Attention-deficit/hyperactive disorder: making a case for multi-disciplinary management

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Attention Deficit/Hyperactivity Disorder (AD/HD) is characterized by a cluster of age-inappropriate behavioral abnormalities comprising inattentivity, hyperactivity and impulsivity. The definition is controverisal and without an accurate diagnosis. Therefore, it seems prudent that a multidisciplinary treatment protocol should begin with non-drug psychological and behavioral strategies plus nutritional intervention.
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INTRODUCTION

Attention Deficit/Hyperactivity Disorder (AD/HD) is a condition that comprises the cluster of age-inappropriate behavioral abnormalities comprising inattentivity, hyperactivity and impulsivity. AD/HD has been rather controversial in its definition, diagnosis and treatment. At a recent National Institutes of Health (NIH) consensus development meeting, an expert panel had difficulty in developing a decisive consensus statement on AD/HD, leaving several unresolved issues including some that questioned the very validity of the condition. The following is an excerpt.

"There is no consistency in treatment, diagnosis or followup for children with ADHD. It is a major public health problem," said panel chair Dr. David J. Kupfer, Thomas Detre Professor and Chair, Department of Psychiatry, University of Pittsburgh.

"These children are subjected to a fragmented treatment system that reaches beyond health care into a wide range of social and educational support services. Its impact on individuals, families, schools, and society is profound, and it demands our immediate attention," Dr. Kupfer said.

The problem is compounded by the fact that an accurate diagnosis for ADHD remains elusive and controversial yet continues to be a commonly diagnosed behavioral disorder of childhood. One of the most important, immediate research needs is to develop standardized diagnostic criteria based on age and gender, the panel said.

While the panelists concluded that the absence of a simple, consistent diagnostic test for ADHD continues to pose validity problems for the disorder, they agreed that the 3 to 5 percent of school age children grappling with ADHD experience an inability to sit still and pay attention in class, peer rejection, and disruptive behaviors, which can lead to academic and social difficulties. Other long-term consequences include higher rates of accidents as well as alcohol and drug abuse and criminal behaviors when ADHD is accompanied by conduct problems.[1]

Notwithstanding this debate at the scientific level, it is useful to remember that parents of children who are inattentive or hyperactive often express their wish that their child would stay still or focused for just a moment. These comments are usually based upon comparisons with their child's peers. Such expressions are observed across all cultures and socio-economic classes and clearly warrants medical attention where deemed necessary.

The current state of the empirical literature regarding the treatment of AD/HD is necessarily focused on psychopharmacological management techniques. While this article will also review drug therapy, special emphasis will be given to the emerging role of special dietary factors as an adjunct to the management of AD/HD.

DEFINITION

The essential feature of AD/HD is a persistent pattern of inattention and/or hyperactivity-impulsivity that is more frequent and severe than is typically observed in individuals at a comparable level of development (criterion A). Some hyperactive-impulsive or inattentive

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symptoms that cause impairment must have been present before 7 years, although many individuals are diagnosed after the symptoms have been present for a number of years (criterion B). Some impairment from the symptoms must be present in at least two settings (e.g., at home and at school or work) (criterion C). There must be clear evidence of interference with developmentally appropriate social, academic, or occupational functioning (criterion D). The disturbance does not occur exclusively during the course of a Pervasive developmental Disorder, Schizophrenia, or other Psychotic Disorder and is not better accounted for by another mental disorder (e.g., a Mood Disorder, Anxiety Disorder, Dissociative Disorder, or Personality Disorder) (criterion E).[2]

Sub-criteria definitions attempt to provide a framework to the inattention, hyperactivity, impulsivity, and behavior manifestations of the condition. However, three distinct subtypes are recognized to make a diagnosis. These are as follows:

- AD/HD, Combined Type.
- AD/HD, Predominantly Inattentive Type.
- AD/HD, Predominantly Hyperactive-Impulsive Type.[2]

INCIDENCE / PREVALENCE

Affecting approximately 1 in 200 children in the UK[3], the reported prevalence of AD/HD is estimated to be higher at 3% to 5% of school age children in the United States. Data on teenage and adults are limited. AD/HD is more frequently reported in males than in females in ratios ranging from 4:1 to 9:1 respectively. It is reported to occur in various cultures and countries, however, it is interesting to note that international community studies have yielded prevalence rates between 1.7% and 17.8%.[4,5] While this disparity in prevalence estimates are partly due to diagnostic criteria applied and the population assessed, it raises the distinct possibility that the condition is both over diagnosed or under diagnosed in certain populations.

