective assessment of the impact of a disorder on functioning, whilst QoL is the subjective self-perception of one's own well-being (health related QoL is used to describe the impact of a disease or disorder on this sense of well-being). Both impairment and QoL can be measured using either generic or disorder-specific measures. Disorder-specific measures maximise sensitivity and are especially valuable for measuring treatment effects and change (14). Generic measures are more comprehensive in their cover but are less likely to be sensitive to treatment-related change. Generic measures do, however, allow comparison between different disorders across different patient groups and are potentially very useful for commissioning and planning services (15). For planning individual treatment, combined disease-specific and generic measures may be the most appropriate.

The Children's Global Assessment Scale (CGAS) (16) is a quick and easy-to-use generic measure of impairment that, in our opinion, should be used at every visit for all children being seen by health services for mental health problems. The Weiss Functional Impairment Rating Scale (WFIRS; available from the Canadian ADHD Resource Alliance [CADDRA] website http://www.caddra.ca/) is a validated, disorder-specific tool for measuring ADHD-related impairment that is available in both parent and self-report versions. Whilst there is one validated ADHD-specific QoL measure (the ADHD Impact Module [AIM]) its use is limited by cost. Fortunately there are several other generic measures of QoL that have been demonstrated to be valid, reliable and sensitive to change (14). These include the Child Health Illness Profile Child Edition (CHIP-CE), http://www.childhealthprofile.org/index.asp?pageid=49, which has been shown to be sensitive to the QoL impairments associated with ADHD as rated by parents (17), and to a lesser degree patients (18) as well as the treatment-related changes in QoL (18). The Pediatric Quality of Life Inventory (PedsQL), www.pedsqol.org/, is another slightly shorter, generic measure of QoL that has also proved useful in ADHD research and that could be considered for use within the clinic (19).

Whilst space does not allow a full discussion of other, potentially important measures of outcome, such as those relating to adverse effects, safety or cognitive performance we would like to highlight one finding from our own research which, if replicated, may have a significant impact on how we understand ADHD and measure outcomes. In a neuropsychopharmacological study investigating the effects of methylphenidate on cognitive and clinical outcomes (20) we identified that ADHD is associated with a range of cognitive deficits. Treating these previously stimulant-naive boys with methylphenidate resulted in the expected clinically important reduction in symptoms for around 70% of subjects as well as striking improvements in cognitive performance on some, but not all, of the tasks with which they had previously struggled. What was surprising was that the improvements in clinical and cognitive functioning were not correlated with each other (i.e. those that improved clinically did not necessarily improve cognitively). If we had only measured either symptoms or cognitive performance we would have missed some important medication effects. On the one hand
these findings underline the importance of measuring change across a range of different aspects of functioning whilst on the other they remind us of the complex relationships between different aspects of functioning and raise questions about whether the current DSM description of ADHD fully describes the problems faced by those who suffer from this important condition. Unfortunately the assessment of cognitive functioning in ADHD is not well standardised and considerable further work is required before clear recommendations can be made regarding the use of neuropsychological testing within routine clinical practice.

Conclusions

Different outcome measures should be used for different purposes in the assessment of ADHD and in monitoring response to treatment. Some suggested scales for these different purposes are summarised in the table that follows.

Table 1: Instruments to consider using in routine clinical practice for monitoring treatment in ADHD

<table>
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<tr>
<th>Domain of interest</th>
<th>Measure/instrument</th>
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<td></td>
<td>SNAP-IV (ADHD and ODD sections (6))</td>
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<td>SKAMP (9; 10)</td>
<td>Teacher</td>
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<tr>
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<td>CHIP-CE (17; 18)</td>
<td>Parent</td>
</tr>
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<td></td>
<td>PedsQL (19)</td>
<td>Parent</td>
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</table>

GP Comment.

What have I learned from this paper?

1. The findings from research using outcome measures have confirmed that ADHD itself is a condition that can involve impairment in several different areas of functioning, even before any comorbidities are considered.

2. It is particularly interesting to know that improvement in one area does not necessarily correspond to improvement in another when ADHD is treated. For example, it seems that improvement in cognition might or might not be related to improvement on measures of quality of life.

3. This paper makes it clear that some of the outcome measures used for ADHD are very easy and quick to use. This makes me wonder whether I can expect my colleagues in child and adolescent psychiatry to provide me with specific results of outcome measures each time the child with ADHD visits the clinic and whether those results will reflect real changes in quality of life for the family.

Dr Tom Inskip, GP, Bedford.
Reference List


### Declaration of Interest

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ADHD and Comorbid Conditions – A Conceptual Model

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Assistant Clinical Professor of Psychiatry, Yale University School of Medicine
and Associate Director of the Yale Clinic for Attention and Related Disorders

Abstract

A very high proportion of both children and adults with ADHD have at least one other psychiatric disorder. These comorbid disorders can be dynamic, implying that they may change with age or may wax and wane over the lifetime of the individual. “Subthreshold” psychiatric disorders, that do not meet strict diagnostic criteria but nevertheless impair the quality of life of the individual significantly, can also occur with ADHD. It is suggested that ADHD is a “foundational disorder” underlying many other psychiatric conditions and increasing the vulnerability to them.

Introduction

Despite the increased recognition of attention deficit hyperactivity disorder and the benefits of its treatment, overly simplistic understanding of ADHD persists among many professionals in medicine, psychology, and education, as well as in much of the general public. Many continue to see this syndrome as simply a behavioural disorder characterized by excessive restlessness and distractibility, a problem that usually remits during childhood but occasionally persists into adulthood. They are unaware of important new understandings, supported by considerable evidence, that provide the basis for a new paradigm to describe attention deficit disorders. Key elements of this new paradigm include the following.

1. ADHD is essentially a complex disorder in unfolding development of the unconscious self-management system of the brain.

2. Impairments resulting from ADHD usually include chronic difficulties in self-regulation of emotion and in self-regulation by emotion.

3. ADHD symptoms may be noticeable during early childhood but often are not apparent until the individual encounters challenges of adolescence or adulthood.

4. ADHD appears to be a problem of insufficient willpower, but it is actually a problem in chemical dynamics within the brain.

5. Causes of ADHD appear to be primarily genetic, although environmental stressors and supports may modify expression of symptoms.

6. ADHD is not just one of many different psychiatric disorders; it is a foundational disorder that substantially increases a person’s risk of experiencing additional cognitive, emotional, or behavioural disorders across the life span.

This article will elaborate on the sixth new understanding about the syndrome currently known as ADHD or attention deficit hyperactivity disorder and its relation to other disorders; it concludes with a discussion of how this new conceptualization of ADHD and its comorbidities is related to a broader change of paradigm in psychiatry, psychology, and neuroscience.

Comorbid—or co-occurring—disorders

More than any other psychiatric diagnosis, ADHD tends to appear in combination with other disorders of learning, emotions, and behaviour. This comorbidity has been reported in both children and adults. The Multimodal Treatment Study of Children with ADHD found that 70% of 579 children ages 7-9 years
met full diagnostic criteria for at least one other psychiatric disorder within the year preceding their enrolment in that study (1). Adults with ADHD assessed in the replication of the National Comorbidity Survey had more than six-fold incidence of having had at least one, and often many more than one, other psychiatric disorder at some point in their life (2). Several different types of comorbidity are seen.

Among various studies, comorbidity is not always consistently defined. In some cross-sectional studies (such as the MTA), a child was considered to have a comorbid disorder if that child fully met DSM-IV diagnostic criteria for that additional disorder within 6-12 months preceding the child’s entry into the study. In other studies (2), respondents were asked whether they had ever experienced symptoms associated with various comorbid disorders at any point in the last year or at any other point in their lifetime. Cross-sectional and longitudinal measurements yield quite different estimates of psychiatric comorbidity.

In the cross-sectional view, depression is rarely comorbid with ADHD if the sample includes only prepubescent children, yet the overlap of ADHD and depression is very substantial if assessment is undertaken in adolescence or adulthood. Some psychiatric disorders emerge during childhood and may worsen or improve as the child grows older. Other psychiatric disorders do not usually appear during childhood; they are typically characterized by an onset late in adolescence or sometime in adulthood.

Types of comorbidity

Both the cross-sectional and the lifetime analyses of comorbidity have another fundamental problem: neither is sensitive to what has been referred to as the dynamic comorbidity of ADHD and other disorders. This term refers to the tendency of some disorders to wax and wane over an individual’s life span, possibly in response to situational influences, the presence or absence of specific stressors or supports, or unfolding developmental factors.

Some individuals with significant psychiatric impairments at some point in childhood or adolescence do quite well as adults. Other individuals, similarly impaired during their earliest years, continue to fare poorly throughout their lives. Data from most surveys of lifetime or cross-sectional comorbidity of psychiatric disorders do not provide a way to differentiate these very different outcomes. In a survey of lifetime comorbidities in adults, a 45-year-old person with ADHD who had experienced a year of drug or alcohol abuse while in university at age 19 years would be counted as having ADHD comorbid with substance abuse, even if the person had experienced no problems with substance abuse over the subsequent quarter century. Most clinicians are familiar with many patients who have had one or numerous episodes of depression, substance abuse or dependence, tics, anxiety, conduct disorder, obsessive-compulsive disorder, or other psychiatric disorders while having no indications of such impairments over many years of their lives. Much of comorbidity is dynamic.

Another type of comorbidity occurs when clusters of symptoms of a disorder that may not fully meet the official diagnostic criteria for one or both disorders overlap, yet the symptoms have a significant effect on the individual, possibly over a long time. This has been referred to as comorbidity of “subthreshold conditions” or as the overlap of “shadow syndromes”. For example, an individual may fully meet official diagnostic criteria for ADHD and also struggle with chronic obsessional worries that do not fully meet diagnostic criteria for either obsessive compulsive disorder or generalized anxiety disorder. Although full diagnostic criteria are not met, that person’s excessive worrying may interfere with his or her daily life in a variety of ways, one of which may be worrying about whether it is safe to take medications prescribed for ADHD.

Another type of comorbidity that has received insufficient attention thus far is the overlap and reciprocal influence of medical and psychiatric conditions—that is, situations in which a person has a medical problem (e.g. diabetes, asthma, infection) that overlaps with a psychiatric problem such as depression, anxiety, or ADHD. Some studies suggest that a psychiatric disorder may contribute significantly to a medical condition. Studies of the onset of obsessive-compulsive disorder after certain types of streptococcal infection suggest that a medical condition may be causative of a psychiatric
condition. Ample evidence shows a more-than-chance correlation between certain medical disorders and specific psychiatric disorders, but much remains to be learned about the mechanisms and timing of reciprocal influences over the life span. More research could be useful in this area; data is insufficient to address medical comorbidities that may be especially important to ADHD (such as the influence of diabetes on cognition or the effect of menopause on working memory).

A foundational disorder?

Regardless of how comorbidity between ADHD and other disorders might be defined and measured, the incidence of overlap tends to be much higher than for other combinations of disorders. One obvious question arises from these high rates of comorbidity. Why are individuals with ADHD so much more likely to have additional psychiatric disorders? The sequence of appearance of these disorders offers a clue: usually ADHD is the first psychiatric disorder to appear, whereas other disorders emerge later in childhood, adolescence, or adult life.

One possible explanation is that ADHD is not just one more among other psychiatric disorders; it may be foundational in the sense that a person with ADHD-related impairments of executive function is more vulnerable to other psychiatric disorders. One might compare ADHD to chronic problems in the operating system of a computer that affect a wide range of software used, as distinguished from problems in a specific computer software program that impair a narrower range of functions. ADHD impairments can bring a cascade of additional problems in adaptation. It may also be linked to increased genetic vulnerability to other disorders that exacerbate problems in adaptation.

Our current diagnostic system in psychiatry, DSM-IV, describes more than 200 disorders as distinct entities. Within the current system, each psychiatric diagnosis is conceptualized as though it were a particular kind of fruit, each growing on its own type of tree, totally independent of any others. Comorbidity among these disorders is often discussed as though it were simply a chance composite in which separate fruits just happen to fall together to form a salad. This model is not adequate to describe relations between comorbid disorders in which impairments of one disorder may cause an individual to have increased vulnerability to another and in which many psychiatric disorders are complex hybrids.

Bruce Pennington, a leader in the emerging field of developmental cognitive neuroscience, has challenged the notion of psychiatric disorders as totally separate entities (3). He highlighted common neurobiological factors underlying various disorders and noted that current definitions of disorders are “regions with fuzzy boundaries in continuous multivariate space”. He suggested that various disorders are likely to be distinguished more by variable weighting of different risk factors, and by different epigenetic (other than genetic) and developmental interactions that result from that weighting, than by a distinct set of risk factors for each disorder.

Some researchers have observed that executive function impairments are not specific to ADHD but are characteristic of many other disorders as well. This observation suggests a view of ADHD comorbidity quite different from the fruit salad construct. The high incidence of comorbidity of ADHD with other psychiatric disorders and the typically earlier onset of ADHD suggest that this syndrome is a primary or foundational disorder, underlying many other disorders, heightening vulnerability of affected individuals to other psychiatric impairments. For many individuals with ADHD, it is not only that the conductor of the brain’s orchestra is impaired but also that elements of the woodwinds and/or another instrumental section may fail to function adequately.

How might disorders be related?

ADHD and other disorders might be related in two primary ways:

1. ADHD may cause adaptive impairments that render an individual more vulnerable to environmental stressors that increase risk of another disorder, or
2. An individual with ADHD may have genetic vulnerability to additional disorders that combine to cause more specific impairment than ADHD alone might bring.

Or there may be a combination of both of these factors.

Substance use disorders offer an example of how adaptational problems resulting from ADHD may heighten risk of another disorder. Unless children with ADHD are treated with appropriate medications, they have at least double the risk of developing a substance use disorder sometime during adolescence compared with children without ADHD.

Researchers who studied substance use in adolescents with ADHD compared with that in adolescents without ADHD found that severity of inattention symptoms of ADHD in adolescence, more than hyperactive or impulsive symptoms, was associated with lower academic grades and with increased risk for heavier use and abuse of tobacco, alcohol, and other drugs by the teenage years (4). They suggested that students with inadequately treated ADHD are more vulnerable to academic failure and are thus more likely to gravitate away from peers who value academic success and toward nonconformist peer groups in which heavier substance use is modelled and tolerated. Thus, the ADHD impairments may indirectly cause affected individuals to be exposed to increased risk for developing a substance use disorder.

An example of the second type of comorbidity, ADHD with an additional genetic vulnerability for intensified impairment of a specific function, can be found in ADHD with a reading disorder (dyslexia), another inherited syndrome. A child with the executive function impairments that constitute ADHD would be more likely to meet diagnostic criteria for a reading disorder than would one without ADHD impairments because executive functions such as working memory and speed of information processing play a critical role in a person's learning to read, in developing reading fluency, and in being able to comprehend what has been read.

However, a person with an appropriate diagnosis of reading disorder would have additional impairments beyond those involved with ADHD. That person is likely to have specific impairments in speech-language processing and word retrieval that are not characteristic of most other individuals with ADHD. Thus, comorbidity can be seen as involving impairments in the more general foundational cognitive functions and also in more specific cognitive functions involved in speech language processing and word retrieval.

Some researchers have presented evidence that a common genetic cause that increases risk for reading disorder and for ADHD is likely, with each individual's final traits being determined by additional genetic and environmental influences that affect that particular person (5). Findings from that study suggested that information-processing speed is probably the most important cognitive function impaired in both reading disorder and ADHD. Some studies have suggested a specific gene that may be one component of the genetic underpinning of both disorders, although those researchers emphasized that the contribution of that one specific gene falls far short of explaining all the shared variance between the two disorders (6). Other genetic influences, shared and divergent, are also likely to be involved in each disorder. Similar overlap of shared and divergent genetic influences is likely to be involved in many other comorbid combinations.

In many disorders comorbid with ADHD, symptoms overlap - causing uncertainty about whether a given individual simply has a severe variant form of ADHD - or has ADHD and an additional comorbid disorder. In recent years, nowhere has this uncertainty been more controversial than in ADHD and juvenile-onset bipolar disorder. Many child psychiatrists are quick to diagnose bipolar disorder in children with ADHD who show significant impairments in their ability to regulate their moods, especially anger and aggression. Other investigators dispute this approach, stating that moodiness and irritability are common characteristics of children with ADHD and children with bipolar disorder. Sometimes the dispute can be resolved on grounds of the severity of the impairment.
In a large sample of children with ADHD, investigators found that severity of irritability differentiated children with only ADHD from those with ADHD and unipolar depression and from children who also had full bipolar disorder (7). This finding is consistent with the view that many individuals with ADHD have chronic difficulty in regulating their frustration and irritability—but some individuals with ADHD, who can be reliably distinguished by their much more intense levels of chronic irritability and aggression, exceed the normal range of mood problems usually associated with ADHD and have additional symptoms that fully qualify for a specific diagnosis of mood disorder.

In other cases, some individuals who qualify for an ADHD diagnosis also qualify for an additional diagnosis that involves symptoms quite different from a typical ADHD profile. For example, many children with ADHD, particularly those who are hyperactive or impulsive, seem fearless in their willingness to seek out novel situations and to engage in high-risk behaviours, whereas many others who also fully meet diagnostic criteria for ADHD are so fearful that they qualify for the diagnosis of generalized anxiety disorder or multiple phobias.

Alternative new views of ADHD

The six understandings mentioned above constitute one possible model to reconceptualise ADHD. Several researchers have recognized that current diagnostic formulations of ADHD are inadequate. Many have recognized the need to develop a conceptual model of ADHD that more adequately recognizes the diversity among individuals with ADHD and that takes more seriously the two-way interactions between biological impairments of ADHD and changing developmental and environmental influences that alter the ADHD traits during the course of the individual's life experiences.

Most proposed solutions to this problem tend to use approaches that have, thus far, proved inadequate to account for the complex characteristics of ADHD and its extensive comorbidity with other disorders. It would seem that a more radical reconceptualization is needed, one that recognizes that ADHD is essentially impairment in development of executive functions and that these executive function impairments constitute an important aspect of most other psychiatric disorders.

In many areas of psychiatry and psychology, there is increasing recognition that most psychiatric disorders are better seen as dimensional rather than categorical, on a wide spectrum of impairment, often overlapping with other disorders. Much work remains to be done to refine our understanding of ADHD and other psychiatric disorders, both in their own complexity and as they relate to one another.


Editors notes.

1. The original article referred primarily to “attention deficit disorder” which was abbreviated ADD. This has been altered to ADHD, in keeping with UK practice.

2. This paper does not discuss the detailed management of ADHD comorbidities but this important subject is covered, at least in part, in other papers in this issue, including those on Substance Misuse, Learning Disability, Autism and Epilepsy, in association with ADHD.
GP Comment

What have I learned from this paper?

1. A child with ADHD is likely to be at high risk of developing psychiatric disorders, especially in the teenage and adult years.

2. The high rate of other psychiatric disorders in people with ADHD is likely to be the result of both genetic and environmental factors.

3. It is important for GPs to be aware that the child with ADHD is liable to develop other psychiatric disorders so that they can be followed closely and referred promptly for additional specialist help if the need arises.

Dr Talib Mearza
GP, Flitwick, Bedfordshire.

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ADHD in children and young people - How common are the comorbid conditions?

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Abstract

ADHD is often associated with comorbid (coexisting) medical conditions. It is important to be aware of and screen for these conditions during the assessment of children and young people with ADHD. This short article presents a table with comorbid conditions and their prevalence figures derived from a number of sources in the literature.

Introduction

In clinical practice it is not uncommon to see a child with ADHD presenting with more than one diagnosis (see paper by Thomas Brown in this issue). About 50% to 75% of children with ADHD have one or more comorbid conditions (1).

There are several developmental and psychiatric conditions (Table 1) that are often found in association with ADHD but may not be apparent at the initial clinical assessment. It is important for the clinician to assess carefully in order to diagnose comorbid conditions. Prompt and effective intervention, both for the ADHD and for the comorbid conditions, offers the best chance of a favourable outcome.

Table 1

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<thead>
<tr>
<th>Psychiatric conditions</th>
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</tr>
<tr>
<td>Anxiety disorders</td>
<td>• Specific learning disorders</td>
</tr>
<tr>
<td>• Separation anxiety disorders</td>
<td>- Reading disorder/ dyslexia</td>
</tr>
<tr>
<td>• Avoidant disorder</td>
<td>- Mathematic disorder (dyscalculia, disorder for written expression)</td>
</tr>
<tr>
<td>• Overanxious disorder</td>
<td></td>
</tr>
<tr>
<td>• Obsessive Compulsive Disorder, also an anxiety disorder</td>
<td></td>
</tr>
<tr>
<td>• Depressive disorder</td>
<td>• Smoking, alcohol and substance misuse disorders</td>
</tr>
<tr>
<td>• Tic disorder and Tourette syndrome</td>
<td>• Sleep problems/disorders</td>
</tr>
<tr>
<td></td>
<td>• Obstructive Sleep Apnoea</td>
</tr>
<tr>
<td></td>
<td>• Restless Leg Syndrome</td>
</tr>
<tr>
<td></td>
<td>• Delayed Sleep Phase Syndrome</td>
</tr>
</tbody>
</table>
Prevalence of certain comorbid conditions seen in association with ADHD (1)

GP Comment

What have I learned from this paper?

1. Behavioural disorders (such as conduct and oppositional defiant disorder), developmental/learning disorders, anxiety disorders and tic disorders are all common in individuals with ADHD.

2. The table showing the prevalence of comorbid disorders has increased my awareness of the importance of diagnosing and managing these conditions in people with ADHD; if the ADHD is adequately treated but the comorbid disorder is not, I shall have a low threshold for referring back to specialist child and adolescent psychiatry services.

3. As a result of reading this paper I shall raise the awareness of the common associated disorders with family and carers who attend GP appointments with the patient who has ADHD, and encourage early reporting of any concerns.

Dr Talib Mearza
GP, Flitwick, Bedfordshire.
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ADHD and Sleep problems

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2. Dr Chinnaiah Yemula, Consultant Community Paediatrician, Union Street Clinic, Bedford

Abstract

Sleep is a vital process not only for survival but also to maintain physical and psychological health. ADHD is often associated with sleep difficulties. A reduction in sleep quality and duration can lead to significant behavioural and psychological manifestations. A comprehensive assessment should be carried out, involving a detailed sleep history, sleep diary, evaluation of any associated primary sleep disorders and an assessment of the role of ADHD medication. Management is ‘diagnostically driven’ and should include sleep hygiene with behaviour interventions, treating other comorbid conditions, optimising ADHD treatment and, if necessary, short-term use of sleep medication.

Introduction

Sleep anatomy and physiology.

