Trends
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Review Article

Are parents with bipolar disorder at higher risk of having offspring with ADHD? A systematic review

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Abstract

Objective: The offspring of parents with bipolar disorder (BD) and with attention deficit hyperactivity disorder (ADHD) have a higher risk of having the same condition. Both disorders also share psychopathological symptoms; however, little is known about their genetic overlap. To examine whether the offspring of parents with BD have a greater chance of being affected by ADHD, we conducted a systematic review.

Methods: From inception to August 12, 2024, we searched the PubMed, SciELO, PsycInfo and Cochrane databases. We included studies if they investigated the association of parental bipolar disorder with offspring outcomes and made a proper investigation of disorders using validated instruments based on the Diagnostic Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD) criteria. Studies were excluded if: parents were under 18 years old or over 70; did not report original data; systematic reviews; in vitro studies; with an animal model; offspring older than 17 years of age or with any comorbid diagnosis with ADHD. To assess risk of bias, two authors independently used the Newcastle-Ottawa Scale quality assessment tool.

Results: 23 articles met the inclusion criteria. The majority of the studies reported that the offspring of parents with BD were at higher risk for ADHD. Particularly, in all case-control studies, the risk of ADHD was higher in the case group than the control group.

Conclusion: The current studies are yet heterogeneous and literature did not uncover the biological correlation of these disorders regarding genetic, biochemical, neuroimaging and neuropsychological aspects.

Keywords: Bipolar, attention, hereditary, offspring, intergenerational.

Introduction

Attention deficit hyperactivity disorder (ADHD) is a highly hereditary, neurodevelopmental disorder that is associated with the risk of other mental disorders later in life, such as anxiety, substance use and depressive disorders.[1-3] Bipolar disorder (BD) is a mood disorder that is frequently associated with mental comorbidities but is rarely diagnosed in childhood.[4]

Various studies have already shown that bipolar disorder is also highly hereditary[5,6]; some have reported a seemingly higher chance of individuals with ADHD being diagnosed with BD later in life,[7] but few have focused on the risk of mental disorders other than BD, especially neurodevelopmental disorders, among the offspring of parents with BD.

Both BD and ADHD present some psychopathology similarities, such as mood lability, psychomotor agitation and distractibility.[8] The neurobiology and neural circuitry deficiencies associated with bipolar disorder onset are not yet fully known, but the common symptomatology could indicate that these two disorders

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have some neurobiological correlation. Furthermore, evidence from genome-wide association studies have already identified significant single nucleotide polymorphism-based genetic correlation between these disorders and risk loci with shared effects on the two of them consistent with the existence of genetic overlap between BD and ADHD.

To the best of our knowledge, this is the first review intended to investigate whether parents with bipolar disorder may have a greater chance of having offspring with ADHD. Positive findings may reinforce perspectives that suggest ADHD symptoms might be an initial phase of a longitudinal development of bipolar disorder.[7,8]

Methods

This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines[9] and was conducted following an a priori established protocol on PROSPERO[10] (CRD42023431438).

Database selection and search strategy

From inception to August 12, 2024, PubMed database was searched using the following terms: "bipolar disorder," "offspring," "progeny," "inheritance," "family history," "familial history," "attention deficit hyperactivity disorder" and "ADHD." SciELO, PsycInfo and Cochrane databases were also searched using these terms: "bipolar disorder," "manic depression," "bipolar affective disorder," "children" "descendants," "parents," "genetic," "family background, "family history," "familial history," "attention deficit hyperactivity disorder," "hyperactivity disorder," "attention deficit disorder" and "ADHD." To avoid publication bias, non-English language studies and grey literature (for example, conference abstracts) were included. A structured search strategy based on the PICOS framework was used.[11] Studies were included if they met the following criteria: a) enrolled adult parents with bipolar disorder and their offspring; b) investigated the association of parental bipolar disorder with offspring outcomes; c) conducted a proper investigation of bipolar disorder among parents made by a psychiatrist or using validated instruments based on the Diagnostic Statistical Manual of Mental Disorders (DSM-IV, DSM-IV TR, DSM-5) or the International Classification of Diseases (ICD-9 and ICD-10) criteria; d) conducted a proper investigation of ADHD among the offspring of parents with BD made by a psychiatrist or using validated instruments based on DSM-IV, DSM-IV TR, DSM V, ICD-9 or ICD-10 criteria; e) used any study design; f) a comparison group was preferable, but not mandatory. When reported in the study, both parents and offspring should have the control group. Studies were excluded if: enrolled parents who were adolescents under 18 years of age and elderly people (over 70); systematic reviews; studies that did not report original data; studies with an animal model; in vitro studies; enrolled offspring who were not under 18 years of age or had any comorbid diagnosis with ADHD. The systematic search protocol and full search terms for each database are detailed in Supplementary Materials S1 and S2.

