World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2019 September 6; 7(17): 2420-2426

DOI: 10.12998/wjcc.v7.i17.2420

ISSN 2307-8960 (online)

MINIREVIEWS

Attention deficit hyperactivity disorder and comorbidity: A review of literature

Sundar Gnanavel, Pawan Sharma, Pulkit Kaushal, Sharafat Hussain

ORCID number: Sundar Gnanavel (0000-0003-0384-7357); Pawan Sharma (0000-0003-4983-7568); Pulkit Kaushal (0000-0002-4609-268X); Sharafat Hussain (0000-0001-9209-2421).

Author contributions: Gnanavel S conceptualised and synthesised the review; Sharma P and Kaushal P contributed to different parts of the review; Hussain S proof read the manuscript, provided inputs for revising the manuscript.

Conflict-of-interest statement: None of the authors have any conflicts of interest to declare pertaining to content of this manuscript.

Manuscript source: Invited Manuscript

Received: April 6, 2019
Peer-review started: April 8, 2019
First decision: June 21, 2019
Revised: July 10, 2019
Accepted: July 27, 2019

Sundar Gnanavel, Child Mental Health Services, Tees, Esk and Wear Valleys NHS Foundation Trust, Durham DH1 4LW, United Kingdom

Pawan Sharma, Department of Psychiatry, Patan Academy of Health Sciences, Patan 44700, Nepal

Pulkit Kaushal, Sharafat Hussain, Northumberland, Tyne and Wear NHS foundation Trust, Newcastle NE3 3XT, United Kingdom

Corresponding author: Sundar Gnanavel, MD, Doctor, Child Mental Health Services, Tees, Esk and Wear Valleys NHS Foundation Trust, North End, Durham DH1 4LW, United Kingdom. sundar221103@yahoo.com
Telephone: +44-73-41672503

Abstract

Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder with onset in early childhood. It is a clinically heterogenous condition with comorbidity posing a distinct challenge to diagnosing and managing these children and adolescents. This review aims to provide an overview of comorbidity with ADHD including other neurodevelopmental disorders, learning disorders, externalising and internalising disorders. Challenges in screening for, diagnosing and managing comorbidity with ADHD are summarised. Also, methodological challenges and future directions in research in this interesting field are highlighted.

Key words: Attention deficit hyperactivity disorder; Comorbidity; Review

Core tip: Attention deficit hyperactivity disorder (ADHD) is a clinically heterogenous condition that is typically complicated by extensive comorbid conditions. Screening for comorbidity is imperative for appropriately managing these children and adolescents presenting with complex difficulties. Further research is required for elucidating the implications of comorbidity in terms of diagnosing and managing children with ADHD.

Citation: Gnanavel S, Sharma P, Kaushal P, Hussain S. Attention deficit hyperactivity disorder and comorbidity: A review of literature. *World J Clin Cases* 2019; 7(17): 2420-2426
URL: https://www.wjgnet.com/2307-8960/full/v7/i17/2420.htm

Article in press: July 27, 2019
Published online: September 6, 2019

P-Reviewer: El-Razek AA
S-Editor: Cui LJ
L-Editor: A
E-Editor: Xing YX

DOI: https://dx.doi.org/10.12998/wjcc.v7.i17.2420

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is characterized by pervasive and impairing symptoms of inattention, hyperactivity, and impulsivity according to Diagnostic and Statistical Manual of Mental Diseases (DSM-V)[1]. It is a common childhood onset mental disorders with reported prevalence rates of 5%-8% in school children[2]. ADHD has been identified as an extremely clinically heterogenous disorder with one of the reasons being high rates of comorbidity with other childhood onset disorders. It is estimated that around 60%–100% of children with ADHD also exhibit one or more comorbid disorders that often continue into adulthood[3,4], This narrative review aims to provide an overview of current research (including recent research findings) on comorbidity with ADHD, methodological issues with such studies and implications for nosological systems, clinical management as well as future research. The scope of this review includes comorbid mental health disorders but not physical illnesses. The review also highlights the need for a dimensional construct, particularly after release of DSM V diagnostic criteria[1].

