Nature or Nurture? A Review of the Aetiology, Diagnosis, and Treatment of Attention Deficit Hyperactivity Disorder

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Abstract

Attention deficit hyperactivity disorder (ADHD) is a common neurobehavioural disorder characterised by developmentally inappropriate levels of hyperactivity, impulsiveness and inattention. Heritability data from twin studies of ADHD attribute about 75 percent of ADHD aetiology to genetic factors. The remaining 25 percent is attributed to environmental influences. ADHD affects 3 to 5% of children and a smaller percentage of adults. Diagnosis is based on criteria from the DSM-IV or ICD-10 and determined by a complete physical and behavioural evaluation. Psychoactive medication is consistently the most effective approach to managing ADHD and many effective pharmacological treatments are currently available.

Introduction

ADHD is a neurobehavioural disorder that affects both children and adults. It was first identified over a century ago by Dr. Heinrich Hoffman in children who acted impulsively and had significant behavioural problems. Research later determined that the behaviour was not caused by poor child rearing, but by a genetic predisposition. Sir George F. Still described the genetic predisposition in a series of lectures he presented to the Royal College of Physicians in England in 1902. Since that time, thousands of studies have been performed concerning ADHD.

Formerly, ADHD was known as Attention Deficit Disorder (ADD) but was renamed ADHD in 1994 to encompass the hyperactivity which may present in the disorder. The main symptoms of ADHD are hyperactivity, impulsiveness and inattention. Typical symptoms include excessive running and climbing, squirming in seat, careless mistakes on assignments, difficulty awaiting turn, and excessive talking. The child displays these symptoms in the classroom and home. The prevalence of ADHD is between 3 to 5% of school children worldwide[1]. It was recently estimated to occur in 5 to 10% of Irish children[2]. Boys are approximately three times more likely to have ADHD than girls, although the reason for this is not understood[3].

Theories of Causation

No definitive cause has been established for ADHD. The disorder cannot be identified by any distinct genetic, environmental, or neurobiological factors[4]. Family, twin and adoption studies have indicated that ADHD has a strong genetic foundation. It has been firmly established that ADHD is not simply the result of a poor social environment; however there is a correlation between specific environmental factors and ADHD. Finally, neurobiological studies indicate that ADHD may be caused by alterations in neurological

circuitry or specific structural changes in the brain. Ultimately, ADHD is most likely due to an interaction between these factors in genetically predisposed individuals.