Two reviewers working independently considered the potential eligibility of each of the abstracts retrieved via the search strategy. Full-text articles were obtained unless both reviewers decided that an abstract was ineligible, with disagreements resolved by a third reviewer. The overall interobserver agreement of abstract selection was $K = 0.70$, which is deemed good to excellent agreement. Each full-text report was assessed independently by two reviewers for final study inclusion, and the agreement for final texts inclusions was $K = 0.90$.

Data abstraction and risk of bias assessment

Data on study-, parent-, and offspring-related characteristics were abstracted using a standardized form, and conducted independently by 2 researchers, with disagreements resolved by a third researcher. The following variables were extracted from all studies: authors, year of publication and subject characteristics of the parent and offspring groups. The risk of bias assessment of the individual studies was conducted independently by two authors (LLF and LAQ) using the Newcastle-Ottawa Scale quality assessment tool.[12] The overall interobserver agreement of methodological quality assessment was $K = 0.64$, which is deemed good to excellent agreement. Any disagreements were settled following discussion with a third reviewer (AEN). The details of the quality assessment are reported in Supplementary Table S1.

Results

366 studies were found using the previously described strategy. Four duplicate records were removed. 424 records were screened, and after reading the abstracts, 94 systematic reviews and 261 reports which did not meet the inclusion criteria of enrolling adult parents with BD and/or their offspring were excluded. 69 studies were then assessed for full reading, and 46 of them were disqualified based on this article's inclusion and exclusion criteria. Finally, a total of 23

papers representing individual studies were included. A PRISMA diagram is shown in Figure 1.

Study characteristics

The key study characteristics are presented in Table 1. We obtained results from studies published between 2000 and 2023. This was reflected in the categorical measurement used: the DSM-IV or DSM-IV-TR and adaptations of both. The most commonly used diagnostic tools were the Structured Clinical Interview for DSM Disorders (SCID) for the parents and the Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children (K-SADS) for their offspring.

Parent results

The age of the parents ranged from 24 to 47 years old among the total sample. Thirteen studies identified the sex of the parents. In two of them, only female patients were included. All of the others identified the sex from a randomized sample selection, and noted the mother as being the most affected parent. Six studies identified substance use disorder as a comorbidity among parents, and five of them provided the percentage, which varied from 8% to approximately 85% among the investigated parents. Other comorbidities were also found, with one study pointing out that all parents had an associated Axis I disorder in addition to BD.[26] In two studies, 21.8%[7] and 20%[29] of the parents were also diagnosed with ADHD. A study comparing comorbidities between parents in the bipolar and control groups found that any Axis I disorder was more common among parents with bipolar disorder.[20] Anxiety disorders were also found to be highly correlated with bipolar disorder, especially in two studies that identified an association between both disorders with proportions of 84%[23] and 80.8%.[7] Two studies reported the duration of disease among the parents, varying from 19[25] to 21 years.[23] Only two studies presented the current mood episode of the parents, and they all were euthymic at the time of the study.[29,30]

