ADHD: Pathophysiology, Management, and Assessment Scales

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Abstract
Attention-Deficit/Hyperactivity disorder (ADHD) is the most prevalent childhood behavioural disorder diagnosed in the outpatient setting. Due to the broad impact of ADHD, the disease is likely to have serious economic implications for children and their families leading to increased costs in healthcare. Functional and anatomical dysfunction in the brain's frontal cortex and basal ganglia segments of the cortico-basal ganglia-thalamocortical circuitry have been observed in patients of ADHD. A combination of psychoeducation, Cognitive behavioral therapy, and pharmacotherapy with psychostimulants like Methylphenidate are used for the management of ADHD symptoms. Various rating scales help in the assessment of severity of disease, treatment planning, and monitoring the level of improvement.

Keywords: ADHD, assessment scales, Conners’ scale, Vanderbilt Scale.

Introduction
ADHD is characterized by a decreased sustained attention and higher levels of impulsivity in a child or adolescent than expected for someone of that age and developmental level1. The worldwide prevalence of ADHD is 7.2%2. ADHD is likely to have considerable economic implications for their families and the government. Research has only recently begun to explore these economic costs, suggesting that ADHD leads to increased costs in healthcare3.

Although the aetiology of ADHD is mainly genetic, there is a growing consensus that the condition involves functional and anatomical dysfunction in the brain’s frontal cortex and basal ganglia segments of the cortico-basal ganglia-thalamocortical circuitry4. The diagnosis of ADHD is established by 5th edition Diagnostic and Statistical Manual of Mental Disorders (DSM-5) of the American Psychiatric Association5.
Psychostimulants like methylphenidate that increase dopamine concentration and nonstimulant medications like atomoxetine which increases noradrenaline levels are used in the treatment of ADHD by targeting the central nervous system. Various studies have established the usefulness of Conners’ Rating Scale, Vanderbilt ADHD Rating Scale and Clinical Global Impression (CGI) rating scale in ADHD.

**Methodology**

Electronic databases of MEDLINE (PubMed) and Google Scholar search engines were searched for relevant studies and reviews published from 1990 to 2017. The keywords used were “ADHD,” “Pathophysiology,” “assessment scales,” “Vanderbilt ADHD Rating Scale,” “CGI rating scale,” and “treatment.” The reference list of recently published relevant articles and reviews were also screened. Titles, abstracts, and full texts of peer-reviewed articles about related topics published in English were included.

**Pathophysiology of ADHD**

Evidence from neuropsychological, pharmacological, and brain-imaging studies implicates dopamine and norepinephrine neurotransmitter systems of frontostriatal circuit in the pathophysiology of the disorder. Global brain volume is reduced by 3–5%, with the gray matter, preferentially affected. More marked volume loss, correlated with the severity of the symptom of ADHD, is seen in the prefrontal areas, the basal ganglia, and the cerebellum. Cortical maturation is delayed, particularly in the prefrontal areas.

The multifactorial aetiology of ADHD corresponds to the heterogeneous profile of cerebral structural abnormalities and functional neuropsychological and psychopathological disturbances.

Epidemiological studies show an association between ADHD and various environmental factors. These primarily include pre- and perinatal risk factors (maternal stress, smoking or alcohol consumption during pregnancy, low birth weight, prematurity), environmental toxins (organophosphates, polychlorinated biphenyls, lead), unfavourable psychosocial conditions (severe early-childhood deprivation, maternal hostility), and dietetic factors.

ADHD tends to run in families. First degree relatives of patients with ADHD have an increased risk of developing ADHD. Structural and functional neuroimaging has studied the deficits of prefrontal cortex in ADHD. Dopaminergic and noradrenergic dysregulation is associated with a loss of inhibitory processes critical for adaptive heart rate neural regulation. It seems that the prefrontal cortex dysfunction could represent one of the underlying mechanisms of the impaired catecholaminergic regulation. The genetically mediated abnormalities in the neurotransmission could contribute to the discrete dysfunctions in the prefrontal cortex, limbic system, locus coeruleus-noradrenergic system and other related brain structures that are also included in the neuro-cardiac complex regulation.