For decades, research has shown that ADHD is primarily the result of genetic factors and is transmitted in families. ADHD occurs 5 to 7 times more frequently in family members with the disorder[5]. A recent longitudinal study showed that the parents of children with ADHD had significantly increased rates of ADHD as compared with the parents of children who did not have ADHD[6]. The child of an adult with ADHD has approximately a 25% chance of developing ADHD[7]. In agreement with these findings, studies found that adoptive relatives of children with ADHD are less likely than biological relatives to have the disorder or associated syndrome. A large scale study identified a 75 to 91 percent heritability across familial relationships (twin, sibling, and twin-sibling)[8]. This finding, along with numerous other studies, estimates the heritability to be 0.76 on average (Figure 1)[9]. A twin study reported a monozygotic probandwise concordance rate of 51 percent and dizygotic concordance rate of 33 percent[10]. Together, these studies provide compelling evidence that ADHD is a highly heritable disorder. Although no single genomic region is responsibility for ADHD, a number of genetic abnormalities have been associated with the disorder.
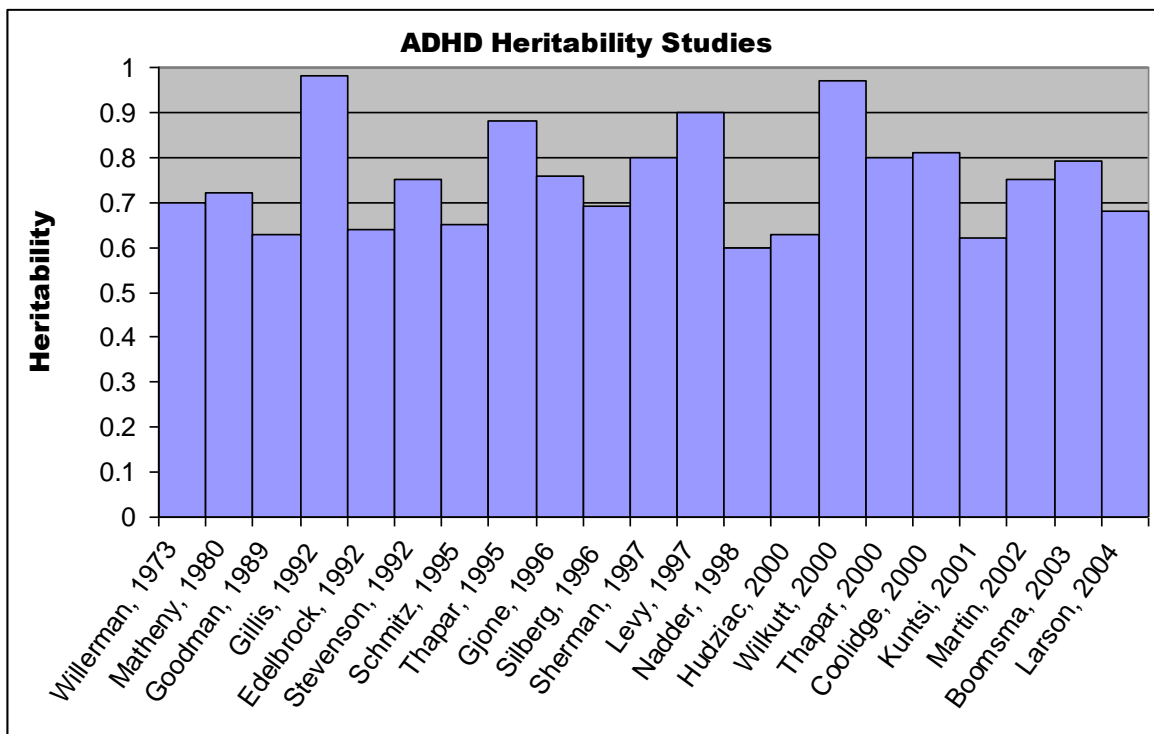

Figure 1[9]. This figure demonstrates the correlation in data from heritability studies.

Linkage findings provide evidence of a susceptibility locus on chromosome 16p13. A polymorphism in the GRIN2A (glutamate receptor, ionotropic, N-methyl D-aspartate 2A) gene, which maps to this locus, has been associated with increased risk of ADHD[11, 12]. Despite findings such as this, genomic regions implicated by linkage studies do not show significant correlations and several different loci have been connected with ADHD. These include 5p13, 5q33.3, 6q12, 7p13, 9q33, 11q22, 15q15 and 17p11[9]. Given the absence of repeated results across the spectrum of studies to date, it is reasonable to speculate that

genes with moderately large effect do not exist and that predisposition to ADHD is the result of a combination of genetic factors.

Meta-analyses have implicated polymorphisms in dopamine receptors *DRD4*, *DRD5* and the dopamine transporter *SLC6A3*. DRD4 is also prevalent in the frontal-subcortical networks that are implicated in ADHD pathophysiology[9]. Imaging studies of adults with ADHD have demonstrated a reduction in dopamine-transporter binding[9]. Accordingly, the dopamine tranporter is a primary target of the most frequently prescribed pharmacological treatments, methylphenidate and amphetamine.

There are multiple environmental factors which contribute to the risk of developing ADHD. The child is most vulnerable in utero where chronic exposure to certain toxins, including alcohol, nicotine and cocaine, is associated with an increased risk of ADHD. Delivery complications also increase the risk of ADHD. This includes foetal hypoxia, premature delivery and significantly low birth weight[9, 13]. Notably, the basal ganglia, which are associated with ADHD, are particularly sensitive to hypoxic insults[9].

