Attention deficit hyperactivity disorder — a review

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SUMMARY

The topic of attention deficit hyperactivity disorder (ADHD) is fascinating and controversial. A variety of stances have been taken by different clinicians, support groups, and the media. A nature/nurture argument has developed that may have a tendency to polarize views. This review aims to present research findings that inform the debate. It deals with symptomatology, aetiology, and prevalence, with assessment for diagnosis, management, and outcome. The importance of comprehensive management taking into consideration not just attention abilities but a range of other factors that have an impact upon them is stressed. Management should be pragmatic, multifaceted, and based around the establishment of good working relationships with family and school.

Keywords: attention difficulties; attention deficit hyperactivity disorder; hyperkinetic disorder; children.

Introduction

AS early as 1902, a group of restless children was described with 'abnormal incapacity for sustained attention' and deficits in 'volitional inhibition'.[1] In 1937, it was discovered that amphetamine could reduce levels of hyperactivity and behavioural difficulties.[2] Although the term 'minimal brain damage' (MBD) was often applied to children with these symptoms in the 1950s, there was no evidence of neurological dysfunction in most cases. By 1960, the emphasis shifted from the 'unknown' biological basis of the disorder to the 'known' behavioural expression of the symptoms and the labels attention deficit disorder (ADD) and attention deficit hyperactivity disorder (ADHD). The symptoms, impulsiveness, and inattention in ADD (and also over-activity in ADHD) became the syndrome.[3] There is an ongoing debate about whether ADHD is a continuum representing a risk factor for future adversity or whether it is a discrete disorder.[4]

The symptoms and their weighting have altered with each new diagnostic system, and we have now reached a situation where ICD-10 (the World Health Organization diagnostic system) describes Hyperkinetic Disorder and DSM-IV (the American Medical Association system) describes Attention Deficit Hyperactivity Disorder (ADHD), and these are very similar to each other. Recent research focuses on cognitive processing, genetic factors, brain function abnormalities, and the significance of comorbidity in ADHD.[5]

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Classification

The core symptoms of ADHD are poor ability to sustain attention, impulsivity, and overactivity.[6,7] However, there are long standing differences between clinicians that some have suggested illustrate a dichotomy between Europe and other countries such as North America, Australia, and South Africa. These revolve around the severity required for diagnosis and the constellation of symptoms (and previously the pervasiveness), resulting in higher rates of diagnosis in some places than in others. These differences are being resolved, at least diagnostically, but there is still a wide variation in the clinical use of medication,[8,9] although this involves individual clinicians within countries as well as differences between countries.

ICD-10 and DSM-IV criteria for attention deficit hyperactivity disorder (ADHD)

Both ICD-10[6] and DSM-IV[7] criteria require symptoms of ADHD to be:

- pervasive; that is, symptoms must occur in two or more settings (e.g. home and school),
- present before the age of seven,
- persistent for more than six months,
- out of keeping with developmental level,
- maladaptive, and
- significantly impairing social, academic, or occupational functioning.

ICD-10 criteria ADHD

ICD-10 criteria for hyperkinetic disorder with disturbance of activity and attention are that there are six of the following symptoms of inattention for at least six months:

A. Attention problems
- poor attention to detail/careless errors,
- often fails to concentrate on tasks or play,
- often appears not to listen,
- often fails to finish things (but not for developmental or oppositional reasons),
- poor task organization,
- often avoids tasks which require sustained mental effort,
- often loses things for tasks,
- often distracted by external stimuli,
- often forgetful.

And three of the following disturbances of motor activity for at least six months:

B. Hyperactivity problems
- often fidgets or squirms on seat,
- often leaves seat when expected to sit,
- excessive inappropriate running or climbing,
- often noisy/difficulty being quiet,
- persistent overactivity not modulated by request or context.

And one of the following symptoms of impulsiveness for at least six months:

C. Impulsiveness problems
- often blurts out answers before the question is complete,
- often fails to wait turn in groups, games, or queues,
- often intrudes into games or conversations,
- often talks excessively without response to social appropriateness.

