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REVIEW

Attention Deficit Hyperactivity Disorder: Advances in Epidemiology, Pathogenesis, and Neurobiology

Trastorno por Déficit de Atención e Hiperactividad: Avances en Epidemiología, Patogénesis y Neurobiología

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ABSTRACT

Introduction: ADHD is a neurodevelopmental condition that affects approximately 5-7 % of children and adolescents and persists in a significant number of cases into adulthood, with an estimated prevalence of 2,5 % in adults globally. The impact goes far beyond school or work performance; it is associated with an increased risk of accidents, risky behaviors, comorbid disorders such as anxiety, depression, substance use disorders, and a significant reduction in quality of life.
Method: a search was conducted in the databases SciELO, Scopus, PubMed/MedLine, Google Scholar, Cochrane Library, as well as Clinical Keys services. The search terms for the search formulation were “ADHD”, “attention deficit disorder”, “Hyperactivity”, “depression”, “autism spectrum”, “anxiety”, as well as their translations into English.
Results: the reported prevalence of ADHD in children ranges from 2 to 18 percent depending on the diagnostic criteria and the population studied. The prevalence in school-aged children is estimated to be between 9 and 15 percent, making it one of the most common childhood disorders. Possible etiological factors include comorbid disorders, oppositional defiant disorder, conduct disorder, anxiety disorder, depression, developmental coordination disorder, autism spectrum disorder, and sleep disorders.
Conclusion: ADHD constitutes a complex neurodevelopmental condition whose impact transcends clinical boundaries to become a multifaceted challenge for public health, neuroscience, and social justice.

Keywords: Attention-Deficit Hyperactivity Disorder; ADHD; Depression; Anxiety; Autism Spectrum Disorder.

RESUMEN

Introducción: el TDAH es una condición del neurodesarrollo que afecta aproximadamente al 5-7 % de niños y adolescentes y persiste en un número significativo de casos durante la adultez, con una prevalencia estimada

del 2,5 % en adultos globalmente. El impacto va mucho más allá del rendimiento escolar o laboral, se asocia con mayor riesgo de accidentes, conductas de riesgo, trastornos comórbidos como ansiedad, depresión, trastorno por uso de sustancias, y una reducción significativa en la calidad de vida.
Método: se realizó una búsqueda de información en las bases de datos SciELO, Scopus, PubMed/MedLine, el buscador Google Académico, Cochrane Library, así como en los servicios Clinical Keys. Los términos de búsqueda para la formulación de búsqueda fueron "TDHA","Trastorno por Déficit de Atención", "Hiperactividad", "depresión", "espectro autista", "ansiedad", así como sus traducciones al idioma inglés.
Resultados: la prevalencia informada de TDAH en niños varía del 2 al 18 por ciento dependiendo de los criterios de diagnóstico y la población estudiada. Se estima que la prevalencia en niños en edad escolar está entre el 9 y el 15 por ciento, lo que lo convierte en uno de los trastornos más comunes de la infancia. Algunos de los posibles factores etiológicos son: trastornos comórbidos, trastorno negativista desafiante, trastorno de conducta, trastorno de ansiedad, depresión, trastorno del desarrollo de la coordinación, trastorno del espectro autista y trastornos del sueño.
Conclusión: el TDAH constituye una condición compleja del neurodesarrollo, cuyo impacto trasciende las fronteras clínicas para convertirse en un desafío multifacético de salud pública, neurociencia y justicia social.

Palabras clave: Trastorno por Déficit de Atención e Hiperactividad; TDHA; Depresión; Ansiedad; Espectro Autista.

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental condition that affects approximately 5-7 % of children and adolescents and persists in a significant number of cases into adulthood, with an estimated prevalence of 2,5 % in adults globally. It is a disorder that manifests in childhood with symptoms of hyperactivity, impulsivity, and/or inattention. Symptoms affect cognitive, academic, behavioral, emotional, and social functioning. ADHD is a disorder that manifests in early childhood with symptoms of hyperactivity, impulsivity, and/or inattention. Symptoms affect cognitive, academic, behavioral, emotional, and social functioning. This disorder is characterized by persistent patterns of inattention, hyperactivity, and impulsivity that significantly interfere with the individual's social, academic, and occupational functioning.[1] Despite its high prevalence, ADHD remains an underdiagnosed, stigmatized, and often misunderstood condition, especially in populations such as women, older adults, and people from disadvantaged socioeconomic backgrounds.[3,4] From a historical perspective, ADHD was initially conceptualized as a childhood disorder with obvious behavioral manifestations. However, advances in cognitive neuroscience, genetics, evolutionary psychiatry, and functional neuroimaging have revealed a much more complex and dynamic basis, where multiple biological, psychological, and social factors converge.[5] Current models of ADHD address it as a neurocognitive self-regulation disorder, in which the front striatal systems responsible for sustained attention, inhibitory control, motivation, and executive function are compromised.[6]

The impact of ADHD goes far beyond school or work performance; it is associated with an increased risk of accidents, risky behaviors, comorbid disorders such as anxiety, depression, substance use disorder, and a significant reduction in quality of life. In addition, the economic costs of treatment, lost productivity, and family impact are significant worldwide, representing a priority challenge for public health systems.