Postnatal environmental conditions have also been associated with ADHD. Rutter *et al* found that combinations of family environmental risk factors, rather than any one factor, contribute to the postnatal incidence of ADHD[14]. The risk factors include a large family size, maternal mental disorder, paternal criminality, severe marital discord, low social class and foster care placement[15]. It is not suggested that these risk factors cause ADHD, but that there is a positive correlation between their presence and the presence of ADHD. Systematic studies discredit theories contending that particular foods or additives or excessive television viewing contribute to ADHD[9]. Despite being associated with ADHD, lead contamination is not found in most children with ADHD and many children with high lead exposure do not develop ADHD[9].

There are two currently held neurobiological models to explain ADHD. The Neuro-Cognitive Model describes ADHD as an executive dysfunction caused by disturbances in the fronto-dorsal striatal circuit and associated dopaminergic branches (e.g. mesocortical pathway). A second account sites altered reward pathways (e.g. delay aversion). These implicate fronto-ventral striatal reward circuits and the meso-limbic branches that terminate in the ventral striatum, particularly the nucleus accumbens. Previously, these models were thought to be competing. However, they are now regarded as complementary accounts of two psycho-patho-physiological subtypes of ADHD with different developmental pathways, supported by different cortico-striatal circuits and modulated by alternative dopaminergic pathways[16]. Both models result in a reduction in attention-monitoring processes, inappropriate cognitive responses and behavioural impulsiveness. Many scientists now believe that cognitive disinhibition is the root cause of ADHD[5, 17].

Scientists have examined the brain's anatomy in order to find further information as to the aetiology of ADHD. Electroencephalogram (EEG) studies show that over 90% of children diagnosed with ADHD demonstrate regulation disturbances in the prefrontal and sensorimotor cortices along with inhibited activity in all cortical areas. These children may be experiencing delayed maturation of the neural pathways because the regulation disturbances were seen in younger children's brains (<8yrs). The average total brain volume of boys with ADHD was found to be 5 percent smaller than that of the control group. The two anterior regions of the corpus collusum, the rostrum and the rostral body, have smaller areas in boys with ADHD compared with the control group[5, 18]. When

compared with controls, ADHD boys were also found to have a smaller right globus pallidus volume, a smaller left caudate volume[19], a smaller right anterior frontal region and a reversal of normal lateral ventricular asymmetry[20]. PET studies have shown that brain activity in adults with ADHD were significantly lower than control groups. The failure to adequately metabolise glucose was also implicated as a direct contributor to ADHD[5]. While these findings support the hypothesis that anatomical and physiological brain abnormalities are the basis of ADHD, no unique brain pattern has been identified. Slight variations of brain size and structure occur normally in the population. ADHD brains still have the same neurological and developmental features as the rest of the population.

Diagnosis

The two main sets of diagnostic criteria for ADHD are the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV) from the American Psychiatric Association and the International Classification of Mental and Behavioral Disorders 10th edition (ICD-10) published by the World Health Organisation. The two sources provide similar criteria for diagnosis of ADHD. The DSM-IV subdivides ADHD into three main categories; inattentive type, hyperactive-impulsive type and combined type. According to a recent study, more children meet the DSM-IV criteria for ADHD diagnosis than the ICD-10 criteria[21]. Therefore, children who have ADHD under the DSM-IV criteria may not be diagnosed under the ICD-10 criteria. This study illustrates the fine line in diagnosis and therefore the importance of a thorough examination. Accurate diagnosis of ADHD is dependent on a lengthy and systematic process that rules out other possibilities. The medical practitioner must therefore be cautious and diagnosis should not be hasty.

Inattentive type

In this subtype, inattention is present without impulsivity or hyperactivity. Children with this form of ADHD tend to be slow moving, slow thinking and sluggish in general. They have trouble with sustained concentration during tasks and play activities, resulting in apparent listening problems. Children with ADHD have difficulty paying attention to detail which is integral to schoolwork and other activities involving organisation. They often lose equipment necessary for completion of tasks and appear forgetful[3].