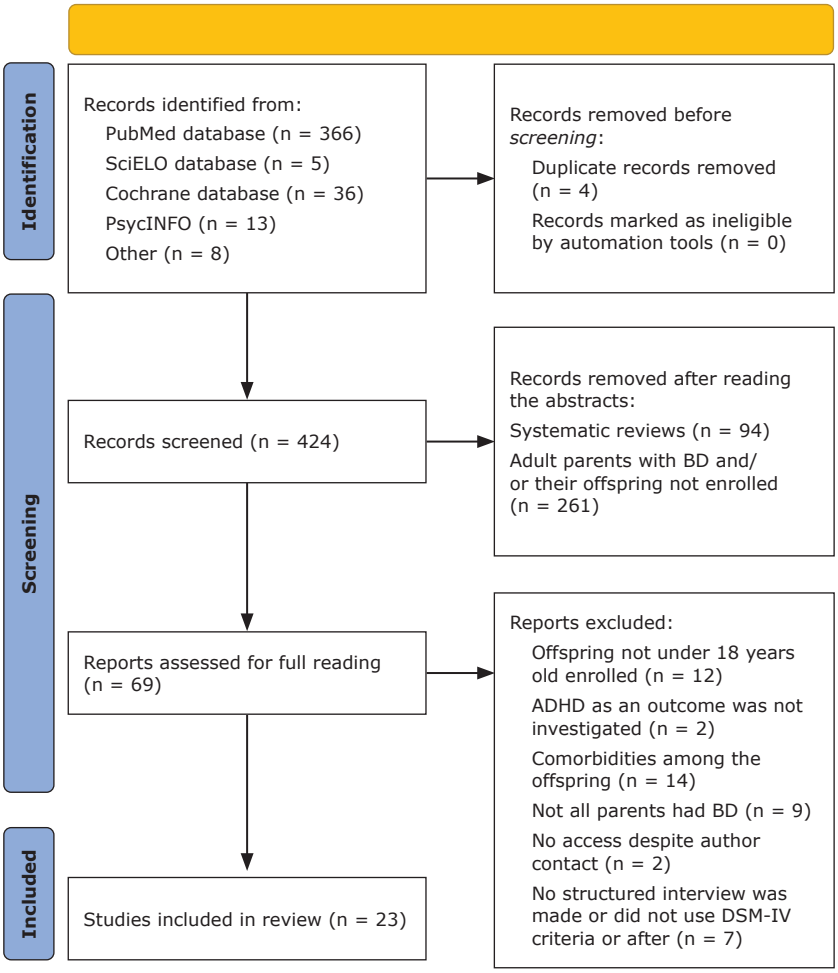

Figure 1 - Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram.[9]