ADHD AND COMORBIDITY

Autism spectrum and other neurodevelopmental disorders

Autism spectrum disorder: While DSM IV precluded a dual diagnosis of ADHD and autism spectrum disorder (ASD), DSM V allows for the dual diagnosis if appropriate diagnostic criteria are met. In a recent nationally representative sample from United States, in children diagnosed with ASD, the rate of comorbidity with ADHD was 42% and the rate of comorbidity with ADHD and learning disability (LD) was 17%, resulting in a 59% total comorbidity rate of ADHD and ASD[5]. In terms of symptomatology, it is widely believed that there is good degree of overlap between symptoms of ADHD and ASD. However, a recent study demonstrated that it was possible to discriminate symptom profiles of ASD and ADHD in children[6]. Another study demonstrated that children and adolescents with combined ADHD and ASD have more severe symptoms across all domains and an additive severity of sleep-related difficulties in this group[7].

Novel neuroimaging techniques including diffusion tensor imaging (DTI) have been utilised to demonstrate neurobiological changes that correspond with clinical severity in neurodevelopmental disorders and this might be a future tool to assess for additive severity of comorbid conditions in this regard[8].

Learning disorders: There is a wide variation in reports of comorbidity between ADHD and learning disorders, ranging from 10%-92%[9]. This is possibly due to differences in diagnosis and discriminating between both the conditions in individual studies[8]. A recent study demonstrated the relationship between learning difficulties and ADHD symptoms, predominantly in the inattentive type[10]. In an earlier study, a LD was present in 70% of the children with ADHD. A LD in writing was two times more common (65%) than a LD in reading, math, or spelling[11].

Tic disorders: In an international study on tic disorders and ADHD, the reported prevalence of ADHD in Tourette's syndrome (TS) was 55%[12]. Previous studies have cited similar numbers as well[13]. The other salient findings from the study were ADHD was associated with earlier diagnosis of TS and a much higher rate of other difficulties including anger management, insomnia, learning difficulties, Obsessive compulsive disorder (OCD), Oppositional defiant disorder (ODD), mood disorder, and self-injurious behaviour[14].

ADHD and internalizing disorders

Depressive disorder: The rate of major depression in youth with ADHD ranges from 12% to 50% which is more than five times higher than in youth without ADHD[13]. It is also shown that this comorbidity is higher in clinical sample than in the community sample[14]. Depressive disorders with ADHD typically occur several years after the onset of ADHD and is independent of other comorbidities[15]. Co-morbid depression is regarded as an outcome of ADHD-related impairments and negative environmental circumstances also called as ADHD-related demoralization by many authors[15-17].

However, ADHD and depression have independent and distinct courses. This proves that ADHD-associated depression reflects a depressive disorder and not merely demoralization[17].

Bipolar disorder: The rates of comorbidity between pediatric bipolar disorder and ADHD have been greater than the chance findings but are dramatically different across studies[18-20]. Evidence suggests some mechanisms for comorbidity including shared risk factors, distinct subtypes and weak causal relationships[21]. However, the clinical diagnosis of ADHD is not a reliable antecedent in the developmental trajectory toward bipolar disorder[22]. The association between these disorders appears more co-incidental than a causal relationship /predictive association. But when these two disorders co-occur the patient will have poorer global functioning, greater symptom severity, and more additional comorbidity than for either of these disorders[23].

Anxiety disorders: The prevalence of anxiety symptoms in ADHD patients range from 15% to 35%[24,25]. The rates of comorbidity may be affected by the symptom overlap and the diagnostic systems[13]. The relationship between ADHD and anxiety appears to be robust, existing in all populations and in children seen by primary care pediatricians as well[24,25]. This co-existence has been described by different psychological as well as biological models[26,27]. In terms of neurophysiology, anxiety in ADHD may partially inhibit the impulsivity and response inhibition deficits, make working memory deficits worse, and may be qualitatively different from pure anxiety. The co-morbid condition has more negative affectivity and disruptive social behaviour and less fearful/phobic behaviour. The anxiety in ADHD may substantially change the presentation and course of the disorder[17]. The co-morbid condition is associated with more attentional problems, school phobia and mood disorders and lower levels of social competence than either ADHD or anxiety alone[14]. However, when the moderation effect of ADHD in anxiety was studied it was seen that ADHD had a limited impact on the manifestation of anxiety disorder giving an evidence that ADHD and anxiety disorders are independently expressed in children[28]. It is widely suggested that due importance be given to assessment of anxiety symptoms while assessing and treating ADHD[29,30].

ADHD and externalizing disorders: Common externalizing disorders comorbid with ADHD include ODD and Conduct disorder (CD). Newer diagnostic categories like Disruptive Mood Dysregulation Disorder (DMDD) and Intermittent Explosive Disorder (IED) have also been shown to exist comorbidly with ADHD[31,32]. It is demonstrated that 30%-50% children with ADHD also fulfill criteria for CD or ODD. Population-based studies usually identify occurrence of comorbidity more in boys than girls[33].