Hyperactivity-impulsive type

Hyperactivity and impulsivity are present in this subtype without inattention. It is characterised by excessive talking and fidgeting. A child with this form may interrupt or intrude frequently and has difficulty waiting for his or her turn. The child has great difficulty controlling immediate reactions and thinking before acting. Teenagers and adults express feelings of internal restlessness and report that they must remain occupied and often try to do several things simultaneously[3].

Combined type

The combined type includes a combination of symptoms from the other two types including inattention, hyperactivity and impulsiveness. It is the most prevalent form of ADHD. The synergy of symptoms results in exponential problems for individuals with this subtype of ADHD[3].

All of these symptoms can mimic childhood behaviours making diagnosis difficult. In order for a child to be diagnosed with ADHD, symptoms must be displayed from one of the ADHD categories before the age of 7. The behaviours must be more severe than those

displayed by children of the same age and must last for at least 6 months. Symptoms should be present both at home and school. No simple medical test exists to detect the presence of ADHD. One tool to aid in diagnosis is the Conners' hyperactivity index, which includes a patient and teacher rating scale. A complete physical and behavioural evaluation is also required for diagnosis to rule out any organic cause. It is also important to rule out the possibility that the behaviour is stress induced such as parental marriage breakdowns, illnesses or any other significant events. Behavioural changes resulting from such traumatic events are not an indication of ADHD. Additionally, children with high IQ's can display characteristics similar to those of ADHD including emotional responses, imagination and resistance to authority[22]. Awareness and thorough investigation of this is necessary to avoid the risk of misdiagnosis.

Many children with ADHD remain undiagnosed and untreated. This is most common in children with the inattentive form of ADHD. They do not show the problems of hyperactivity or impulsiveness associated with the hyperactive-impulsive type. As a consequence, these children are generally better behaved and do not present a problem in school or at home. Research has shown that girls, especially those with the inattentive type of ADHD, are at greater risk of being overlooked. Girls are more likely to become passive and withdrawn, while boys are likely to act out and misbehave[3].

Under DSM-IV criteria, diagnosis with a subtype requires presentation of 6 or more of its specific criteria for at least the past 6 months to a degree that is maladaptive and inconsistent with the developmental level for the childs age. Combined type must meet the criteria for both of the other subtypes. Some hyperactive-impulsive or inattentive symptoms that caused impairment must have been present before age 7 years and must present in two or more settings (e.g., at school and at home). There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning. The symptoms must not be better accounted for by another mental disorder (e.g., Mood Disorder, Anxiety Disorder, Dissociative Disorders, or a Personality Disorder) and do not occur exclusively during the course of a Pervasive Developmental Disorder, Schizophrenia, or other Psychotic Disorder or other Psychotic Disorder[23].

The DSM-IV criteria for inattentive type ADHD are: (a) often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities (b) often has difficulty sustaining attention in tasks or play activities (c) often does not seem to listen when spoken to directly (d) often does not follow through on instructions and fails to finish school work, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions) (e) often has difficulty organizing tasks and activities (f) often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework) (g) often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools) (h) is often easily distracted by extraneous stimuli (i) is often forgetful in daily activities[23].

The criteria for hyperactivity-impulsivity type ADHD are**:** (a) often fidgets with hands or feet or squirms in seat (b) often leaves seat in classroom or in other situations in which remaining seated is expected (c) often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness) (d) often has difficulty playing or engaging in leisure activities quietly (e) is often "on the go" or often acts as if "driven by a motor"(f) often talks excessively(g) often

blurts out answers before questions have been completed (h) often has difficulty awaiting turn (i) often interrupts or intrudes on others (e.g., butts into conversations or games)[23].