Table 1 - Study characteristics

Study	Sample size (affected parents)	Sample size (offspring - proband)	Sample size (non-affected parents)	Sample size (offspring - control)	Affected parents gender (F)	Offspring gender - Proband (F)	Country	ADHD scale	BD scale	Parent comorbidities	Positive correlation between BD in parents and ADHD in offspring?	Effect size
Birmaher B et al.[13]	156	251	180	158	-	-	-	K-SADS/DSM-IV	SCID	None	Yes	OR = 0.19
Propper L. et al.[14]	-	93	-	125	-	51%	Canada	K-SADS-PL/SCID-5	SADS/SCID	None	Yes	OR = 2.67
Yeh TC et al.[15]	5669	430	5699	272	100%	-	Taiwan	ICD-9 criteria	ICD-9 criteria	None	Yes	OR = 1.51
Solberg BS et al.[16]	66211	3477	2381348	-	-	-	Norway	ICD-10 criteria	ICD-10 criteria	None	Yes	OR = 6.2
Goetz, M. et al.[17]	34	43	33	43	44.1%	41.9%	Czech Republic	K-SADS-PL	SADS-L	None	Yes	OR = 5.23
Neslihan Inal-Eiroglu F et al.[18]	29	35	29	33	-	48%	Turkey	T-DSM-IV-S	K-SADS	None	Yes	OR= 2.6
Sanchez-Gistau V et al.[19]	54	90	65	107	55.6%	44.4%	Spain	K-SADS-PL	SCID-I	~33.3% any Axis I disorder	Yes	OR = 2.88
Axelson D et al.[20]	236	391	141	248	80.5%	48.9%	USA	K-SADS-PL	SCID	any Axis I disorder + likely < control	Yes	OR = 1.63
Garcia-Amador M et al.[21]	34	50	25	25	55%	42%	Spain	K-SADS-PL	SCID-I/II	Cluster A: 2 B: 3 C: 6	Yes	OR = 3.34
Singh MK et al.[22]	-	31	-	21	-	48%	USA	K-SADS	SCID	None	Yes	OR = 2.07
Birmaher B. et al.[7]	78	116	79	98	80.8%	51.7%	USA	K-SADS-PL	SCID	DBD: 44.9/ADHD: 21.8/ANX: 80.8/ MDD: 96.2	Yes	OR = 0.45
Sparks GM et al.[23]	233	375	143	241	-	49%	USA	K-SADS-PL	SCID	ANX: 84/ADHD: 56/ODD: 52/ SUD: 80	Yes	OR=1.4
Duffy A. et al.[24]	63	127	41	61	47%	59.7%	Canada	K-SADS-PL	SADS-L	None	Yes	OR = 0.31
Oquendo MA et al.[25]	86	177	234	502	86%	45.7%	USA	K-SADS-PL	SCID	None	No	OR = 1.09
Birmaher B et al.[26]	83	121	65	102	90.4%	51.2%	USA	K-SADS-PL	SCID	100% any Axis I disorder	Yes	OR = 0.40
Palacio-Ortiz JD et al.[27]	65	127	94	150	-	44.9%	Colombia	K-SADS-PL	DIGS	SUD: 46%/ANX: 13.8%	Yes	OR = 3.76
Flinding R. L. et al.[28]	185	167	571	233	57.8%	40.7%	USA	K-SADS	SADS-LB	None	No	OR = 1.1
Chang KD et al.[29]	37	60	-	-	83.7%	42%	USA	K-SADS-PL	DSM-IV criteria	ADHD: 20%	Yes	OR = 0.40
Zappitelli MC et al.[30]	-	35	-	-	82.9%	42.9%	USA	K-SADS-PL	SCID	None	Yes	OR = 0.18
Liang CS et al.[31]	39278	-	6324048	-	57%	47.8%	Taiwan	ICD-10 criteria	ICD-10 criteria	None	Yes	OR = 1.4
Parvaresh N et al.[32]	100	100	100	48	-	46%	Iran	DSM-IV-TR criteria	DSM-IV-TR criteria	None	Yes	OR = 0.2
Chen MH et al.[33]	105	-	932,544	-	100%	-	Taiwan	ICD-9 criteria	ICD-9 criteria	None	Yes	OR = 4.18
Hirshfeld-Becker DR et al.[34]	23	34	170	179	56%	61%	USA	K-SADS	SCID	SUD: 85/ANX: 79/ DBD: 50	Yes	OR = 4.9

M = male; F = female; ICD = International Classification of Diseases; BD = bipolar disorder; ADHD = attention deficit hyperactivity disorder; ANX = anxiety disorder; MDD = major depressive disorder; K-SADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia for School-age Children-Present and Lifetime Version; SUD = substance use disorder; T-DSM-IV-S = Turgay DSM-IV-Based Child and Adolescent Disruptive Behavioral Disorders Screening and Rating Scale; DIGS = Diagnostic Interview for Genetics Studies; ODD = oppositional defiant disorder; DBD = disruptive behavior disorder.

Offspring results

Among the nineteen studies that identified the sex of the offspring, fourteen showed a higher prevalence among males. Nine studies reported the most common school grade among the offspring: in five of them, the majority of the participants were of school age; in three of them, they were of preschool age; one study showed high school as the most common school grade, while another identified the majority of participants as having already graduated.