Although there has been a significant increase in our knowledge over the past few decades regarding the underlying mechanisms which control sleep, its basic function remains unclear. Adequate sleep does, however, appear to represent a “biological imperative”, vital for the maintenance of optimal physical and psychological wellbeing and survival (1-5).

Sleep and wakefulness are normally regulated by coupled homeostatic (“Process S”) and circadian (“Process C”) mechanisms, summarised in Table 1

<table>
<thead>
<tr>
<th>Process</th>
<th>Function</th>
<th>Putative Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homeostatic, -</td>
<td>Influences depth and length of Sleep and “Sleep Drive”</td>
<td>Progressive accumulation of brain metabolites, -e.g. cytokines, adenosine, resulting in an inescapable “sleep debt”</td>
</tr>
<tr>
<td>“Process S”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endogenous Circadian</td>
<td>Influences timing and duration of sleepiness versus daytime alertness</td>
<td>Circadian “clock” in supra-chiasmatic nucleus, - influenced and to a certain extent “entrained” by light dark exposure; also by “clock genes”, resulting in morning “lark” and night “owl” individuals.</td>
</tr>
<tr>
<td>Rhythm, “Process C”</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1 Coupled Mechanisms for Sleep regulation (3,5,6)
Normal Sleep Characteristics in Childhood and Adolescence

From an average of around 16-18 hours at term, sleep duration reduces over childhood to between 7 to 8 hours in late adolescence (see Table 2). Across childhood and adolescence, according to limited data available, the time taken to fall asleep (“sleep onset latency”) averages between 15 to 20 minutes, and does not appear to show much variation depending on age.

<table>
<thead>
<tr>
<th>Age</th>
<th>Average Sleep duration (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Term</td>
<td>16-18</td>
</tr>
<tr>
<td>1 year</td>
<td>15</td>
</tr>
<tr>
<td>2 years</td>
<td>13-14</td>
</tr>
<tr>
<td>10 years</td>
<td>8-10</td>
</tr>
<tr>
<td>Mid Adolescence</td>
<td>8½</td>
</tr>
<tr>
<td>Late Adolescence</td>
<td>7-8</td>
</tr>
</tbody>
</table>

Table 2 Average Sleep Duration at Different Ages (2,3,7,8).

Consequences of disordered sleep

Reduction in the duration and quality of sleep results in a number of daytime manifestations affecting cognitive function and behaviour alongside the familiar symptoms of sleepiness, fatigue, yawning etc., associated with “sleep debt”. Reduced alertness may be accompanied by noticeable hyperactivity, impulsivity, and inattention - the core symptoms observed in ADHD. A synopsis of potential signs and symptoms which may be observed as a consequence of disordered sleep is listed in Table 3. It is important to keep in mind the potential for family disruption and discord to which these symptoms may contribute, as well as possible implications of disturbed parental and sibling sleep (1,2,3,17,18).

- Drowsy, fatigued, yawning, rubbing eyes
- Reduced alertness, falling asleep
- Reduced sleep latency (time to fall asleep) on Multiple sleep latency test
- Increase hyperactivity, impulsivity and inattention
- Reduced cognitive flexibility
- Reduced verbal creativity
- Poor abstract reasoning
- Impaired motor skills
- Memory impairments
- Increased mood lability and aggression

Table 3. Behavioural and Psychological manifestations of Disordered Sleep(2,3,9-16,)

Sleep and ADHD

A clear association between disordered sleep and ADHD is well established, with a reported prevalence that approaches 50% or more (compared to for example 11% of normal 4-12 yr old children) comprising a range of self-reported and parent-reported difficulties, which include bedtime resistance, increased sleep latency and sleep of poor quality (e.g. with frequent wakening) or duration (19,20). The poor concordance between parental accounts and objective measures such as polysomnography and actigraphy is likely to be explained by night-to-night variability in sleep patterns and methodological difficulties such as the challenge of reproducing a “naturalistic” sleep environment in a sleep laboratory setting.
Impaired sleep may result in psychological and behavioural problems identical to those seen in ADHD. Sleep difficulty can not only therefore mimic ADHD but can also potentially cause exacerbation of ADHD symptoms. This can add further to the burden of care within families, such as reported excessive parental tiredness, irritability, social withdrawal, arguments, and time off work, all seriously affecting quality of life.(21,22)

Factors which may contribute to sleep difficulties in children and young people with ADHD (see figure 1).

The aetiology of sleep difficulties in ADHD is complex and not well studied or understood; more than one cause may be implicated in any individual.

Figure 1. Contributing factors to sleep difficulties in ADHD
Primary Sleep Disorders

A “Primary” sleep disorder may result in reduced daytime alertness and daytime ADHD symptoms due to, for example, reduced sleep duration and/or fragmented sleep. Important examples include obstructed breathing and sleep apnoea, restless legs syndrome/periodic leg movement disorder, narcolepsy/cataplexy, and delayed sleep phase syndrome of adolescence. Recognition and specific treatment of these albeit relatively uncommon disorders can be effective and lead to reduced ADHD symptoms. A brief synopsis is in Table 4.

<table>
<thead>
<tr>
<th>“Primary Sleep Disorder”</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructive Sleep Apnoea/ Hypopnea Syndrome (OSAHS) (19,23-27)</td>
<td>Assess for obesity and adenotonsillar hypertrophy. Noisy breathing at night; adenoidal facies; “mouth breathing” ADHD symptoms may be remediable by ENT surgery</td>
</tr>
<tr>
<td>Restless Legs Syndrome/ Periodic Leg movement Disorder (28-31)</td>
<td>Fidgety, on the move, - “growing pains” in extremities. Poor sleep and movements worse when settling at night. Association with caffeine use and low serum ferritin. Increasingly acknowledged as a treatable extrapyramidal disorder, overlapping with ADHD</td>
</tr>
<tr>
<td>Narcolepsy/Cataplexy (32)</td>
<td>Rare. Cataplexy results in episodes of collapse from rapid change in emotion. Disrupted sleep with hypnogogic hallucinations, sleep paralysis and daytime sleepiness, naps, and ADHD symptoms</td>
</tr>
<tr>
<td>Delayed Sleep Phase Syndrome (33-35)</td>
<td>Up to 3% adolescents. Sleep late, wake late if allowed, but pressured to attend school, college etc. Challenging to treat (attempt to recalibrate sleep-wake cycle)</td>
</tr>
</tbody>
</table>

Table 4 Examples of “Primary” Sleep Disorders which may overlap with or mimic ADHD

Behavioural Disruption and Sleep Difficulties in ADHD

Sleep disruption, particularly bedtime resistance and increased sleep latency in ADHD, frequently result from inappropriate and inconsistent parental limit setting combined with oppositional behaviour, exacerbated by poor “sleep hygiene” (i.e. poor control of behavioural and/or environmental factors that can interfere with sleep, including lack of bedtime routine). However, before assuming that in individual cases such sleep difficulties are “behavioural” or environmental, it is important to keep in mind that ADHD-associated CNS dysregulation of arousal and circadian rhythms may be contributory factors (3,36), - not so much a question of “won’t sleep”, but “can’t sleep”.

Internalising Disorders and Autism affecting Sleep in ADHD

Anxiety and depression are well recognised “comorbid” accompaniments of ADHD in many children and young people. Early recognition and screening for these conditions is part of the clinician’s ongoing responsibility, whilst recognising that sleep disruption, with attendant daytime sequelae may result (3, 37). Anxiety is also more likely to be observed in children who lack a capacity for “self-soothing” as part of normal maturation, and in those identified as exhibiting problems such as impaired sensory integration. Similarly children and young people who have autism spectrum disorder with ADHD demonstrate a high rate of potentially refractory sleep difficulties, which correlate positively with the severity of the daytime behavioural problems and communication impairments (2,3,38,39).
Daytime environmental exposures and Sleep problems in ADHD

Overstimulation and excessive exercise close to normal sleep times may contribute to difficulties settling at night; the importance of good sleep routines and environment cannot be understated. Exposure to caffeine-containing drinks and beverages may promote wakefulness and arousal. Specific medications, particularly neurostimulants may also be implicated. Psychostimulants have a potential to increase sleep latency, particularly when administered later in the day or as an extended-release preparation. Although convincing objective research evidence for a link between stimulant medication and disrupted sleep is scanty, it is clear that this is a common clinical problem. (40-42). Other prescribed medications which can impair sleep include antiepileptic drugs (rarely) and antidepressants (3).

Assessing Sleep in ADHD

Assessment is based on appropriate enquiry about sleep routines and evening activities, (including food, beverages, medication), sleep environment, time to get into bed, time to settle to sleep, and the quality and duration of sleep. Any alteration in daytime behaviour or any change in sleep pattern coinciding with medication initiation or modification should also be noted. This information can be captured by self-report, and parental report (2, 3), and ideally by completion of widely available sleep diaries. Systematic evaluation is possible using specific questionnaires (43,44). When relevant, other assessments such as upper-airway assessment for tonsillar or adenoidal obstruction may be required, or when suspecting restless legs syndrome/PLMD, blood assay for ferritin level (30,31). Considering the potential causes of disrupted sleep, careful assessment to detect associated anxiety, low mood, and autism spectrum disorder should not be overlooked.

If a primary sleep disorder is suspected from the history, a referral to a specialist sleep centre for further investigation such as polysomnography/actigraphy is indicated.

Management of Sleep Disorders in ADHD

Management is “diagnostically driven”, and depends on thorough assessment and a formulation to include the likely underlying cause or causes.

Primary sleep disorders

Specific individual management strategies are summarised in Table 5.

<table>
<thead>
<tr>
<th>Primary Sleep Disorder</th>
<th>Management Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructive sleep apnoea/hypopnoea syndrome (OSAHS)</td>
<td>Weight reduction; adenotonsillectomy. (25-27)</td>
</tr>
<tr>
<td>Restless legs Syndrome/periodic limb movement disorder (PLMD)</td>
<td>Oral Iron; avoid caffeine. Dopaminergic agents e.g. Sinemet. Pramipexole. Clonidine. Opiates such as codeine. Gabapentin. (29,30)</td>
</tr>
<tr>
<td>Narcolepsy/cataplexy</td>
<td>Psychostimulants; SSRIs; sodium oxybate. (32)</td>
</tr>
<tr>
<td>Delayed Sleep Phase Syndrome of adolescence</td>
<td>“Chronotherapy” (re-adjusting sleep/wake cycle). Melatonin. Light therapy. (33,34)</td>
</tr>
</tbody>
</table>

Table 5. Management of Primary Sleep Disorders
Management of Primary Sleep Disorders

Psychological/Behavioural Causes and adverse environmental triggers and exposures should be managed in the first instance by well-established strategies, summarised in table 6. It is particularly important not to overlook the potential contribution of anxiety and altered mood to sleep difficulties and specific enquiry should be made about any potential triggers. It is particularly important to assess so-called “sleep hygiene” (see earlier) in this era of multimedia with the plethora of potentially stimulating (and light emanating) devices. These should be strategically and progressively removed from the bedroom environment.

### Table 6. Psychological and Behavioural Strategies for Disordered Sleep in ADHD (2,3)

<table>
<thead>
<tr>
<th>Behavioural Methodology examples</th>
<th>“Sleep Hygiene” issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consistent limit setting</td>
<td>Regular scheduling</td>
</tr>
<tr>
<td>Positive (e.g. token) reinforcement</td>
<td>Appropriate bed time</td>
</tr>
<tr>
<td>Reduce anxiety ; relaxation training/tapes</td>
<td>Bedtime preparation routines</td>
</tr>
<tr>
<td>Avoid negative associations (e.g. bedroom seen as punishment zone)</td>
<td>Relationship to meals, exercise, caffeine, stimulating activity.</td>
</tr>
<tr>
<td>Individual CBT in older children and adolescents</td>
<td>Ambient noise, temperature, light, DVD, Playstation, X-Box etc.</td>
</tr>
</tbody>
</table>

As noted earlier, the use of psychostimulants for control of daytime ADHD symptoms may cause or exacerbate insomnia. Treatment options when faced with sleep difficulties which may be medication related, include stimulant dose reduction, switching to a shorter acting neurostimulant, or in refractory cases discontinuing the medication completely (13,28,45). If the sleep disturbance continues, it may be worth undertaking a brief pragmatic trial of short-acting methylphenidate in the evening, about an hour before the time that the child should be asleep; this is effective in a subgroup of children with ADHD (46), probably those in whom the symptoms of this condition are keeping them awake at night. The usual convention is a trial of half of one of the daily doses, i.e. if the child was taking 20 mg three times daily then a dose of 10 mg would be given in the evening. This need only be tried for one or two nights. If the sleep is improved, it may be continued but if the sleep is worse or unchanged the evening methylphenidate dose should be stopped. If stimulant medication causes a deterioration in sleep, atomoxetine, which is not associated with sleep disruption (47), should be considered as an alternative.

**Medications for sleep promotion in ADHD-Associated Insomnia.**

The use of medication for disrupted sleep in ADHD is rarely the first and only choice; it should be combined with behavioural strategies aiming to sustain improvement and minimise adverse effects. There are no licensed medications for sleep promotion in children and adolescence and indeed the research base is sparse. Prescribing must be initiated on a “named patient”, off-label basis, under “specialist” supervision (See British National Formulary for Children (BNFC) for support and guidance). There is little guidance in the paediatric and psychiatric literature, although recent reviews may be useful (13,28,45,49,50). Prescribing needs to take into account a risk-benefit analysis for the individual patient and medication.

In the UK medications listed for consideration, but not “recommended”, by the BNFC, for “occasional” and/or “short-term” use include chloral derivatives, the antihistamine promethazine (“Phenergan”), and melatonin. Clinicians will need to assess the risks and benefits of longer-term treatment on an individual basis; children may revert to a pattern of poor sleep when sleep medications are withdrawn or inadvertently overlooked.

**Melatonin (MLT),** in both immediate and extended-release forms, is widely prescribed, in “pharmaceutical quality” preparations in the UK. Evidence for the efficacy of MLT for sleep promotion
is based mainly on open studies and case reviews, although a small number of randomised trials have been published (51,52,53). In practice, adverse effects with MLT are relatively uncommon and self-limiting. There is increasingly reassuring evidence that this is a safe medication in hypnotic doses of up to 10mg (54,55). In such doses, administration is recommended 30 minutes before sleep time, and the half-life is short with no likely hangover or morning-after ill effects. Long-term safety of MLT has not been convincingly established and there are some residual questions, including potential adverse endocrine and immunological effects. The effectiveness of MLT may be limited by its short half life (1-2hrs) and rapid elimination in which case an extended-release preparation may be considered. Future potential therapeutic alternatives with longer half-life properties include MLT analogues such as Ramelteon, Tasimelteon, and Agomelatine (48).

Though still in use by some clinicians, there is no evidence base to support the use of Chloral Hydrate. Effectiveness may be limited by gastrointestinal intolerance and sometimes daytime dizziness reflecting the long longer half-life of the main active metabolite trichlorehanol. Cautious short-term use may be justified in treatment-refractory patients.

A wide range of Antihistamines are employed empirically for sleep promotion in children, particularly in primary care. For example, as noted earlier, the BNFC supports lists promethazine (Phenergan) for short-term use; daytime drowsiness, gastrointestinal upset, paradoxical excitation and tolerance may limit effectiveness (56,57).

Clonidine Hydrochloride, a central alpha-2 adrenergic agonist is widely used for sleep promotion in childhood practice in the USA, often in higher doses than would usually be considered in the UK. Onset of action is rapid with peak effects within 2 to 4 hours. Evidence for efficacy from clinical trials is limited and potential adverse effects include postural hypotension, syncope, dry mouth and fatigue (58,59).

The use of Benzodiazepines for insomnia in ADHD is not supported because of significant limitations and adverse effects, including the risk of exacerbating hyperkinesis. Shorter acting Non-Benzodiazepine Receptor Agonists or “Z Drugs” such as Zolpidem, Zopiclone are popular hypnotics in adult practice and may have a limited role in refractory insomnia in ADHD. Potential adverse effects which may limit usefulness include dizziness, headache and hallucinations (60). In the USA Atypical Antidepressants (5-HT Antagonist) such as Trazodone and Mirtazapine are sometimes prescribed for sleep promotion (61,62), although there is little experience with these agents in the UK and no evidence base to support use.

There is no "ideal" hypnotic medication for use in refractory insomnia in ADHD. Pragmatically, ideally short-term prescribing is perhaps worthy of consideration in individual circumstances. Melatonin appears to be the medication associated with the fewest adverse effects but it is not always effective or may appear to lose its effect over time. Whatever medication is tried, periodic breaks from treatment are prudent to assess whether ongoing treatment is necessary. Most hypnotics will remain ineffective in the presence of poor sleep routines, overstimulation at bedtime or the challenges of nocturnal multimedia.

Key Points

- Sleep difficulties are highly prevalent in ADHD, are often multifactorial in origin, and significantly impair quality of life for the child and family.
- Sleep deprivation can produce symptoms that mimic ADHD.
- Sleep difficulties exacerbate daytime ADHD symptoms.
- Shared biological dysregulation in ADHD may contribute to disordered sleep.
- Assessment of ADHD is incomplete without a sleep history.
- Sleep diaries are particularly useful in assessment.
In assessment “Primary Sleep Disorders” (Obstructive Sleep apnoea, Restless leg Syndrome/Periodic leg movement Disorder, Narcolepsy/Cataplexy, Delayed Sleep Phase Syndrome), though rare, need consideration; referral to a sleep specialist may be indicated.

Behavioural disorders, internalising disorders and autism spectrum disorder should be considered/excluded in assessment.

Daytime medication such as neurostimulants may cause/exacerbate sleep problems in ADHD.

Management is “diagnostically driven”; it should always include behavioural intervention and consideration of sleep routines and environment.

Medication (hypnotics) and manipulation of daytime ADHD medications may be used on an individual basis to promote and improve sleep.

If medication is prescribed for sleep in childhood and adolescence this is necessarily “off-label”, ideally short term, and on a named-patient basis under specialist supervision and surveillance.

**GP Comment.**

**What have I learned from this paper?**

1. Disordered sleep is much more common in children with ADHD; self-report and parent-report assessments have suggested a prevalence approaching 50%.

2. Insufficient sleep (“sleep debt”) can result in hyperactivity, impulsivity and inattention, the same core symptoms that are seen in ADHD. In addition, it may contribute to family disruption, adding to family stress and behavioural problems. Treating the sleep problems successfully can resolve the ADHD symptoms in some cases.

3. Sleep disturbance can not only mimic ADHD but can also exacerbate the symptoms in children with established ADHD.

4. Although good “sleep hygiene”, (involving control of behavioural and environmental factors that can interfere with sleep), is important, some children with ADHD have underlying sleep problems that will not resolve with these measures alone.

5. The management of sleep problems in ADHD depends on the underlying diagnosis: obstructive sleep apnoea/hypopnoea, restless legs syndrome, periodic limb movement disorder, narcolepsy and delayed sleep-phase syndrome of adolescence of all require specific management strategies.

6. Medication for ADHD can either worsen or improve sleep; this depends not only on the type of medication but also the characteristics of the individual.

7. There are no licensed medications for treating sleep problems in children with ADHD but melatonin is widely used to decrease time to sleep onset (sleep latency). It may not be very effective in maintaining sleep throughout the night, however.

8. Clonidine can be helpful both in treating ADHD symptoms and in promoting sleep.

**Dr Subash Kanungo, GP, Bedfordshire.**

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ADHD and Learning Disability

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Abstract

Learning disability (mental retardation) can be defined as IQ <70 combined with impairment in social functioning. ADHD is more common in people with learning disability and the prevalence increases as the degree of learning disability increases. However, assessment of ADHD in people with learning disability can be problematic and needs to be undertaken carefully. ADHD occurs more commonly in specific syndromes associated with learning disability. It is also common in people with epilepsy, a condition which occurs more frequently in people with learning disability. Correct management of ADHD in an individual with learning disability depends on careful assessment followed by an approach that is both comprehensive and pragmatic; for example, people with learning disability may be unable or unwilling to swallow tablets, implying that a different formulation or different strategy of medication administration may be required. Despite the challenges, treating ADHD in people with learning disability can be both effective and worthwhile.

Introduction

The diagnosis and treatment of individuals with ADHD and learning disability has lagged behind in CAMHS services and even more so in adult services. In this paper the differences in assessment and management within this population who can definitely benefit from effective treatment are briefly explored.

Definition of Learning Disability

Learning disability is defined as a state of arrested or incomplete development of the mind, which is characterized by impairment of skills manifested during the developmental period, which contributes to the overall level of intelligence, motor, cognitive, language, adaptive, and social skills and abilities. The term generally used at present in the UK is learning disability (LD) and this equates with intellectual disability or mental retardation, the terms used more commonly outside of the United Kingdom. Educational services use the term learning difficulty which can be confusing to professionals and parents as, for example, moderate learning difficulty can include those with a borderline, mild or moderate level of LD.

The ICD 10 (1) uses the terms mild mental retardation (IQ between 50 and 69), moderate mental retardation (IQ between 35 and 49), severe mental retardation (20 to 34) and profound mental retardation (IQ below 20). The current preference is to use the term learning disability as an equivalent to mental retardation. Very few patients have a measured IQ; the level of learning disability is usually assessed based upon their level of functional skills with mobility, daily living skills, communication and social skills. This is generally estimated from their clinical presentation but it can be assessed with a well-validated tool such as the Vineland Adaptive Behaviour Scale (2) or the ABAS (3).

Diagnostic criteria for ADHD in patients with LD.

The ICD 10 or DSM IV (4) criteria are used for diagnosis, using detailed assessment of inattention, hyperactivity and impulsivity. It is vital when assessing those with LD to establish whether these symptoms are inconsistent with the person's developmental level.
The more severe the level of disability, the less applicable many of the diagnostic criteria within ICD10 and DSM IV appear to be. For this reason the DC LD (5) diagnostic criteria for adults with LD was developed. The main differences in the criteria includes the age of onset to be as far back as ‘available history’, increased emphasis on flitting and fleeting activity, lack of sustained and purposeful action, impulsivity and inability to keep still, all not attributable to severity of the learning disability.

Epidemiology

The estimated prevalence of mild LD is 2-3 per cent of the population and moderate to profound LD 0.3- 0.4 per cent of the population. There are more boys than girls with special educational needs in the education system due to boys having higher rates of behavioural problems, and to a smaller degree due to X linked disorders (6). The prevalence of ADHD in children with learning disability is higher than that in the general population (7) and it increases with increasing severity of the LD. The rates of ‘hyperactivity’ among young adults increases markedly with increasing levels of learning disability (8). The prevalence of ADHD declines with age in the general adult population (9). Recent research indicates the possibility of a longer and more persistent course of the disorder in those with LD (10). This also seems to be the case with adults who have borderline or mild levels of LD where a more severe presentation and an uneven and less favourable pattern of improvement across the lifespan has been found (11).

