Attention deficit hyperactivity disorder (ADHD) is among the most prevalent chronic health disorders affecting school-age children. The disorder is the subject of much debate for several reasons, the major one being the diagnostic process, which in some aspects is unstructured and can be relatively easily biased. The impact of undiagnosed or misdiagnosed ADHD on the lives of many children can be severe. Therefore, it is important to understand the complexities of the diagnostic procedure in ADHD, including the cultural bias effect, the limitations of the DSM-IV-TR definitions, the effect of comorbid conditions on the diagnostic process, the gene-environment interaction, and the need to compose an objective, more accurate, and generally accepted diagnostic battery of tests. This review addresses the diagnostic difficulties of ADHD and considers some steps that would make ADHD a more easily identifiable disorder.

**ABSTRACT:** Attention deficit hyperactivity disorder (ADHD) is among the most prevalent chronic health disorders affecting school-age children. The disorder is the subject of much debate for several reasons, the major one being the diagnostic process, which in some aspects is unstructured and can be relatively easily biased. The impact of undiagnosed or misdiagnosed ADHD on the lives of many children can be severe. Therefore, it is important to understand the complexities of the diagnostic procedure in ADHD, including the cultural bias effect, the limitations of the DSM-IV-TR definitions, the effect of comorbid conditions on the diagnostic process, the gene-environment interaction, and the need to compose an objective, more accurate, and generally accepted diagnostic battery of tests. This review addresses the diagnostic difficulties of ADHD and considers some steps that would make ADHD a more easily identifiable disorder.

**KEY WORDS:** attention deficit hyperactivity disorder, diagnosis, bias

ADHD = attention deficit hyperactivity disorder

ADHD Diagnostic Criteria: Possible Bias Effects

ADHD is characterized by a persistent pattern of inattention and/or hyperactivity-impulsivity, which is maladaptive and inconsistent with a comparable level of developmental age [6]. The DSM-IV-TR criteria classify the disorder into three general subtypes [6,7]:

I. Predominantly hyperactive-impulsive: a child who is excessively fidgety and restless, seems to always be “on the go,” and has difficulty waiting and remaining seated, acts immaturely, may not set physical boundaries, and may exhibit destructive behaviors

II. Predominantly inattentive: a child who is easily distracted, forgetful, manifests daydreaming, disorganization, poor concentration, and difficulty completing tasks

III. Combined type.

Children who exhibit the behavioral symptoms of ADHD but demonstrate no functional impairment do not meet the diagnostic criteria [6].

One of the major difficulties in diagnosis is that decisions about the inappropriateness of behavior in children are based on subjective judgments of the observers. Despite efforts of standardization, there are no data to offer a precise estimate of when diagnostic behavior becomes inappropriate [2,7]. So, the behavioral characteristics remain subjective and may be interpreted differently by different observers and in different cultures [2,8,9]. Significant variations in the prevalence rates around the world, based on variations in diagnostic methods, support the hypothesis of the role of diagnostic criteria bias [8].

Comorbidities

Another source of possible bias in the assessment of ADHD is the fact that ADHD often coexists with other conditions – psychiatric, psychological and developmental disorders – that...
sometimes overlap with ADHD symptoms [4,7]. Learning disabilities, oppositional defiant disorder, conduct disorder, anxiety and depressive disorders are the most common comorbidities among ADHD children [2,7]. As many as one-third of children with ADHD have one or more coexisting conditions [2]. Most of these disorders have a commonality, such as similarity in symptoms, the role of genetic factors, and environmental factors, age at onset, and even some aspects of the clinical course. Since the DSM-IV-TR definitions do not take into account diagnoses, cultural or developmental variations in behavior in their list of diagnosis criteria and do not specify which diagnostic tools should be used, it is even more difficult to separate ADHD symptoms from comorbid conditions.

**BIological Markers: Genes and Environment**

Scientific research over the past 30 years has helped characterize biological and genetic components involved in ADHD [4,9,10]. Strong evidence based on various types of genetic investigations of adoption, twins, and family studies demonstrates that ADHD has a genetic component [10,11]. The new possibilities that emerged from the human genome project led to the discovery of specific genes for attention, and the heritability of ADHD was estimated to be about 77% [4,11]. Furthermore, a number of susceptibility gene variant findings for ADHD have been independently validated and meta-analyses have yielded significant evidence of association [4,10,11].