ETIOLOGY

AD/HD is a disorder of unknown etiology. However, data from segregation analysis, adoption, twin and family genetic studies suggest a genetic origin for at least some forms of the condition. Other etiologies are also likely including psychological adversity, perinatal insults, and perhaps other as yet unknown biological causes.[6]

PATHOLOGY

Based on current understanding AD/HD is a disorder of questionable validity. Presupposing a disease component, its underlying pathophysiologic substrate remains unknown. However, an emerging neurophysiological and neuroimaging literature suggests that abnormalities in frontal-striatal dysfunction could be the disorder's underlying neural substrate, and catecholamine dysregulation is its underlying pathophysiological substrate.[6]

DIAGNOSIS

Diagnosis is made based on the criteria set forth in the DSM-IV definition of the condition and is therefore an exclusion driven psychoanalytical assessment. In early childhood it is difficult to distinguish AD/HD from age appropriate behaviors in active children.

There are no laboratory tests established as diagnostic in the clinical assessment of AD/HD, neither are any specific physical features associated with the condition. (Minor physical anomalies such as hypertelorism, high arched palate and low set ears may occur at a higher rate than in the general population).[2]

DRUG MANAGEMENT

Psychostimulant drugs have been the treatment of choice for several decades (Table 1). The most common compounds in this class are methylphenidate, dextroamphetamine and magnesium pemoline. These stimulants are sympathomimetic compounds structurally similar to catecholamines like norepinephrine and dopamine. Several short term controlled studies have shown these drugs to be efficacious but many studies have also consistently shown that approximately 30% of the cases do not respond to these drugs.[5,6]

Another group of compounds used in AD/HD management are tricyclic antidepressants including the tertiary amine amitriptyline and imipramine, and the secondary amines desipramine and nortriptyline. These compounds appear to block reuptake of central nervous system neurotransmitters especially norepinephrine.[6] While these tricyclic antidepressants appear to be an effective treatment alternative, reports of sudden death and asymptomatic increases in heart rate and ECG measures of cardiac conduction times have been reported in the literature. This relegates tricyclic antidepressants to a second line treatment option.

Bupropion hydrochloride, an antidepressant pharmacologically different from other antidepressants, has indirect dopamine and noradrenergic agonist effects. This drug appears to reduce AD/HD symptoms rapidly however causes dermatological reactions.[5,6]

In preliminary studies, monoamine oxidase inhibitors (MAOIs) such as selegiline, clorgiline, pargyline and tranylcypromine appear to be effective in treating AD/HD. However, a major limitation to the use of MAOIs is the potential for hypertension and drug interactions. Serotonin selective reuptake inhibitors are also currently being evaluated but initial indications are that these compounds have limited value. Alpha adrenergic agonists like clonidine have also been recently used with moderate results.

It is evident therefore, that a number of well known drug compounds are available for the treatment of

Table 1. Regimens used in psychopharmacological management of AD/HD. (adapted from Elia J, Ambrosini PJ and Rapoport JL. Treatment of attention deficit hyperactivity disorder, N Engl J Med 1999; 340:780-788).