Differential diagnosis

In addition to the differential diagnoses and co-morbidities discussed in previous papers, children and adults with LD, in environments that are under-stimulating or over-stimulating, may engage in high levels of physical activities as a self-stimulatory behaviour.

Medication adverse effects such as those seen with some antiepileptic drugs may raise the suspicion of ADHD because of behavioural adverse effects (12); a review of the person’s medication history in relation to the onset of symptoms can be illuminating. It is also very important to remember that a person with learning disability may not have the level of communication to express their needs, emotions or desires resulting in behaviours such as those seen in ADHD.

Aetiology

The following chromosomal and genetic syndromes have all been associated with increased rates of ADHD: Fragile X, Smith-Magenis, Angelman, Prader-Willi, Turner, Williams and Cornelia de Lange syndromes (13,14). Children who are preterm and of low birth weight have increased risk of developing hyperactivity (15). Infections during pregnancy and foetal toxins such as alcohol can cause intrauterine foetal damage, for example foetal alcohol syndrome, increasing the risk of developing ADHD (16). Epilepsy is common in children with learning disability; the prevalence increases with the degree of learning disability. There is a high rate of ADHD features in children with epilepsy, typically estimated as being at least 20% (17).

A later age of onset or atypical progression of the symptoms indicative of ADHD can be caused by the following.

1. Neurocutaneous disorders such as neurofibromatosis and tuberous sclerosis
2. Mucopolysaccharidoses such as Sanfilippo, Hurler and Hunter syndromes.
3. Severe head trauma such as road traffic accidents, non-accidental injury and hypoxia.
4. Infective causes such as meningitis and encephalitis.
Referral considerations

The developmental level can be assessed fairly quickly in a clinic appointment with a brief review of developmental milestones, academic skills and current self-help skills. This will be helpful in making a judgement about the degree of ADHD symptoms in relation to ability level in addition to the observation of the person during the appointment. It will also be very helpful when making decisions about referral to the most appropriate service within adult or child health services. It can be useful to request a report from the school if the individual is of school age, as this will clarify whether the symptoms are pervasive across environments and may also give some useful guidance regarding degree of learning disability.

When a referral for assessment to secondary care is made it should include the past medical history, any known information about the pregnancy, birth and neonatal period, family or social issues and a record of all medications prescribed.

Assessment issues

When the young person or adult is assessed in secondary care a full history with symptom onset and evidence of pervasiveness across settings, past medical and mental health history, family history, educational and social history, assessment of family relationships and for older adolescents and adults an educational and forensic history, will be completed.

A detailed assessment using an instrument such as Vineland Adaptive Behaviour Scale or ABAS, can provide clarity about the developmental level so that the assessment of ADHD is in context. A more detailed IQ assessment may be undertaken if there appears to be an uneven or “patchy” cognitive profile.

For children, an assessment of impulsivity, attention and hyperactivity may usefully include observation in school, and collation of information from school, rather than relying on symptoms seen in the clinic setting. The child can be seen in a familiar environment engaging both in activities requiring sustained mental effort and in unstructured time. It is advisable not to rely on the parent or teacher Conners scales when the child has more than mild LD as many items on these scales are not applicable to children with severe or profound learning disability who do not have speech (18). Sleep problems are common in those with learning disability (19) and sleep disturbance may be either the result of or the cause of ADHD symptoms. If sleep is disturbed, further assessment may be required.

For adults, detailed information from family members or carers will be crucial to clarify diagnostic issues. Adult ADHD scales can be difficult to interpret when there is more than a borderline or mild level of learning disability.

Treatment Issues

On completion of assessment and diagnosis, ADHD treatment following the NICE Guidelines (20) is recommended and has been shown to be effective for those with learning disability (14). There are, however, some important treatment considerations for patients with LD, as follows.

1. The capacity of the patient to consent to assessment and treatment should be assessed whenever appropriate and all efforts should be made to enable them to communicate their wishes and preferences clearly throughout the process. This requires ample time to be allocated for this work.

2. The most crucial intervention for a person with LD and symptoms indicative of ADHD is consideration of their environment, routine, activities, communication strategies and coping skills. There also need to be consistent behavioural management strategies, following detailed analysis of the functions of their behaviour. This requires involvement from a multidisciplinary and multiagency team.
3. Regarding groups for parents and children as recommended in the NICE guidelines, unless there are specific groups for children with ADHD and LD those with mild or moderate symptoms will usually need individual management strategies.

4. For those with severe symptoms, or those who do not respond to management strategies, medication is used but individualised baseline measures of symptoms and adverse effects may need to be devised as the child or adult may have difficulty describing their symptoms. Collaboration with the education placement or day provision (with consent from the patient or family) in establishing baselines and development of a management plan can be very valuable.

5. Choice of medication may depend upon the formulation that they can swallow. Many patients with LD and younger children struggle to swallow tablets or capsules. There is no standard liquid formulation of stimulant medication, although ‘special’ liquid formulations are available at significant cost. It is possible to open the capsules of Medikinet and Equasym to sprinkle the slow-release beads onto food such as jam or yoghurt with breakfast. Atomoxetine is available in capsules that contain a powder. It is not advisable to open the capsule of atomoxetine as the powder is unpalatable and can cause irritation if contact is made with the eyes. It may also cause gastric irritation. However, some families try to administer atomoxetine by breaking open the capsules and attempting to disguise the taste in liquids or food; this is not an approved method of administration.

6. Careful consideration needs to be made about any associated medical problems and other medications. It may be useful to liaise with the neurologist or paediatrician if the individual is on antiepileptic medication to ensure stability of seizure control and clarity that there is no interaction between the treatment for ADHD and antiepileptic drug (e.g. methylphenidate inhibits metabolism of phenobarbitone, phenytoin and ethosuximide). It is important to monitor the seizure frequency before and after methylphenidate even though studies indicate that methylphenidate is safe to use and effective for those with epilepsy and ADHD (17). (Also see paper on ADHD and epilepsy in this issue.)

7. There needs to be a baseline assessment of sleep and appetite. Accurate height and weight for children and weight for adults should be recorded. The appropriate growth charts for specific syndromes should be used if available, for example for Down syndrome.

8. There needs to be careful monitoring of all adverse effects and thorough assessment of symptoms which may indicate adverse effects in a person with limited communication skills. For example, if a person has no speech and is spoon fed the only way they may be able to indicate that they have lost their appetite is to spit their food out, and insidious signs of depression may be indicated by reduction in daily living skills.

9. The monitoring of blood pressure and pulse rate should take place but it can be challenging to achieve accurate results in those with severe learning disability and difficult behaviours. A desensitisation programme or social stories to help them accept the monitoring regimes may be useful.

10. A more cautious introduction of medication is generally recommended for those with LD because of their vulnerability to adverse effects.

**GP Comment.**

**What have I learned from this paper?**

1. ADHD is more common in people with learning disability and increases in prevalence as the severity of the learning disability increases.

2. ADHD might be more likely to persist into adulthood in a person with learning disability.
3. The diagnosis of possible ADHD in a person with learning disability needs to take into account a number of confounding factors, including environment, sleep problems and medication adverse effects, all of which can result in changes that can mimic ADHD.

4. Although the diagnosis of ADHD in a person with a disability may be more difficult to make and although adverse effects of medication may be more difficult to assess, treating the ADHD with medication, as part of a comprehensive plan, can be very effective.

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References


Co-occurrence of Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorders (ASD)

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Abstract

The current diagnostic manuals, DSM-IV-TR and ICD-10, do not allow the diagnosis of ADHD to be made separately in the presence of autism (pervasive developmental disorder). However, the characteristics of ADHD are very common in autism, occurring in around 30 to 70%. Surveys of children with ADHD also reveal a high proportion of features of Autism Spectrum Disorder (ASD). Furthermore, treatment of ADHD in the presence of autism is of benefit in a large proportion. The inconsistency in the diagnostic manuals should be resolved in the forthcoming DSM-5 and ICD-11. The results of twin studies have been consistent with the sharing of genetic influences between autism and ADHD symptoms. Genome-wide studies have also shown shared chromosomal regions of interest for susceptibility sites for both conditions. There is an overlap between the executive function deficits in both conditions, although the details of the dysfunction may be different. There is evidence that all the standard treatments for ADHD can be effective in the presence of autism (though to a lesser extent than in pure ADHD): methylphenidate, amphetamines, atomoxetine, clonidine and guanfacine. Atypical antipsychotics such as risperidone and aripiprazole may be of specific importance in managing ASD with irritability, aggression and hyperactivity. The idea that ADHD cannot be diagnosed or treated successfully in those with ASD is a myth that should be dispelled; many of those who have both autism spectrum disorder and ADHD can benefit greatly from the treatment of the ADHD.

Introduction

Pervasive Developmental Disorders (PDD) or Autism Spectrum Disorders (ASD), are early-onset developmental disorders with severe lifelong impact on social functioning, communication and behaviour. Children with ASD often present with interfering symptoms of Hyperkinetic Disorder (HKD) or Attention Deficit Hyperactivity Disorder (ADHD), i.e. symptoms of motor hyperactivity, impulsiveness and inattention requiring treatment (1). There is widespread clinical agreement that severe levels of hyperactivity in a pre-school age child should prompt suspicion that the ‘underlying’ disorder might be autism. It is not unheard of for a child suspected of suffering from severe ADHD (because of extremes of early onset hyperactivity and impulsivity) to be treated with a stimulant,
and for there to emerge autism features in the course of such treatment. In the past, this was often believed to be a side-effect of the treatment per se. While that is a real possibility, a more common link might be the suppression of severe hyperactivity leading to the ‘unmasking’ or ‘surfacing’ of the ASD which was always present but hidden under the more conspicuous symptoms associated with extreme hyperactivity (2).

**Concept of Developmental Co-morbidity**

The term ‘co-morbidity’, coined by Feinstein, is now widely used to refer to the greater than coincidental association of two conditions in the same individual (3). The concept of “developmental comorbidity” looks at the possible influence of age and development on the occurrence of comorbidity in psychiatric conditions such as ADHD and autism, to outline distinct trajectories of symptom progression with possible impact on course and outcome. The occurrence of co-morbid symptoms, for example ASD symptoms, could temporally (i) arise before the appearance of first definite ADHD symptoms (“pre-comorbidity”); (ii) coincide with ADHD symptoms when they reach a clinical significance (“simultaneous comorbidity”); (iii) or rarely appear or be identified after the onset of ADHD (“post-comorbidity”) (4).

**Co-morbidity between HKD/ADHD and PDD/ASD**

The diagnostic nomenclatures do not allow for the concurrent diagnosis of autism and HKD/ADHD. Both ICD and DSM classification systems assume a hierarchical standpoint when dealing with PDD/ASD and HKD/ADHD: the diagnosis of PDD/ASD automatically trumps the diagnosis of HKD/ADHD. The Diagnostic and Statistical Manual of Mental Disorders, 4th- text revision (DSM-IV-TR) (5) does not allow ADHD to be diagnosed if the ADHD symptoms occur only during the course of a Pervasive Developmental Disorder (American Psychiatric Association, 1994). A similar approach is taken by the International Classification of Diseases – 10th Revision (ICD-10) (World Health Organisation, 1992) (6), with the diagnosis of Hyperkinetic Disorders not being allowed if symptoms occur in the context of a PDD (synonymous to ASD). This reluctance to make co-morbid diagnosis of ASD and HKD/ADHD has treatment implications because ASD subjects with HKD/ADHD symptoms may not be identified or diagnosed, resulting in delayed treatment or even denial of treatment for the HKD/ADHD (2). This hierarchical diagnostic framework for ADHD and ASD is very likely to be removed from DSM-5 and ICD-11.

**Clinic-based Studies of ADHD and ASD**

Historically, Clark and colleagues estimated the rate of autism features within a sample of 49 DSM-IV ADHD children, using a retrospective, case-note-based extraction of symptoms as reported on the Autism Criteria Checklist (a 12-item parent-rated questionnaire): 65-85% of these children were reported as having significant difficulties in social interaction (particularly in empathy and peer relationships), and communication (particularly in imaginative ability, nonverbal communication and maintaining conversation) (7). Another review of 309 child & adolescent patients with ICD-10 Hyperkinetic Disorder (HKD) found that 40% of the HKD group had “social reciprocity problems,” 24% had “speech and language difficulties” and 9% had “repetitive behavior” (8). Interestingly, substance use and alcohol use was only present in ASD adolescents if they had concurrent ADHD (9).

When ASD children were evaluated for ADHD, between 30 and 70% met symptom criteria for ADHD (10,11,12).

**Population-based Studies of ADHD and ASD**

Due to the obvious referral biases, the clinical samples described above will show increased psychiatric comorbidity, and hence it is important to investigate the association between ADHD and ASD in population-based samples. Reiersen and colleagues showed that children with ADHD selected from a general twin population have elevated levels of autism traits. DSM-IV combined subtype and the
population-derived severe combined subtype had the highest mean scores for each of the three autism symptom domains, with a substantial proportion of individuals scoring in the clinically significant range (13).

The Twins Early Development Study (TEDS), a study on a community sample born in England and Wales has also reported on the association between ADHD and ASD. They found significant correlations between autism and ADHD traits in the general population (0.54 for parent data, 0.51 for teacher data). They concluded that there are some common genetic influences operating across autism traits and ADHD behaviours throughout normal variation and at the extreme, and that it is relevant for molecular genetic research, as well as for psychiatrists and psychologists, who may have assumed these two sets of behaviours are independent (14).

Motor problems and high levels of autism traits are common in individuals with combined-type ADHD. Individuals with the combination of motor problems and ADHD were more likely to have high levels of autism traits than those with ADHD alone (15).

Another population-based study confirmed the association between autism and ADHD symptoms in a young adult twin sample assessed by self-report, and showed that in young adults, a substantial proportion of the genetic influences on self-reported autism and ADHD symptoms may be shared between the two disorders (16).

Biopsychosocial Risk Factors in ADHD and ASD

Genetic factors

Some studies in the early 1990s did suggest a strong familial overlap of the conditions (17,18). There is, perhaps unexpectedly, rather more to suggest a biological link between the two diagnosed conditions at the molecular genetic level. It has been suggested that the serotonin transporter gene is down-regulated in both ADHD and ASDs (19). Genome scan studies of autism have suggested certain chromosomal regions of interest for autism susceptibility genes, and genome scan studies of ADHD have demonstrated that some of these regions, e.g. on chromosomes 2q, 15q, and 16p, are also susceptibility sites for ADHD (20, 21).

Neuroanatomy and neurophysiology

At the brain biological level, the evidence linking the two conditions is highly contradictory. On the one hand there are many studies suggesting brainstem, cerebellar, basal ganglia, and frontal dysfunction in both conditions, even though it is not clear that the types of dysfunction are shared across them. On the other hand, some studies do suggest markedly different brain pathologies in the two disorders. For instance, in systematic studies, autism is quite often associated with macrocephaly (in about 20% of the cases) (22), whereas ADHD is often reported to be linked to smaller overall brain size (23).

Neuropsychological Findings in ADHD and ASD

To date, there are few studies that have compared executive functions (EF) in ASD and ADHD. Ozonoff and Jensen (24) compared children with ADHD, ASD or Tourette syndrome, as well as controls with typical development (TD) and reported that the ASD group showed more perseveration and poorer planning than any other group, while the ADHD group was poorer than TD controls on tasks of inhibition (25).

Geurts et al. conducted a study attempting to map distinct profiles of EF in ASD and ADHD. They compared 6-12 year olds (mean age 9) with ADHD, high-functioning autism, or TD (whose IQ was higher than the clinical groups) on a large battery of EF tasks. The ASD group showed deficits on all
EF tasks except interference control and working memory, and greater impairments than the ADHD group on planning and cognitive flexibility. The ADHD group, by contrast, was most impaired on inhibition of pre-potent response and verbal fluency. The authors conclude that EF problems are more severe in ASD, although poor performance in this group on non-EF control tasks was also noted (26). Another study concluded that spatial working memory is impaired in both ADHD and High Functioning Autism (HFA), and more severely in ASD. No differences were found between ADHD and ASD children on response inhibition, planning and flexibility tasks (27).

When the age and IQ matched groups with ASD, ADHD, or typically developing children were compared on tasks tapping planning, working memory and response inhibition, both clinical groups showed significant EF impairments compared with the typically developing group. At older (but not younger) ages, the ASD group outperformed the ADHD group, performing as well as the typically developing group on many EF measures. EF scores were related to specific aspects of communicative and social adaptation, and negatively correlated with hyperactivity in ASD and typically developing children. The overall findings suggested less severe and persistent EF deficits in ASD than in ADHD (28).

Learning, attention, graphomotor, and processing speed scores were analyzed in 149 typical control children and 886 clinical children with normal intelligence. Control children performed better than children with ADHD and autism in all areas. Children with ADHD and autism did not differ, except that children with ADHD had greater learning problems. Attention, graphomotor, and speed weaknesses were likely to coexist; the majority of children with autism and ADHD had weaknesses in all three areas and these scores contributed significantly to the prediction of academic achievement (29).

A community-representative sample of Swedish children with late developing language at 2.5 years of age had persisting difficulties with oral narrative skills at age 7-8 years (30). Compared to Normal Control (NC), children with HFA and with ADHD showed generalised pragmatic deficits and impairments in pragmatic language use, which did not vary with age (26).

In contrast to the well-established literature on the behavioural and cognitive deficits of children with ADHD, much less is known about the social deficits of this population. Wheeler et al. suggested that the social deficits of the ADHD subtypes could be best explained as social skills deficit, social performance deficit, self-control skill deficits and self-control performance deficit (31). Another concept considering social skills deficiencies of children with ADHD is that self-regulation of affect, motivation and arousal represents an important area of impairment in ADHD, beneath working memory, utilization of speech and reconstitution (32). Moreover, it has been reported that some socially inappropriate behaviours (eg. blurt out answers to questions, interrupting or intruding on the conversations of others, handling frustration in an impulsive, aggressive manner, etc.) seem directly related to the core features of ADHD (33). On the other hand, other social deficits in ADHD children, such as failing to comprehend the impact of one’s actions on others, misinterpreting social information and possessing a limited repertoire of social responses, may be closer to the autism type of social difficulties. This is rarely discussed in the literature and it may be an important link to autism (34). The same hypothesis might be a plausible explanation for the research revealing that children with ADHD have difficulties in responding appropriately to the continuous changes in demands and cues that characterizes the flow of social interaction (35; 36).

**Reasons why Symptoms Overlap**

Over the past few years, in our Developmental Neuropsychiatry Clinic, we have seen a significant number of children with high functioning autism being referred who have been previously diagnosed as having only ADHD. Various reasons for the hyperactivity can be put forward. The inability of the child to switch attention from one task (overcircumscribed interest) to another may lead the child to return constantly to the original task, thus preventing sustained attention in other tasks. Apart from this, stimulant treatment in itself may lead to increased perseveration and over-focused attention, leading to inability to pay attention to routine tasks. Motor mannerisms can be mistaken for hyperactivity. Poor social skills and reciprocity can lead to inappropriate questioning and comments,
which are impulsive. Cognitive rigidity and language and communication impairment lead to oppositional and challenging behaviours.

**Treatment of ADHD co-morbid with ASD**

Methylphenidate has been considered the first-line treatment for children with ADHD without significant co-morbidity (other than co-morbid conduct disorder). A recent large open-label study found no statistically significant difference between children with ASD plus ADHD symptoms and children with ADHD alone, in the degree of improvements or rate of adverse effects (37). The most frequently reported adverse effect was decrease in appetite. The randomised, controlled, crossover trial of methylphenidate in ASD with hyperactivity showed that about half of these children responded to methylphenidate, although this treatment was less effective than that seen in typically developing children with ADHD. Moreover, methylphenidate was frequently associated with adverse effects leading to discontinuation (38). Similar results were found in the randomised, placebo-controlled, crossover study of methylphenidate for ADHD symptoms in pre-school children with developmental disorders, including ASD and intellectual disability (39).

Amphetamines have been used but recent studies in ASD are lacking. Two studies conducted in the early seventies did not show any significant improvement. In a placebo-controlled crossover study of 16 children (40), dextroamphetamine yielded no significant improvement. Another study, with levoamphetamine, a double-blind crossover trial of 12 children, showed only minimal positive effect (41).

Atomoxetine has been used to treat inattention and hyperactivity in ASD, with three open-label studies suggesting that it may be effective in children and adolescents with ASD for symptomatic treatment of hyperactivity, impulsivity and oppositionality (42, 43, 44). If methylphenidate has been ineffective, atomoxetine can be considered as another option. A placebo-controlled crossover pilot trial showed that atomoxetine appeared to be safe and effective for treating hyperactivity and the effect appeared as large as in a multisite methylphenidate trial in the same population, with fewer intolerable adverse effects (45). Other authors studied the efficacy and tolerability of atomoxetine in high-functioning boys with ASD and comorbid ADHD, showing significant reductions in ADHD symptoms rated by parents and by teachers, with half of the participants classified as clinical responders. In addition, most children tolerated the drug well (46).

**Risperidone**

Risperidone is licensed for use in autism to manage marked irritability and challenging behaviour. The Research Units of Paediatric Psychopharmacology (RUPP), Autism Network, conducted a double-blind placebo-controlled study in children and adolescents with autism and reported improvements in tantrums, aggression or self-injurious behaviour in children, and also of hyperactivity (47). Improvement in irritability and hyperactivity has been replicated in another Canadian multi-centre trial (48).

**Aripiprazole**

Aripiprazole is an atypical antipsychotic and is a 5-HT1a agonist, partial dopamine D2 agonist and serotonin 5-HT2A antagonist. Two recent double-blind randomised, placebo-controlled studies concluded that aripiprazole was effective in children and adolescents with irritability associated with autism disorder and was generally safe and well tolerated (49, 50). Hyperactivity was reported to have improved in both studies (49, 50). Monitoring to rule out hyperprolactinaemia and emergence of metabolic syndrome is important when using atypical antipsychotics.

**Clonidine**

Clonidine is an alpha-2-adrenergic agonist that is useful in ASD with ADHD/Tourette syndrome.
Two double-blind, placebo-controlled crossover trials in the early nineties reported some benefits with clonidine in treating overactivity in children with autism, although the sample size was small. Fankhauser reported that patients on transdermal clonidine experienced fewer sensory responses, less affectual reactions and improvement in social relationships (51). Another study reported a decrease in irritability, stereotypy, hyperactivity, inappropriate speech and oppositional behaviour during patient treatment (52). Both studies reported sedation and fatigue as major adverse effects, along with decreased activity (53). Clonidine was effective in reducing sleep initiation latency and night awakening, and to a lesser degree in improving attention deficit and hyperactivity, mood instability and aggressiveness (54).