Associated Problems

Longitudinal studies have shown that children with ADHD are more prone to learning, behavioural and emotional problems during childhood and adolescence. Childhood ADHD pre-disposes to specific disadvantages such as less formal schooling (2 years less, on average)[24]. Children diagnosed with ADHD are more likely to fail academically in school despite scoring in the average to above average range on standardised ability tests and achieve a lower occupational status [25].

People with ADHD are more likely to have co-existing or associated psychiatric problems. Studies have shown that about 50-60 percent of children with ADHD also have oppositional defiant disorder (ODD), about 50 percent meet the criteria for conduct or mood disorder, 18% experience depression and 25% have anxiety disorders. The person may have difficulty in various social settings, in particular those where co-occurring conditions are present[5, 26]. Children with ADHD are also more likely to have tics[26], problems with motor co-ordination, psychosocial functioning and sleep[27]. For these reasons, it is accepted that treatment is necessary to manage ADHD and reduce the possibility of adverse outcomes.

Treatments

Many treatments are currently available for ADHD. These treatments consist of three general approaches; pharmacological therapy, behavioural treatment and a combined approach. Over the past decade, numerous scientific studies have examined each treatment to establish which are most effective. Pharmacological treatment has a greater effect on behaviour than counselling, however counselling results in better educational outcomes [28]. Results from a large scale study showed that both the pharmacological and combined approaches show a significantly greater improvement in ADHD symptoms than behavioural treatment alone [29]. There is still an ongoing debate as to which drug is the most effective for general ADHD treatment. Since each approach has its strengths and weaknesses, it is prudent for healthcare specialists to decide treatments on a case-by-case basis. The American Academy of Pediatrics (AAP) issued modern clinical practice guidelines for the treatment of school-aged children (six to 12 years) with ADHD in 2001. Clinical guidelines are also being developed by the National Institute of Clinical Excellence (NICE) in the UK for treatment of ADHD [30].

Pharmacological therapy

Stimulants

Stimulant drugs are by far the most popular class of drugs used to treat ADHD in adults and children. They account for about 75% of the medications prescribed for children [31]. Stimulants are the most effective treatment of ADHD, producing significant relief of symptoms in 75 to 90% of children.

Methylphenidate hydrochloride (Ritalin)
Methylphenidate is the most widely used drug for the treatment of ADHD. It provides safe, effective relief from the symptoms of ADHD with improvements in social interactions, academic performance and self-esteem. It decreases impulsivity and hyperactivity while also increasing attention. Methylphenidate is a psychomotor stimulant which has pharmacological similarities to the amphetamines, although the drugs differ in their neurochemical mechanism of action. Methylphenidate appears to enter the brain primarily by passive diffusion. It then enhances dopaminergic transmission in a dual action, augmenting dopamine (DA) release while simultaneously inhibiting dopamine reuptake transporters. This is done with potency comparable to that of cocaine but without activating the reward circuitry that leads to addiction in cocaine users[32].

Analogous to its effects on dopaminergic pathways, methylphenidate is also thought to increase CNS synaptic concentrations of noradrenalin (NA) by inhibiting the NA reuptake transporters[33]. In addition, research has suggested that methylphenidate indirectly increases cortical acetylcholine levels by stimulating cortical dopamine D1 receptors. It is not thought to affect the serotinergic pathways or their transporters. It is postulated that the therapeutic relief provided by methylphenidate is mediated by its effects in the CNS on DA concentrations and to a lesser extent NA concentrations. Methylphenidate also significantly increases the rate of glucose metabolism in the cerebellum and decreases it in the basal ganglia. It has been suggested that the increased metabolism seen in the cerebellum is the result of DA or NA concentration changes [34, 35]. Methylphenidate's activation of cerebello-thalamo frontal circuits may be a contributing factor in its therapeutic effects since the cerebellum plays an important part in higher cognitive functions such as learning, memory and attention[32].