DSM-IV ADHD

DSM-IV uses exactly the same symptoms, but differs from ICD-10 in the way that it operationalizes them to achieve diagnoses. Six symptoms from box A (attention problems) are required to be present (as with ICD-10), but it amalgamates hyperactivity and impulsiveness (boxes B and C) and requires six symptoms in total from these to be present (i.e. different from ICD-10). It allows diagnoses to be made if *either* of these two strands is present. In this way three diagnoses are possible:

1. ADHD combined type (inattention *and* hyperactivity/impulsiveness criteria met),
2. ADHD predominately inattention (six of the symptoms for inattention but does not require that the criteria are met for hyperactivity/impulsiveness), and
3. ADHD predominately hyperactivity (six of the symptoms for hyperactivity/impulsiveness but does not require that the criteria are met for inattention).

The way that the disorders and associated difficulties have been conceptualized and organized has changed over the years. As a result, both the names given to the disorders and the criteria to merit any specific diagnosis have changed. Consequently, some of the research is not strictly comparable because different diagnostic criteria were used.

In terms of the diagnostic schedules, ICD-10 criteria probably define a more severe group of children than DSM-IV, with impulsiveness as well as overactivity and attention problems. However, the rest of this review will use the term ADHD (the most popular term) to include diagnoses of ADHD or hyperkinetic disorder.

Aetiology

A difficult issue with respect to aetiology centres around the nature (genetics)/nurture (environment) debate. It can be very difficult to tease out the influences of one or the other. It therefore becomes necessary to consider the various aetiological associations that have been proposed in the literature under the following headings.

Genetics

There are studies showing higher rates of ADHD and behaviour problems in relatives of sufferers,[10,11] although this does not necessarily prove genetic linkage. However, studies of twins show high rates of inheritance, supporting the importance of genetics.[12-14] Some children have an underlying language disorder,[15] while some have inherited cognitive difficulties including a tendency to respond impulsively, difficulties with sustaining and shifting attention, and with planning.[12] Although there is still some debate about this, most researchers agree that ADHD has a hereditary component. Whether this is a predisposition that interacts with the environment, a definite single biological dysfunction, a polygenic phenomena leading to a continuum of difficulty within the population, or a heterogeneous group with sub-groups within it remains to be seen. Given the evidence in this review, it is very unlikely to be one single biological dysfunction or one single gene that is responsible for ADHD as we now know it.

Structural brain damage

Striking similarities have been noticed in behaviour problems between children with ADHD and people who had suffered injury to the frontal lobes of the brain. Relatively new scanning techniques, such as SPECT (single photon emission computed tomography) and PET (positron emission tomography), are able to indicate the areas that are being relatively under- or overused. Areas implicated by studies showing apparent underuse include the caudate neulei/subcortical striatum, the prefrontal and frontal areas, the limbic system, the posterior periventricular regions, and the corpus callosum.[5,16-21]

Some have questioned whether these findings mean that these areas of the brain are abnormal, leading to attention and other problems, or whether attention problems (whatever their cause) lead to the differential glucose utilization in these parts of the brain.[22] The direction of the effect is important.

One year after suffering a closed head injury, almost 40% of children met DSM-III R criteria for ADHD, and, on retrospective analysis, only half of these did so before the trauma.[23] If substantiated, this implies that structural head injury may lead to symptoms of ADHD (particularly where psychosocial adversity is present),[23] but also, interestingly, that children with ADHD may be more likely to put themselves in situations where they suffer head injury.