In recent decades, advances in diagnostic technologies such as neuroimaging, quantitative electroencephalography (qEEG), artificial intelligence, and genomic analysis are enabling an evolution from a categorical approach to a multidimensional and personalized one, recognizing the heterogeneity of the disorder and its expression throughout the lifespan.[9,10] On the other hand, new digital therapies, therapeutic video games, non-invasive brain stimulation, and neurofeedback-based approaches are emerging as complements or alternatives to traditional pharmacological treatments. [11]

This context presents a historic opportunity: to rethink ADHD from a multidimensional, interdisciplinary, and person-centered approach that transcends symptoms to focus on human potential. This review follows a narrative approach, synthesizing current advances in the understanding of the epidemiology, pathogenesis, and neurobiology of ADHD. While this is not a systematic review, our goal was to highlight key advances and areas for future research based on the recent literature.

METHOD

A search for information was conducted on January, 2025 in the SciELO, Scopus, PubMed/MedLine, Google Scholar, Cochrane Library, and Clinical Keys databases, using search formulas with Boolean operators such as "AND" and "OR," adapted to the specific syntax of each database. The search terms used to formulate

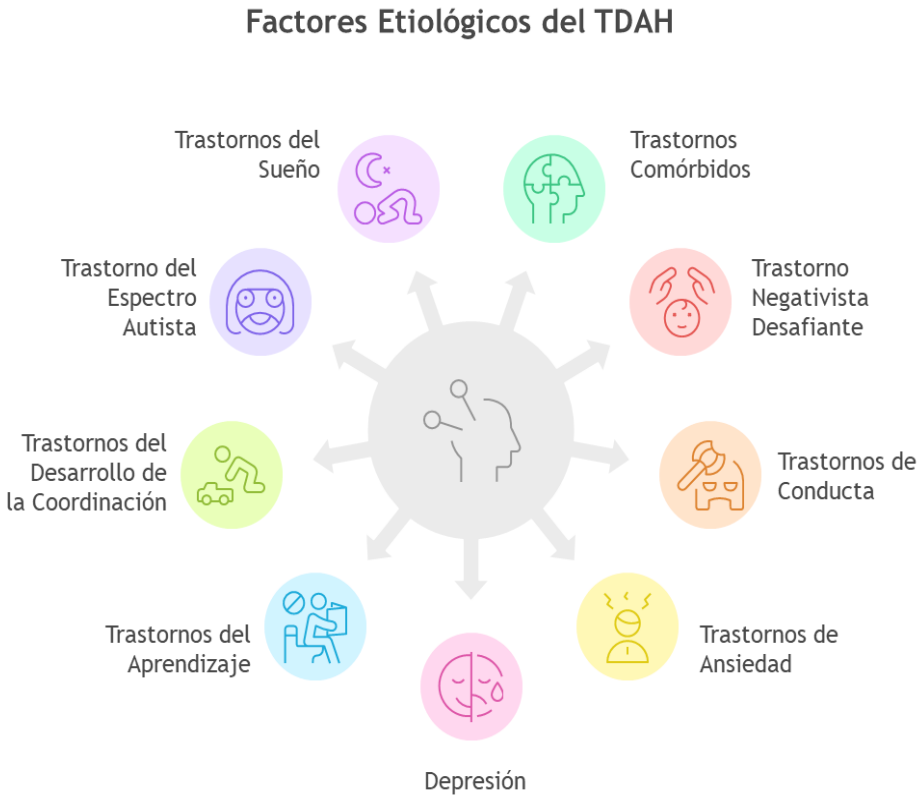
the search were "ADHD," "Attention Deficit Disorder," "Hyperactivity," "depression," "autism spectrum," "anxiety," as well as their translations into English: "ADHD," "Attention Deficit," "Hyperactivity Disorder," "depression," "anxiety," "autism spectrum disorder." From the resulting documents, those written in the last 10 years, in Spanish or English, that provided updated information on Attention Deficit Hyperactivity Disorder were selected. It should be noted that, although this time frame was prioritized, some systematic reviews covered longer periods, such as the last 5 years, the last 10 years, or did not apply a specific date limit.