Guanfacine is another alpha-2-adrenergic agonist that has been shown to reduce hyperactivity in ASD. A retrospective case-note analysis of 80 patients with ASD on guanfacine showed that most patients tolerated it well (55). In a more recent eight-week prospective open trial of guanfacine in children with ASD, a significant decrease in hyperactivity was reported (56). Sedation, constipation, headache, increased irritability, aggressiveness, sleep disruption and decreased appetite are adverse effects reported in studies (55,56).

Conclusion

It is timely and important to examine the diagnostic approaches critically with regard to ADHD and ASD, with the goal of translating research evidence into treatments. Although it is unclear whether there are shared underlying causes producing both ADHD and ASD symptoms, it is clinically clear that a combination of these symptom domains can cause severe impairment, deserving special attention. Diagnosing ADHD in ASD is important as the ADHD can be pharmacologically treated and non-pharmacological interventions may need appropriate modifications. Parents, carers, and professionals need appropriate psychoeducation about developmental comorbidity to achieve optimal outcomes.

GP comment.

What have I learned from this paper?

1. The previous idea that ADHD could not be diagnosed in the presence of autism was misleading.

2. Children with both autism and ADHD can benefit from treatment of the ADHD with the usual medications, including methylphenidate, dexamphetamine, atomoxetine, risperidone and aripiprazole.

3. There is debate about why the two conditions overlap but there is some evidence for a common genetic susceptibility.

4. As a GP, this paper has made me more aware of the possibility of ADHD in a child with autism. As a result, I shall have a low threshold for referring children with autism spectrum disorder for specialist assessment and treatment of the ADHD.

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References


ADHD and Epilepsy

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Abstract

ADHD symptoms occur in about 30% of children with epilepsy. The causes include “classical ADHD”, other forms of brain dysfunction, some antiepileptic drugs and the epilepsy itself. Management of the ADHD will depend on the cause. Standard ADHD treatment, such as methylphenidate, dexamfetamine and atomoxetine, is effective in about 70% of cases and is very unlikely to exacerbate seizures.

Introduction

ADHD is one of the more common comorbidities in children with epilepsy. It is typically reported in about 30% of children with epilepsy compared to 3-6% of controls (1;2). Approximately 70,000 school-age children in the UK have epilepsy and about 20,000 of these will have both epilepsy and ADHD. However, probably only a fraction of these children are treated for the ADHD. Reluctance to treat may be related to diagnostic issues but is more likely to be related to concerns about possible seizure exacerbation.

Epidemiology

Hermann et al. (1) studied 75 children aged 8–18 years with new or recent onset idiopathic epilepsy and compared them with 62 controls. ADHD was found in 31% of the children with epilepsy and 6% of the controls. Hesdorffer et al. (3) carried out a population-based study in Icelandic children under 16 years of age. They found that ADHD was 2.5 times more common in children with recent-onset epilepsy than in the controls. Dunn et al. (4) reported results on 175 children (90 M, 85 F) who had a history of epilepsy of at least six months duration. Of the 175 children, a total of 66 (38%) had ADHD of one type or another. There was an equal male to female ratio in the children with epilepsy and ADHD. Sherman et al. (5) reported on a population of children with more severe epilepsy in a tertiary centre. Of 203 children, over 60% met screening criteria for ADHD.

Gonzalez-Heydrich et al. (6) found that 61% of 36 children with both epilepsy and ADHD, aged 6 to 17 years, had a comorbid disorder: 36% had anxiety disorders and 31% had oppositional defiant disorder.

Possible causes of overactivity in children with epilepsy

There are many possible causes of the features of attention deficit hyperactivity disorder in children with epilepsy, including the following.

1. “Classical” ADHD.
2. Other psychiatric disorders.
3. Associated/underlying brain damage or dysfunction.
4. Causes related specifically to the epilepsy including: frequent epileptiform discharges: Rolandic discharges, frontal discharges or generalised spike-wave discharges.
   Post-ictal elevated mood.
   Inter-ictal manic psychosis.
5. Adverse effects of medication.
Other psychiatric disorders, not necessarily related to the epilepsy, may present with features of ADHD but careful assessment should distinguish them as being different. These disorders include conduct disorder, generalised anxiety disorder and elevated mood states such as hypomania or mania.

Associated underlying brain damage or dysfunction may include global developmental delay and specific frontal lobe damage or dysfunction. It is interesting to note that, although these children may not present with the classical history of ADHD, they may nevertheless, in at least some cases, respond to the standard medication prescribed for this condition.

Causes related specifically to the epilepsy

Frequent epileptiform discharges

Holtman et al. (7) examined the frequency of Rolandic spikes in the EEGs of 483 ADHD children, aged 2 to 16 years. These were compared to 3726 normal school-age children. Rolandic spikes were found in 27 (5.6%) of the ADHD children. The Rolandic spike frequency in children with ADHD was said to have been significantly higher than expected. ADHD in the children with Rolandic spikes presented earlier; these children had more hyperactive-impulsive symptoms. In a further study, the same group (8) studied 48 children 6.7 to 14.9 years, of whom 16 had ADHD and Rolandic spikes, 16 had ADHD without epileptiform discharges and 16 were healthy controls. Rolandic spikes were associated with increased impulsivity, deficient inhibition and decreased interference control.

Sinzig and Gontard (9) analysed EEGs of 8132 children and adolescents retrospectively. A new diagnosis of absence seizures was made in only 12 of these (0.44%) in the first centre and none in the second. They concluded that there was a minimal occurrence of absences in child and adolescent patients and that this was therefore not the main differential diagnosis that has to be considered in children with ADHD. However, they added that it was important to regard absence seizures as a rare differential diagnosis. From the current author’s own experience, in specialist centres, children certainly present with ADHD symptoms because of very frequent absence seizures or epileptiform discharges.

Elevated mood states

Children and teenagers who present with post-ictal elevated mood or inter-ictal manic psychosis certainly have some features of ADHD. However, the history should distinguish clearly between the two conditions, in most cases. For example, in the case of post-ictal elevated mood changes, the history of recent seizures, typically a cluster, is characteristic and usually diagnostic. Above all, for both post-ictal and inter-ictal elevated moods the nature of the condition is intermittent, in contrast to the persistence of the ADHD symptoms, although inter-ictal elevated mood states may persist for long periods, for example several weeks.

Antiepileptic drugs

Antiepileptic drugs that can cause symptoms of ADHD in children include the benzodiazepines, phenobarbitone and vigabatrin. It is also important to consider adverse drug interactions. For example, if lamotrigine is added to carbamazepine in someone who is unable to express their experiences verbally and the patient develops diplopia and/or dizziness, they may present with distressed and overactive symptomatology. Treatment of these symptoms with ADHD medication would be inappropriate; this situation can readily be resolved by decreasing the carbamazepine dose. The history should distinguish this situation clearly.

Should children with both epilepsy and ADHD be treated for the ADHD?

In the past there has been considerable reluctance about treating ADHD in the presence of epilepsy because of concern of possible seizure exacerbations. Are these fears justified by the evidence? What
are the ADHD treatments of choice in children with both conditions?

The first step in the management of the child with epilepsy and ADHD must be to consider the possible causes already described. The management might need to be very different, depending on the cause. For example, if frequent absence seizures are causing the ADHD symptoms, additional or different antiepileptic medication may be appropriate. In contrast, if the child is overactive because of the adverse effects of antiepileptic medication such as the benzodiazepines, medication reductions or a change in antiepileptic medication rather than increasing antiepileptic medication will be appropriate.

The first-line treatment for children with ADHD, regardless of whether they have epilepsy or not, remains methylphenidate. The second-line treatment is atomoxetine. Third-line treatments include dexamfetamine, clonidine and, particularly in children with learning disability and autism spectrum disorder in addition to the epilepsy, low-dose risperidone; the risperidone might act through decreasing agitation/anxiety rather than treating core ADHD symptoms. Neither clonidine nor risperidone is licensed for treating ADHD in children but both may be of benefit. How safe are these drugs for treating ADHD in children with epilepsy? What is the risk of seizure exacerbation? Formularies such as the British National Formulary recommend "caution" when prescribing methylphenidate and dexamfetamine, suggesting that these drugs may exacerbate seizures. What does the published evidence reveal with regard to possible seizure exacerbations?

Gross-Tsur et al. (10) reported a study on 30 children with ADHD and epilepsy, aged 6.4 to 16.4 years. For the first two months they were treated with antiepileptic medication only. Methylphenidate was added in the next two months. None of the 25 children who had been seizure free had attacks with methylphenidate. Of five children with active seizures, three had an increase in seizures and the other two had no change or a reduction in seizures. There were no statistically significant changes in seizure control. If children with active epilepsy are treated with any additional medication, or indeed with no additional medication, the expected outcome would be that some might have fewer seizures, an approximately equal number would have more frequent seizures and some would have no change in seizure frequency. This is exactly the outcome that was reported in the study by Gross-Tsur et al. It would appear that no conclusions can be drawn from the study or, perhaps more accurately, it could be concluded that methylphenidate has no major effect on seizure control. The same authors also reported that there were no significant EEG changes with the methylphenidate and that, in terms of the ADHD symptoms, 70% derived benefit. They concluded that methylphenidate was effective in treating children with epilepsy and ADHD, and added that it was safe in children who were seizure free. They commented that “caution is warranted for those who are still having seizures while receiving AED therapy”; although it would appear that they had no evidence whatsoever from the results of their own study to support this statement.

Hemmer et al. (11) presented results on 234 children with complicated ADHD of whom 36 (15.4%) had epileptiform abnormalities. 40% of the abnormal EEGs had Rolandic spikes. 60% of the abnormal EEGs had other focal abnormalities. 205 of the 234 (87.6%) were treated with stimulant medication. Seizures occurred only in the treated group; 1/175 patients with a normal EEG had seizures and 3/30 with epileptiform discharges i.e. 10% (95% confidence interval 0%, 20.7%). Seizures occurred in two of the 12 children (16.7%) with Rolandic spikes. It is very difficult to draw any conclusions from these results other than that children with epileptiform abnormalities on the EEG are more likely to have seizures than those who do not, regardless of what treatment is given. The authors stated the following conclusions. “These data suggest that a normal EEG can be used to assign children with ADHD to a category of minimal risk of seizure. In contrast, an epileptiform EEG in neurologically normal children with ADHD predicts considerable risk for the eventual occurrence of seizure. The risk, however, is not necessarily attributable to stimulant use.”

Gucuyener et al. (12) compared 57 patients with ADHD and active seizures and 62 patients with ADHD and EEG abnormalities before and after treatment with methylphenidate. They found that seizure frequency did not change from baseline. The EEG appeared to improve, leading them to state that methylphenidate had a beneficial effect on the EEG. They concluded that methylphenidate is safe and
effective in children with ADHD and concomitant active seizures or EEG abnormalities.

There have been several reviews on ADHD and epilepsy, (Parisi et al. (13), Hamoda et al. (14), Torres et al. (15), Baptista-Neto et al. (16) and Dunn and Kronenberger (17)), all of which have drawn broadly the same conclusions, namely that there is no evidence that methylphenidate causes seizure exacerbations when used to treat ADHD in people with epilepsy.

Both evidence and opinion suggest that previous concerns about methylphenidate causing seizure exacerbations in children with epilepsy and ADHD were probably not justified. Dexamfetamine has been considered to be even less likely to worsen seizure control and it has even been suggested that it might improve seizure control.

**Safety of other drug treatments for ADHD**

Wernicke et al. (18) reviewed two independent Eli Lilly databases: the Atomoxetine clinical trial base and the Atomoxetine post-marketing spontaneous adverse event database. The crude incidence rates of seizure adverse events were between 0.1 and 0.2%; there was no significant difference between atomoxetine and placebo. These authors concluded that, although children with ADHD are increasingly recognised as being at an elevated risk of seizures, treatment of the ADHD with atomoxetine does not appear to elevate this risk further.

Gonzalez-Heydrich et al. (19) studied the seizure risk in 21 young people with epilepsy and psychiatric disorders, mean age 12 years, who were treated with risperidone 2.4 ± 3.5 mg/day. They reported that the psychiatric symptoms improved in 71% and the seizures were no worse in any patient. It should be noted, however, that there have been anecdotal reports of seizure exacerbations with higher doses of risperidone.

**Conclusions**

1. ADHD is under-diagnosed and under-treated in children with epilepsy.

2. There is a broad differential diagnosis for the causes of ADHD symptoms in children with epilepsy, including some antiepileptic drugs and the epilepsy itself. The management of ADHD in the child with epilepsy will depend on the cause.

3. Approximately 70% of children with ADHD and epilepsy will benefit from standard treatment such as methylphenidate and there appears to be no firm evidence that the usual treatments are likely to exacerbate seizures.

**GP Comment**

**What have I learned from this paper?**

1. As a GP, I am very cautious about prescribing medication to children and adults with epilepsy, in case it might cause seizure exacerbations. However, it appears that there is no evidence to confirm that methylphenidate exacerbates seizures.

2. ADHD is a risk factor for seizures. Children with ADHD often have abnormal EEGs. If seizures occur, it might be the result of a pre-existing tendency but is unlikely to be the result of medication prescribed to treat the ADHD.

3. ADHD is common in children with epilepsy and there are many causes but it can often be treated successfully.

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Reference List


ADHD and Substance Misuse in Young people: From cutting edge research to the coal face reality of clinical practice

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Abstract

Children with ADHD are at high risk of developing substance misuse in adolescence and adulthood. The abuse potential of stimulant medication and the impact of medication treatment on long-term risk of substance misuse are areas of ongoing controversy. Existing literature indicates that treatment of ADHD with medication does not increase the risk of development of substance misuse in the treated individual. Stimulant medications can, however, be diverted or misused, either for subjective euphoric effects or for effects on performance. Integrated treatment of both substance misuse and ADHD should be provided. Strategies to minimize the risk for misuse or diversion of medications include use of extended-release formulations of currently used stimulant medications, new non-stimulant medications and novel pro-drugs. This article provides a brief overview of the extant literature and offers practical guidelines for the management of young people with ADHD and co-morbid substance misuse.

Keywords: substance misuse, substance dependence, substance abuse, co-morbidity, children, young people, abuse potential.

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Declaration of interests

K.A.H Mirza has served on the advisory boards of Janssen, Eli Lily and Shire pharmaceuticals and has received research and educational grants from Glaxo Smith Kline, and Shire pharmaceuticals. He has received honoraria for speaking at conferences organized by Janssen, Eli Lilly and Shire pharmaceuticals.

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Introduction

Attention deficit hyperactivity disorder (ADHD) is a common, heterogeneous neuropsychiatric condition with significant levels of morbidity. ADHD can persist into adolescence and adulthood. Children with ADHD are at higher risk of developing substance misuse in adolescence and adulthood; the risk is higher if there is co-morbid conduct disorder and/or social adversity. Pharmacological treatment is a central component of intervention in children with ADHD and there is a robust body of evidence to attest the efficacy and safety of medications, at least in the short term (1). The global rise in ADHD diagnosis in children and the increasing rates of stimulant prescription over the previous two decades have led to a vigorous, often polemic, debate as to whether pharmacotherapy may in fact increase the risk of development of substance misuse. Critics of drug treatment point out that methylphenidate and other stimulants have strikingly a similar pharmacological profile to cocaine and...
pharmacotherapy may increase the risk of development of substance misuse in young people (2,3). There have been reports of intranasal and intravenous abuse of methylphenidate and non-prescribed use of stimulants by university students in the USA (4) and diversion of methylphenidate into the illegal drug market in the UK (5,6). The aim of this review is to explore the complex relationship between ADHD and substance misuse and to provide clinical guidelines for treating children and young people.

**Relationship between ADHD and substance misuse: causal pathways and Mechanisms**

There are a number of complex pathways and mechanisms to describe the relationship between ADHD and substance misuse. Among drugs of abuse, specific risk from ADHD is most significantly associated with tobacco misuse. The risk of developing nicotine dependence may be mediated by self-medication, as nicotine appears to alleviate the symptoms of ADHD (7). Co-morbid conduct disorder was thought to be responsible for most of the risk with all other classes of drugs. More recent studies suggest that both ADHD and conduct disorder contribute to the risk of developing all drug and alcohol misuse, but conduct disorder poses the most significant risk (8).

**Does stimulant medication lead to substance misuse?**

We aim to address this controversy by exploring the evidence from animal, clinical and pharmacological studies. A comprehensive review of animal studies concluded that there is insufficient evidence at present to suggest that exposure to stimulants would lead to long-term risk of addiction (9). It is difficult to extrapolate findings from animal studies to human beings for a variety of reasons.

Drugs of abuse such as cocaine and stimulants act by increasing dopamine in the mesolimbic and mesocortical dopamine pathways (10). However, seminal studies by Nora Volkow and colleagues from the National Institute of Drug Abuse have shown that the route of administration and dosages of stimulants are the most important variables, determining the abuse potential (11). Thus methylphenidate, when taken orally in therapeutic doses and within a clinical context, appears to be associated with a much lower abuse potential than cocaine.

A meta-analysis of the prospective and retrospective clinical studies conducted before 2003 reported that those treated with stimulant medication were protected against the development of substance-related problems by a factor of two (Odds Ratio 1.9) (12). Three prospective studies since 2003 concurred with the above (13,14,15). Furthermore, 36 month follow-up of the Multimodal Treatment Trial (MTA) has suggested that medication does not contribute significantly to the risk for substance misuse in adolescence and behaviour therapy is associated with reduction of risk (16).

**Diversion of stimulants: “to get a high” or to enhance academic performance**

Stimulant medications are controlled drugs and have the potential for misuse and diversion, either for subjective effects or for effects on performance. Methylphenidate can be misused intranasally by crushing the tablets and snorting the powder or intravenously by dissolving the powder in water for injection. More commonly, oral stimulants can be misused to enhance performance in sports or some kinds of cognitive tasks and examinations (17,18,4). Diversion of stimulants into the illegal drug market is rife in North America and there is early indication that the above phenomenon is not entirely uncommon in the UK (5,6).

**Summary and clinical implications**

Children with ADHD are at high risk of developing substance misuse. Consequently, prevention of substance misuse should be a target for ADHD services. At least a substantial amount of the risk is mediated by conduct problems (or the social adversity leading to them). Reduction of conduct
problems could be helpful in reducing the risk of substance misuse and hence psychological and social measures should be included in the long-term treatment of ADHD. As stimulant medication does not appear to increase the risk of substance misuse, it is not contraindicated for that reason. It is, however, important to note that stimulants do have the potential to be misused, especially by people without ADHD.

Guidelines for assessment and practical management

Young people presenting with substance misuse and ADHD pose significant challenges for assessment and treatment. Defining substance misuse in young people is not easy and developmentally sensitive classificatory systems are useful in everyday clinical practice (19). Pointers such as drug-misusing relatives, being in a drug-misusing peer group, the combination of absence of effect with ongoing requests for prescriptions and frequent mysterious “loss” of prescriptions, should alert clinicians to the risk of diversion and misuse of prescribed medication.

Treatment

a. General principles

Integrated, multimodal treatment of both substance misuse and ADHD has been found to be useful in clinical practice (20) and specific treatment for ADHD and substance misuse should, ideally, be provided under the same roof. Substance misuse, especially if it is chaotic, is often the first issue to be addressed before initiating ADHD treatment. Although abstinence is ideal prior to initiating medication treatment for ADHD, achieving complete or sustained abstinence may not be a realistic expectation.

b. Specific treatment of ADHD: evidence base for medications

There is some empirical data to guide treatment. Although debate about the role of medication to treat ADHD continues, it appears that stimulant medication is indeed helpful, although it has been argued that it might add little or nothing to a well-delivered program of CBT (21). Medication does, however, appear to be safe and does not worsen substance misuse.

Pharmacological strategies to reduce the abuse potential of medications

Long-acting or controlled-release formulations are less likely to be misused than short-acting agents (23). The lower risk for misuse of extended-release formulations of methylphenidate may also be related to the fact that active components cannot be rapidly extracted from the beaded or osmotic extended-release preparations of these stimulants (18). Atomoxetine, a selective norepinephrine reuptake inhibitor, has been reported to have little abuse potential, as evidenced by animal studies and small-scale studies in human volunteers (24). Other pharmacological strategies to reduce intranasal or intravenous abuse include use of a methylphenidate transdermal patch, (25) or a prodrug such as Lis-dexamfetamine Dimesylate (LDX). In its intact form, LDX is pharmacologically inactive. When taken orally, LDX is converted in the red blood cells by rate-limited enzymatic hydrolysis to L-lysine, a naturally occurring essential amino acid, and d-amphetamine. Neither of these is available in the United Kingdom yet.

In summary, the choice of a medication is dependent on the personal and family history of substance misuse, in particular the potential risk of misuse and diversion. In young people with non-chaotic substance abuse/dependence, and in the absence of significant family history of substance misuse, long-acting preparations of stimulant medication may be the preferred option, in view of its superior efficacy. However, if there is personal or family history of stimulant misuse and the substance misuse is chaotic, atomoxetine or other non-stimulants should be considered as the drugs of choice.
Conclusions

Substance misuse in adolescence is a major public health problem with substantial levels of morbidity and mortality. ADHD is a significant risk factor for the development of substance misuse through a number of complex causal pathways. Medication for children with ADHD is unlikely to increase the long-term risk of substance misuse. Given the consistent findings of misuse of stimulants (either illicit use or for enhancing performance), General Practitioners, CAMHS clinicians, youth offending officers, substance misuse workers, teachers and other professionals should be made aware of the scope of the problem. Extended-release stimulants, non-stimulants or pro-drugs may be less likely to be misused or diverted. Identification and optimal treatment of ADHD in children and adolescents may, hopefully, result in lower rates of substance misuse and diversion of stimulants but research will be needed to establish whether interventions are effective.

GP Comment

What have I learned from this paper?

1. As a group, people with ADHD are more at risk for substance misuse than the general population.

2. Treatment of ADHD should include psychological and social measures to prevent development of conduct disorder and substance misuse.

3. Despite previous concerns, treating ADHD almost certainly does not increase the risk for substance misuse.

4. Careful consideration needs to be given to the management of the ADHD patient with risk factors for substance misuse, such as a personal or family history of substance misuse.

5. Illicit diversion of medication used to treat ADHD can be minimised by using controlled-release/extended-release stimulants or by using non-stimulant drugs such as atomoxetine.