Some have sought to link some of the structural findings to function, such as the ability to control and direct what we attend to, suggesting that a filter, allowing important information in and keeping interfering information out, may be dysfunctional.[24] Some hypothesize that abnormalities may be related to a dysfunctional inhibitory control system,[25] which is markedly similar to the effects of closed head injury.[23]

Brain receptor sites

There have been studies that show that some receptor sites in the brain may have certain configurations that are more common in this group of children than in the remainder of the population. The genes coding for dopamine receptors, such as the D4 site,[26] are implicated, and research is ongoing into other dopamine receptor sites. The fact that the main neurotransmitters affected by methylphenidate are dopamine and noradrenaline[27,28] lends support to the importance of dopamine receptors. Since stimulants have an effect on the dopaminergic pathways, many have postulated that methylphenidate's action is mediated here.[24]

Thyroid function

Up to 5% of children with ADHD may have abnormal thyroid function,[29] although the significance of this is unclear since other studies have not found such high rates.[30]

Birth experiences

When very low birthweight children were compared with healthy controls at the age of 12, 23% of them met the criteria for ADHD against 6% of their peers.[31]

Early life experiences

Studies looking at children brought up in institutions found significantly higher than expected rates of impulsiveness and attention problems.[32]

Parenting and parental mental health

Children with ADHD are more likely to have a parent with a history of ADHD,[33] although it should be noted that a parent is integral to both nature and nurture. Within the home environment, parenting styles, psychosocial support, socioeconomic status, and parental psychopathology have been identified as significant.[34]

With respect to parenting style, parents of hyperactive children have been observed to be more directive and give more frequent commands, reprimands, and corrections. They are also reported as giving fewer rewards for compliance and to attend less to appropriate behaviours than parents with children without these difficulties. Furthermore, mothers who rewarded their children less and controlled them more were associated with conduct disorder and ADHD together compared with normal children or children with ADHD alone.[35] Critical parenting and limited parenting skills have been shown to be associated with hyperactivity, even when controlling for conduct disorder symptoms.[36]

With respect to home environment, there is a suggestion that children who have not experienced a home that has promoted, fostered, or modelled attention skills (e.g. very chaotic home lives), may be more likely to display attention difficulties at school.[37] Hyperactivity is associated with families where there is marital disharmony,[38] family dysfunction,[39] and where there is overt hostility between child and parent.[40,41] However, we should be cautious given that any particular style of parenting may have developed partly in response to their child's behaviour[34] as well as being influential in it. We should always consider the direction of such associations (and the fact that there is often comorbid conduct disorder), and we should acknowledge that associations are probably best understood dynamically rather than in a linear way.

Parental mental health is an important factor in a child's development. Nigg and Hinshaw[33] showed that there was a much higher rate of maternal depression in the year previous to diagnosis than in a comparison group confirming previous findings of associations between maternal depression and symptoms of ADHD.[42,43]

Other psychosocial factors

In later life, the symptoms of ADHD may be exacerbated by adverse social factors.[44] A study of the effect of social factors on the development of ADHD found higher scores on a social adversity scale were related to increased ADHD symptoms and to the presence of the comorbid symptoms of depression and anxiety.[45] Interestingly, children with higher levels of psychosocial adversity were more likely to develop symptoms of ADHD (using DSM-III R criteria) after head injury than children without.[23]

In just the same way that it is acknowledged that factors affecting parenting behaviour and style may be both heritable and environmental,[46] we should not be surprised to find that childhood behaviour is as well.

Prevalence

The symptoms required to make the diagnosis are behavioural and therefore subjectively judged, and will in part be dependent on factors such as the experience the observer has with the child, the behaviour of the child on assessment days or across different situations. It will also depend on the information provided by other observers who may have different perceptions about what is normal and what is abnormal. Hence, studies have found that those receiving a diagnosis may not be a homogenous group. For example, one study looking at children on treatment for ADHD in two general hospitals found that only half of those being treated with medication met the DSM-IV diagnostic criteria.[47]

The rates quoted for how many children suffer from ADHD are very variable, and some studies suggest that as high as 17% of children are sufferers.[48] Rates depend on the diagnostic criteria being used and who applies them (this study was in a sample of boys aged 10 to 13 years using DSM-III R criteria). The tighter World Health Organization diagnostic schedules (ICD-10) put the rate at 0.5% to 1% of the total child population.[49] DSM-IV criteria produce a higher rate (approximately 5%).