The majority of the studies found that parents with bipolar disorder had a higher risk of having offspring who developed ADHD. In three of these studies, this correlation was highly positive (OR = 2.67),[14] (OR = 1.51),[15] (OR = 2.88).[19] Three other studies also confirmed that there was an association between bipolar disorder in parents and a higher prevalence of ADHD in offspring (OR = 0.19),[13] (OR = 2.6),[18] (OR = 1.63).[20] Seven case-control studies compared the prevalence of comorbidities among parents with bipolar disorder and healthy controls, also reporting that the offspring of parents with bipolar disorder were more affected by ADHD than the offspring of control parents.[7,21,22,24-26,34] In one of these studies, this correlation even reached 39% of the sample.[22] In the study conducted by Hirshfeld-Becker DR et al., the control group was formed by patients with panic disorder and major depressive disorder (MDD), which had a prevalence of occurrence of ADHD of 8.4% among the offspring meanwhile offspring of parents with BD had 23.5%.[34] Two longitudinal studies also identified a significant prevalence of ADHD among parents with bipolar disorder of 28% and 40%, respectively.[29,30] Specifically, maternal bipolar disorder was linked to a higher risk of ADHD in offspring in two studies.[31,33] In the study conducted by Chen MH et al., women who developed bipolar disorder after giving birth and their children were followed for investigation and among those patients the prevalence of having offspring with ADHD in the follow-up was significant (OR = 4.18).[33]

A study comparing the frequency of ADHD, conduct disorder (CD) and emotional disorders among children of parents with BD, drug dependence and control found that the prevalence of ADHD among the offspring of parents with BD was higher than control. However, it was equivalent to the group of parents with drug dependence, suggesting that ADHD may be more frequent among parents with psychiatric disorders in general than control (OR = 0.2).[32] Two studies found a meaningful correlation only before controlling for comorbid parental diagnoses and demographic variables.[17,23] In the study conducted by Goetz et al. to investigate quality of life (QoL) in offspring of a parent with BD using the self-report questionnaire KIDSCREEN, between-group differences in parental and self-assessment were controlled for co-occurring conditions (DSM-5 disorders) with the use of logistic regression. Cross-informant (parent–child) agreement in the assessment of symptoms of mood and anxiety disorders was calculated as Kendall's rank correlation coefficient (tau) and concordance correlation coefficient (CCC) for an ordinal rating and Cohen's kappa for a dichotomous rating. To compare the KIDSCREEN (QoL) between groups, the raw scores were converted to the T scores (The KIDSCREEN Group Europe 2006) and unpaired t-tests were conducted followed by Cohen's d calculation and least-square multiple regression to control for between-group differences for current psychopathology and family status.[17] Sparks et al. used Odds ratios (ORs) to estimate the risk of disruptive mood dysregulation disorder based on status as offspring of bipolar parents or community control parents were calculated using generalized linear mixed models with family of origin used as a random effect variable. The model was initially constructed as a univariate model. Subsequently, demographic variables (age, gender, race, SES, and offspring living with both biological parents) and proband parent non-BD lifetime diagnoses (ADHD, depressive disorder, anxiety disorder, ODD/CD, and substance use disorder) were entered as potential covariates. Models were constructed with backward model selection procedures, removing demographic variables and parental diagnoses with $p > 0.10$ iteratively in order of magnitude until all variables remaining in the model were significant.[23]

One study did not find a higher prevalence of ADHD among the offspring of parents with bipolar disorder in comparison to control parents. In this study, this correlation was definitely negative.[28] A study evaluating psychopathology in offspring of both parents with bipolar disorder and major depressive disorder (MDD) reported ADHD as being no more likely among the offspring of parents with bipolar disorder than among those of parents with MDD.[25] In a 2021 case–control study comparing the most prevalent mental disorders among the offspring of parents with bipolar disorder, parents with ADHD and control parents, it was found that ADHD was more prevalent among offspring of parents with bipolar disorder than among offspring of control parents; however, it was not more prevalent among offspring of parents with ADHD.[16]

Discussion

This systematic review shows that many studies in the literature point to a higher risk for parents with bipolar disorder of having offspring predisposed

to ADHD. The majority of the investigated studies reported that, in comparison to control parents, parents with bipolar disorder had a higher prevalence of having children being affected by ADHD. The follow-up of the longitudinal studies that investigated only the offspring of parents with bipolar disorder indicated a high risk of ADHD among their children as well.