Adverse effects include headache, insomnia, abdominal discomfort, diminished appetite, weight loss and increased nervous behaviours. The majority of these effects are mild and dissipate with cessation of treatment. However, potentially dangerous affects on the heart rate and blood pressure can occur due its action as an agonist at NA post synaptic terminals. Caution must be used in treating patients with coexisting heart conditions. Other contraindications include use with Monoamine Oxidase (MAO) inhibitors since high doses of methylphenidate also inhibit monoamine oxidase, possibly leading to hypertensive crisis. Methylphenidate can also cause a transient increase in intraocular pressure and must be used with caution in patients with glaucoma[32]. As with other psycho-stimulants, 'behavioural rebound' may occur after about 5 hours when the medication effect diminishes leading to increased irritability, over talkativeness, excitability and hyperactivity. However, this rebound can be controlled by administration of a small dose of methylphenidate. Despite previous reports which suggested that stimulants may intensify tics in children with ADHD, a recent study provides evidence that methylphenidate may actually be used to treat these children[36]. Methylphenidate is a controlled substance with potentially addictive properties and therefore constitutes an abuse liability.

The dosage of methylphenidate can vary from about 10 mg/day up to a maximum of 60mg/day. Methylphenidate has a short half life of approximately 2.5-3 hours and therefore is usually taken in two or three doses during the day. The Concerta brand of methylphenidate consists of coated beads that dissolve at different rates to provide a steady response that can last up to 12 hours.

Dextroamphetamine sulphate (Dexedrine)
Dextroamphetamine is another stimulant commonly used for treatment of ADHD. It acts by a mechanism similar to methylphenidate, stimulating DA release and reducing reuptake. Side effects are similar to those of methylphenidate although it may cause a more severe headache[37]. Dextroamphetamine observes the same contraindications as methylphenidate. It has a short half life of 4-6 hours and is taken in two or three daily doses. Dextroamphetamine therapy may be initiated with a dose of 2.5 mg/day and increased to the required level, but may not exceed a maximum dose of 40mg/day in children.

Amphetamine Salts (Adderall)
Adderall is commonly used to treat ADHD. It is a mixture of amphetamine salts consisting of three forms of d-amphetamine and one of 1-amphetamine. Studies have shown that Adderall is at least as effective as methylphenidate at reducing ADHD symptoms and improving academic performance[38]. It is twice as potent, although doses higher than 7.5mg/day do not produce incremental improvement. Its dose range is between 2.5mg/day and a maximum of 40mg/day. Its effects are longer lasting than methylphenidate due to its longer half life of 6 or 7 hours[26]. Similar to methylphenidate, Adderall produces side effects including restlessness, dizziness, headache, insomnia, dryness of the mouth and weight loss. Sudden death has occurred in some patients taking this medication, which has resulted in the suspension of sales in some countries.

Antidepressants
Tricyclic antidepressants (TCA) such as desipramine (Norpramin) and imipramine (Tofranil) are used for the treatment of ADHD when psychostimulant use has proven ineffective. The therapeutic relief provided by TCA's is postulated to be mediated by its CNS inhibition of both serotonin and noradrenalin reuptake which thereby increases their concentration and enhances their transmission. TCA's also stimulate phospholipase C (PLC) and the production of the second messenger inositol 1,4,5-trisphosphate (IP3). PLC activation leads to the activation of diacylglycerol (DAG) and protein kinase C (PKC) production. It is postulated that this pathway modifies the activity of glutamatergic neurons[39].

Studies comparing the efficacy of TCA's with psychostimulants have yielded inconclusive results[40]. They have longer half lives of about 24 hours and can therefore be given once daily. Behavioural rebound is not as problematic with TCA's as with stimulants. TCA's are especially useful when treating children with ADHD and concomitant depression. Side effects of TCA use in children can be substantial and include dry mouth, constipation, decreased appetite, fatigue, headaches, abdominal discomfort, dizziness, insomnia and increased blood pressure. TCA's should not be used concurrently with MAO inhibitors.