The strikingly high rates of comorbidity could at least be partially attributed to shared genetic origin[34]. Longitudinal studies suggest that the correlation between ADHD-like and externalizing traits increases across age (from childhood to adulthood) and ADHD-like traits may exacerbate externalizing tendencies in the transition from adolescence into adult life[35]. With regard to predictive environmental factors, researchers have found that children with ADHD suffering from neuropsychological dysfunction, early aggressive behaviour, and adverse family circumstances are at increased risk for comorbid externalizing disorders[36].

CD and oppositional defiant disorder: The combined impact of ADHD with other externalizing disorders on functioning can be profound. Higher rate of academic problems in children with above comorbidity like reading disorder, impaired verbal skills, visual motor integration and visuospatial skills on neuropsychological measures is well documented when compared with children without such comorbidity[36]. Furthermore, ADHD/CD children are more likely to abuse drugs, engage in criminal behaviour, have driving-related outcomes and are more likely to adult antisocial personality disorder than children with ADHD alone[37-39]. ADHD/CD has also been found to be associated with higher expulsion and dropout rates in school than in children with ADHD alone[40] (Table 1).

Apart from impact on clinical course and symptomatology, such comorbidities also pose a diagnostic challenge for clinicians. With several overlapping clinical features, distinction between ADHD and CD can sometimes be unclear. Thus, a hybrid disorder hyperactive CD with an earlier onset and an outcome worse than of either disorder alone is now recognized[41]. Similarly, most of the patients who have been diagnosed as DMDD also fulfilled the diagnostic criteria for ODD/CD with ADHD and it becomes difficult to diagnose them as comorbid disorders[41].

Disruptive mood dysregulation disorder and IED: Sagar-Ouriaghli *et al*[31] thus

Table 1 Summary of some key studies on comorbidity with attention deficit hyperactivity disorder in children and adolescents

Comorbidity with attention deficit hyperactivity disorder	Incidence (%)	Ref.
Autism spectrum disorder	59	Stevens *et al*[5]
Learning disorders	10-92 70	Biederman *et al*[9] Mayes *et al*[11]
Tic disorders	55	Freeman *et al*[12]
Depressive disorder	12-50	Angold *et al*[13]
Bipolar disorder	5-47	Galanter *et al*[18]
Anxiety disorders	15-35	Jensen *et al*[25]
Conduct disorder	3.5-10	Barkley *et al*[40]
Oppositional defiant disorder	30-50	August *et al*[37]

postulated that DMDD appears to be an alternative way of describing the presence of ODD/CD with either anxiety or ADHD. Symptoms of aggression, anger and impulsivity are also seen in IED and high rate of comorbidity are reported in literature. An early onset and common core clinical features of both these disorders suggest a strong association between these disorders[42].

IMPLICATIONS

Phenotypes and endophenotypes of ADHD

Genetic studies on ADHD and comorbid disorders is one of the key methods to investigate the putative ADHD phenotypes based on comorbidities. For example, the study addressed the question of how the association between ADHD and reading disability (RD) might arise. The clear conclusion from subsequent studies investigating their co-occurrence is that there is a common genetic aetiology[43-49]. This raises two possibilities: either that RD and ADHD in general are influenced by the same genes or when they co-occur this comorbid group have a distinct genetic origin from those acting on RD and ADHD in isolation[50].

Studies focusing on dimensional constructs of ADHD like executive dysfunction in "pure" cases *vs* comorbid cases is another method to disentangle the association. For example, in a recent study comorbid problems including autistic traits, motor coordination problems and reading problems were just associated phenotypically, were also related to the executive function (EF) and motor ADHD-endophenotypes after correction for ADHD[51]. These findings may point towards a shared underlying neuropsychological dysfunction that may give rise to both ADHD and comorbid disorders. These familial and shared neuropsychological endophenotypes appear to have multiple behavioural consequences (pleiotropy)[52].

This gives rise to the question whether ADHD with comorbidity is viewed as a distinct phenotype or simply accentuates the severity of ADHD symptoms. A number of studies suggest that the combination of ADHD with a comorbid problem may not be best conceptualized as a distinct phenotype since the interaction between ADHD and the comorbid condition did not have predictive value on the core deficits (*e.g.*, EF) over and beyond the independent effects of ADHD and the comorbid condition[13,53-56].