RESULTS

Epidemiology

The reported prevalence of ADHD in children ranges from 2 to 18 percent depending on the diagnostic criteria and the population studied. The prevalence in school-aged children is estimated to be between 9 and 15 percent, making it one of the most common childhood disorders.[12,14,15,16,17,18,19] In a meta-analysis of 175 studies (including 1,023,071 subjects over the age of 36), the estimated pooled prevalence of ADHD was 7,2 % (95 % CI: 6,7 to 7,8).[2] The studies were geographically diverse (Europe, Asia, North America). Most were conducted in school-aged children. The prevalence of ADHD in children has been increasing.[20,21,22] In the National Health Interview Survey (NHIS), caregivers reported that 11,3 % of children aged 5 to 17 years in the United States had ever received a diagnosis of ADHD,[21] an increase from 9,6 % in 2017 to 2018 in children aged 3 to 17[22] and from 6 % in 1997 to 1998 in children aged 4 to 17.[20]

Prevalence was higher among children living in non-metropolitan areas compared with large central metropolitan areas (13,9 % vs. 9,4 %). Prevalence increased with age in both geographic areas (children aged 5 to 11 years: 10,8 % in non-metropolitan areas vs. 6,9 % in metropolitan areas; children aged 12 to 17 years: 17,1 % in non-metropolitan areas vs. 12,1 % in metropolitan areas). Previous surveys have shown a similar increase in prevalence with age. ADHD is more common in males than in females (the male-to-female ratio is 4:1 for the predominantly hyperactive-impulsive presentation and 2:1 for the predominantly inattentive presentation).[23] In the National Health Interview Survey (NHIS), the prevalence of ADHD was 12,9 % in males and 6,2 % in females.[2] In the same report, the prevalence was highest in non-Hispanic black and non-Hispanic white children (11,4 % and 10,9 %, respectively). Possible explanations for the apparent increase in the prevalence of ADHD over time include greater awareness and identification of cases by primary care professionals, educators, and parents, or more frequent exposure to some of the possible etiological factors described below (figure 1).



Source: Own elaboration

Figure 1. Etiological factors of ADHD

Comorbid disorders

Children and adolescents with ADHD often have psychiatric and neurodevelopmental disorders, including oppositional defiant disorder (ODD), conduct disorder, depression, anxiety disorder, autism spectrum disorder (ASD), and learning disorders.[24,25,26,27,28,29,30] Comorbid conditions may be primary or secondary. In either case, they require treatment independent of, but often additional to, treatment for ADHD.[14,31,32]

Oppositional defiant disorder (ODD): coexists with ADHD in approximately 50 to 80 % of cases.[23,29,33] It is more common in children with combined and hyperactive-impulsive manifestations.[34,35] Their excessive activity, impulsive response style, and uninhibited emotional expression often bring them into conflict with their caregivers and other adults.

Conduct disorder: coexists with ADHD in up to one-third of cases. [23,24,29] Like ODD, it is more common in combined and hyperactive-impulsive presentations.[34,35]

Anxiety disorder: coexists with ADHD in approximately 20 to 40 % of cases.[23,24,29,33] It occurs more frequently in the inattentive presentation.[23,34,35] Anxiety may develop as a secondary disorder in children with ADHD; however, in many cases, anxiety appears to be a distinct disorder and may be independent of ADHD.[25,36]

Depression: coexists with ADHD in up to one-third of cases.[23,24,29,33] It appears to be more common in inattentive and combined presentations.[34,35] Children with ADHD and comorbid mood disorder may have family members with a history of major depressive disorder. [27] Adolescents with ADHD and mood disorder are at increased risk for suicide attempts.[37,38,39]

Learning disorders: the co-occurrence of learning disorders and ADHD is estimated to range from 20 % to 60 %.[23,24,28,40] In a population-based birth cohort, approximately 40 % of children with ADHD also had reading difficulties, and approximately 60 % of children with ADHD also had written language disorder.[41,42] Learning disorders appear to be more common in children with inattentive and combined ADHD.[34,35] Data on the rates of co-occurrence of specific types of learning disorders and ADHD are lacking. In a study of 445 ninth-grade students, children with reading difficulties were twice as likely to meet the diagnostic criteria for inattentive presentation as the general population (15 % vs. 7 %).[43] Conversely, individuals with ADHD were at greater risk than the general population of having reading difficulties or phonological awareness deficits (36 % vs. 17 %).

Developmental coordination disorder: approximately half of children with ADHD meet the criteria for developmental coordination disorder (DCD). The association between ADHD and DCD is discussed separately.