It was expected that with the advanced genetic knowledge, a biological marker for the diagnosis of ADHD would be available [11,12]. However, even the researchers who discovered attention genes are aware of the fact that the course of this disorder cannot be explained solely by genes. A number of environmental factors appear to be significantly associated with ADHD [4,10,13]. Family environment and psychometric studies have suggested separate etiologies and pathophysiological mechanisms for ADHD [14].

The relationship between nature and nurture and genes and environment is still not well understood. This led to the introduction of the endophenotype concept, which divides behavioral symptoms into more stable phenotypes with a clear genetic connection [10,12]. The endophenotypes are inheritable quantitative traits that index an individual's potential to develop or manifest a given disease. In ADHD research the endophenotype concept "lags somewhat behind" [12]. Again, one of the difficulties is related to the bias in clinical diagnosis since "the current use of multiple variations of tests for the same cognitive domains prevents thorough generalization of the research findings" [12].

Geneticists and neuroscientists are "well aware that genes do not control behavior directly, that almost all behavioral traits emerge from complex interactions between multiple genes and environments, and that the brain bases of both personality and psychopathology are distributed across complex neural networks and are usually not caused by single loci" [15]. We assume that genetic and environmental interactions may be the reason for the phenotypic complexity of ADHD [11]. The disorder might have its origins in genes, but the course of the disorder is probably influenced by the way these genetic factors interact with and affect an individual's response to the environment [11].

Currently there is no available biological marker for the diagnosis of ADHD that can be used in clinical practice [4]. It is notable that many of the environmental risk factors for ADHD occur early in development, which is consistent with the idea that ADHD is a neurodevelopmental condition [1,16].

It is destined for future studies to discover the interactions between environmental and genetic factors, and to determine whether early recognition of these interactions might provide more effective management [16]. The literature suggests that multiple replications are necessary before a true association can be made between a given marker or candidate gene and ADHD [4,10]. Thus, more individuals with ADHD and their families need to be recruited for these studies [4,12]. Meanwhile, even though genetic tests are reliable and/or environmental factors indisputable, the clinician cannot rely on them to diagnose ADHD on a routine basis.

**Clinical Diagnosis**

There is a discrepancy between the clinical based procedure of ADHD diagnosis and the expanding scientific, biological, genetic and imaging knowledge. In the absence of available biological markers that would support diagnostic tests, clinicians are asked to continue to use a structured interview based on DSM-IV-TR clinical criteria, together with behavior rating scales [2,6,17]. As mentioned above, this process is subjective and might be easily biased. Given the absence of methods to confirm ADHD diagnosis by other means, it is important to recognize the limitations of the DSM-IV-TR definitions by adding more objective means of assessment to the diagnostic process [2].

**Questionnaires**

Several questionnaires and rating scales were developed to differentiate between ADHD and comorbid disorders, and to detect coexisting conditions in ADHD children [2,7]. The
use of general clinical impressions or descriptions within the domains of attention and activity is insufficient to diagnose ADHD or to differentiate between ADHD and non-ADHD children [2,7]. Therefore, these tools are not recommended for the diagnostic process [2].

The ADHD-specific questionnaires and rating scales have been shown to have sensitivity and specificity greater than 94% under ideal conditions, but much less in primary care settings even when based on self-report [2,7,18]. The use of questionnaires and rating scales as a developmental screening tool has demonstrated that the sensitivity and positive predictive values were much too low to allow a routine screening procedure for ADHD with these items among children [18]. Like other measures of clinical criteria assessment, questionnaires and rating scales are subjective and subject to bias, so their results may convey a false sense of validity and cannot always be relied upon [2,18]. Therefore, ADHD questionnaires and rating scales add important data to the clinical diagnostic process but cannot serve as a single reliable diagnostic tool.

CONTINUOUS PERFORMANCE TESTS

There has long been interest in developing laboratory-based measures that could support ADHD diagnosis. The interest derives from the potential advantages that objective laboratory-based measures might have over more traditional measures [19].