Response to treatment

Comorbid conditions with ADHD have a definite bearing on selection of treatment modality as well as treatment response. For example, the landmark Multimodal treatment of ADHD study demonstrated that subjects with both ADHD and anxiety disorders are particularly responsive to behavioural therapy, compared with subjects in other comorbidity groups including those with ODD/CD[25,52]. Patients with ADHD, anxiety disorders and ODD/CD subjects were preferentially responsive to combination interventions with both medication and behavioural therapy. In children with only ADHD, and ADHD with ODD/CD behavioural intervention in isolation didn't appear beneficial[25,54].

Nosological systems

Evaluating the presence of comorbidity between different psychiatric conditions offers a method of both correcting and validating psychiatric nosology[13]. The co-occurrence of ADHD and comorbidity is partly due to shared familial/heritable neuropsychological deficits and motor dysfunction[56]. This implies that these symptoms cannot be diagnosed or treated independently of one another. This has

definite theoretical implications in future nosological systems, particularly when we consider this in the framework of RDoC (research domain criteria) of NIMH (National institute of mental health) that postulates linking basic dimensions of functioning to behaviour[57].

Methodological issues in research on ADHD and comorbidity

For an accurate interpretation of studies on ADHD and comorbidity in relation to implications in clinical management as well as future research, it is important that we consider the results in light of certain methodological limitations. The choice of information sources (*e.g.*, clinician, parent, teachers self-report, behavioural observation) as well as method of arriving at a diagnosis (*e.g.*, Standardized scales or clinical interview) were heterogenous across different studies[58]. A combination of information from different sources might sometimes lead to overdiagnosis of comorbidity and vice versa. There is also a possibility of Berkesonian bias in referred clinical population with typically more severe symptomatology, more comorbid disorders or more severe comorbid disorders[14]. In addition to this, use of different classificatory systems may lead to differences as well *e.g.*, ASD can be co-diagnosed with ADHD in DSM V but not in DSM IV[1,59].

CONCLUSION

Cross-disciplinary research combining genetics, symptom dimensions, core deficits, choice of treatment and treatment response on a large sample size is likely to shed more light on this complex but exciting area[60]. This would aid in more personalized and precise matching of patients to treatment modality using patients' comorbidity profiles and result in much better treatment gains for individual patients. A comprehensive screening for comorbidity in cases diagnosed with ADHD should be mandatory to achieve the above objectives.