Autism spectrum disorder: ASD often coexists with ADHD, although many children with ADHD do not have ASD.[44,45] In children with comorbid ADHD and ASD, the initial diagnosis of ADHD may delay the diagnosis of ASD. [46] Children with comorbid ADHD and ASD tend to have more severe cognitive impairment, behavioral problems, and psychopathology than children with ADHD or ASD alone.[47,48,49,50]

Sleep disorders: children with ADHD may have comorbid sleep disorders.[14] In addition, sleep disturbances underlie behavioral symptoms.

Table 1. Pathogenesis of ADHD: Possible influences

Author(s)	Year	Type of study	Possible influence	Main Results
Faraone et al.[51]	2015	Systematic review	Genetics	The heritability of ADHD is estimated at ~76 %. Multiple genes associated with dopamine (DRD4, DAT1) were identified, affecting inhibitory control and sustained attention.
Demontis et al.[52]	2019	Multicenter study	Polygene genetic basis	They identified 12 genetic loci associated with ADHD; these genes regulate neuronal and synaptic functions, especially in the prefrontal cortex and basal ganglia.
Rubia et al.[6]	2018	Review of functional neuroimaging	Neurodevelopment (affected brain networks)	Evidence of dysfunction in fronto-striatal networks, cerebellum, and parietal cortex. Delayed cortical maturation of up to 3 years in key regions for self-control.
Shaw et al.[53]	2007	Longitudinal study with brain MRI	Delayed cortical maturation	Children with ADHD showed delayed peak cortical thickening, especially in the prefrontal cortex, compared to controls (~108 vs. 123 months).
Sciberras et al.[54]	2017	Narrative review	Environmental factors (prenatal and postnatal)	An association was found between prenatal exposure to alcohol, tobacco, low birth weight, and the development of ADHD. A negative family environment also contributes.
Cortese et al.[55]	2020	Meta-analytic review	Structural and functional brain abnormalities	Reduced volume in the caudate nuclei, putamen, and cerebellum. Hypoactivation in cognitive control and sustained attention tasks.

Loo & Makeig.[56]	2012	EEG study	Imbalance in cortical activity (EEG)	Children with ADHD show an increased theta/beta ratio in frontal areas, suggesting cortical immaturity and attentional dysregulation.
Pliszka et al.[57]	2007	Clinical study + neuroimaging	Dopaminergic dysfunction	Decreased dopaminergic activity in prefrontal and subcortical regions; this affects motivation, attention, and impulse control.

Neurobiological basis

Adequate levels of dopamine (DA) and noradrenaline (NA) are required in the prefrontal cortex for executive functions (EF), including attention. Dopaminergic activity within the corticostriatal pathway is involved in motor functions and impulse control, while NA plays a role in shifting attention in the parietal lobes and regulating wakefulness in the brainstem. Given that the drugs used to treat this disorder have an effect on both catecholamines, the dopaminergic and noradrenergic systems are believed to play a fundamental role in the neurobiology of ADHD.[58] Glutamate is a regulator of DA in the prefrontal cortex and striatum. A possible role for the serotonergic and cholinergic systems in the development of ADHD has also been proposed, based on the fact that the former is involved in impulse control, while the latter is involved in memory and cognitive functions.

Neurophysiology

Studies of cranial electrical activity and blood flow have shown reduced blood flow and activity in the prefrontal cortex, parietal lobe, and basal ganglia of individuals diagnosed with ADHD.[5,62]Electroencephalography (EEG) studies have demonstrated increased theta wave activity and rreduction in alpha and beta wave activity in ADHD, which normalized with treatment.[62,63] Event-related potential studies showed smaller N2 and P3 amplitudes among ADHD patients, suggesting that this could be related to impulse control problems that may be alleviated with treatment.[62,63,64] In addition, ADHD may be related to problems in areas of the brain linked to daydreaming.[65]

CONCLUSION

Attention deficit hyperactivity disorder (ADHD) is a complex neurodevelopmental condition whose impact transcends clinical boundaries to become a multifaceted challenge in public health, neuroscience, and social justice. Our understanding of ADHD has evolved significantly in recent decades, particularly in the fields of epidemiology, pathogenesis, and neurobiology, allowing us to reframe this disorder beyond a mere childhood behavioral dysfunction. From an epidemiological perspective, recognition of its persistent prevalence into adulthood, along with the identification of diagnostic gaps in historically invisible groups such as women and people in disadvantaged socioeconomic contexts, has highlighted the urgent need to improve detection, differential diagnosis, and access to services at all stages of the life cycle. In terms of pathogenesis, the reductionism of single-factor models has been overcome in favor of a multifactorial paradigm. The integration of these advances represents a paradigm shift toward a more inclusive, transdisciplinary, and person-centered model that recognizes the diversity of ADHD trajectories and promotes a more humane, functional approach tailored to the specific needs of each individual.

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