6. As a GP who used to run an ADHD clinic and who now offers a substance misuse clinic I was certainly interested by this paper. I was previously unaware of the link between ADHD and smoking but will undoubtedly share this information with patients in the future. I had prior understanding that pharmacological treatment of ADHD reduces risk of subsequent substance misuse and it was interesting to note that the risk actually relates more to the associated condition of conduct disorder. As a GP this paper will be useful for providing knowledge based reassurance to parents that stimulant medications are an appropriate therapy and counter-intuitively do protect them from the risk of substance misuse. It seems that perhaps GPs could be alert to the more conduct disordered children amongst those who suffer ADHD and seek to ensure that these children do not simply receive a repeat prescription for methylphenidate but are enrolled onto therapeutic programmes. Diversion is an important consideration and I would need to have greater understanding of the different extended release preparations as it seems that some exist that would resist the option of simply being crushed to allow misuse. It is disappointing that the more novel preparations are not yet available in the UK. Finally there should perhaps be more onus on those of us running substance misuse clinics to have a lower threshold for suspecting ADHD amongst our adult clients but this would then have implications for the commissioning of services which I understand are currently very limited.

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References


The Challenge of ADHD and Youth Offending

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Abstract

Research suggests that ADHD youths are vulnerable to committing crimes and that there is a disproportionately high proportion of individuals with ADHD involved with the criminal justice system. UK studies of offenders have indicated around 45% of youths and 24% of male adults screen positive for a childhood history of ADHD, 14% of whom have persisting symptoms in adulthood. Young people with persisting ADHD symptoms begin offending at a significantly younger age and more commonly re-offend. They find it difficult to control their behaviour in institutions and are therefore less likely to be eligible for early release. Although there are international guidelines available for the treatment of ADHD in young people and adults, these do not take into account the more complex and comprehensive interventions serious offenders with ADHD require, such as psychological interventions containing a prosocial competence component. Diagnosis and ongoing intervention should be offered to young people with ADHD who are excluded from school and/or come into contact with the criminal justice system, to try to reduce the risk of offending.

Keywords: ADHD, youth offending, recidivism, intervention, crime, prison.

The relationship between ADHD and offending

Growing evidence is confirming an association between ADHD and offending. Studies published in the 1980s and 1990s reported that ADHD youths were more likely to be arrested, to receive convictions (1-5) and to begin criminal activity at a younger age (6-8). When comprehensive clinical assessments using DSM-IV criteria are conducted in prison settings, rates of inmates with persistent ADHD symptoms are around 45% for youth offenders (6,7,9) falling to 30% for male adults (8) and 10% for female adults (10). It is likely that reported rates overestimate the real picture, with a high number of false positives being obtained from self-rated checklists for childhood/adulthood symptoms. Nevertheless the rates are undoubtedly considerably higher than community prevalence rates in children of 5% (11) and adults 2.5% (12).

The most comprehensive study to date of the characteristics of male offenders with ADHD was carried out in Aberdeen Prison, Scotland (13-15). This study identified that the group with current ADHD symptoms were significantly younger than the non-ADHD group at the time of first conviction, had more total previous convictions (particularly for property and violent offences) and were more likely to re-offend. Drug and alcohol misuse featured strongly in the sample.

The authors investigated the relationship between childhood ADHD, symptom persistence into adulthood and drug and alcohol use, with the motivation for offending. Offences were categorized into total offences, violent offences, drug offences, property offences and ‘other’ offences (e.g. breach of bail, criminal damage, arson and sexual offending). When predictors of offending for each category were analysed, the most powerful predictor of total offending was regular heroin use, followed by childhood ADHD. The most striking finding was that the most powerful predictor of violent offending was childhood ADHD, followed by alcohol dependence. Drug offences were predicted by crack...
cocaine use, and ‘other’ offences by heroin use. There were no significant predictors of property offending. A similar pattern of results was found in the model when replacing a childhood history of ADHD with persistent symptoms.

Within the institution, the ADHD prisoners were involved in eight times more aggressive incidents than other prisoners, and six times more incidents when controlling for antisocial personality disorder. An evaluation of the highest frequency (10%) of critical incidents showed a clear relationship between participation in critical incidents and persistence of ADHD symptoms. Thus ADHD inmates are likely to be seen as challenging individuals who are difficult and expensive to manage. Behavioural disturbance within prisons, especially staff assaults and prisoner-on-prisoner assaults, are of major concern and many such aggressive incidents lead to formal adjudications which, in turn, reduce the possibility of early release.

Why are young people with ADHD vulnerable to involvement with the criminal justice system?

1. Engagement in antisocial activities.

Young people with ADHD tend to commit offences that are reactive and opportunistic rather than well planned and organized. They are therefore more easily apprehended. They are more impulsive and less likely to appreciate the seriousness of their actions; 40-60% of children and adolescents with ADHD develop conduct disorder or oppositional defiant disorder (16). Young people with ADHD and these comorbid disruptive disorders appear to have clinically and genetically more severe variants of their independent disorders (17).

2. Coping within the Criminal Justice System.

ADHD youths may be less able to cope with arrest, the police interview and court process. They may struggle to sustain attention during lengthy questioning under pressure or focus on questions whilst involved in other tasks such as looking at exhibits or sketching maps of locations. Young people are more susceptible to interrogative pressure than adults (irrespective of whether they have ADHD or not) and, to avoid this, they are more likely to accept or comply with the suggestions of authority figures (18,19). When adults with ADHD are put under interrogative pressure they may appear evasive by engaging in a strategy of responding “I don’t know” even to questions that they should be able to answer. This may be because they do not trust their memory in these circumstances of stress and pressure (20). They may also be motivated to comply with requests and avoid conflict and confrontation (21,22). All of these factors may contribute to the reported increase in false confession by people with ADHD (21,23).

3. In offender Institutions

Once incarcerated, individuals with untreated ADHD, even those in partial remission, seem to have great difficulty tolerating the stress of prison life, resulting in high rates of aggressive incidents in secure settings (24,13,25). Several factors associated with ADHD may contribute to this, including impulsive responding (26), mood instability, low frustration tolerance (27,28) and a chaotic/disorganised personality style (29). Conversely some young offenders may find the structure and security of the institution beneficial, especially when they are provided with education at an appropriate level (30).

4. Re-offending.

Once released, young offenders with ADHD often have little family or community support and they may not have the resources to obtain and hold down a job. They may also have substance misuse disorders and for those who are untreated, substance use may be an attempt to self-medicate (31). Re-offending is frequent and the cycle continues.
Can we reduce the likelihood of young people with ADHD becoming offenders?

ADHD in young people is increasingly being recognised, leading to treatment with psychological and pharmacological methods. There is, however, no robust research into whether current ADHD management strategies will reduce the risk of offending in ADHD youth. Taylor et al. (32) reviewed the current status of young people aged over 14 years in a UK paediatric service and suggested that outcomes could be better than suggested in previous literature. Future research needs to include long-term outcomes for children with ADHD and comorbid conduct disorder. We need much more long-term follow-up data.

Interventions for ADHD offenders

As a neurodevelopmental disorder that crosses the lifespan, the window for intervention is not a one-off opportunity and appropriate interventions can be offered at any age (33). Nevertheless the most effective intervention is prevention. For example, by offering assessment for ADHD at the point of second fixed-term exclusion from school it would be possible to identify some children at risk and ensure they are treated at an earlier stage.

In the UK, the National Institute for Health and Clinical Excellence guidelines (34) recommend treatment with medication as the first-line for children and adults with severe ADHD, and psychological treatment as first-line for those with less severe symptoms. The guidelines state that drug treatment for ADHD should always include a comprehensive treatment programme addressing psychological, behavioural, educational or occupational needs. However, when treating serious offenders with ADHD, even more complex and comprehensive interventions are likely to be needed. The aims of ‘treatment’ in such cases must be the following.

1. Conferring health gain to the individual by reducing ADHD symptoms and associated impairment, improving function and quality of life.
2. Rehabilitating the individual by providing targeted treatments, e.g. to address antisocial attitudes and thinking styles, to develop insight into offending and victim empathy.
3. Considering public protection issues and reducing risk to society.
4. Delivering justice in a fair and reasonable way.

Medication alone is unlikely to achieve these aims fully. There is growing evidence from studies in children suggesting that multimodal treatments (involving psychological and drug treatments) lead to greater effects on comorbidity and greater long-term effects. Indeed, most psychosocial treatments have evolved from interventions designed for children with disruptive behavioural problems (33). By contrast, psychosocial treatments developed for non-offending ADHD adults specifically target the reduction of ADHD symptoms and the improvement of executive function skills, e.g. time-management, planning and organization skills (35,36). If these are provided to offenders with ADHD, the outcome may not be the acquisition of prosocial competence (defined as competence in behaving in a way that benefits others, such as helping, sharing, co-operating and volunteering), but antisocial competence. Thus it is essential that the psychosocial treatments that are delivered to ADHD offenders (and given the high rates of comorbidity with conduct disorder, perhaps also ADHD non-offenders) include a prosocial competence component. One such programme is the R&R2 for ADHD Youths and Adults (37) which is a manualised 15 session CBT group programme. R&R2 is a revision of the earlier R&R programme which has demonstrated high efficacy with a 14% reduction in re-offending when delivered in institutional settings and a 21% reduction when delivered in community settings (38). R&R2 has been evaluated in a randomized controlled trial in a sample of non-offending clinically referred ADHD patients (39). Results suggested medium to large treatment effects for ADHD symptoms, which increased further at three month follow-up. Comorbid problems (anxiety, depression, antisocial behaviour, social functioning) also improved at follow-up, with large effect sizes. Thus antisocial behaviour significantly decreased even though participants were not
specifically referred for this reason. A controlled pilot study of the R&R2 intervention delivered to offenders with severe personality disorder and ADHD symptoms has also reported significant improvements at outcome with medium effect for social problem solving and emotional stability, while reducing ADHD symptoms, violent attitudes and reactive anger (40).

Conclusions

It is now well established that there is a disproportionately high prevalence of ADHD within the prison population. Those who commit non-indictable offences e.g. drunk and disorderly behaviour and less severe acts of public order or criminal damage are also more likely to have ADHD. Individuals with ADHD enter the criminal justice system at a younger age, often as a result of being apprehended for impulsive and violent crimes. They often become ‘revolving door’ recidivists and their aggressive behaviour within institutions means that they are ineligible for early release. Yet ADHD in young offenders is all too often being missed, misdiagnosed or inadequately treated. Appropriate treatment and support is likely to reduce symptoms, improve behavioural and emotional control, and improve prosocial skills. Moreover, with early recognition and a goal-directed intervention, there is the potential to divert youths away from a criminal trajectory, offering a better future for both the individual and the community. We know the solutions; we just have to start to implement them. Is this so challenging?

GP Comment

What have I learned from this paper?

1. The rate of ADHD in both teenage and adult offenders is high but the condition is often untreated.

2. Early recognition of the ADHD, for example screening for ADHD after a second school exclusion, followed by effective treatment, might prevent some offending behaviour.

3. Management of ADHD should include not only medication but teaching of prosocial skills to prevent offending/re-offending.

4. This paper emphasises two points in particular.
   • First, the need for early recognition of ADHD. This implies that there should be appropriate training and systems for identification in primary care, schools, children’s services, social care and young offenders services.
   • Second, the need for access to psychological assessment and treatment for those diagnosed with ADHD.

Dr Morgan Walters, GP, Bedford.

References


Pathways to social failure within the ADHD community - it’s criminal how much we get wrong.

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Abstract

People with ADHD are much more likely to encounter difficulties at school, at work and socially. They are more liable than the general population to misuse drugs and to commit criminal acts. Management of ADHD involves far more than simply decreasing the scores on behavioural scales. Because the consequences of the impairment of executive function can be so profound, attention needs to be paid to ways in which these deficits can be overcome by adopting a broader approach to assessment and management.

Introduction

Whilst watching my 14 year old daughter play competitive hockey last weekend I was drawn to a parallel of life that relates strongly to the subject under discussion in this paper. One of her team mates was struck in the face by the ball, never a pleasant experience. Naturally people flocked to assist her and make sure she was all right. Whilst this was going on, and throughout the morning, a young lad had been climbing up the railings, running round and shouting at his parents. No-one was flocking to his or their assistance or setting out to see if he was OK. In fact they were avoiding them as a family. He was not OK. He was bored. He had no one to mix with and play with and he was frustrated. Knowing him, and his parents, I suspect to this day he has a behavioural disorder such as ADHD. That is the issue. I knew the girl had been hit in the face, and needed help. I could only suspect the lad was poorly, and most people around had no clue as to what could have been wrong and what to do. They shunned him. ADHD is an unseen disability. Yes, we see the manifestations of the disorder, but we do not see the cause. That affects how we react.

In this paper I seek to outline a number of entry pathways that are frequently ‘taken’ by the young person with ADHD into what I label ‘negative social outcomes’. Often seen as failures for the individual, I argue that it is the professionals working with these young people that have failed them if this is the outcome. Low self-esteem, unlawful drug taking, acquisitive crime, road deaths and injuries are all discussed with an over-riding message that in clinical settings more can be done to reduce these risks if the clinician is sensitised to the issues above and beyond their understanding of rating scales and behavioural measurement charts.

My thesis is that the unseen nature of the disorder, ADHD in conjunction with, but not reliant on, co-occurring conditions, gives rise to a heightened risk of criminal behaviour in adolescents and adults. We have a low tolerance for ‘abnormal behaviours’ and the law sets tolerances about what is acceptable often, if not at all times, regardless of the causes of errant behaviour. Those facts alone heighten the risk of young people with ADHD coming into contact with the legal system.

Pathways to Success or Failure

ADHD is commonly referred to as ‘a neuropsychiatric disorder that becomes apparent when the child’s functioning is negatively impacted upon by inattention, hyperactivity and impulsivity’ (1). I find that definition to be stifling, and by using three words that have become the common language, we do little to assist in people’s understanding of what ADHD really is. This therefore constrains what we do about it.

To be able to see forward into the predictable outcomes for a person with ADHD, which are more often
than not negative outcomes, a more meaningful definition is necessary. I find that defining ADHD in terms of executive function impairments assists practitioners to recognise the impact on life and the scale of the issues more readily. Executive functioning is described as ‘neurocognitive processes that maintain an appropriate problem-solving set to attain a later goal: in particular responses to inhibition, vigilance, working memory, and planning’ (2). Barkley (3) and other commentators are clear on the link.

ADHD is a deficit in self-control – what some professionals call the executive functions, critical to carrying out human behaviour over time.

Brown breaks down executive functioning into 6 key areas, all of which operate in unison in the human brain, a fact that he states separates us out from other animals on the planet (4). When these key areas are drawn to the attention of professionals I have found that they begin to observe and grasp how deficits in these areas can lead to a social crisis for the person with ADHD. Their understanding is far greater through this analytical route than by merely discussing inattention, hyperactivity and impulsivity. Brown has summarised the areas of executive functioning as follows.

• Organising, prioritising and activating work
• Focusing, sustaining and shifting attention to tasks
• Regulating alertness, sustaining effort and processing speed
• Managing frustration and modulating emotions
• Utilising working memory and assessing recall
• Monitoring and self-regulating action

A lengthy analysis of executive functioning is not possible in a brief paper. My aim is to stimulate debate on how awareness of this functioning capability and its deficits can lead to a more appropriate care regime, one that aims at improving social outcomes rather than only reducing symptoms. This care regime commences within the medical provision and clinical setting. In real-life terms and by way of an example, consider the following.

Imagine crossing a road alone for the first time. The difficulties that this may pose for any youngster are many fold. Now imagine you have ADHD and your ability to function executively is greatly reduced. This is now not a frustrating task, it is a dangerous one. Judging traffic speeds, regulating action to a point where you will stop on the pavement long enough to cross safely, recalling what went on from your left whilst looking to your right, organising your thoughts to block out distractions and to focus on the road width, approaching cars speed, etc, staying alert and thinking to act expediently when safe... It is all too obvious where this exercise can and does go wrong. In 1998 DiScala concluded that those with ADHD, in particular boys, were significantly more likely to be injured as pedestrians and severely injured (12.5% v 5.4%), as measured by the Injury Severity Score (5).

This is a fundamental point relating ADHD to life outcomes; it is not just about distracted children in the classroom – it is real everyday life that can and should be the focus of management by all professionals charged with responsibility.

However, the school setting is very important. Within the school setting, executive functioning is a major contributor to success, or often for those with ADHD, lack of it. Practitioners recognise, for ICD 10 or DSM IV and other current assessment criteria, that the school setting is a primary source of evidence for impairment. Studies found that students with ADHD, compared to students without ADHD, had persistent academic difficulties that resulted in lower average marks, more failed grades, more expulsions, increased dropout rates, and a lower rate of college undergraduate completion (6). In 2004 the UK Audit commission reported that children excluded from school are twice as likely to commit crime. Biederman reported in 2006 that the suspension rate for school aged children with ADHD was significantly higher than those without (21% v 71%) (7). Research in both the UK and US
(8) found that children with ADHD are noticeably shunned by their peers from the age of 6 years as a consequence of school behaviour. They are no longer invited to play in the playground, go on after school outings or attend sleep-overs and parties.

This exclusion from friendships and the subsequent drop in self-esteem was said by one young interviewee to be ‘the most impactful and upsetting time in my life’ (9). The constant lowering of self-esteem leads inevitably to inappropriate friendships, and for boys this is frequently with older boys. Many case studies report the typical escalation of actions that arise from such friendships: feeling a sense of belonging for the first time, proving ability by currying favour, stealing when challenged from a parent, drinking / drug-taking to be part of the [older] group.

Substance abuse is a common co-occurring condition that occurs in the adolescent or adult (10). Molina (11) found that ADHD is a predictor of substance abuse in young people by the age of 16 years. The relationship between illicit substances and ADHD is worthy of further examination (see elsewhere in this issue). Avoidance of this harmful social outcome should be a fundamental concern of medical staff in clinical settings. The taking of unlawful drugs by a person with ADHD has been described as ‘a way of stopping the tumble drier in my head’ (12) and is very common. However, in contrast to prescribed medications for ADHD, which are approved, titrated, measured and controlled, unlawful self-medication regimes are not, and the heightened risk that results is often life threatening. For over half of the community abusing unlawful drugs, such as heroin, the primary form of income is acquisitive crime (13), such as burglary and vehicle-related theft.

Qualitative research in Newcastle, England undertaken by the University of Central Lancashire (14) on behalf of the author found that the success of treatment regimes for people with ADHD and substance abuse issues is often directly related to the environment and conduct of the clinical setting and its sensitivity to the primary disorder of ADHD: in short, people with ADHD do not perform well in traditional clinical / care settings, with their ADHD becoming a frustration to success.

This is perhaps easily explained by imagining sitting a group down to discuss their unlawful drug taking habits, with say 2 of the 10 attendees having ADHD. The disruptive nature of the disorder to such settings and formalities can and often does cause withdrawal from the programme, and the nature of the rehabilitation processes underway. The almost complete nationwide absence of such clinical sensitivities and awareness can be argued as part of the problem when discussing the high recidivism figures for substance abusers that can be as high as 60% (15). What is clear that completing treatment programmes has a significant effect on substance abusers returning to their unlawful behaviours (16).

The Challenge for Professionals

I therefore challenge professionals, particularly but not exclusively clinical practitioners, to begin to analyse ADHD differently.

1. Ask yourself and the patient about lifestyle in terms of self-esteem; challenge parents to be aware of the need to manage this from the beginning, especially if the child is shunned by peers.

2. Be aware of the increased dangers of road use for young people with ADHD, whether on a bicycle, driving a car or as a pedestrian. Advise parents and carers of these risks at the time of diagnosis and remind them on repeat clinical visits.

3. Coach young people with ADHD (and their carers) on their life skills, particularly with regard to executive functioning as a set of areas for individual plans and coping strategies.

4. See success not as reduced behavioural patterns on rating scales, but as improved social outcomes for the patient and those around them. This is a harder but more rewarding outcome for which to strive.
These are four straightforward areas that, when managed well, can assist a person with ADHD to avoid following pathways to failure. People with ADHD will challenge us in public, on the sports field, in class or in the clinic. The task facing parents, clinicians and other professionals is not only to understand the condition better but also to have a more positive attitude to the individual with ADHD, knowing that sound management can lead to a much better outcome.

**Conclusion**

Clinical practitioners should adopt treatment regimes that seek to do more than reduce the symptomatology in well-documented rating scales. By assessing the impact of the condition, particularly of the executive function deficits, on the individual’s life, treatment should seek to improve longer-term outcomes. As a result, it should be possible for medical teams to reduce the propensity for people with ADHD to fall into a life of crime.

But we should be clear about ADHD and criminal behaviour. ADHD is an explanation and can never be an excuse for errant and disruptive, unlawful behaviour. I have often been held to account for allegedly trying to make excuses for young people’s behaviour to let them ‘off the hook’. We have a set of laws in the country that we should all seek to abide by. However, the legal process should not be used as an excuse for failing to assess, manage and treat the individual with ADHD in an appropriately professional way.

We have a judicial system that seeks to rehabilitate offenders to prevent laws being broken again. My observation is that with disorders such as ADHD not enough is understood about the drivers that allow lawlessness to manifest, and we can all, whatever the setting, learn and do more for these poorly people. It is especially important, if not vital, for clinicians to push for transition services into adulthood for people with ADHD; how can we allow a system to prevail that treats young people for a period determined by biological age, and just at the time of academic challenge, hormonal development removes the very regime that allows them to executively function because they reach the age of 16. It’s a very clear ‘welcome card’ to the criminal justice system for most, and this is inexcusable.

It is not inevitable that the individual with ADHD will follow a pathway to failure and poor social outcomes, but, in many cases, avoiding this and assuring success will depend on sensitive, skilled management by a multi-discipline team working in harmony.

**GP comment.**

**What have I learned from this paper?**

1. Because ADHD is an “unseen” condition, it may go undiagnosed and untreated for long periods.

2. Formal definitions of ADHD are in terms of hyperactivity, inattention and impulsivity but the deficits in the executive function can lead to a much broader range of issues that need to be addressed by the individual, the family and professionals.

3. The deficits in executive function in ADHD imply that there can be problems in organising, sustaining or shifting attention appropriately, sustaining effort and processing speed, managing frustration/emotions, using working memory appropriately, planning, and monitoring with self-regulation of action.

4. The individual with ADHD may not only follow a pathway of social failure but may also encounter the legal system or even be imprisoned. Understanding of the implications of the condition and providing appropriate, timely professional management might lead to a very different pathway.

Dr Murari Agrawal, GP, Bedfordshire.
References.