Computerized continuous performance tests were intended to serve as an objective measure that would aid in the clinical assessment of ADHD. CPT are generally characterized by the rapid presentation of continuously changing stimuli among which there is a designated “target” stimulus or “target” pattern. Most CPT measure the number of correctly detected stimuli as well as response time [2,20]. CPT have several advantages: they are cost effective, are relatively free from bias, provide immediate information, are easy to administer, rely only on the individual being evaluated, and can be administered in a variety of settings [19]. Thus, although not recommended by the American Academy of Pediatrics, CPT are reported to be the most popular clinic-based measure of ADHD [20,21]. The clinical utility of CPT in the diagnosis of ADHD is the subject of much controversy due to the relatively high number of false negative errors and low overall utility [2,20,21].

CPT were found to distinguish between ADHD and non-ADHD children but have been inconsistent in differentiating ADHD from other clinical groups [19,22]. Although some studies indicate that CPT are potentially clinically useful tools in ADHD evaluation, others did not provide support for the validity of the available CPT as an attention measure and failed to demonstrate the discriminant validity of any score regardless of the behavior rating scales used [2,19-21,23]. Most researchers concluded that the data supporting the validity of the CPT are limited and stress the need for further validity studies [2,19,21]. The American Academy of Pediatrics concluded that the current data do not support the use of any CPT in the diagnosis of ADHD [2]. Other tests might be available, but a detailed description of these is beyond the scope of this review.

CONCLUSIONS

It is important to recognize the complexities of the diagnostic procedure in ADHD. The first significant step is the understanding that ADHD is the extreme end of a continuum and not an isolated disorder [4]. Concluding that “ADHD is unlikely to exist as an identifiable disease” [5] is probably short-sighted since it might leave many children neglected, undiagnosed and suffering. The impact of undiagnosed ADHD on the lives of so many could be severe and a better attitude is warranted.

Several recent studies demonstrate this point [7,18]. Elkins et al. [24], who explored whether there is a prospective relationship between ADHD and initiation of substance abuse disorder, concluded that ADHD predicts later substance abuse problems, even when only a single symptom exists. They also claimed that the failure in previous research to consistently observe relationships between ADHD and substance abuse outcomes could be due to reliance on less-sensitive categorical diagnoses [24].

Langley and co-researchers [25] recently suggested that individuals with ADHD represent a high risk group for serious antisocial behavior and impose a significant cost to society as well as to the individual. They recommend that any long-term clinical treatment of individuals with ADHD include monitoring and interventions even at diagnostic subthreshold levels.

Clearly, the diagnostic process of ADHD requires the development of more definitive measures [2]. The solution lies in more research that will guide us towards better diagnostic tools. In conclusion:

- It is important to recognize the limitations of the DSM-IV-TR definitions. Since current criteria do not take into account gender, cultural bias, or developmental variations in behavior, there is a need to verify the DSM criteria in a more specific way that takes all these issues into account [2].
Coexisting and comorbid conditions are common among children with ADHD [2,7]. Additional research is required, particularly regarding the neural substrates and biomarkers of comorbid conditions. Until research results become available there is a need to carefully assess the occurrence of comorbid conditions among ADHD children by using specific diagnostic tools validated for these conditions.

The etiology of ADHD is a combination of genetic and environmental factors [11,12]. The early recognition, prevention and treatment of environmental causes may provide more effective management and reduce the reliance on symptom modification with medications [16,26]. Future research needs to determine whether modifying environmental risk factors can lead to preventive interventions [11,16].

Genetic research must be enhanced by new technologies, combined with imaging, neurophysiologic and neuropsychological measures [12].

There is a need to compile a mandatory, more accurate, and generally accepted diagnostic battery of tests for all clinicians who assess ADHD children.

Composing a set of objective diagnostic tests based on computerized (objective) tests including a broad range of tasks that have been examined for validity and reliability will let clinicians use the same battery of tests at the primary care setting and will add better tools for clinical diagnosis [2,12].

These and other improvements of the diagnostic process can be implemented. Such improvements will allow us to develop better measurements of assessment and treatment of ADHD that can be applied even in the primary care setting [2,26] and might make ADHD a more easily identifiable disorder. In view of the high prevalence of ADHD, such improvements will likely have a significant effect on public health.

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