It is well known that a family history of bipolar disorder is associated with a higher risk for the condition.[5] In addition, ADHD symptoms in childhood are commonly discussed as possible prodromes for adult bipolar disorder,[7,8] conduct disorders[35] and substance use disorders.[36] Identifying epidemiological findings that suggest that ADHD could also be a significant outcome for the offspring of parents with BD may help to improve knowledge about the chances of children to have ADHD being in fact higher if their parents have BD.

Some studies have already demonstrated that ADHD shares a positive genetic correlation with major depressive disorder, insomnia and depressive symptoms in general,[37] which are not uncommon among BD patients. A meta-analysis of family genetic studies examining the comorbidity between ADHD and BD type I found a significantly higher prevalence of ADHD among relatives of bipolar I probands and a significantly higher prevalence of bipolar I disorder among relatives of ADHD probands.[38] An analysis of shared heritability in common disorders of the central nervous system searching to understand the joint effect exerted by a pool of several small effect genomic variants which are in turn used to estimate the heritability that seems to be shared in between disorders pointed out that a common variant risk for psychiatric disorders was shown to correlate significantly especially among attention deficit hyperactivity disorder, bipolar disorder, major depressive disorder and schizophrenia.[39] Moreover, genome-wide association studies (GWAS) have already found overlapping genes among the two disorders. In a cross-trait meta-analysis of GWAS on schizophrenia, bipolar disorder, autism spectrum disorder, attention deficit hyperactivity disorder and depression, the SORCS3 gene was highlighted due to the fact that it was involved in all the five conditions of study.[40] In an analysis of genome-wide single-nucleotide polymorphism (SNP) data from the Psychiatric Genomics Consortium for the same five disorders, SNPs at four loci – regions on chromosomes 3p21 and 10q24, and SNPs in two L-type voltage-gated calcium-channel subunits, CACNA1C and CACNB2 – exceeded the cutoff for genome-wide significance ($p < 5\times10(-8)$) in the primary analysis.[41]

Besides the genetic evidence, according to the current DSM-5 diagnostic criteria for ADHD, it also shares a psychopathology overlap with BD, such as talkativeness, hyperactivity and distractibility presented as manic episodes, in addition to emotional features seen in mood instability and irritability, which are also common in both disorders. The common overlap of psychopathology alterations between BD and ADHD could be related to shared neurocircuitry alterations.[42]

Another similar neurobiological alteration between these disorders was found in a cerebrospinal fluid (CSF) monoamine metabolite concentrations analysis of ADHD and BD patients, which identified that both disorders were associated with higher CSF homovanillic acid (HVA) concentration in that sample.[43]

These previous findings suggest that these two mental disorders are somewhat correlated despite the present lack of robust information about the neurobiological mechanisms of BD. Regardless, clinical and epidemiological studies have shown rates of BD in subjects with ADHD are proportionally more elevated than other psychiatric conditions, and previous results from family studies show increased incidence of ADHD in offspring of probands with BD.[8] Given that several staging models of bipolar disorder have been proposed over time, including an initial prodromal phase where mild symptoms of mood disorder similar to ADHD such as overactivity and impulsivity could happen before culminating in a first threshold episode of illness, it is possible that many ADHD symptoms that correlate with BD psychopathology may be involved in the first stage of a longitudinal development of bipolar disorder.[44]

The present review had a number of limitations. Performing a meta-analysis was not possible due to the heterogeneity of the results. Given that only a few studies were not originally from America, the cross-cultural validity and applicability of the findings of this review to the global youth population is limited. It is worth noting that since ADHD is the most prevalent psychiatric disorder in children, it could also be that the results which show a higher prevalence of this disorder among the offspring of parents with bipolar disorder only represent the well-known higher prevalence of disorders in general among offspring of individuals with psychiatric disorders. Eight studies have indicated that parents with bipolar disorder also have comorbidities such as anxiety disorders, MDD or ADHD, which might represent confounders. Despite these limitations, our analysis of the evidence showed a methodologically robust corpus of studies.