Desipramine is the most studied and the most popular TCA used for ADHD. It significantly improves behaviour in doses ranging from 1–3.5 mg/kg/day. The most serious side effect of desipramine and other TCA's is cardiotoxicity, most commonly presenting as sinus tachycardia. It is recommended that children receive an electrocardiogram (ECG) before administration of TCA's, as well as before dose changes.

Bupropion (Wellbutrin) is an antidepressant medication that is used as a second line treatment for ADHD. It affects the noradrenergic and dopaminergic systems and has been shown to ameliorate the symptoms of ADHD. Bupropion has greater efficacy than Pemoline and clonidine but is not as effective as methylphenidate or dextroamphetamine.

Bupropion is given in a daily dosage range of 50-300 mg (3.0 to 6.0 mg/kg/day) as Wellbutrin, although several formulations are available. Side effects include seizure activity in 0.1% of patients prescribed with dosages under 300 mg/day. The risk of seizures are reduced if bupropion is taken in doses over 8 hours apart, medication is slowly titrated upward in dose, sustained release (SR) formulation is used, and the regular formulation is not administered in high doses. Bupropion is contraindicated in patients with epilepsy or eating disorders. Drug interactions are minimal and it does not lead to cardiac conduction delays[41].

Antihypertensive Agents

Clonidine (Catapres) and guanfacine (Tenex) have been shown to be somewhat effective in the management of ADHD. They are central acting alpha2 adrenergic receptor agonists and bind to the presynaptic terminal to produce inhibition of adenylate cyclase and a subsequent decrease in cAMP formation. This results in inhibition of noradrenaline (NA) and acetylcholine (Ach) release.

Clonidine has a dose range of 0.05 mg/day to 0.3 mg/day while guanfacine's dose range is between 0.5 mg/day and 3.2mg/day[42]. Side effects are generally limited and may include sedation, hypotension, headache, dizziness, stomach-ache, nausea, depression and cardiac arrhythmias[43]. Patients should have their blood pressure, pulse, liver function tests and ECG closely monitored[44]. Contraindications include use with other antihypertensive drugs such as beta blockers. Also, the drugs should not be abruptly discontinued due to risk of rebound hypertension[26].

New drug treatments - Atomoxetine (Strattera)

Atomoxetine is the first non-stimulant drug approved for use in children, adolescents and adults, for the treatment of ADHD [45, 46]. The American Academy of Child and Adolescent Psychiatry recently approved Atomoxetine as a first line treatment for ADHD[47]. Atomoxetine provides relief of core symptoms of ADHD and also improvements in social and family functioning and self-esteem. Its mechanism of action is the selective inhibition of noradrenalin reuptake through inhibition of the presynaptic NA transporter. Atomoxetine has a low affinity for various receptors, such as cholinergic, serotonergic, adrenergic, and histaminic. The recommended dose is 1.2 mg/kg/day in children and adolescents weighing less than 70 kg and 80mg/day for children, adolescents and adults weighing over 70kg[45]. A single daily dose provides continuous symptom relief throughout the day.

Clinical trials have shown Atomoxetine to be safe and well tolerated in the short term but studies examining long term use are unavailable[45]. Atomoxetine is not a controlled substance and carries a negligible risk of abuse. Adverse effects include appetite loss, stomach ache, headache and nausea. These effects are mostly mild and temporary in nature. Modest increases in heart rate and blood pressure were also reported but steadily decreased after cessation of treatment[48]. Other drugs, such as selective serotonin reuptake inhibitors may increase the blood level of atomoxetine and intensify its actions by competing for the attention of liver enzymes that metabolize it. Overall, atomoxetine represents an important advance in the pharmacological treatment of ADHD.

Discussion

ADHD is caused by a combination of genetic and environmental risk factors. These contribute approximately 75% and 25% respectively to ADHD susceptibility. The presence of certain genetic variations influences brain development in such a way that children with these configurations are more likely to develop inattention, hyperactivity and impulsivity. Environmental factors can exacerbate these behaviours. However, it is not yet known which environmental factor has the most prominent effect on each genetic continuum of ADHD.