Developing an ADHD Integrated Care Pathway (ICP)

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Abstract

One of the key recommendations of the National Institute for Health and Clinical Excellence (NICE) guideline on the diagnosis and management of attention deficit hyperactivity disorder (ADHD) in children, young people and adults in September 2008 (1) is that Health Trusts, in collaboration with major stakeholders, develop ADHD Specialist teams that will be instrumental in implementing integrated care pathways. An ADHD integrated care pathway (ICP) can provide a valuable structure for patient identification, referral, assessment, diagnosis, management, support and follow up. By assisting a patient through their healthcare journey, an ICP can help to facilitate effective clinical governance. An ICP should set standards for interventions that are evidence based in line with the definition of clinical governance by the Commission for Health Improvement (CHI). In this paper, the advantages of an Integrated Multiagency ADHD Care Pathway, together with the steps required in its development and implementation are considered.

Key words
Integrated care pathway, ADHD, NICE, Clinical governance, Stakeholders

Introduction

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental conditions underlying behavioural and academic difficulties in children and young people. It is a heterogeneous behavioural syndrome characterised by symptoms of inattention, impulsivity and hyperactivity.

The report of the National group of chairs of the NHS next stage review (2) in June 2008 made the following recommendations.

1. Commissioning of pathways of care delivered by staff with the relevant skills in evidenced based interventions.

2. This will require a combination of general skills for frontline practitioners and a stepped care approach to more specialised competencies. For example, appropriate competencies in liaison psychiatry are required to back up the generalist knowledge of clinical staff working in any acute physical health care service.

3. Commissioners, providers and regulators should work together to ensure that contracts encourage high-quality staff into mental health commissioning and service provision.

4. Develop and maintain staff skills to deliver improved outcomes and reduce the stigma of mental health services by promoting the field as an important career choice for the long term emotional, social and economic wellbeing of the country.

5. Training and continuing professional development should be driven by service design based on effective care pathways to address local need, rather than existing skill sets driving service design.

The above recommendations can be achieved by the implementation of a clear and robust integrated care pathway involving all major stakeholders.
Definition

There are many definitions for an integrated care pathway.

One of the earliest formal definitions states that an integrated pathway is a tool which is determined and agreed locally; multidisciplinary; based on guidelines and evidence when available; forms part or all of the clinical record; documents care given and facilitates the evaluation of outcomes for continuous quality improvement (3).

The European Pathway association (EPA) as suggested by Vanhaecht et al in 2007 (4) defined this as: ‘A complex intervention for the mutual decision making and organization of predictable care of a well defined group of patients during a well defined period’.

Historical perspectives

Pathways were introduced in the Healthcare system in the early 1980s in the USA (5). Prior to their introduction in healthcare, certain non-health industries had already been using care pathways. The first use of clinical pathways was in Boston USA in 1985 and 1987. This was as a result of introduction of diagnosis-related groups in 1983. By the late 1990s the majority of US hospitals were using some form of clinical pathway (6).

Clinical care pathways were introduced in the 1990s in the UK. Care pathways are now used worldwide.

Aims of an Integrated Care Pathway (7).

Figure 1

- Identify research and development questions
- Facilitate guidelines and continuing audit into clinical care
- Improve overall clinician patient communication and patient satisfaction
- Improve multidisciplinary communication, including primary care
- Aim for or exceed existing clinical quality standards
Integrated patient care becomes possible when the patient remains the central focus

Patient-centred pathways occur when all major stakeholders including service users and providers work together in partnership. It is important to incorporate the views of patients during this process and there are different methods to achieve this (8).

Vanhaecht et al, 2010 described 3 different care pathway models (5):

Chain models are used for high predictability processes like elective surgery or chemotherapy teams. They require a high level of agreement between the members of the multidisciplinary teams.

Hub models are used for less predictable processes like psychiatry and palliative care. The key or lead worker leads the organization and planning of the care process around the patient.

Web models are also used in unpredictable care processes where it is essential to have frequent and regular meetings to enable organization and structuring of the process.

The goal of these models is to enhance multiagency and multidisciplinary team working.

Advantages/benefits of integrated care pathways (7)

Integrated pathways:

- Encourage multidisciplinary working and communication.
- Facilitate the introduction of local protocols, research and audit.
- Promote patient-focused care.
- Improve patient information.
• Result in a more efficient data collection and encourage changes in practice.
• Encourage the use of evidence-based care into clinical practice.
• Provide clear and concise standard of care.
• Provide the framework for the management and reduction of clinical risk.
• Are cost effective by reducing hospital stays.
• Enhance communication between different care sectors.
• Support education and training.
• Provide a baseline for future initiatives.
• Provide a standardised system for progress and monitoring of care.

Campbell et al. (7) further described concerns about integrated pathways as being:

• Investment of time that could be spent in other clinical activities.
• Discouragement of appropriate clinical judgement in certain individual cases.
• The stifling of innovation and progress.
• Being difficult to develop in situations with multiple pathologies or variable clinical management.

Developing an Integrated ADHD Care Pathway - Key considerations

• Identify a specific area for further development
• Recognise that an ADHD ICP is needed to enhance patient experience and produce better outcomes for all.
• Identify bench-marks e.g. NICE guidelines which can be used to support your rationale for an ICP development.
• Identify a project facilitator or lead.
• Solicit the support/ involvement of team members and educate them about the ICP.
• Identify, involve and manage key stakeholders.
• Map out ICP process and timelines for development.
• Agree ICP with all major stakeholders.
• Implement pathway.
• Review and audit pathway regularly.

Identifying a specific area for further development

- The Rationale for ICP development

Audits, surveys and research can help to identify and strengthen the value of an ADHD ICP. It is important to obtain feedback from service users and also to review and audit existing patient data. Regularly updated ADHD patient databases make the process of data collection for audit or research purposes easier.

Information can be obtained from service users by issuing survey cards, conducting short interviews, organising focus groups or arranging workshops. Service users may also be accessed via voluntary organizations or multiagency meetings.

National and local clinical standards and guidelines can provide a rationale for developing an ADHD ICP. The ICP should have a strong evidence base. The evidence base should contain the relevant clinical standards/benchmarks and best practice.
Some of the key documents that should support an ADHD ICP include:

- NICE guidance 2008 (1).
- SIGN guidance 2006 (9).
- Every child matters integrated working (10).
- Every child matters Lead Professional (11).
- Department of Health 2010 New Horizons (12).

**Identify a project lead or facilitator**

A designated facilitator or lead should manage the ICP process. The facilitator should have the relevant skills to manage all the major stakeholders effectively. He or she will provide leadership, ongoing support and education, acting as a link between different professional groups.

Gaining support of Team members and colleagues is vital to the success of the ICP. The project lead or facilitator may be the clinical ADHD lead or a specialist working with children and young people with ADHD.

Colleagues, managers and commissioners should be made aware of the need and rationale for an integrated pathway. Colleagues may have very little knowledge about the condition particularly if they do not assess and manage ADHD regularly.

Team member involvement and education will involve providing information about the role, aims, objectives and benefits of an ADHD ICP. It will also involve explanation of how the ICP may affect practice, cost effectiveness and the role of the team in contributing to the overall process. Team members may feel sidelined if their views are not solicited and represented in the process. It is very important that the project lead or facilitator communicate effectively with the team.

Once interested team members are identified, a steering or working group can be formed and roles delegated to key members.

It is essential to widen membership to members of other multidisciplinary/multiagency teams. This should include all providers of ADHD care and support, including representatives from parent support groups, voluntary organizations, social care and education. Service users, including families and young people, should also be included in this process.

Hussein (13) makes the following points about the importance of the inter/multidisciplinary nature of pathways.

Team members should reflect all the disciplines involved in delivery of care. Communication at all levels is essential. Exchanging resources across different agencies and disciplines is cost effective. Availability of various sources of data is integral to decision making. Every discipline is important, regardless of the degree of involvement.

The importance of incorporating the views of service users (patients/carers) into the process has been stressed by the Irish society for quality and safety in Health Care (14). They state that the benefits of involving patients and their carers include:

Better quality of services for patients resulting in improved outcomes.
Patient-focused planning and decisions.
Enhanced communication between organizations and the communities they serve.
Elimination of waste by identifying well in advance services required for specific purposes.
Examples of key stakeholders forming part of an ADHD ICP working group are:

**Preschool**

- Preschool teachers/advisory teachers.
- Nursery nurses.
- Health visitor.
- Family liaison worker.
- Community nurse.
- Pre School SENCO.
- GP.
- Paediatrician.
- Clinical psychologist.
- Psychiatrist.
- Voluntary organizations.
- Parent/carers.
- Social Care.
- Commissioners.

**School Age**

- Educational psychologist.
- SENCO.
- Teacher/teaching assistant.
- Clinical psychologist.
- Behaviour support team.
- Youth offending team (YOT).
- Social Services.
- Voluntary Organizations.
- Paediatrician.
- Psychiatrist.
- Commissioners.

**Designing an ADHD ICP**

Brainstorming sessions chaired by the project lead/facilitator will identify the rationale for the ICP, aims/objectives and how the pathway should be designed. The design should be simple and easy to understand.

The pathway should include evidence-based standards of practice, allow for regular analysis, should form a single record of use by the whole multidisciplinary/multiagency team and should be easily accessible (15). It is essential for the ICP to be incorporated into organizational strategy thus empowering service users.

The ideal ADHD ICP maps a framework for identification, diagnosis, management, follow up and progress at each step of the patient’s journey. It has the potential to shorten the patient’s journey from
time of identified concerns, referral, management and support. An ADHD ICP will also raise the profile of ADHD within a certain geographical area. Services are more visible, clear, robust and streamlined. Communication is enhanced between primary and specialist care providers. Lack of a clear pathway can lead to a ‘pot luck’ system of referral from primary care or universal services into specialist services further lengthening the patient journey. An ADHD ICP will ensure the provision of a uniform service in a wider geographical area thus eliminating a possible ‘postcode lottery’. Standardizing the whole process should result in a more efficient and cost-effective service.

Mapping the patient journey by the method of process mapping captures the delivery of care at each stage of the patient’s journey, providing a detailed view of the process and outcome. Process mapping identifies the strengths and weaknesses in delivery of care whilst providing robust evidence to support the need to review and develop solutions for change. It also identifies delays, duplication of care, gaps in the patient’s journey, deviations from best practice and quality/safety issues (15).

Process mapping involves a number of stages (16). These are:

- Identifying what occurs along a patient’s journey from their experience.
- Analyzing the map to identify waste, duplication, errors, blockages and unnecessary steps to the flow of health delivery.
- Developing solutions to any identified issues.
- Testing possible solutions and their impact on care delivery.
- Implementing necessary changes to improve the patient’s journey.
- Evaluating impact of change on the care continuum.
- Reviewing regularly to ensure continuous quality improvement.

Launching and implementing the pathway should involve all the members of the working group. This entails education and training of all major stakeholders in the proper use of the ICP, together with audit and review of the ICP periodically to ensure updated standards are continually incorporated. An effective ADHD ICP supports the audit process and assists in maintaining clinical governance standards. Members of the working group should identify and agree on outcome measures at the start of the pathway development process.

**Conclusion**

A well developed ADHD ICP should shorten the patient’s care journey, empower patients and carers, make services more visible and uniform, and support both providers and commissioners in providing a more accessible service appropriate for the needs of service users.

**GP Comment**

*What have I learned from this paper?*

1. An integrated care pathway may be of particular benefit in the management of ADHD because this is a condition that affects the individual in many different settings, is often associated with comorbidity and generally involves a large number of professionals.

2. An integrated pathway can facilitate referral, management, audit and measurement of outcome; by incorporating NICE and other relevant guidelines, regularly updated with the best available clinical evidence, it can help to maintain high standards in managing complex conditions such as ADHD. This is very much in keeping with the concept of Clinical Governance.

3. Because shared-care arrangements with general practice are an essential aspect of the integrated care pathway, it is very relevant to the GP in managing patients with ADHD.
4. In this paper, the lists of professionals and others who should be involved in the care of the individual with ADHD at different ages provide a valuable aide-memoire to assist us in ensuring that appropriate comprehensive management is being provided.

Dr Vinita Manjure, GP, Milton Keynes.

References


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Shared Care Guidelines for Effective Management of ADHD

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2. Dr John Kedward, General Practitioner, London Road Surgery, Bedford

Abstract

It is important to produce local protocols for a Shared Care arrangement between specialists and primary care providers for effective management of ADHD in children and young people. This article outlines the roles and responsibilities of the specialist and the GP, emphasising the need for clear communication between them.

Introduction

In the current climate, there is an increasing awareness about ADHD, its impact on the child's home and school life and methods of treatment including medication, not only amongst health professionals but also education staff and the general public. The National Institute for Health and Clinical Excellence (NICE) has issued guidance on ADHD diagnosis and management in children, young people and adults (1), recommending that drug treatment for children and young people with ADHD should always form part of a comprehensive treatment plan that includes psychological, behavioural and educational advice and interventions.

NICE Guidance

According to the NICE guidance, it is important for health professionals to ensure drug treatment is offered as first-line treatment for children and young people with a severe form of ADHD and also for those with moderate ADHD, who do not respond to behavioural treatments alone. There is also a clear expectation that both the diagnosis of ADHD and initiation of drug treatment should be carried out by a specialist psychiatrist, paediatrician or other health professional with training and expertise in the management of ADHD (1). In addition, NICE guidelines recommend that a multidisciplinary ADHD team and/or clinic should produce local protocols for Shared Care arrangements with primary care providers, and ensure that clear lines of communication between primary and secondary care are maintained (1).

What is Shared Care?

For some conditions, including ADHD, GPs have been asked to continue to prescribe medication that they would not normally initiate and which, in some cases, they might feel uncomfortable about prescribing. An arrangement for “Shared Care” implies that, although the GP takes over the prescription of the medication when this has been stabilised, the hospital/community specialist who initiated the medication continues to provide ongoing monitoring and review of the patient for a period of time.

Who can develop these guidelines?

The guidelines can be drawn up by a panel consisting of the local specialist/lead for ADHD service (Paediatrician/Child and Adolescent Psychiatrist), pharmacist and a GP with a special interest in ADHD and subsequently ratified by the local area prescribing committee. However, the membership of the panel can vary depending on the needs of the local area.
Responsibilities of the specialist (Paediatrician/ Child and Adolescent Psychiatrist) may include the following.

• To discuss the benefits and adverse effects of drugs and monitoring programme with the child/young person and their parent/carer, providing them with relevant written information.
• To advise the parent/carer that the drug treatment will not be prescribed if they do not keep the appointments.
• To inform the GP when the diagnosis of ADHD has first been made and will explain what regime of methylphenidate, dexamfetamine or atomoxetine has been prescribed.
• To inform the child’s school about the ADHD diagnosis and treatment including medication, after permission from the family has been obtained.
• To monitor the patient’s ADHD and drug therapy regularly, retaining responsibility for making dose alterations when needed and informing the GP in writing.
• To liaise with the GP to agree to share care once the child/young person is stable and benefiting from a certain therapeutic dose of the drug (which may take 3 to 6 months).
• To ask the GP to prescribe the appropriate drugs, only in accordance with their product licence.
• To provide the GP with a brief summary sheet with details of the child/young person, the drug, dose and its adverse effects and monitoring requirements (see the Shared Care guidelines for methylphenidate, appendix 1 - a similar Shared Care guidelines Protocol for dexamfetamine and atomoxetine should be developed).
• To ask the GP to monitor the patient’s weight, height, pulse rate and blood pressure at periodic intervals (6 monthly).
• To decide when to stop or periodically withdraw drug treatment to assess progress.
• To liaise with the GP regarding transition arrangements and onward referrals to a specialist adult team, if drug treatment is required beyond the age of 18 years. (It should be noted, however, that several areas in the UK do not yet have the necessary agreed transitional arrangements in place.)

Responsibilities of the GP may include the following.

• To prescribe methylphenidate, dexamfetamine or atomoxetine, in line with the respective product licences.
• To check if the child/young person is keeping the review appointments with the specialist prior to issuing repeat prescriptions.
• To monitor the patient’s overall health and wellbeing.
• To inform the specialist in writing of measurements of the patient’s weight, height, pulse rate and blood pressure.
• To inform the specialist if there are any adverse effects. (For example, for methylphenidate see the ADHD Methylphenidate Monitoring Form, appendix 2).
• To contact the specialist to discuss the patient’s progress when necessary, particularly if there are any concerns, for example with regard to adverse effects or medication compliance.

Responsibilities of the parent/carer may include the following:

• To read and understand the product’s patient information.
• To store the medication safely and to ensure compliance with the medication, as prescribed.
• To inform the GP/specialist of all the medications the child is taking currently.
• To report any unusual symptoms or adverse effects to the GP/specialist.
• To maintain regular review with the specialist to monitor treatment.
What else the guidelines should cover

- Brief information about how ADHD is diagnosed.
- Indications and adverse effects of drug treatment with methylphenidate, dexamphetamine and atomoxetine.
- Contact details of the specialist and pharmacist.
- An agreement of the Shared Care arrangement between the specialist and the GP.
- References.

Prescription requirements for controlled drugs (CDs)
As methylphenidate and dexamphetamine are controlled drugs, they should be prescribed carefully to ensure compliance with the legal framework. A prescription for Schedule 2 and 3 CDs (with the exception of temazepam and preparations containing it) must contain the following details, written so as to be indelible, (e.g. handwritten in ink, typed or computer-generated) (2).

- The patient’s full name, address and, where appropriate, age. An email address or PO Box is not acceptable. ‘No fixed abode’ is acceptable as an address for homeless people.
- The name and form of the drug, even if only one form exists.
- The strength of the preparation, where appropriate (if more than one strength exists).
- The dose to be taken.
- The total quantity of the preparation, or the number of dose units to be supplied, in both words and figures.
- Signed by the prescriber with their usual signature (this must be handwritten) and dated by them (the date does not have to be handwritten).

Establish good communication and record keeping

Shared Care requires good communication between the specialist, primary care prescriber and the patient. Good record keeping of all the verbal and written communications as well as copies of the prescriptions aids this process.

Conclusion

Agreement of Shared Care guidelines between the specialist and GP facilitates high-quality care for the patient with ADHD by ensuring that roles and responsibilities are clearly defined and good communication is maintained.

GP Comment

What have I learned from this paper?

1. The NICE guideline and other policies indicate that GP’s have a vital role in Shared Care arrangements and should take over prescription of standard ADHD medication when this has been stabilised; Shared Care guidelines can help to ensure clarity of roles between the specialist and the GP, so that this process can be managed safely and efficiently.

2. Shared Care guidelines should improve communication between the specialist and the GP, adding to patient safety and facilitating co-ordinated, well-planned management.
3. As also stated in the ADHD pathway paper, in light of the current financial climate, it is essential that the interface between primary and secondary care remains as seamless as possible. These guidelines will help the healthcare professionals achieve that and beyond, ensuring patient-centredness remains the main aim.

Dr Vinita Manjure, GP, Milton Keynes

References

1. Attention Deficit Hyperactivity Disorder – diagnosis and management in children, young people and adults, NICE clinical guideline 72, Developed by the National Collaborating Centre for Mental Health, Sep 2008

## Appendix 1

Shared Care Guidelines for the use of methylphenidate in the treatment of ADHD in children and young people.

### Brief summary

<table>
<thead>
<tr>
<th>Patient’s name</th>
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<tbody>
<tr>
<td>Date of birth</td>
<td></td>
</tr>
<tr>
<td>NHS number</td>
<td></td>
</tr>
<tr>
<td>Patient’s address</td>
<td></td>
</tr>
<tr>
<td>Consultant’s name</td>
<td></td>
</tr>
<tr>
<td>Consultant’s contact details</td>
<td></td>
</tr>
<tr>
<td>GP’s name</td>
<td></td>
</tr>
<tr>
<td>GP’s contact details</td>
<td></td>
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<table>
<thead>
<tr>
<th>Drug dose, formulation and frequency</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Methylphenidate standard release (generic), 5–20 mg tds</td>
<td></td>
</tr>
<tr>
<td>□ Ritalin® (methylphenidate standard release), 5-20 mg tds</td>
<td></td>
</tr>
<tr>
<td>□ Medikinet® (methylphenidate standard release), 5-20 mg tds</td>
<td></td>
</tr>
<tr>
<td>□ Equasym®XL (methylphenidate modified release), 10-60 mg od</td>
<td></td>
</tr>
<tr>
<td>□ Medikinet® XL (methylphenidate modified release), 5-60 mg od</td>
<td></td>
</tr>
<tr>
<td>□ Concerta® XL (methylphenidate modified release), 18-54 mg od</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Higher doses than shown in the table may be prescribed according to NICE guidance</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s diagnosis</td>
<td>ADHD</td>
</tr>
</tbody>
</table>

### Adverse effects

**Very common adverse effects include (≥1/10):**
- Insomnia, nervousness, headache

**Common adverse effects include (≥1/100 to <1/10):**
- Decreased appetite, dizziness, somnolence, abdominal pain, nausea, vomiting, dry mouth, tachycardia, palpitations, arrhythmias, changes in blood pressure and heart rate (usually an increase), rash, urticaria, pruritus, fever, alopecia, moderately reduced weight and height gain during prolonged use in children

**Very rare adverse effects include (<1/10,000):**
- Anaemia, leucopenia, thrombocytopenia

### GP monitoring requirements and frequency

GP to monitor height, weight, BP and pulse rate every 6 months. If the child falls off the centile in his/her growth and any parental concerns arise, the GP should refer the child to the paediatrician

### When to refer back to consultant

Report to and seek advice on any aspect of patient care that is of concern to the GP and may affect treatment

### How often will the patient be reviewed by the specialist

Children with ADHD will be reviewed every 12 months by the specialist (Paediatrician/Child and Adolescent Psychiatrist)
Appendix 2

ADHD Methylphenidate Monitoring Form

<table>
<thead>
<tr>
<th>Physical parameters</th>
<th>Measurement</th>
<th>Centiles and trends (stable/falling/rising)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height in cm</td>
<td>Centile</td>
<td>Trend</td>
</tr>
<tr>
<td>Weight in kg</td>
<td>Centile</td>
<td>Trend</td>
</tr>
</tbody>
</table>

- Give advice if growth is compromised
- Consider referral to dietician and alert the specialist

<table>
<thead>
<tr>
<th>BP in mm Hg</th>
<th>Systolic</th>
<th>Centile</th>
<th>Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diastolic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Contact ADHD specialist if BP persists above 95\textsuperscript{th} centile

<table>
<thead>
<tr>
<th>Pulse rate/min</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-12 years</td>
<td>80-120/min concern if &gt; 120/min</td>
</tr>
<tr>
<td>&gt;12 years</td>
<td>60-100/min concern if &gt; 100/min</td>
</tr>
</tbody>
</table>

- NICE guidelines on ADHD say ‘sustained resting tachycardia, arrhythmia or systolic BP greater than 95\textsuperscript{th} percentile measured on two occasions should prompt dose reduction and referral to a paediatrician

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<thead>
<tr>
<th>Any side effects</th>
<th>Yes /no</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced appetite</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep onset problems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td></td>
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<tr>
<td>Tics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug misuse/diversion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Current medication/s and the dosage</th>
<th>Methylphenidate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Atomoxetine</td>
</tr>
<tr>
<td></td>
<td>Dexamfetamine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of the doctor</th>
<th>Signature</th>
<th>Date</th>
</tr>
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</table>

Table adapted from Hertfordshire Shared care Guidelines
Adult ADHD

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Abstract

The diagnosis of ADHD has only relatively recently been acknowledged in adult psychiatry. Education of healthcare professionals in the appropriate management of this condition has yet to be widely achieved. A brief overview is given of the symptoms, impairment and comorbidity. An ultrashort screening list is presented; diagnostic assessment and treatment are discussed. ADHD in adulthood is a psychiatric condition that begins in childhood and can lead to chronic impairment but, once recognised, it can usually be treated effectively.