While it is well established that BD and ADHD might have a neurobiological and genetic linkage, the current studies are yet heterogeneous and literature did not uncover the biological correlation of these disorders regarding gene expression, biochemical pathways,

neuroimaging aspects and neuropsychological processes. Therefore, more studies are needed in order to elucidate these aspects and improve knowledge about these disorders.

Disclosure

No conflicts of interest declared concerning the publication of this article.

Data availability statement

Not applicable.

Author contributions

Leandro L. Ferreira: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing
Antonio E. Nardi: Writing – review & editing
Laiana A. Quagliato: Conceptualization, Supervision, Writing – review & editing
All authors have read and approved of the final version to be published.

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References

1. Daviss WB. A review of co-morbid depression in pediatric ADHD: etiology, phenomenology, and treatment. J Child Adolesc Psychopharmacol. 2008;18:565-71.
2. Dirks H, Scherbaum N, Kis B, Mette C. [ADHD in adults and comorbid substance use disorder: prevalence, clinical diagnostics and integrated therapy]. Fortschr Neurol Psychiatr. 2017;85:336-44.
3. Schatz DB, Rostain AL. ADHD with comorbid anxiety: a review of the current literature. J Atten Disord. 2006;10:141-9.
4. Parry P, Allison S, Bastiampillai T. 'Pediatric bipolar disorder' rates are still lower than claimed: a re-examination of eight epidemiological surveys used by an updated meta-analysis. Int J Bipolar Disord. 2021;9:21.
5. Chang K, Steiner H, Ketter T. Studies of offspring of parents with bipolar disorder. Am J Med Genet C Semin Med Genet. 2003;123C:26-35.
6. Lau P, Hawes DJ, Hunt C, Frankland A, Roberts G, Mitchell PB. Prevalence of psychopathology in bipolar high-risk offspring and siblings: a meta-analysis. Eur Child Adolesc Psychiatry. 2018;27:823-37.
7. Birmaher B, Merranko J, Hafeman D, Goldstein BI, Diler R, Levenson JC, et al. A longitudinal study of psychiatric disorders in offspring of parents with bipolar disorder from preschool to adolescence. J Am Acad Child Adolesc Psychiatry. 2021;60:1419-29.
8. 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;141:143-59.
9. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
10. Page MJ, Shamseer L, Tricco AC. Registration of systematic reviews in PROSPERO: 30,000 records and counting. Syst Rev. 2018;7:32.
11. Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: a key to evidence-based decisions. ACP J Club. 1995;123:A12-3.
12. Lo CK, Mertz D, Loeb M. Newcastle-Ottawa Scale: comparing reviewers' to authors' assessments. BMC Med Res Methodol. 2014;14:45.
13. Birmaher B, Hafeman D, Merranko J, Zwicker A, Goldstein B, Goldstein T, et al. Role of polygenic risk score in the familial transmission of bipolar disorder in youth. JAMA Psychiatry. 2022;79:160-8.
14. Propper L, Sandstrom A, Rempel S, Howes Vallis E, Abidi S, Bagnell A, et al. Attention-deficit/hyperactivity disorder and other neurodevelopmental disorders in offspring of parents with depression and bipolar disorder. Psychol Med. 2023;53:559-66.
15. Yeh TC, Bai YM, Hsu JW, Huang KL, Tsai SJ, Chu HT, et al. Bipolar women's antepartum psychotropic exposure and offspring risk of attention-deficit/hyperactivity disorder and autism spectrum disorder. J Affect Disord. 2021;295:1407-14.