Research into the genetic aetiology of ADHD has enhanced understanding of the disorder and resulted in an increased appreciation of the genetics involved. The multifactoral model of ADHD maintains that ADHD cannot be attributed to a single inherited gene, but is a complex disorder caused by a combination of genetic and environmental risk factors. Despite the identification of specific risk factors, their exact contribution and specific interaction have yet to be determined. If an individual's cumulative susceptibility exceeds a certain threshold, he or she will manifest the symptoms of ADHD[9]. In the future, genetics may provide an avenue of very early diagnosis, even before the symptoms of the disorder present. However, more work is required before data can provide a new diagnostic approach for ADHD. A better appreciation of the genetics involved in ADHD susceptibility may allow for the selective use of medications which are more suited to the specific gene and neurobiological differences of each individual with ADHD.

Similarly, brain imaging studies have been useful in providing information on both the structural and functional characteristics of the brains of people with ADHD. Emerging knowledge of the cause and pathophysiology of ADHD is creating an improved understanding of the underlying neural mechanism involved. This should allow for improvements in both diagnostic and treatment strategies[9].

Given the prevalence of ADHD among school aged children, primary care clinicians should have a strategy for diagnosis and long term management of the condition. The practice guidelines issued by the AAP provide a solid framework for the treatment of children with ADHD without major co-morbidity. According to the AAP, physicians should recognise ADHD as a chronic condition, the treatment of which requires partnership with the family, child, teachers, nurses, psychologists and counsellors. The physician must serve as a source of information for the family and child while co-ordinating resources as necessary. As with other chronic conditions, new data may impact upon the treatment of ADHD and physicians should therefore closely monitor the literature. Given that the primary symptoms of ADHD impact the child's performance in various circumstances, the main focus of treatment should be to maximize function. The AAP recommends that treatment plans be tailored for each child to achieve between three and six specific changes such as improvements in relationships, self-esteem and school performance, and a decrease in disruptive behaviours[49].

The AAP guideline recommends methylphenidate or dextroamphetamine (short-, intermediate-, and long-acting formulations) stimulants as the first-line treatment. Based on data indicating that the majority of children who do not respond to one stimulant will respond to an alternate one, the AAP recommends that if one stimulant does not work at the highest feasible dose, the physician should recommend another. Nonstimulant medications do not fall within the scope of the guidelines. The only other medications indicated for ADHD in the guideline are the tricyclic antidepressants (imipramine,

desipramine) and bupropion. Physicians are advised to titrate upward from an initially low dose so as to achieve the highest efficacy with minimal side effects. If adverse effects or no further improvement occurs, a downward titration is recommended. Behavioural therapy has also been advocated as a separate treatment or in addition to medication[49].

Psychoactive medication has consistently proven to be the most effective approach to managing ADHD. A wide range of very effective pharmacological treatments are currently available for the management of the disorder. Stimulants such as methylphenidate and Adderall have proven very capable first line medications for ADHD treatment and are supported by a number of other pharmacological options. Atomoxetine provides a novel non-stimulant ADHD treatment for all ages. It has recently been accepted as a first line treatment and may yet surpass stimulants in terms of use.

The AAP recommends a series of follow up visits with the child to determine if target outcomes have been achieved and whether or not adverse effects exist. Information from parents, the child, teachers, and any other professionals involved can be used for this assessment. In cases where the selected treatment plan for a child with ADHD has not met target outcomes, physicians should evaluate the original diagnosis, use of all appropriate treatments, adherence to the treatment plan, and presence of coexisting conditions[49].

Although the parameters of the disorder are vague and diagnosis can sometimes be difficult, it is very important to identify and treat people with ADHD. With the help of their medical practitioner, most people can find the treatment which is right for them. Successful treatment is paramount to allowing sufferers of ADHD to break free from the constraints of the disorder and fulfil their potential. Research continues to unravel the intricacies of ADHD and may provide scope for the introduction of early behavioural treatments in the future to tackle the disorder before its symptoms even present.

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