Boys are five to nine times more likely to be affected with ADHD than girls. It is possible that girls have previously been under-identified and undertreated because ADHD girls are less likely to show behavioural problems,[50] and the drive for referral may therefore be lower. Girls are also more likely to show cognitive impairment, depression, and low self-esteem when compared with boys suffering from ADHD.[51]

Children with inattention but not overactivity appear to be a different group from those with ADHD. They are characterized as suffering from anxiety more and they are more likely to be quiet and introverted.[52] This group is more likely to have learning difficulties[36,53] and come from a household with lower socioeconomic status.[36] They are far less likely to be at risk in the same way as the children with ADHD, particularly for behaviour disorders and comorbid psychiatric disorder,[17] and the natural history and prognosis is probably different.

Difficulties with diagnosis

There is no current acceptable biological measure of ADHD.[34] ADHD therefore tends to be measured by behavioural symptoms.[37,54] This can be problematic in that:

- Many other disorders can be mistaken for ADHD owing to the similarities in behavioural presentation. For example, poor attention can be caused by hearing difficulties; seizures; drugs; trauma; head injury; autism; neurobiological illnesses (e.g. Hurler's Syndrome, Hunter's Syndrome, Fragile X); language disorders; specific learning disabilities; infections; anaemia; poor nutrition; insufficient sleep; inappropriate educational provision; multiple rejections; repeated traumatic experiences; and abusive, disruptive, or chaotic home circumstances.
- Children can have ADHD *and* other disorders. Between 50% and 80% of children with ADHD meet the diagnostic criteria for other disorders.[10] The research shows that many children with a diagnosis of ADHD or ADD also suffer from anxiety (around 25%),[51] depression (15% to 20%),[42] and specific learning disabilities (20%).[42] Conduct disorder and oppositional defiant disorder are commonly associated with ADHD (between 40% and 90%),[55,56] and include antisocial activity[44] as well as aggression and rule-breaking.[44,57] Different rates of comorbidity are found in different settings. Taylor believes that ADHD puts children at risk of suffering other problems, perhaps because ADHD children cannot meet the expectations of family, peers, and teachers, resulting in social, educational, and psychological problems for the child.[4] These factors often result in a complex differential diagnosis.
- The scoring of assessment tools such as questionnaires can be heavily influenced by disruptive behaviour.[58]
- It is often difficult to assess the degree to which social factors and/or ADHD and/or other disorders contribute to the behaviours manifested by children.

Diagnosis and assessment

It is perhaps too easy to apply the label attention deficit hyperac-

tivity disorder when problems with attention are present, and it is a more difficult task to elucidate the nature of the problems with attention and closely explore other physical, emotional, and social factors that impact upon attention. In this sense, diagnosis is complicated, and so assessment should be as thorough as possible. The diagnostic interviews should include the following:

- An interview with parents to establish the child's developmental history, family history, presenting problems, and other relevant information, including systematic information about the presence or absence of diagnostic criteria.
- Reports from and discussion with teachers, including systematic information about the presence or absence of diagnostic criteria and special educational needs.
- Rating scales and checklists used by clinicians. There are many, but examples include the 'strengths and difficulties' questionnaire,[59] Achenbach's child behaviour checklist,[60] Conners' parent and teacher's rating scales,[61] Rutter's parent[62] and teacher[63] scales, and the Barkley and Du Paul ADHD rating scale.[64]
- Observation of the child.
- Medical evaluation to exclude physical causes of attention or activity problems.
- Cognitive testing is not usually performed routinely, but can be useful in the evaluation of specific difficulties.

The difficulties in assessment and treatment have prompted some to have multi-disciplinary or even multi-agency teams to facilitate the process.[65,66]

Treatment

The debate about treatment options can be as contentious as those surrounding aetiology and diagnosis. Educational interventions, behavioural interventions, and medication are the three main groups of treatment. Adjunctive therapies include social skills training, family work, and cognitive therapy.