REFERENCES

1 **American Psychiatric Association**. Diagnostic and Statistical Manual of Mental Diseases (DSM-V), 5th ed. Washington, DC, American Psychiatric Publishing. 2013 [DOI: 10.1176/appi.books.9780890425596]
2 **Faraone SV**, Sergeant J, Gillberg C, Biederman J. The worldwide prevalence of ADHD: is it an American condition? *World Psychiatry* 2003; **2**: 104-113 [PMID: 16946911]
3 **Gillberg C**, Gillberg IC, Rasmussen P, Kadesjö B, Söderström H, Råstam M, Johnson M, Rothenberger A, Niklasson L. Co-existing disorders in ADHD -- implications for diagnosis and intervention. *Eur Child Adolesc Psychiatry* 2004; **13** Suppl 1: I80-I92 [PMID: 15322959 DOI: 10.1007/s00787-004-1008-4]
4 **Biederman J**, Faraone SV, Spencer T, Wilens T, Norman D, Lapey KA, Mick E, Lehman BK, Doyle A. Patterns of psychiatric comorbidity, cognition, and psychosocial functioning in adults with attention deficit hyperactivity disorder. *Am J Psychiatry* 1993; **150**: 1792-1798 [PMID: 8238632 DOI: 10.1176/ajp.150.12.1792]
5 **Stevens MC**, Gaynor A, Bessette KL, Pearlson GD. A preliminary study of the effects of working memory training on brain function. *Brain Imaging Behav* 2016; **10**: 387-407 [PMID: 26138580 DOI: 10.1007/s11682-015-9416-2]
6 **Mayes D**, Calhoun L, Mayes D, Molitoris S. Autism and ADHD: Overlapping and discriminating symptoms. *Research in Autism Spectrum Disorders* 2012; **6**: 277-285 [DOI: 10.1016/j.rasd.2011.05.009]
7 **Sadeh A**, Pergamin L, Bar-Haim Y. Sleep in children with attention-deficit hyperactivity disorder: a meta-analysis of polysomnographic studies. *Sleep Med Rev* 2006; **10**: 381-398 [PMID: 16846743 DOI: 10.1016/j.smrv.2006.03.004]
8 **Abdel Razek A**, Mazroa J, Baz H. Assessment of white matter integrity of autistic preschool children with diffusion weighted MR imaging. *Brain Dev* 2014; **36**: 28-34 [PMID: 23398955 DOI: 10.1016/j.braindev.2013.01.003]
9 **Biederman J**, Milberger S, Faraone SV, Kiely K, Guite J, Mick E, Ablon S, Warburton R, Reed E. Family-environment risk factors for attention-deficit hyperactivity disorder. A test of Rutter's indicators of adversity. *Arch Gen Psychiatry* 1995; **52**: 464-470 [PMID: 7771916 DOI: 10.1001/archpsyc.1995.03950180050007]
10 **Rucklidge JJ**, Tannock R. Neuropsychological profiles of adolescents with ADHD: effects of reading difficulties and gender. *J Child Psychol Psychiatry* 2002; **43**: 988-1003 [PMID: 12455921 DOI: 10.1111/1469-7610.00227]
11 **Mayes SD**, Calhoun SL, Crowell EW. Learning disabilities and ADHD: overlapping spectrumn disorders. *J Learn Disabil* 2000; **33**: 417-424 [PMID: 15495544 DOI: 10.1177/002221940003300502]
12 **Freeman RD**; Tourette Syndrome International Database Consortium. Tic disorders and ADHD: answers from a world-wide clinical dataset on Tourette syndrome. *Eur Child Adolesc Psychiatry* 2007; **16** Suppl 1: 15-23 [PMID: 17665279 DOI: 10.1007/s00787-007-1003-7]
13 **Angold A**, Costello EJ, Erkanli A. Comorbidity. *J Child Psychol Psychiatry* 1999; **40**: 57-87 [PMID: 10102726 DOI: 10.1111/1469-7610.00424]
14 **Spencer T**, Biederman J, Wilens T. Attention-deficit/hyperactivity disorder and comorbidity. *Pediatr Clin North Am* 1999; **46**: 915-927 [PMID: 10570696 DOI: 10.1016/S0031-3955(05)70163-2]
15 **Blackman GL**, Ostrander R, Herman KC. Children with ADHD and depression: a multisource, multimethod assessment of clinical, social, and academic functioning. *J Atten Disord* 2005; **8**: 195-207 [PMID: 16110050 DOI: 10.1177/1087054705278777]