Drug	Initial Dose	Suggested increment	Maximum single dose	Maximum daily dose	Doses per day	Comments
Stimulants						
Methylphenidate standard	5mg	5mg	20-30mg	60mg	2 to 3	First line drug
Sustained release dextroamphetamine First line drug	20mg		20mg	20mg	1	Not consistently effective
Dextroamphetamine sulphate alone and in combination with other salts	2.5-5mg	2.5-5mg	20mg	40mg	2	Higher doses have been given safely but not tested in clinical trials
Sustained release Pemoline	5mg	5mg	15mg	15mg	1mg	Consistently effective
Pemoline	37.5mg	18.7mg	112.5mg	112.5mg	1mg	Effective, rare risk of hepatic failure
Antidepressants						
Imipramine	1mg/kg	0.5mg/kg	1.5mg/kg	3mg/kg	2 to 3	Not as effective as stimulants. Risk of sudden death
Desipramine	1mg/kg	0.5mg/kg	1.5mg/kg	3.5mg/kg	2 to 3	
Bupropion	3mg/kg	3mg/kg	3mg/kg	3 to 6mg/kg	2	Not as effective as stimulants. Causes dermatologic reactions
Alpha-adrenergic agonist drugs						
Clonidine	0.05mg	0.05mg	0.1mg	0.3mg	1 to 3	Questionable efficacy
Clonidine transdermal patch	0.05mg	0.05mg	0.1mg	0.3mg	1 every 5 days	Questionable efficacy Causes skin reactions.

AD/HD. However, there appear to be a number of individuals that do not respond adequately or are unable to tolerate the adverse effects of the drugs.[6] Given the limitations of drug therapy, the lack of a convincing pathophysiological basis for the condition, and anecdotal evidence of successful non-drug treatments, a multidisciplinary approach to manage the symptoms is essential.

NON-DRUG MANAGEMENT

There is a long history of a number of non-drug interventions for Attention Deficit/Hyperactivity Disorder (Table 2). These include cognitive treatments like problem-solving strategies, self-monitoring, modeling, individual psychotherapy or play therapy. Other nondrug interventions include dietary replacement, dietary exclusion, dietary supplementation, various vitamin, mineral, or herbal regimens, biofeedback, vestibular and sensorimotor integration, perceptual stimulation and a host of others techniques.[1,6]

Non-drug psychosocial management of AD/HD includes the following behavioral strategies:

- Contingency management typically conducted in the classroom using point-token reward systems, time-outs, response cost etc.
- Parent training where the parent is taught child behavior management skills.
- Clinical behavior therapy where both parent and teacher are taught contingency management techniques.
- Cognitive-behavioral techniques that involve self-monitoring, verbal self-instruction, problem-solving strategies, self-reinforcement etc.

Clinical behavior therapy, parent training, and contingency management have produced beneficial effects. However, cognitive-behavioral treatment has not been found to yield beneficial effects in children with AD/HD. Intensive direct interventions in children with AD/HD have produced improvements in key areas of functioning. However, no randomized control trials have been conducted on some of these intensive interventions alone or in combination with medication.[1]

Studies that compared stimulants with psychosocial treatment consistently reported greater efficacy of stimulants. Although these interventions have generated considerable interest and there are some controlled and uncontrolled studies using various strategies, the state of the empirical evidence regarding these

Table 2. Examples of a few non-drug AD/HD management techniques

Psychological	Dietary management	Other
Self monitoring	Dietary replacement	Biofeedback
Verbal self-instruction	Dietary exclusion	Vestibular/Sensorimotor integration
Problem solving	Dietary supplementation	Perceptual stimulation
Self reinforcement	Fatty acid	supplementation regimens
Point-token reward System	Vitamin, mineral regimens	
Time-outs Herbal regimens		
Response costs		

interventions is uneven, ranging from no data to well-controlled trials.[1] While controlled studies are yet to show effectiveness of these non-drug management strategies, anecdotal evidence and wide spread use of these strategies appear to indicate that some benefits are being realized. Herein, specific non-drug dietary strategies have shown intriguing results and warrant special mention.

ROLE OF SPECIAL NUTRIENTS IN MANAGEMENT OF AD/HD

Given the emerging evidence of a cerebral and neural substrate based etiology for AD/HD, and that contemporary drugs exert their effects on the same cerebral and neural substrate, it is reasonable to hypothesize that structural components of the neural substrate would affect not only cellular function but also response to drug therapy.