Gordon[67] quotes five core needs with respect to psychosocial treatment of children with ADHD. Namely:

1. Clearly specified rules, expectations, and instructions;
2. Frequent, immediate, and consistent feedback on behaviour and redirection to task;
3. Reasonable and meaningful consequences for both compliance and non compliance;
4. A package of adult interventions designed to compensate for the child's distractibility, limited organizational skills, and low frustration tolerance; and
5. A well-integrated and functioning system of parents, teachers, administrators, and clinicians who communicate often and work together to create a structured and supportive environment.

Behavioural approaches

There is no doubt that behavioural interventions can produce short-term benefits in children with ADHD.[68] Fior, Becker, and Nero reviewed 150 largely non-pharmacological intervention studies.[69] Although the evidence remains contradictory, the following interventions seemed the most useful: positive reinforcement, reprimands and redirection, response costs, parent or family training, self-instruction/cognitive behaviour training, and task or environmental stimulation/biofeedback. Behavioural treatment approaches have been shown to be effective in improving on-task behaviour,[70] reducing aggression,[71] and improving short-term academic and behavioural performance.[72] However, despite improvement in outcome targets, Abikoff and Gittleman found that the primary symptoms of attention, impulsivity, and activity remained largely unchanged after an eight-week behavioural programme for ADHD children,[71] suggesting that programmes need to be for more than the short term. Parents of children with ADHD often need help in developing strategies to deal with the primary, secondary, and comorbid symptoms. Studies show family approaches to be successful.[73] They may increase behaviour compliance[74,75] and reduce behaviour problems,[76] and may reduce subsequent delinquency.[77]

Cognitive–behavioural interventions

As cognitive processes appear to be strongly linked with the symptoms of ADHD, cognitive behavioural therapy (CBT) would seem to be ideally suited as an intervention. However, research evidence to date has not shown significant benefits. Whalen, Henker, and Hinshaw reviewed cognitive behavioural approaches in the literature, and concluded that evidence for benefit was weak for many studies.[78] Kendall and Braswell found that CBT reduced impulsivity but had little effect on other features of ADHD.[79] Abikoff and Gittleman examined the combination of cognitive behavioural treatments with medication. The results showed limited benefit over medication alone.[77] However, in consideration of the findings in the literature, it is important to recognize that there is considerable variation in the type of CBT throughout the studies.

Educational interventions

Educational interventions to enhance learning may improve attention problems.[81] Systematic behavioural management techniques have been shown to be of benefit in schools.[82] In the classroom, ADHD symptoms were reduced in formal versus informal classrooms[83] when children were in small classes with front row seats,[84] when work was given in small quantities with breaks in between,[85] when tasks were novel and with multimodal presentation,[84,85] and when noise levels were reduced.[86]

Diet

Several dietary factors have been suggested as causing or exacerbating symptoms. The 'Feingold' diet is one such diet.[87] This and other approaches were not the revolutionary answer hoped for.[88] Concerns have been raised about routinely using dietary interventions because of low response rates, high placebo response, and potential for diets that may be nutritionally damaging.[78] When there is a very powerful history of association with food, such strategies should be considered, but preferably under professional guidance.[89] A high intake of caffeine in drinks and food may be enough to cause symptoms of restlessness.[90] Anecdotally implicated substances such as sugar[85] and aspartame[91,92] have not been shown to be significant causes of ADHD-related difficulties in controlled trials.