16 **Herman KC**, Lambert SF, Ialongo NS, Ostrander R. Academic pathways between attention problems and depressive symptoms among urban African American children. *J Abnorm Child Psychol* 2007; **35**: 265-274 [PMID: 17211727 DOI: 10.1007/s10802-006-9083-2]
17 **Biederman J**, Mick E, Faraone SV. Depression in attention deficit hyperactivity disorder (ADHD) children: "true" depression or demoralization? *J Affect Disord* 1998; **47**: 113-122 [PMID: 9476751 DOI: 10.1016/S0165-0327(97)00127-4]
18 **Galanter CA**, Leibenluft E. Frontiers between attention deficit hyperactivity disorder and bipolar disorder. *Child Adolesc Psychiatr Clin N Am* 2008; **17**: 325-346, viii-viix [PMID: 18295149 DOI: 10.1016/j.chc.2007.11.001]
19 **Biederman J**, Faraone S, Mick E, Wozniak J, Chen L, Ouellette C, Marrs A, Moore P, Garcia J, Mennin D, Lelon E. Attention-deficit hyperactivity disorder and juvenile mania: an overlooked comorbidity? *J Am Acad Child Adolesc Psychiatry* 1996; **35**: 997-1008 [PMID: 8755796 DOI: 10.1097/00004583-199608000-00010]
20 **Skirrow C**, Hosang GM, Farmer AE, Asherson P. An update on the debated association between ADHD and bipolar disorder across the lifespan. *J Affect Disord* 2012; **141**: 143-159 [PMID: 22633181 DOI: 10.1016/j.jad.2012.04.003]
21 **Youngstrom EA**, Arnold LE, Frazier TW. Bipolar and ADHD Comorbidity: Both Artifact and Outgrowth of Shared Mechanisms. *Clin Psychol (New York)* 2010; **17**: 350-359 [PMID: 21278822 DOI: 10.1111/j.1468-2850.2010.01226.x]
22 **Duffy A**. The nature of the association between childhood ADHD and the development of bipolar disorder: a review of prospective high-risk studies. *Am J Psychiatry* 2012; **169**: 1247-1255 [PMID: 23212056 DOI: 10.1176/appi.ajp.2012.11111725]
23 **Arnold LE**, Demeter C, Mount K, Frazier TW, Youngstrom EA, Fristad M, Birmaher B, Findling RL, Horwitz SM, Kowatch R, Axelson DA. Pediatric bipolar spectrum disorder and ADHD: comparison and comorbidity in the LAMS clinical sample. *Bipolar Disord* 2011; **13**: 509-521 [PMID: 22017220 DOI: 10.1111/j.1399-5618.2011.00948.x]
24 **Busch B**, Biederman J, Cohen LG, Sayer JM, Monuteaux MC, Mick E, Zallen B, Faraone SV. Correlates of ADHD among children in pediatric and psychiatric clinics. *Psychiatr Serv* 2002; **53**: 1103-1111 [PMID: 12221308 DOI: 10.1176/appi.ps.53.9.1103]
25 **Jensen PS**, Hinshaw SP, Swanson JM, Greenhill LL, Conners CK, Arnold LE, Abikoff HB, Elliott G, Hechtman L, Hoza B, March JS, Newcorn JH, Severe JB, Vitiello B, Wells K, Wigal T. Findings from the NIMH Multimodal Treatment Study of ADHD (MTA): implications and applications for primary care providers. *J Dev Behav Pediatr* 2001; **22**: 60-73 [PMID: 11265923 DOI: 10.1097/00004703-200102000-00008]
26 **Schatz DB**, Rostain AL. ADHD with comorbid anxiety: a review of the current literature. *J Atten Disord* 2006; **10**: 141-149 [PMID: 17085624 DOI: 10.1177/1087054706286698]
27 **Levy F**. Synaptic gating and ADHD: a biological theory of comorbidity of ADHD and anxiety. *Neuropsychopharmacology* 2004; **29**: 1589-1596 [PMID: 15114344 DOI: 10.1038/sj.npp.1300469]
28 **Hammerness P**, Geller D, Petty C, Lamb A, Bristol E, Biederman J. Does ADHD moderate the manifestation of anxiety disorders in children? *Eur Child Adolesc Psychiatry* 2010; **19**: 107-112 [PMID: 19543790 DOI: 10.1007/s00787-009-0041-8]