A large portion of the brain, and therefore the neural substrate, is made up of special long chain fatty acids. Four fatty acids are particularly important in the brain. They are dihomogammalinolenic acid (DGLA), arachidonic acid (AA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). AA and DHA make up approximately 20% of the dry mass of the brain and their structural and functional roles have been studied and well documented. DGLA and EPA play minor structural roles but along with other fatty acids have critical functional roles as eicosanoid precursors. The eicosanoid complex include the very highly biologically active compounds comprising prostanoids (prostaglandins, thromboxanes, prostacyclins) and leukotrienes. These compounds impact numerous body systems including the eye, brain and nervous system.[7,8]

As structural components of cell membranes, these fatty acids have membrane proteins embedded that serve as receptors to elicit electrical or chemical signaling pathways and function to transmit signals between nerve cells. The precise fatty acid composition of the membrane can therefore affect these membrane bound receptors and their associated neurotransmitter functioning. These receptor sites are also targeted by contemporary drugs used in psychiatry. It is therefore reasonable to assume that deficiency of these fatty acids will affect not only the function of the brain, eye and nervous system, but also impact response to contemporary AD/HD drug therapy. Indeed such a fatty acid deficiency hypothesis appears to support rather than conflict with current neurotransmitter models of AD/HD management.[8]

EVIDENCE OF FATTY ACID DEFICIENCY IN AD/HD

Early evidence of fatty acid deficiency in AD/HD was provided in 1981 by Colquhoun and Bunday.[9] They surveyed 214 hyperactive children in the UK and found signs of fatty acid deficiency (FAD) in a number of subjects, leading them to propose that hyperactivity may be the result of fatty acid deficiency which in turn led to a deficiency in prostaglandins. Further research has confirmed that levels of specific fatty acids are significantly lower in some individuals with AD/HD and supplementation of the diet with these fatty acids can have a beneficial reduction of some symptoms of the condition.[8-17] While not suggesting that fatty acids have drug type effects on AD/HD, the research makes a strong case to supplement the diets of AD/HD individuals with these vital fatty acid nutrients.

In the presence of these vital fatty acids, a healthy cell membrane environment is fostered to promote nerve and brain cell function, improve the transmission and communications between the cells, and aid in contemporary treatment modalities. Inadequate amounts of these long chain fatty acids, or excess consumption of saturated and trans fats, can potentially effect and even alter the structure and function of these organs - and modern diets tend to contain excessive amounts of saturated and trans fats.

This issue is critical since these much needed fatty acids cannot be manufactured by the body and must be

obtained from the diet. It is therefore vital to eat the right types of foods, or alternatively supplement the diet with these essential fatty acids. Green leafy vegetables, fish, fish and vegetable oils are known sources of these vital fatty acid nutrients.

CONCLUSION

Absence of a simple consistent diagnostic test and pathophysiologic evidence of the condition will continue to pose validity problems for AD/HD. However, it is likely that co-morbid conditions confound the diagnosis making it difficult to devise a simple diagnostic test. Further, the absence of anatomic or pathophysiological evidence of a disease does not negate the validity of the condition. AD/HD could well be a heterogenous disorder, partly evident from the differing but definite responses to drug therapy. At the same time overzealous use of drug therapy, and dismissing the relevance of alternate approaches, is not advisable. Given the variations in clinical presentation and treatment response it appears prudent to use a multi-disciplinary approach to managing AD/HD.

Along with non-drug psychological and behavioral strategies, dietary factors can influence not only the type and amount of medication to be taken, but also the effect it will have on the body. In the case of Attention Deficit/Hyperactivity Disorder, proper nutrition will help foster normal growth and development and a healthy cellular environment, thereby helping the body regulate itself and to better respond to standard treatment protocols. Therefore, a multidisciplinary treatment protocol can begin with behavioral and nutritional interventions while evaluating appropriate drug treatment.

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