Elimination diets may be warranted in special circumstances but do not usually demonstrate large behavioural differences and may be burdensome and unpleasant.[93] Megavitamin therapy has been advocated by some, but consistent advantages have not been demonstrated.[94]

Social skills training

Some improvement is noted in the behaviour of ADHD children after social skills training.[95] However, behaviour may not reach normal levels, and generalization to natural settings remains a problem.[96]

Psychotherapy, counselling, and play therapy

Mendelson, Johnson, and Stewart found psychotherapy, counselling, and play therapy relatively ineffective in altering the

behaviour of children with ADHD.[97] Other researchers have looked at psychoanalysis, suggesting improvement in a third of children, but there were methodological problems including small numbers, old criteria for diagnosis, and closed case notes.[98]

Medication and behavioural intervention combined

The research literature suggests that the sole treatment approaches of either medication or behavioural modification have several shortcomings. Pelham suggests that these can be reduced when the two approaches are combined, with suggestions that the primary symptoms are most successfully treated by medication, and the secondary symptoms by behavioural approaches.[99] Gittleman and colleagues investigated the efficacy of three treatment approaches of behaviour modification plus placebo, behaviour modification plus methylphenidate, and methylphenidate alone.[80] The combination of behaviour modification plus methylphenidate was the most effective followed by methylphenidate alone and then behaviour modification plus placebo.

Medication

There has been criticism of the rates of prescription in different countries, but the research shows that even within countries such as America and Australia there are very different prescribing rates, and these are of the same magnitude of difference as that between countries or between Europe and America.[9] There are numerous research papers to show that stimulants of the phenylethylamine variety, such as methylphenidate and dexamphetamine, do have very clear short-term benefits for children with ADHD.[100-103] Not all stimulant groups work so effectively. For example, the xanthine stimulants, such as caffeine, have a beneficial effect on concentration but tend to lead to a short-term increase in restlessness and levels of activity.[90]

The benefits of the phenylethylamine stimulants include reduction in errors of commission and omission, improvement in vigilance tasks, improvement in search tasks, improvements in maze tracing, and improvements in arithmetic and spelling tasks, and children handing in more correctly done work over the short term; but, despite this, expected resultant improvements in longer-term scholastic achievement have been extremely disappointing.[104-111] Being on medication not only increases academic task successes but is associated with more positive attributions to failure experiences,[112] perhaps because there are fewer of them. Benefits are not just restricted to childhood, with adolescents also showing improvements.[113]

Methylphenidate also reduces disruptive behaviours.[110] Aggression in naturally observed situations is diminished.[114] Relationships within the family appear to improve,[115-116] presumably by the systemic effects that an improvement in symptoms sparks. Some have questioned whether this represents more positive interactions or less negative parenting,[21] although this is likely to be too simplistic. Although ADHD children are likely to have poor social communication skills,[117] peer relationships may also improve with stimulants.[118]

Some researchers have suggested that increasing the dose loses the educational (concentration-based) effects in favour of the effects on behaviour,[119] although other researchers have not agreed with this finding.[120] Twenty-five per cent of children with ADHD may not respond to one stimulant (e.g. methylphenidate),[102,121] although some of these may then respond to the alternative (e.g. dexamphetamine). Predictors of the response to drug treatment (i.e. what factors predict which children are likely to respond) have been very hard to find.[103] The prevalence of anxiety or depression reduces the effectiveness of psychostimulants.[121] When considering children with severe to moderate learning difficulties, the use of stimulants is not so clear cut. For example, dexamphetamine may increase aggressiveness in autistic children,[123] and methylphenidate works less well in this group.[124] Children with organic impairments[107] or neurodevelopmental impairments[124] are likely to respond less well to stimulants. They also appear to be far less effective in children with severe learning disabilities,[125] although children with mild learning difficulties respond just as well as children of normal intelligence.[124] Additionally, adverse socioeconomic factors reduce effectiveness of medication in children with learning difficulties.[126]

Other than the two main stimulants used (methylphenidate and dexamphetamine), Pemoline was used in the past but was withdrawn recently because of concerns of adverse effects on the liver in a minority of children. Tricyclic antidepressants, such as imipramine, have also been used,[127,128] particularly where anxiety/depression is present (when methylphenidate may be less effective). Desipramine has been used and may be useful in ADHD sufferers who also suffer with Gilles de la Tourette syndrome,[129] but some reports of sudden death[93] led to many clinicians opting for imipramine if they are using a tricyclic. Clonidine has been shown to be useful in treating ADHD, particularly with comorbid conduct disorder.[130,131] Other drugs, such as serotonin re-uptake inhibitors, have been suggested, and systematic studies on their efficacy are awaited.