**Diagnosis**

ADHD is a behavioural and neurocognitive condition characterized by developmentally inappropriate and impairing levels of gross motor overactivity, inattention, and impulsivity. As with many psychiatric disorders, there is no simple objective test, such as a blood test, that can aid in making the diagnosis. ADHD can be reliably diagnosed if the diagnostic criteria are carefully scrutinized, and differential diagnoses are excluded.

The clinical interview in conjunction with assessment scales are the primary tools for the diagnosing ADHD. The most important source of information is from the parents and the school teachers. Patient interview, although unreliable in young children, should also be part of the assessment. Comparing the patient’s functional impairment against children of a similar age is necessary for an ADHD diagnosis.

There are five main diagnostic criteria: (1) an onset before age 12 years (2) duration greater than 6 months; (3) an 18-item symptom list of which 6 of 9
inattention or 6 of 9 hyperactive/impulsive symptoms have persisted for at least 6 months to the degree that is maladaptive as well as inconsistent with developmental levels; (4) impairment in two or more settings (home and school); and (5) symptoms that do not occur exclusively during the course of schizophrenia, psychotic disorder, a pervasive developmental disorder, or other and are not better accounted for by another mental disorder, such as depression.

According to DSM-5 the presence of either 1 or 2 is confirmatory of the presence of ADHD:

1. Six or more symptoms of inattention which persist for at least six months to the degree that is inconsistent with developmental level.
2. Six (or more) symptoms of Hyperactivity-impulsivity has persisted for at least six months to the degree that is inconsistent with developmental level.

Differential Diagnosis and comorbidities
Anxiety can accompany ADHD either as a secondary feature or can manifest in the form of over-activity and easy distractibility. A child with ADHD can become demoralized and, in some cases, may develop depressive symptoms in reaction to persistent frustration with academic difficulties and resulting low self-esteem. Mania and ADHD share many core features, such as excessive verbalization, motor hyperactivity, and high levels of distractibility. Frequently, conduct disorder and ADHD coexist, and both must be diagnosed. Learning disorders of various kinds must also be distinguished from ADHD; a child may be unable to read or do mathematics because of a learning disorder, rather than because of inattention. ADHD often coexists with one or more learning disorders, including reading disorder, mathematics disorder, and disorder of written expression. ADHD and obsessive-compulsive disorder (OCD) are common developmental neuropsychiatric disorders associated with significant distress and dysfunction. ADHD is characterized by inattention, hyperactivity and impulsiveness present since childhood, whereas OCD is characterized by intrusive obsessions and compulsions that are typically performed in response to those obsessions.

Prognosis
ADHD is associated with psychosocial functional impairment and a markedly reduced subjective health-related quality of life. Patients with ADHD are about four times less likely than their peers to obtain a college degree and attain a lower socioeconomic status on an average. Their relationships with parents, siblings, peers, and partners are often conflict-ridden.

Symptoms of ADHD persist into adolescence or adult life in approximately 50% of cases. In the remaining 50%, they may remit at puberty, or in early adulthood. In some cases, the hyperactivity may disappear, but the decreased attention span and impulse-control problems persist. The symptoms of overactivity are usually the first symptoms to remit, and distractibility is the last to go.

Treatment
Treatment guidelines now recommend a combination of multiple, individually adapted treatment components (multimodal treatment). The foundation of all therapeutic interventions is psycho-education to impart information about the disorder to the parents, as well as to the patient in an age-appropriate manner. Cognitive behavioural therapy techniques are also used, in both individual and group settings. Alongside these treatments, pharmacotherapy is a further essential component of ADHD treatment.

Psychostimulants are the first-line treatments for the disorder and are more effective at treating ADHD symptoms than behavioural therapy alone. Methylphenidate is one of the most commonly used medications for ADHD treatment.