Keywords: ADHD, adult, prevalence, gender, diagnosis, treatment

Introduction

The importance of acknowledging the possibility of the diagnosis of ADHD in adults has only recently been recognised. Adults with ADHD are easily distracted, have poor planning and organisational abilities, and are liable to both mood fluctuations and fits of temper. They seek out excitement and risks in order to be better able to concentrate. They often use drugs and alcohol, and they are impulsive and restless. Furthermore, they almost always have one or more additional disorders. They may consequently have problems with functioning in their studies, at work and in relationships. There is often a history of having repeated a class at school. At work they may be a “jack of all trades and a master of none”. They also have accidents, including car accidents, more often than average, are more often ill and are less productive. They often have chronic physical stress-related complaints that are not well understood. Once a diagnostic assessment has been made, the disorder can generally be treated satisfactorily. The road ahead tends to be long because of a lack of understanding of the person by those involved and a lack of knowledge among healthcare providers, whose training has usually not covered the diagnosis and management of adult ADHD.

Prevalence and gender distribution

The prevalence of adult ADHD is estimated as 3-5%. These figures are based on population research in the USA, in Europe and elsewhere (1-5). Epidemiological research in adults indicates a more equal gender distribution for ADHD than in children (2-4,6). Population research in children has revealed that boys predominate (7). In clinical populations boys are referred for help much more often than girls. Girls are probably underdiagnosed because GPs and other healthcare providers are less aware of the possible diagnosis in girls. Another explanation could be that girls tend to have the inattentive subtype of ADHD and have less disturbing comorbidity, causing less of a problem to those around them, resulting in fewer referrals (8-11).

Symptoms

The core symptoms of ADHD are inattention, hyperactivity and impulsivity. In addition, 90% of adults also suffer from lifetime mood swings (4-5x/day) and anger outbursts (12). Inattention problems are: being easily distracted, difficulty finishing things, having no overview, poor planning, difficulty making decisions, forgetfulness, often losing things. Hyperactive behaviour is being busy, talkative, difficulty sitting still, inner restlessness, inability to relax. Impulsive behaviour is manifested by blurting out, interrupting others, impatience, acting without thinking.
Impairment and comorbidity of ADHD

Impairment in adults with ADHD (13) may be expressed through the following.

- Being educated below the intellectual level or not having finished an education.
- Underachievement in work (below the educational level).
- Continuously changing jobs or positions as a result of conflicts or being easily bored.
- Having relationship problems as a result of not sticking to agreements, not taking enough responsibility, irritability or the need for variety and easily giving in to infatuations.
- Social problems or social isolation as a result of fear of failure, social fear, shame as a result of failure, poorly developed social skills.
- Inability to organise daily life, keep finances and housework under control.
- More accidents and speeding violations.
- More teenage pregnancies.
- Earlier onset of alcohol and drug abuse.

ADHD in outpatients is accompanied by one or more associated psychiatric disorders in three-quarters of cases. The average number of comorbid disorders in referred patients with ADHD is three (12,14,15). In the National Comorbidity Survey Replication (NCS-R) in the general population in the US the same pattern of comorbidity was found in non-referred patients. The presence of three comorbid disorders increased the chance of ADHD in the general population 8.3 times (16). Main comorbid disorders in adult ADHD are depression, bipolar disorder (mainly type II), anxiety disorders, sleep disorders (mainly delayed sleep phase syndrome), addiction and personality disorders (13). This means that ADHD is not an innocent condition but is often an undiscovered disorder in patients who have already sought help for complex, possibly therapy-resistant problems. This research showed that ADHD that was not in remission or that was untreated led to chronicity of comorbid disorders. This was mainly the case in mood disorders (including bipolar disorder), post-traumatic stress disorder, generalised anxiety disorder, panic disorder and dependency on drugs. The chances of ADHD in a mood disorder were 20%, in an anxiety disorder 17% and in addiction 18%. Vice versa, mood disorders occurred in 31% of those with ADHD, anxiety disorders in 51% and addiction in 14%.

Screening

A short screening instrument can be very useful when ADHD is suspected and when more information is needed regarding the usefulness of further testing. A screening test is not, however, a diagnostic tool. It is always advisable to perform further tests if there is a chance of ADHD.

Ultra-short screening list for ADHD in adults (13)

1. Do you usually feel restless? (for example: nervous, difficulty sitting still, fidgeting, a lot of exercising or being active)
   
   Yes / no

2. Do you usually act first and then think? (for example: blurring things out, spending too much money or being impatient)
   
   Yes / no

3. Do you usually have concentration problems? (for example: being easily distracted, not finishing things, being easily bored, forgetful or chaotic)
Yes / no

If the answer to questions 1 and/or 2 and/or 3 is yes:

4. Have you always had this? (as long as you can remember, or have you been like this most of your life)

Yes / no

If the answer to question 4 is yes, then please consider further diagnostic assessment for ADHD.

This questionnaire has not yet been validated in research, but it does use the DSM-IV requirements for the diagnosis: the chronic persistence of the three core symptoms, with childhood onset.

Diagnostic assessment

The purpose of the diagnostic phase is to assess whether the ADHD characteristics meet the DSM-IV criteria. This implies that the ADHD symptoms should have the following characteristics.

- Started in childhood.
- Are sufficiently severe.
- Have been present throughout the patient's life.
- Have led to dysfunction from onset, throughout the patient's life.

The diagnosis will not be made or rejected on the basis of the impression someone makes during the diagnostic interview or on the basis of a neuropsychological test. This is because ADHD patients can, as a result of the tension associated with the interview, be temporarily more calm and focussed than they are normally. Neuropsychological tests so far lack sufficient sensitivity and specificity to serve as diagnostic tools. A detailed history will give the definitive answer as to whether the patient meets the criteria for ADHD.

Aside from interviewing the patient, the method for diagnosing adult ADHD consists of, if possible, also interviewing the partner for current complaints, and parents or other relatives for the childhood symptoms.

The diagnostic assessment can be performed using the structured Diagnostic Interview for ADHD in adults (DIVA 2.0) (13). DIVA 2.0 is free online, in different languages, at www.divacenter.eu. In this diagnostic interview, for every DSM-IV criterion, concrete examples are given for both childhood and adulthood. It makes it easier for patients and family to recognise symptoms that occur in different life phases. The assessment of impairment due to the symptoms in five life areas is also accompanied by concrete examples. The validity of the DIVA will be studied in the near future. If the ADHD diagnosis is made, further assessment of potential comorbidity and treatment advice should follow.

Treatment

The treatment of adults with ADHD consists of the following.

- Psychoeducation.
- Medication for ADHD and comorbidity.
- Joining a patient support group.
- Coaching/cognitive behaviour therapy.
Psychoeducation is provided for the patient and family when the diagnosis is made. This includes information on the heritability of the disorder, the relationship with lifetime impairment and treatment options.

The most effective and safe treatment is ADHD medication, above all stimulant drugs. However, as three quarters of adults with ADHD also have one or more other psychiatric disorder(s), these disorders also have to be treated, usually before the ADHD. Clinical experience shows that stimulants can be combined well with antidepressants (SSRIs), mood stabilisers and even antipsychotics (13).

Stimulant drugs are effective in 50-70% of children and adults with ADHD as long as they are taken regularly (15,17-22). If doses are skipped or the medication is stopped, the symptoms return. The effects of stimulant drugs can be measured using cognitive performance or learning performance and even IQ (23,24), via clinical variables such as symptom lists or behavioural observations (15,19), and in scientific research using PET scans, which display the effects of stimulant drugs on the dopamine transporter (25).

In adults most medication, including methylphenidate (Ritalin), is prescribed off label in most countries. Methylphenidate and atomoxetine are registered for ADHD in children, but in most countries not for adults (although they are in the USA). Research into the determination of effectiveness, dose and side effects of both these drugs in adults is being carried out with a view to licensing in Europe. However, it should be noted that the most recent National Institute for Clinical Excellence (NICE) guideline for ADHD includes recommendations for the treatment of adults with stimulant medication and atomoxetine.

<table>
<thead>
<tr>
<th>Table 1. Overview of effectiveness and side effects of ADHD medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effectiveness</strong></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
</tbody>
</table>
Contraindications for stimulant drugs are pregnancy, current psychosis and congenital heart rhythm disorders. Relative contraindications are epilepsy (but this has been challenged - see paper on ADHD and Epilepsy in this journal), hyperthyroidism, hypertension, glaucoma, heart rhythm disorders and anxiety disorders.

Table 2. Initial dose, duration of action, dosage frequency, usual and provisional maximum dose per stimulant drug in adults with ADHD, based on clinical experience

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial dose</th>
<th>Duration of action in hrs</th>
<th>Number of doses a day*</th>
<th>Usual maintenance dose</th>
<th>Provisional maximum dose/day</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Concerta® XL (C)</strong></td>
<td>36 mg</td>
<td>7-10</td>
<td>1 - 2</td>
<td>C 72 mg and C 36 mg</td>
<td>150 mg/day</td>
</tr>
<tr>
<td>(Extended-release methylphenidate)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Equasym® XL (E)</strong></td>
<td>30 mg</td>
<td>5-8</td>
<td>2</td>
<td>E 20 mg or 30 mg and C 72 mg or E 2x 30 mg and C 36 mg</td>
<td>150 mg/day</td>
</tr>
<tr>
<td>(Extended-release methylphenidate)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Medikinet® XL (M)</strong></td>
<td>30 mg</td>
<td>5-8</td>
<td>2</td>
<td>M 20 or 30 mg and C 72 mg or M 2x 30 mg and C 36 mg</td>
<td>150 mg/day</td>
</tr>
<tr>
<td>(Extended-release methylphenidate)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Methylphenidate</strong></td>
<td>4 x 10 mg</td>
<td>2-4</td>
<td>6 - 8</td>
<td>6 - 8x10 mg or 4x 15 mg and 2x 10 mg or 4x 20 mg and 2x 10 mg</td>
<td>150 mg/day</td>
</tr>
<tr>
<td>(Ritalin®/Medikinet®)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Standard formulation, sometimes called “immediate-release”)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dexamfetamine</strong></td>
<td>3 x 5 mg</td>
<td>4 - 5</td>
<td>3 - 4</td>
<td>3 - 4 x 7.5 -10 mg</td>
<td>75 mg/day</td>
</tr>
<tr>
<td>(Dextroamphetamine)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

* Adults have a longer wakeful day for 12-16 hours and so they may need to take the medications twice a day, for example, Concerta® XL twice a day or Equasym® XL followed by Concerta® XL or Medikinet® XL followed by Concerta® XL.

**Psychological treatment**

After psychoeducation and starting medication, coaching is provided. Coaching is an important part of the treatment. It provides the patient with support in achieving their practical goals, for example time management and finishing tasks in work or education. Spending time with the partner can also be part of the plan.

Cognitive behavioural therapy for adults with ADHD may focus on the cognitive component as well as on the acquisition of practical skills (26,27). Both coaching and cognitive behavioural therapy can be given individually or in a group. Groups have the advantage of shared recognition and offer more support to the patient. Cognitive behavioural therapy can be indicated in cases of comorbidity with anxiety or depression, for fear of failure, perfectionism, difficulties with impulse control and to increase social skills. Relationship counselling can be part of the treatment program. Finally, patients are advised to contact adult ADHD advocacy groups for support and information.
Conclusions

Adult ADHD is underdiagnosed and undertreated. It is associated with a high rate of psychiatric comorbidity. Recognition and appropriate management of both the ADHD and the comorbidity can be of great benefit.

GP comment.

What have I learned from this paper?

1. Contrary to previous beliefs, childhood ADHD often persists into adulthood and may need ongoing treatment.

2. A very simple screening instrument can be used to identify adult patients who may need further assessment for ADHD.

3. About three quarters of adults with ADHD have an additional psychiatric disorder, which may require additional management.

4. In a large proportion of cases, the symptoms of ADHD in adults will respond to the same medication that is used in children.

5. As is the case for children, the medication should form part of a comprehensive management program, which involves much more than just providing the prescriptions.

Dr Paresh Lathia, GP, Bedfordshire.

References


Setting up Adult ADHD Service in the United Kingdom

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Abstract

A high proportion of children with ADHD, around 70-80%, continue to have this condition into adulthood and the rate of comorbidity is high. The NICE (2008) guideline on attention deficit hyperactivity disorder (ADHD) recommends the development of services and/or clinics specialised in the treatment of adults with ADHD. This is a challenging endeavour in times of austerity measures. We illustrate how existing and recently started adult ADHD clinics/services can be used as models for new service development projects in the United Kingdom.

Introduction

Adult ADHD is a significant and relatively common psychiatric disorder with prevalence rates of 2-4% (1). It carries high social and economic costs for the individual and the society.

ADHD was originally thought to be a developmental disorder that resolved by late adolescence/early adulthood. However, studies, some dating back to 1960s, have consistently shown that up to 70-80%
of those diagnosed with ADHD as children continue to present with symptoms of ADHD into their adulthood (2) (also see paper by Kooij in this issue).

As is common in children with ADHD, up to 80% of adults with ADHD have psychiatric co-morbidity. Personality disorder, depression and anxiety disorder, alcohol and drug misuse are some of the common co-morbidities. Additionally, they have difficulties with poor self-esteem, anger outbursts, poor organisation and time management, mood dysregulation and sleep (3).

Untreated ADHD has serious consequences in the form of poor academic and work related outcomes, family and relationship problems and increased involvement with the criminal justice system (2,4).

Adult ADHD is still under-recognised and a number of factors have contributed towards this, including stigma in the general population and among professionals due to negative propaganda and misperception about the diagnostic validity and its treatment. Lack of awareness and training often leads to ADHD being mistaken for other common mental health problems (2).

The NICE (2008) (5) guideline was a major step forward in giving adult ADHD the recognition it deserves and set out clear standards regarding the need for services for adults with ADHD and how to set up such services. Despite this guideline, there are only a few established services available in the country. On a positive note, there is much activity taking place in many areas to develop new services.

Adults with ADHD fall into three broad groups: First, those who can be described as transition patients, i.e. being transferred from children’s services (CAMHS and Community Paediatric Services). Second, those who were known to childhood services but dropped out of follow up, either due to lack of transition/adult services or non-compliance with treatment (6). These patients are now returning to adult mental health services via primary care or other agencies. Third, there are patients who are presenting for the first time for an ADHD assessment (7).

Because of a variety of factors, adults with ADHD continue to experience difficulties in accessing appropriate services in most parts of the country. This situation persists despite NICE recommendations suggesting that if there were services developed they should be able to provide, as a minimum, a diagnostic service, psychological support and a drug monitoring service (8).

The NICE guideline makes clear recommendations for assessment and management of ADHD in all age groups, from children to adults. The guideline recommends two service models: a generic service model in which general adult psychiatrists diagnose and manage patients (within secondary care) and a specialist neurodevelopmental model, described as tertiary care model which delivers care to adults with ADHD.

**Current state of adult ADHD services in UK**

Despite NICE recommendations, there appears to be great variation in the availability of treatment and services for adults with ADHD throughout the UK.

A limited number of adult ADHD services have been established and they operate with different arrangements for funding and with different service models. Information on the following representative services was obtained from lead clinicians, published and internet sources.

The South London and Maudsley (SLAM) National Adult ADHD Service (tertiary service) was the first adult ADHD clinic in the UK and has been operating for more than 15 years. This clinic is an internationally recognised research and training centre. The National Adult ADHD Service provides comprehensive multidisciplinary assessment for ADHD in adults. Referrals are received from various sources, locally and nationally, from within the NHS and externally. After confirmation of the diagnosis, treatment recommendations are made to the referring organisation and supervision of treatment initiation and monitoring can be provided but needs to be funded by the referring team.

The Avon and Wiltshire Mental Health Partnership NHS Trust adult ADHD service (tertiary service)
was established in 2007 and covers all Bristol areas. Referrals are accepted from other areas on a spot purchase basis. It provides follow up for a period of six months or maximum one year.

The South West Yorkshire Mental Health NHS Trust (tertiary service) established a specialist adult ADHD service in April 2009, which provides a comprehensive service with a well-staffed multidisciplinary team led by a consultant psychiatrist. This service also receives referrals for funded patients from the Midlands.

The Sheffield Adult ADHD service (generic/secondary care service) is one of the first adult ADHD clinics integrated into general adult mental health services. There is an exemplary shared-care protocol, where medication is initiated in secondary care and GPs continue the prescribing once the patient’s condition is stable (8).

The Leicester Adult ADHD service offers a combined model (secondary and tertiary service). This service has been operating since 2002, initially as a special interest clinic and since January 2009 as a commissioned service. The model is based on joint work between a specialist ADHD clinic and generic general adult psychiatry team. The generic psychiatry team carries out the initial screening assessment, and all care needs including CMHT support and co-morbidities are assessed and treated by the generic psychiatry team. The adult ADHD clinic carries out the ADHD assessment and, when necessary, initiates and stabilises the treatment. Stabilized patients are gradually transferred back to their generic psychiatry teams. At a later stage, when the patients have been stable for a period, and have no unmet needs, they are discharged back to the primary care with the provision of yearly review as per the NICE guideline. Once the treatment has been stabilised, prescribing is taken over by primary care in keeping with the agreed shared-care protocol. The aim of the service model is that once appropriate training has been completed, all general adult psychiatrists will be able to carry out initial assessments and initiate and monitor treatment. The ADHD clinic will then function as a second opinion service to deal with complex cases.

The Adult ADHD Research Clinic (tertiary service) in Cambridge was funded in 2000 and has a strong academic background. This clinic is a joint venture between the Department of Psychiatry, University of Cambridge, and the regional mental health trust, Cambridgeshire & Peterborough NHS Foundation Trust (CPFT). The clinic has provided diagnostic assessments and treatment recommendations for more than 500 patients from Cambridgeshire and the rest of East Anglia. A number of senior trainees and consultants who were supervised in this clinic have opened new adult ADHD clinics in the region. Future NHS-funding of the service provided by the Adult ADHD Research Clinic in Cambridge is being negotiated.

The Lothian Adult ADHD service based at Royal Edinburgh hospital is Scotland’s first service that provides diagnostic assessments and treatments for adults with ADHD. Individuals are usually referred by their GPs or their psychiatrists and although referrals from outside Lothian area are considered, the service is primarily aimed for those in the Lothian regions.

A number of mental health trusts throughout the UK are either in the process of or are planning to establish services for adults with ADHD, including in Bedford, South Essex Partnership University NHS Foundation Trust (SEPT), through the effort of lead author (RZ).

Why do we need specialist adult ADHD services?

ADHD is one of the most common psychiatric disorders in children. As already stated, in the majority of cases the condition does not disappear on reaching adulthood and continues to cause impairment. It is important to recognise that the manifestation of many classical symptoms of childhood ADHD is altered by biological, emotional, cognitive and social changes of adulthood. In adults with ADHD, there appears to be a more prominent deficit in executive functions and self-regulation of affect, but less obvious impulsivity and hyperactivity, although the latter can be often experienced as internal restlessness.
Although the number of symptoms and their severity often reduces with age, the overall impact on psychosocial functioning can be greater due to a different set of demands faced by adults. Individuals with ADHD often face educational and occupational failures. They are more likely to misuse alcohol and suffer from substance use disorders, display antisocial and criminal behaviour and indeed face emotional and relationship difficulties. Adults with ADHD often have comorbid conditions, which include, anxiety, depression, bipolar disorder, personality disorders and other neurodevelopmental disorders, as well as, generalized and specific learning disabilities (9,2).

The current state of knowledge suggests that adult ADHD is a common psychiatric disorder with significant morbidity and co-morbidity. There are large unmet needs that are currently not being addressed by primary care and secondary mental health services. This unsatisfactory situation is improving only slowly in the current financial climate. The UK Adult ADHD Network (www.ADHD.org) has made significant contributions towards awareness, training and support of the development of services.

Effective management of adult ADHD not only requires specialised pharmacological treatment, but also non-pharmacological treatments, which include, CBT, psycho-education, counselling and other psychosocial interventions (10) (see table 1).

Table 1. Psychosocial interventions in adults with ADHD address

| • Low self esteem |
| • Poor anger management |
| • Poor social and communication skills |
| • Time management |
| • Organising, or planning activities |
| • Relationship difficulties |
| • Work/vocational difficulties |

Setting up a service for adults with ADHD

Setting up a dedicated service for adults with ADHD within the NHS has many challenges. There are a number of factors that would need to be considered when planning to develop a new service (see table 2).
Table 2. Preconditions for local / regional adult ADHD service development project in the UK:

- Willingness on part of health authority, Primary Care Trusts/Care Commissioning Groups, NHS mental health trusts and clinicians to recognise this unmet need/gap in service delivery and be willing to address it.

**Essential decisions and requirements:**

- Diversion of existing or identification of new funds
- Agreement on service model that meets local/regional needs
- Training of clinicians (psychiatrists, GPs, nurses, pharmacists etc.)