Precautions and side-effects of methylphenidate

From time to time the use of methylphenidate has been criticized in the media or by sections of society as unethical or too risky. There may be several reasons for this, not least because it is a drug that is marketable on the streets as a recreational drug, and also because studies have shown that it may induce paranoid symptoms in some adults[132] and may provoke relapse in schizophrenics.[133] Parents or carers may abuse the medication[134] but there is no evidence that drug tolerance or future abuse develops in children who are prescribed it.[135] These facts, in conjunction with a distinct absence of personality development research in the developing brain of children taking it, have created some concerns among some clinicians. Some have suggested that opting for the simple solution of medication may adversely affect the motivation of carers and teachers to seek other interventions that would additionally benefit the child.[103] Another concern relates to the attributional effects on the child with a potential to reduce perceived autonomy, choice, or responsibility for behaviour. Similarly, the attributional effects on parents may reduce responsibility for change of behaviour management style or expectations of the child. Others have argued that medication facilitates good behaviour management and that the explanations of the clinicians are crucial. It has been widely used throughout the world for some time without apparent serious adverse physical effects.

Simple tics may be precipitated in 2% of children after treatment with methylphenidate (and these disappear after dose reduction or withdrawal of medication), but it appears to be safe in children who already suffer with simple tics.[136] Stimulants are usually avoided where there is a genetic predisposition to severe tic disorders such as Tourette's syndrome,[137] and some have suggested that methylphenidate may precipitate symptoms of Tourette's syndrome in predisposed individuals.[138] However, methylphenidate can abate symptoms of ADHD in children with established Tourette's syndrome.[139] Some studies suggest the avoidance of stimulants in patients suffering with epilepsy,[89] but, despite theoretical risks of a reduced seizure threshold, other studies have shown that average dosages of methylphenidate do

not seem to increase seizure frequency.[140,141] Stomachaches and headaches may occur, especially in the first week of treatment with methylphenidate.[142] Stimulants can also reduce appetite, prevent sleep, and cause weepiness.[89] Such side-effects occur early in treatment, may abate with time, and are dose-related.[142] Rarely there may be blood dyscrasias involving white cells or platelets.[89] Stimulants should not be used with monoamine oxidase inhibitors, and can increase blood pressure and pulse especially when used concurrently with antidepressants or other stimulants.[94] Growth velocity may be affected by prolonged treatment. It is not entirely clear why this should be. It does not appear to be related to reduced appetite,[143] total daily growth hormone release, or sleep patterns,[144] although there are significant effects on the diurnal release patterns of growth hormone.[145,146] The evidence is that if the child is on medication for two years or less, and it is stopped before age 13, then the ultimate height in adulthood will not have been affected.[147] Low or standard doses (up to 20 milligrams) are not thought to be too problematic with respect to growth,[148,149] although studies of children who have been on it throughout childhood are not available. When growth velocity is affected, it rebounds (with catch-up growth) during periods of time without medication.[150] 'Drug holidays' have been found to result in compensatory growth spurts,[143] and many clinicians operate drug holidays periodically to allow for this and to monitor how children respond without medication.

With antidepressants, side-effects may include a dry mouth, constipation, blurred vision, rash, cardiac arrhythmias, and other rarer side-effects including rare sudden death.[94] Before starting medication, height, weight, and blood pressure are measured and some suggest that liver function tests and electrocardiograph tests should be performed.[94] Some clinicians also take intermittent full blood counts.