With treatment, the symptoms of ADHD improve leading to more productive lives for affected children. Methylphenidate acts by inhibiting the reuptake of dopamine and noradrenaline. PET studies with Methylphenidate challenge show increased competition at postsynaptic D2/3-receptors, thus indirectly revealing presynaptic dopamine release.
Methylphenidate is a pure blocker of the norepinephrine and dopamine transporters. The amphetamines also block the reuptake of both catecholamines, but they also release all three monoamines, norepinephrine, dopamine, and serotonin, from presynaptic vesicles. Amphetamines are the most robust agents in increasing synaptic dopamine levels since they do so regardless of the endogenous level in the neurons. Blockade of noradrenergic reuptake in the prefrontal cortex may also indirectly increase prefrontal dopamine levels. There is also evidence that the noradrenergic effects are mediated by alpha-2a noradrenergic receptors.

Clinical and epidemiological studies had equivocal results regarding growth retardation in children and adolescents with ADHD treated with methylphenidate. Some studies report growth retardation with a catch-up of growth during drug-holidays or after ceasing treatment. Bange et al. have reported an increase in Heart Rate (HR) and Blood pressure (BP) after treatment with Methylphenidate in patients of ADHD. The fact that Methylphenidate was associated with an increase in HR and BP could be attributed to the adrenergic effects. They have however found no increase in Myocardial infarction, stroke, and sudden cardiac deaths with methylphenidate.

ADHD Rating Scales
The usefulness of Conners' rating scale and Vanderbilt ADHD Rating Scale has been established by various studies. The Clinical Global Impression (CGI) rating is essential for providing a global rating of illness severity, improvement and response to treatment. The ADHD Rating Scales can be used as a clinician-administered and scored tool for assessing the severity of ADHD symptoms in paediatric patients.

Conners' rating scale
The initial Conners' Rating Scale (CPRS) was developed in 1970 as a comprehensive checklist for acquiring parental reports of the fundamental presenting problems for children referred to an outpatient psychiatric setting. This scale used to be the basis for the parental interview about the child's problems. In its original form, the CPRS contained items grouped regarding problems with sleep, problems with eating, problems with the temper, problems with keeping friends and difficulties in school. Later, an "additional" problems category was added that included item covering the cardinal symptoms of ADHD: hyperactivity, impulsivity, and inattention. Since the introduction, the psychometric properties of the CPRS have been well studied. Several versions of the CPRS are currently in use including a 48-item questionnaire improvised by re-standardization of a subset from the original scale. The CPRS is valuable research and clinical tool for obtaining parental reports of childhood behaviour problems. Advantages of the CPRS include a corresponding factor structure with the Conners' Teacher Rating Scale-Revised and comprehensive symptom coverage for ADHD and related disorders.

A 10-item abbreviated questionnaire was constructed from the items with the best factor loadings. The abridged version of Conners' rating scale revealed to be useful not only for diagnosis but also as an instrument to evaluate the effectiveness of the treatment of ADHD with Methylphenidate.

Vanderbilt ADHD Diagnostic Rating Scale (VADRS)
Among many ADHD rating scales, the VADRS, published in 2002 by the Association for Academic Psychiatry (AAP) and National Institute for Children’s Healthcare Quality, was designed to capture standardized ADHD symptom information from parents and teachers reporting on children’s behaviours. This rating scale was also intended to assist providers in screening Oppositional Defiant Disorder (ODD) and other common comorbidities.

Rating scales are reliable, valid, and efficient in measuring ADHD symptoms in children. They are helpful in research and clinical work.
also help in the treatment planning and ensure accountability in practice.\(^3\)\(^3\)\(^4\).

**Clinical Global Impression (CGI) rating scale**

CGI rating scale is amongst the most widely used of assessment tools in psychiatry. It is a 3-item observer-rated scale that measures illness severity (CGI-S), global improvement or change and therapeutic response. The illness severity score is measured before and after treatment, whereas CGI global improvement and CGI Clinical efficacy sections of the instrument are administered only after treatment. The illness severity and improvement sections of the CGI rating scale are used more frequently than the therapeutic response section in both clinical and research settings. Efficacy index is derived by dividing the therapeutic score by side effect score. The primary purpose of CGI rating is to provide a global evaluation of illness severity, improvement and response to treatment.\(^11\) The usefulness of CGI rating scale to monitor treatment response in ADHD has been variously studied.\(^35\)\(^36\).

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