29 **Jarrett MA**, Wolff JC, Davis TE, Cowart MJ, Ollendick TH. Characteristics of Children With ADHD and Comorbid Anxiety. *J Atten Disord* 2016; **20**: 636-644 [PMID: 22863769 DOI: 10.1177/1087054712452914]
30 **March JS**, Swanson JM, Arnold LE, Hoza B, Conners CK, Hinshaw SP, Hechtman L, Kraemer HC, Greenhill LL, Abikoff HB, Elliott LG, Jensen PS, Newcorn JH, Vitiello B, Severe J, Wells KC, Pelham WE. Anxiety as a predictor and outcome variable in the multimodal treatment study of children with ADHD (MTA). *J Abnorm Child Psychol* 2000; **28**: 527-541 [PMID: 11104315 DOI: 10.1023/A:1005179014321]
31 **Sagar-Ouriaghli I**, Milavic G, Barton R, Heaney N, Fiori F, Lievesley K, Singh J, Santosh P. Comparing the DSM-5 construct of Disruptive Mood Dysregulation Disorder and ICD-10 Mixed Disorder of Emotion and Conduct in the UK Longitudinal Assessment of Manic Symptoms (UK-LAMS) Study. *Eur Child Adolesc Psychiatry* 2018; **27**: 1095-1104 [PMID: 29730721 DOI: 10.1007/s00787-018-1149-5]
32 **Gelegen V**, Tamam L. Prevalence and clinical correlates of intermittent explosive disorder in Turkish psychiatric outpatients. *Compr Psychiatry* 2018; **83**: 64-70 [PMID: 29604524 DOI: 10.1016/j.comppsych.2018.03.003]
33 **Bird HR**, Canino G, Rubio-Stipec M, Gould MS, Ribera J, Sesman M, Woodbury M, Huertas-Goldman S, Pagan A, Sanchez-Lacay A. Estimates of the prevalence of childhood maladjustment in a community survey in Puerto Rico. The use of combined measures. *Arch Gen Psychiatry* 1988; **45**: 1120-1126 [PMID: 3264147 DOI: 10.1001/archpsyc.1988.01800360068010]
34 **Dick DM**, Viken RJ, Kaprio J, Pulkkinen L, Rose RJ. Understanding the covariation among childhood externalizing symptoms: genetic and environmental influences on conduct disorder, attention deficit hyperactivity disorder, and oppositional defiant disorder symptoms. *J Abnorm Child Psychol* 2005; **33**: 219-229 [PMID: 15839499 DOI: 10.1007/s10802-005-1829-8]
35 **Kuja-Halkola R**, Lichtenstein P, D'Onofrio BM, Larsson H. Codevelopment of ADHD and externalizing behavior from childhood to adulthood. *J Child Psychol Psychiatry* 2015; **56**: 640-647 [PMID: 25303006 DOI: 10.1111/jcpp.12340]
36 **Moffitt TE**, Silva PA. Self-reported delinquency, neuropsychological deficit, and history of attention deficit disorder. *J Abnorm Child Psychol* 1988; **16**: 553-569 [PMID: 3235747 DOI: 10.1007/BF00914266]
37 **August GJ**, Stewart MA, Holmes CS. A four-year follow-up of hyperactive boys with and without conduct disorder. *Br J Psychiatry* 1983; **143**: 192-198 [PMID: 6193828 DOI: 10.1192/bjp.143.2.192]
38 **Barkley RA**, Fischer M, Smallish L, Fletcher K. Young adult follow-up of hyperactive children: antisocial activities and drug use. *J Child Psychol Psychiatry* 2004; **45**: 195-211 [PMID: 14982236 DOI: 10.1111/j.1469-7610.2004.00214.x]
39 **Herrero ME**, Hechtman L, Weiss G. Antisocial disorders in hyperactive subjects from childhood to adulthood: predictive factors and characterization of subgroups. *Am J Orthopsychiatry* 1994; **64**: 510-521 [PMID: 7847567 DOI: 10.1037/h0079567]
40 **Barkley RA**, Fischer M, Edelbrock CS, Smallish L. The adolescent outcome of hyperactive children diagnosed by research criteria: I. An 8-year prospective follow-up study. *J Am Acad Child Adolesc Psychiatry* 1990; **29**: 546-557 [PMID: 2387789 DOI: 10.1097/00004583-199007000-00007]
41 **Malhotra S**, Aga VM, Balraj, Gupta N. Comparison of conduct disorder and hyperkinetic conduct