Long-term outcome with medication

Compared with the large number of studies looking at short-term outcome, there is a relative paucity of studies following children on medication into adulthood. The few studies available have produced disappointing results in that hyperactive children on medication were no more likely to go to university than hyperactive children not on medication,[151] nor were ADHD children on medication less likely to become delinquent than those not on medication.[152,153] However, the methodological problems of conducting a randomized controlled trial in this area are huge.[103] They include ethical issues, high attrition rates, cross-over from one group to another, problems with compliance, and inconsistency in taking medication. In addition to this is the difficult task of controlling for all the other relevant educational, developmental, familial, and social factors.

Are stimulants a diagnostic test for ADHD?

It is clear that the beneficial effects of stimulants are not specific to children with ADHD. They improve reaction time and vigilance in enuretic children without ADHD.[154] They reduce activity as well as improving memory and vigilance tasks in normal children.[155,156] Benefits have been shown with both methylphenidate[156] and dexamphetamine.[155]

It has also been shown to have beneficial effects on normal adults, with improved task performance and concentration.[157] Since these stimulants seem to improve concentration in most people, they should not be considered a diagnostic test for ADHD.

Natural history and outcome

Children with ADHD and comorbid conduct disorder are more likely to be referred for specialist help than those without the comorbidity.[158] Some (though by no means all) children with ADHD move into adolescence and take a path towards conduct disorder and delinquency.[152] Some authors believe that they may be more likely to suffer incidents such as head injury because of risk-taking behaviour.[159] Many children improve significantly with time. As children move into adolescence, most of them improve with respect to overactivity, and just under half of them improve with respect to inattentiveness and impulsivity.[160] In adolescence, low self-esteem and poor peer relationships remain a feature.[161] Predictive factors for those who do not improve are more related to conduct disorder symptoms and family dysfunction than the hyperactive symptoms themselves.[162]

Thorley looked at what happened to hyperactive children by early adult life.[163] It was found that they were more likely to have been expelled from school and more likely to have suffered accidents than psychiatric controls. Six to 12-year-old males who were followed up were twice as likely than controls to be arrested or convicted when older.[164] Comorbid conduct disorder has a contributory effect with worse outcome.[165,77]

Restlessness, concentration difficulties, and reduced stability in both personal relationships and employment persist.[162] Interestingly, outcome was more determined by intelligence, social class, and conduct disorder symptoms than hyperactivity symptoms,[163] and Weiss and Hechtman confirm these as well as parental psychopathology and dysfunctional family status as predictors.[162] Treatment with medication has not been shown to be a significant outcome predictor.[166] Satterfield and Schell found that, although children with ADHD had an increased risk of both juvenile and adult criminality, children with ADHD and no conduct problems appear to have no increased risk of later criminality.[167]

Conclusion

In order to assess and treat children with ADHD it is essential to obtain detailed information from a variety of sources (e.g. parents, teachers, clinicians) using a variety of methods (history-taking, questionnaires, direct observation). The complex combination of primary, secondary, and comorbid symptoms, as well as social factors, should be considered for each individual child in order to plan and carry out the most effective treatment approaches.

The outcome efficacy studies show that results from cognitive behavioural approaches, psychotherapy, and social skills are inconsistent. Family therapy and parent training, behavioural interventions, and stimulant medication were on the whole found to be more effective, with combined behavioural and stimulant medication approaches showing the greatest potential for improvement of all symptoms. Pelham and Bender support this view and suggest that treatment approaches for children with ADHD should begin with behavioural management and parent training. They suggest that only when these methods are not successful should medication trials be implemented.[95] We would suggest that a pragmatic approach should be taken in conjunction with the family, with a careful weighing up of the various risks and benefits of the options. On occasion, behavioural interventions may be all that is needed. On other occasions this is not the case, with methylphenidate generating a benefit that facilitates successful behaviour management. Finally, there should be a strong emphasis on multi-agency cooperation (e.g. therapists, parents, teachers, educational psychologists, special educational needs coordinators, behaviour support teachers, and general practitioners) to enable the most successful interventions.

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