**Key requirements:**

- Development of care pathways
- Transition agreements
- Shared care agreement with general psychiatry and other sub-specialities
- Shared care protocols with primary care
- Peer supervision arrangements
- Clinical governance

**What would be the benefits of establishing a local, NHS-funded, adult ADHD service?**

As discussed above, adults with ADHD often present with co-morbid psychiatric conditions. A local NHS-funded service would be best geared to address the needs of these patients. Close links with a variety of regional agencies and stakeholders within the NHS and externally are essential. At times, patients with complex needs, during transition from children services to adult mental health services, require joint working which will be more easily achieved within a local pathway. Additionally, a local service with robust transition arrangements will help reduce the likelihood of poor transition outcomes, which remain a concern (11). New patients and their families (who provide valuable information on developmental history) will find it easier to access local services. Additionally, local services will have better access to and liaison with other local NHS services, law-enforcement agencies, prison services and voluntary agencies. It will be easier for local services to negotiate shared care arrangements with all agencies/departments involved.

Overall, a local and NHS funded Adult ADHD service is likely to play a more effective role in better diagnosis and management of adults with ADHD. It will allow continuity of care during transition (from childhood to adulthood and from secondary to primary care) and aid quicker recovery, improve morbidity; it is likely to reduce the social and economic burden on individuals and local populations that it aims to serve.

**GP Comment.**

**What Have I learned from this paper?**

1. The NICE ADHD guideline recommends service for adults with ADHD but the availability of such services in the UK is currently very patchy.
2. A well-organised adult ADHD service could greatly facilitate the coordinated care of patients.

3. Because 70-80% of children with ADHD continue to have this condition into adulthood, with a high rate of psychiatric comorbidity, the provision of adult ADHD services is an important issue.

4. Reading this paper raised several issues for me as a GP, including the following.

• How many cases of adult ADHD go unrecognised?
• What training is needed in primary care to enable us to recognise and assist such patients?
• Where should we refer such patients for secondary care?
• What would be the best model for a locality service – should each district have a separate centre or should there be a “hub-and-spoke” model with links to a centre of excellence?
• What would be the best way of coordinating the adult services with the child and adolescent services for ADHD and how should education/probation and prison services be involved?

Dr Morgan Walters, GP De Parys Surgery, Bedford

References


Living with a child who has ADHD and special needs - a parent’s perspective

Mrs Deborah Townson, author.

“He’s just got Character!”

That’s what my husband used to say to me when I rang him at work for some much needed adult conversation and support after another exhausting day with our son Jake.

Jake is now nearly 12 years old and has still got bags full of what we call character. He was born just before Christmas 1999 after a difficult pregnancy and birth but was average weight and healthy. Specialists have since stated to us that a difficult pregnancy can play a part in your child’s development and I sometimes wonder if injecting myself every day with heparin (due to having lupus) had any bearing on Jake’s development. We were also told that genetics play a part and my family medical history is certainly colourful. My mum was sent away as a child several times to convalesce and was put on tranquillizers because of a diagnosis of St. Vitus dance, a condition involving involuntary movements. In addition, my sister, my cousin and I had what were called ‘funny habits’ as children. I believe we all have some traits of the things that Jacob has since been diagnosed with.

Jake was diagnosed at the age of 5 with ADHD, OCD, Tourette syndrome, dyspraxia, autism, tip-toe walking (gait and tendon problems) and neurodevelopmental delay. I still remember the day my husband and I walked out of the consultant’s office both stunned and speechless. We knew that Jacob was different and quirky but when someone actually labels your child and tells you that they will not be able to do certain things in their life that is a different matter. It then becomes real in some way and you feel like you have lost your child and he has suddenly become someone different that you do not now know. I remember talking, discussing and worrying over the same questions for days; we felt like our whole lives had changed just because of a few words a consultant had uttered that day. My husband buried his head in the sand and I became the practical one, researching everything on the internet. In the end, however, after talking to various specialists, other parents and various support groups and associations, you realize that you have to deal with the issues you face yourself. Talking to other parents, which is the best medicine ever, helps you focus on the fact that every child is different even if they are diagnosed with the same condition; your child is still an individual. You and only you have to find your own individual way of helping and guiding your own child through their milestones in life. What works for Jacob might not work for another child. You can certainly exchange helpful tips and tried and tested methods from other parents and give them a go but in the end some things may work and not others. In fact, some things may work on some days and not others. That is a big point to make. You think you have found a solution to a particular issue then the next day that solution sends Jacob into a rage or an emotional wreck. We have found, to our detriment on many occasions, that bribery, not reward charts are a great tool to use, even if it does cost us a fortune!

Within the first couple of years of Jake’s life we knew that there was something different and quirky about him. I was a stay-at-home mum and it was exhausting, challenging but also rewarding on a daily basis looking after Jake. He never slept during the day, I remember driving or walking around for hours. He never liked to lie down or just sit. He wanted to be picked up or held all of the time. My hips would be aching by the end of the day! To this day Jake has never fallen asleep on the sofa in front of the television like other children and, apart from the times when he had measles and chickenpox, he has never slept during the day in his whole 12 years. He also never sleeps on car journeys. We have travelled to France and Scotland in the car and he was awake the whole time. Again this is very draining and stressful as you need to make sure you have enough things to entertain Jake for the whole journey but more importantly 9-10 hours of Jake talking, singing and tapping is very draining! When Jake has been ill or just overtired due to recurring bad nights or general lack of sleep he never catches up and gets very stressed and irritable. This is when he becomes uncontrollable with either outbursts of rage or emotion. He has damaged doors in the house and broken items and toys in these outbursts. He is so frustrated and upset with himself afterwards for doing it, he has often asked: “Why do I do this?”
It would also take Jake ages to settle at night. As a baby we would be stroking him for hours and as he has got older he would often say that he felt ‘weird’ and could not explain how he felt. This then led to endless talking and calming down. He would also wake several times during the night, and still does, again saying he feels weird or with pains in his legs. He has tight tendons and foot problems, sees an Orthotic Consultant and has physiotherapy for this but his sleep problems mean that my husband and I both feel like zombies most of the time; it's surprising we are still together!

Jake's appetite has always been very poor. As a baby it would take him twice as long to finish a bottle. Weaning was a nightmare. He would sit for hours in his high chair just pushing the food around or plastering the walls with it! He just grazed on little 'picky bits' as we called them. We developed a system, as he got older, that we called 'play and eat'. Jake would never sit still at the table so we would put food on a plate on the table and he would take a bite then go and play then return etc. This was the only way we could get him to eat as he was always too busy and too interested in moving to eat. Where he got his everlasting energy from we did not know and still don't to this day. We often compare him to the Duracell bunny! This obviously made it difficult to go out as a family or to places where people did not know us and Jake. He was always very active and into everything right from the word go. He was a very inquisitive baby and was walking by 10 months. He talked very early and everyone commented on his speech. In fact, the incessant non-stop talking drives you to distraction and still does today, along with his need to either be singing, pawing all over you or tapping or banging on something. We have since brought Jake a set of drums so that his banging and tapping can be channelled, hopefully into something constructive!

I met up with my ante-natal group on a weekly basis with our babies and started to compare Jake with the others. What a fatal mistake that was! Jake would never just lie under his baby gym, sit still or sleep in my arms like my friends' babies did. He would be wandering around the house looking in cupboards, eating cat food, running up and down stairs or just doing his usual talking. He would never leave your side. I remember frequently having to go to the toilet with him on my lap. If I got the chance to take a shower he would be in the bathroom with me. This separation anxiety has got worse as Jake has got older. It started with him hanging onto my legs when we first tried playgroup and school. It took weeks for him to settle and he still has issues at the start of every new term. Now it has got to the point of his not wanting to go into a different room or up the stairs without me. He will not go to the local shop on his own or with friends; he will not even go into a shop on his own if I am not with him. He will not stay in a car on his own whilst I fill up with petrol, let me post a letter or run into a shop without him, even if he has a friend in the car with him. This again obviously puts great demands on trying to complete even the simplest of tasks.

Jake has never been good at playing on his own. He constantly wants my attention and company and I have to do everything with him. This has consequently meant that is has been difficult to have a conversation with other people or do household tasks if I am on my own with him. As Jake has got older this has had more of an impact when trying to teach him to be independent as projects for school, homework, even washing, dressing, brushing teeth and normal day to day activities have to be done with one of us. Jake cannot tackle a task without that level of support, which makes life very stressful and demanding at all times. Jake receives a lot of emotional and practical support whilst in school and together we try to work on strategies that will help him try to become more independent. However, he does have a lot of issues to contend with, so again this is an ongoing project. Jake is also not good at making friends and has never approached others in play or for company. As parents, we have always had to instigate this on his behalf. Due to his anxieties about almost everything, he lacks confidence and self-esteem, needing constant reassurance and praise. Luckily Jake has built up a good group of friends since playgroup, who accept him for who he is. He is a kind and caring boy with a sensitive nature. He cannot see the bad in anyone and cannot understand when anyone is nasty to him. This obviously has its problems as he is very trusting of people and lives in a world where he thinks everything is safe and just. His sense of fair play has been evident since early on and, although he has his issues, he has been compassionate towards others who also have difficulties.

As well as Jake's hyperactivity, his little quirks and habits were also evident at an early stage. Jake easily becomes obsessed with anything and once a habit sets in you cannot get out of it. He could not and
still cannot go anywhere or to bed without his numerous toys or objects, especially his “sad tissues” (tissues that have been used if he is upset). He surrounds himself in bed with these objects and when we go out or away on holiday, he has certain rituals that have to be completed at bedtime and when getting dressed. These have to continue wherever we are. Again, no respite! When he was a toddler he used to sit in the washing basket or in cardboard boxes with this stuff and pretend to be an animal or some sort of creature. He has a vivid imagination. At parents evening, his first teacher mentioned to us that Jake had an extraordinary imagination as when all the children were asked to name their favourite animal the others mentioned cats and dogs Jake replied his favourite was a chameleon! He has favourite even numbers; odd numbers are the work of the devil! He likes objects to be in a certain positions. Again this causes him problems at school with concentration in lessons and when trying to complete day-to-day tasks.

He has had various tics since early on, from spitting, excessive nose-blowing to the point of bad nose bleeds, constant coughing (we had some comments made to us once whilst in a theatre - “Can’t you shut that child up”), head-shaking resulting in bad headaches, coprolalia, pulling at clothes, scratching and making himself bleed, looking up at the sun to the extent that we had to take him to the opticians who prescribed reactive glasses, eye-blinking, clothes-pulling and the list could go on! These tics, for Jake, can make normal everyday tasks difficult but more importantly it’s about social acceptance. We try to come up with strategies to divert attention away from Jake’s current tic of the time. We just try to encourage him to talk about how it makes him feel and laugh about it together. Otherwise we would constantly end up crying about it.

I think overall the best piece of advice we could give any parent facing the diagnosis of any disability is to join as many support groups and associations as you can. Parents that have already experienced and been through what you are about to encounter are your saviours. They know exactly what you are talking about and will know how to point you in the right direction for help. Obviously you need to seek advice from specialists and make sure your communication with school is constant but nobody knows your child like you do and you need to come up with your own strategies that work for you. It is hard work and can be tiring and frustrating. Parents need more of a voice when it comes to legislation with regard to children with disabilities. We are the ones that live with them 24 hours a day and I often say I am going to video a day in our life just so other people can see how demanding it can actually be. Life with Jake continues to be demanding and sometimes very frustrating but it is also very rewarding. He is our son and we would not change him for the world.

GP Comment.

What have I learned from this paper?

This is a moving and very personal account of what it is like to live with a child who has not only ADHD but other special needs.

The paper raises several issues for the GP. These include the following.

1. The doctor and professional team not only have the task of providing a diagnosis, they also need to face the challenge of supporting the family with the implications of the diagnosis.

2. There has often been a delay before professionals have made a diagnosis of ADHD, despite families continually asserting that there was something wrong with the child.

3. Although it would be unwise to generalise, it is not unusual for fathers to be in denial with regard to ADHD or other special needs and for the mother to be left with the task of coping with the demands.

4. The sleep disturbance that often accompanies ADHD affects not only the child but the whole family. The comment of Jake’s mother that she and her husband “both feel like zombies most of the time” was very telling.
5. The emphasis on the importance of parents identifying sources of support seems very appropriate.

6. The lack of understanding that other people often have of ADHD can be very hurtful for parents, especially when inappropriate comments are made.

7. Above all, it is an inspiration to see how parents can continue to love a child despite the extraordinary demands that he places on them; this makes us very aware that, as professionals, we must endeavour to understand the extent of the pressures that are placed on families and that we must do whatever we can to support them.

Dr Murari Agrawal, GP, Bedfordshire.
ADHD: A GP’s Perspective

Dr John Kedward, General Practitioner, London Road Surgery, Bedford

Abstract

Good communication between the GP and specialist secondary care services is essential in the management of children and adults with ADHD. The NICE recommendations have clarified what is required for treatment and management. This is far broader than simply prescribing medication. The GP may be well placed to appreciate the wider social context. The general practitioner should provide a six-monthly review of all children treated for ADHD and should communicate any concerns to the secondary care team promptly.

The NICE recommendations for comprehensive assessment (assessment of the person’s needs, coexisting conditions, social, familial and educational or occupational circumstances and physical health; and an assessment of their parents’ or carers’ mental health) and other treatment options (referral to a parent-training/education programme as the first-line treatment) goes some way towards allaying the concerns that many GPs have had about ADHD and its treatment.

For many GPs, with their detailed knowledge of the wider social and family issues for these children, there is a concern that these issues are not addressed if it is easier to treat the child with medication.

What is undoubtedly true is that children who are accurately diagnosed using the appropriate criteria generally respond well to treatment with methylphenidate, resulting in far fewer problems at school and at home.

The key to the successful support of children with ADHD and their families, is a secondary care service that is able fully to implement the NICE recommendations, that establishes good communication and liaison with GP practices and has an agreed local shared-care protocol for monitoring and treatment in primary care. For a comprehensive approach to work well, there needs to be good access to parent-training/education programmes, cognitive behavioural therapy and social-skills training for the child or young person.

A GP practice should aim to see all children treated for ADHD in secondary care every six months, with a brief physical examination and medication review. Using a shared-care protocol information can be sent back to secondary care, which supports the ongoing monitoring and treatment.

An adult-based ADHD service is now required to manage the increasing number of children reaching the age of eighteen for whom it is felt necessary to continue treatment. Many areas will now have commissioned adult ADHD services to provide ongoing care.

GP Comment.

What have I learned from this paper?

1. General practitioners are well placed to have knowledge and understanding of the wider social and family issues surrounding the individual who has ADHD.

2. Good ADHD management requires good communication between the GP and secondary care, which is not always easy to establish.

3. The realisation that many children with ADHD continue to have this condition into adulthood can present new challenges for the GP with regard to transition arrangements and adult services, both of which may be poorly developed.

Dr Subash Kanungo, GP, Bedfordshire.
Future Directions for Research and Management of ADHD

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Abstract

Clinicians have been aware of the problems of overactivity and inattention for over 200 years and many advances have been made in this time. However, ADHD remains a very common and challenging condition that does not always respond well to treatment. Some of the areas of research that might prove fruitful in terms of future management include pharmacogenetics, better definition of ADHD subtypes, ADHD across the age range from preschool children to the elderly, the role of health psychology, ADHD in the presence of other conditions such as autism, bulimia or personality disorder, intervention strategies using computers and a focus on emotional dysregulation. The aim of research into these and other areas will be to provide better management of people of all ages with ADHD in the future.

Introduction

While the disorder has not always been called ADHD, the history of the clinical syndrome of inattention and overactivity dates back over 200 years beginning with Melchior Adam Weickhard in Germany in 1770 (1) and in the U.S. by Alexander Crichton in 1798 (2). In the last 200 years since these early descriptions, much has been learned about ADHD, leading to important advances in the diagnosis and management of this common psychiatric disorder. Despite this progress, there is still much we do not know about this condition. The purpose of this paper is to outline several potential areas of clinical and research endeavour that may hold merit for improving the lives of individuals with ADHD.

Pharmacogenetics

One of the more recent advances has been the tremendous explosion of technology permitting improvements in our understanding of genetic mechanisms in ADHD. In the light of the finding that 60-80% of the ADHD behavioural phenotype variance is due to genetic factors (3), the field of pharmacogenetics represents an opportunity to improve medication response rates by using individual candidate genes and genetic polymorphism information to predict individual response. For example, knowing that an individual has a specific gene variant which affects receptor or transporter activity or metabolizing enzymes might help to inform prescribing practice to minimize adverse effects and improve outcomes. This is currently a long way from being standard clinical practice, yet a clear future direction for ADHD research is investigating candidate genes, gene-gene interactions and effect modifications by environmental stimuli. All of these may be related to medication response rates and may even result in the development of new medications. The potential clinical utility of this research is strong and eventually prescribing physicians may have treatment efficacy and adverse effect prediction algorithms based on individual genotyping to guide prescribing practice.
The validity of the DSM-IV ADHD subtypes

Another future direction for research which may hold merit is investigating the validity of ADHD subtypes. Classifying ADHD is clinically and scientifically important, with ongoing discussion on how best to reflect this in DSM-V (to be published in 2013). DSM-IV includes three subtypes: primarily inattentive, primarily hyperactive / impulsive and combined (4). Conversely, Europeans using the International Statistical Classification of Diseases, 10th Revision (ICD-10) do not distinguish subtypes. Previous research, much of it inconclusive, has focused on differentiating the Inattentive and Combined subtypes, with mixed success (5-7). For example, existing family data provide only weak evidence of discriminant validity between the DSM-IV Inattentive and Combined subtypes (8). The subtypes are also unstable over development and are cross-contaminated, in part due to age effects. Molecular genetics may hold more promise for determining whether the subtypes are distinct (as outlined in the DSM-IV) or are better represented as a continuum trait (like hypertension). One approach to subtyping having some merit is distinguishing individuals with sluggish cognitive tempo (SCT) from those with ADHD. SCT is characterized by slow processing of information, staring, daydreaming, mental fogginess or confusion, lethargy, and hypoactivity. Recent evidence suggests that SCT is a distinct disorder from ADHD yet may overlap with it in up to half of all cases (9).

ADHD in the age ‘extremes’ (preschool, elderly)

Although ADHD was long considered to be only relevant to children (10), in the past 30 years longitudinal evidence has accumulated, suggesting that ADHD often persists into adulthood (11-13). Much of what we know about ADHD in adulthood relates to young adults. There is less information on middle-aged adults and far less data on ADHD in old age / geriatric populations. Given our aging population, far more research should focus on ADHD in the context of middle and old age. Are treatments as effective? What types of psychiatric comorbidity are there? What is the relationship between ADHD and cognitive decline? These are all questions that currently remain unanswered. Similarly, because of increased recognition and awareness, more preschool children are being diagnosed with ADHD and treated with stimulants, for example the Preschool ADHD Treatment Study (PATS) (14). While there is some evidence that standard child pharmacological (15) and psychosocial interventions (16) are effective, far less is known about treatment outcomes in the preschool population compared with what is known about older children.

Health Psychology

Traditional research and clinical domains of health psychology such as quality of life, treatment adherence, obesity, cardiovascular disease, stress, etc. have not received much research attention in relationship to ADHD, although evidence shows that ADHD contributes to these and other health risks (11). These domains all go well beyond simple ADHD symptoms and speak to the need to focus not only on symptom reduction but also functional improvement. For example, it might be anticipated that ADHD symptom reduction would be strongly associated with quality of life improvement. However, this is not always the case (17). Furthermore, if stimulant medications are effective at reducing ADHD symptoms, it might be anticipated that treatment adherence would be high. This too is not always the case (18). Inadequate adherence to treatment is not unique to ADHD; poor treatment adherence has been documented for a variety of serious medical diseases and mental health disorders, such as HIV and schizophrenia (19, 20). Individuals with ADHD may experience forgetfulness and disorganization as part of their condition. These symptoms may make it difficult for an individual to adhere to their medication as prescribed (21). Further strategies to improve treatment adherence are greatly needed.
ADHD in the context of autism spectrum disorders, bulimia, borderline personality disorder

While much is known about ADHD that is comorbid with anxiety, mood disorder, substance misuse and disruptive behavioural disorders, far less is known about ADHD in the context of other disorders which can be characterized by impulsivity, for example autism spectrum disorder (22), bulimia (23) and borderline personality disorder (24). Is ADHD a risk factor for developing bulimia as recent evidence (25) suggests, or for a subtype of borderline personality disorder (26)? How does comorbid ADHD affect treatment outcome in these subgroups?

Computerized remediation interventions

Many parents of children with ADHD anecdotally report that their child is “addicted” to video games and/or the computer. Recent evidence supports these reports (27). It is consequently not surprising that some researchers have assessed the utility of computerized interventions towards reducing ADHD symptoms (28, 29). However, far more research is needed before any firm conclusions can be reached about whether computerized interventions might represent a viable treatment option. In particular, research assessing the efficacy of computerized interventions for teaching academic skills is a particular area of research need.

Emotional dysregulation

Much previous research has focused on the cognitive aspects of ADHD. A clear research need is to focus more on the emotional aspects of ADHD, specifically emotional dysregulation. A few studies have directly assessed emotional dysregulation (30, 31) in ADHD but these have been largely descriptive and have focused exclusively on boys. More recent studies do suggest that impulsive emotion and poor emotional self-regulation are closely linked to ADHD symptoms and are specifically predictive of various impairments beyond ADHD symptoms alone (32). More research addressing emotional dysregulation across the lifespan, in females with ADHD and how best to intervene is clearly needed.

Conclusions

While much has been learned about ADHD over the past 200 years, there is still a great deal that we do not yet fully understand. A number of areas of investigation that might prove fruitful in terms of guiding the future management of this challenging condition over the lifespan have been discussed but these only serve to underline the fact that there are still many uncertainties about ADHD and a great need for further research.

GP Comment.

What have I learned from this paper?

Potential future advances that might improve the management of ADHD include the following.

1. Genotyping to guide the prescription of medication for ADHD and subtypes.

2. Gaining a greater understanding of the subtypes of ADHD and what the implications of these might be.

3. The recognition that ADHD might affect not only school-age children, teenagers and young adults but also pre-school children and the elderly.

4. Developments in non-medical strategies to improve the life of people with ADHD
5. Development of a greater understanding of the relationships between ADHD and comorbidities, including autism spectrum disorder.

6. Because some children with ADHD are very attracted to computer games, exploring the possibility of using these therapeutically.

7. The development of improved strategies for managing the disinhibition and emotional dysregulation that are often a very troublesome aspect of ADHD.

As a general practitioner, it is interesting for me to know what the future advances in the understanding and management of ADHD might be but I wonder whether further research on behavioural strategies and social manipulation might be just as valuable in bringing benefit to the lives of the patients with ADHD and their families as the “high-tech” advances. Perhaps one of the more feasible suggested advances might be the use of computers to teach and reinforce self-regulation strategies.

Sarah Griffith, GP, Shefford Health Centre, Bedfordshire.

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1. Concerta® XL 27 mg Summary of Product Characteristics, June 2011
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