disorder: a retrospective clinial study from north India. *Indian J Psychiatry* 1999; **41**: 111-121 [PMID: 21455373]
42 **Coccaro EF**, Lee R, McCloskey MS. Relationship between psychopathy, aggression, anger, impulsivity, and intermittent explosive disorder. *Aggress Behav* 2014; **40**: 526-536 [PMID: 24760575 DOI: 10.1002/ab.21536]
43 **Liszka SR**, Carlson CL, Swanson JM. ADHD with comorbid disorders: Clinical assessment and management. New York, NY, United States: Guilford Press; 1999.
44 **Bowen R**, Chavira DA, Bailey K, Stein MT, Stein MB. Nature of anxiety comorbid with attention deficit hyperactivity disorder in children from a pediatric primary care setting. *Psychiatry Res* 2008; **157**: 201-209 [PMID: 18023880 DOI: 10.1016/j.psychres.2004.12.015]
45 **Ostrander R**, Crystal DS, August G. Attention deficit-hyperactivity disorder, depression, and self- and other-assessments of social competence: a developmental study. *J Abnorm Child Psychol* 2006; **34**: 773-787 [PMID: 17066222 DOI: 10.1007/s10802-006-9051-x]
46 **Brand N**, Geenen R, Oudenhoven M, Lindenborn B, van der Ree A, Cohen-Kettenis P, Buitelaar JK. Brief report: cognitive functioning in children with Tourette's syndrome with and without comorbid ADHD. *J Pediatr Psychol* 2002; **27**: 203-208 [PMID: 11821503 DOI: 10.1093/jpepsy/27.2.203]
47 **Stevenson J**, Asherson P, Hay D, Levy F, Swanson J, Thapar A, Willcutt E. Characterizing the ADHD phenotype for genetic studies. *Dev Sci* 2005; **8**: 115-121 [PMID: 15720369 DOI: 10.1111/j.1467-7687.2005.00398.x]
48 **Willcutt EG**, Pennington BF. Comorbidity of reading disability and attention-deficit/hyperactivity disorder: differences by gender and subtype. *J Learn Disabil* 2000; **33**: 179-191 [PMID: 15505947 DOI: 10.1177/002221940003300206]
49 **Banaschewski T**, Becker K, Scherag S, Franke B, Coghill D. Molecular genetics of attention-deficit/hyperactivity disorder: an overview. *Eur Child Adolesc Psychiatry* 2010; **19**: 237-257 [PMID: 20145962 DOI: 10.1007/s00787-010-0090-z]
50 **Biederman J**, Newcorn J, Sprich S. Comorbidity of attention deficit hyperactivity disorder with conduct, depressive, anxiety, and other disorders. *Am J Psychiatry* 1991; **148**: 564-577 [PMID: 2018156 DOI: 10.1176/ajp.148.5.564]
51 **Caron C**, Rutter M. Comorbidity in child psychopathology: concepts, issues and research strategies. *J Child Psychol Psychiatry* 1991; **32**: 1063-1080 [PMID: 1787137 DOI: 10.1111/j.1469-7610.1991.tb00350.x]
52 **Jensen PS**, Hinshaw SP, Kraemer HC, Lenora N, Newcorn JH, Abikoff HB, March JS, Arnold LE, Cantwell DP, Conners CK, Elliott GR, Greenhill LL, Hechtman L, Hoza B, Pelham WE, Severe JB, Swanson JM, Wells KC, Wigal T, Vitiello B. ADHD comorbidity findings from the MTA study: comparing comorbid subgroups. *J Am Acad Child Adolesc Psychiatry* 2001; **40**: 147-158 [PMID: 11211363 DOI: 10.1097/00004583-200102000-00009]
53 **Sokolova E**, Oerlemans AM, Rommelse NN, Groot P, Hartman CA, Glennon JC, Claassen T, Heskes T, Buitelaar JK. A Causal and Mediation Analysis of the Comorbidity Between Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD). *J Autism Dev Disord* 2017; **47**: 1595-1604 [PMID: 28255761 DOI: 10.1007/s10803-017-3083-7]
54 **Molina BS**, Hinshaw SP, Swanson JM, Arnold LE, Vitiello B, Jensen PS, Epstein JN, Hoza B, Hechtman L, Abikoff HB, Elliott GR, Greenhill LL, Newcorn JH, Wells KC, Wigal T, Gibbons RD, Hur K, Houck PR; MTA Cooperative Group. The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. *J Am Acad Child Adolesc Psychiatry* 2009; **48**: 484-500 [PMID: 19318991 DOI: 10.1097/CHI.0b013e31819c23d0]
55 **Hinshaw SP**, Arnold LE; For the MTA Cooperative Group. ADHD, Multimodal Treatment, and Longitudinal Outcome: Evidence, Paradox, and Challenge. *Wiley Interdiscip Rev Cogn Sci* 2015; **6**: 39-52 [PMID: 25558298 DOI: 10.1002/wcs.1324]
56 **Ter-Stepanian M**, Grizenko N, Cornish K, Talwar V, Mbekou V, Schmitz N, Joober R. Attention and Executive Function in Children Diagnosed with Attention Deficit Hyperactivity Disorder and Comorbid Disorders. *J Can Acad Child Adolesc Psychiatry* 2017; **26**: 21-30 [PMID: 28331500]
57 **Cuthbert BN**. Translating intermediate phenotypes to psychopathology: the NIMH Research Domain Criteria. *Psychophysiology* 2014; **51**: 1205-1206 [PMID: 25387702 DOI: 10.1111/psyp.12342]
58 **Jensen PS**, Martin D, Cantwell DP. Comorbidity in ADHD: implications for research, practice, and DSM-V. *J Am Acad Child Adolesc Psychiatry* 1997; **36**: 1065-1079 [PMID: 9256586 DOI: 10.1097/00004583-199708000-00014]
59 **American Psychiatric Association**. Diagnostic and Statistical Manual of Mental Diseases (DSM-IV), 4th ed. Washington, DC, American Psychiatric Publishing, 1994.
60 **Gnanavel S**. ADHD: Need for a dimensional approach. *J Indian Assoc Child Adolesc Ment Health* 2018; **14**: 128-131

Published By Baishideng Publishing Group Inc
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
Help Desk:https://www.f6publishing.com/helpdesk
https://www.wjgnet.com