16. Solberg BS, Hegvik TA, Halmøy A, Skjaerven R, Engeland A, Haavik J, et al. Sex differences in parent-offspring recurrence of attention-deficit/hyperactivity disorder. J Child Psychol Psychiatry. 2021;62:1010-8.
17. Goetz M, Sebela A, Mohaplova M, Ceresnakova S, Ptacek R, Novak T. Psychiatric disorders and quality of life in the offspring of parents with bipolar disorder. J Child Adolesc Psychopharmacol. 2017;27:483-93.
18. Neslihan Inal-Eiroglu F, Ozerdem A, Miklowitz D, Baykara A, Akay A. Mood and disruptive behavior disorders and symptoms in the offspring of patients with bipolar I disorder. World Psychiatry. 2008;7:110-2.
19. Sanchez-Gistau V, Romero S, Moreno D, de la Serna E, Baeza I, Sugranyes G, et al. Psychiatric disorders in child and adolescent offspring of patients with schizophrenia and bipolar disorder: a controlled study. Schizophr Res. 2015;168:197-203.
20. Axelson D, Goldstein B, Goldstein T, Monk K, Yu H, Hickey MB, et al. Diagnostic precursors to bipolar disorder in offspring of parents with bipolar disorder: a longitudinal study. Am J Psychiatry. 2015;172:638-46.
21. Garcia-Amador M, de la Serna E, Vila M, Romero S, Valenti M, Sánchez-Gistau V, et al. Parents with bipolar disorder: are disease characteristics good predictors of psychopathology in offspring? Eur Psychiatry. 2013;28:240-6.
22. Singh MK, DelBello MP, Strakowski SM. Temperament in child offspring of parents with bipolar disorder. J Child Adolesc Psychopharmacol. 2008;18:589-93.
23. Sparks GM, Axelson DA, Yu H, Ha W, Ballester J, Diler RS, et al. Disruptive mood dysregulation disorder and chronic irritability in youth at familial risk for bipolar disorder. J Am Acad Child Adolesc Psychiatry. 2014;53:408-16.
24. Duffy A, Alda M, Crawford L, Milin R, Grof P. The early manifestations of bipolar disorder: a longitudinal prospective study of the offspring of bipolar parents. Bipolar Disord. 2007;9:828-38.
25. Oquendo MA, Ellis SP, Chesin MS, Birmaher B, Zelazny J, Tin A, et al. Familial transmission of parental mood disorders: unipolar and bipolar disorders in offspring. Bipolar Disord. 2013;15:764-73.
26. Birmaher B, Axelson D, Goldstein B, Monk K, Kalas C, Obreja M, et al. Psychiatric disorders in preschool offspring of parents with bipolar disorder: the Pittsburgh Bipolar Offspring Study (BIOS). Am J Psychiatry. 2010;167:321-30.
27. Palacio-Ortiz JD, Peña-Quintero CE, Gómez-Valero MA, Bustamante-Gómez PA, Arroyave-Sierra PH, Vargas-Upeguí CD, et al. [Lifetime psychiatric disorders: a comparision study between offspring of parents with bipolar disorder type-I versus the offspring of community controls parents]. Rev Colomb Psiquiatr. 2017;46:129-39.
28. Findling RL, Youngstrom EA, McNamara NK, Stansbrey RJ, Demeter CA, Bedoya D, et al. Early symptoms of mania and the role of parental risk. Bipolar Disord. 2005;7:623-34.
29. Chang KD, Steiner H, Ketter TA. Psychiatric phenomenology of child and adolescent bipolar offspring. J Am Acad Child Adolesc Psychiatry. 2000;39:453-60.

30. Zappitelli MC, Bordin IA, Hatch JP, Caetano SC, Zunta-Soares G, Olvera RL, et al. Lifetime psychopathology among the offspring of Bipolar I parents. Clinics (Sao Paulo). 2011;66:725-30.
31. Liang CS, Bai YM, Hsu JW, Huang KL, Ko NY, Yeh TC, et al. Associations of parental mental disorders and age with childhood mental disorders: a population-based cohort study with four million offspring. Eur Child Adolesc Psychiatry. 2023;32:825-33.
32. Parvaresh N, Ziaaddini H, Kheradmand A, Bayati H. Attention deficit hyperactivity disorder (ADHD) and conduct disorder in children of drug dependent parents. Addict Health. 2010;2:89-94.
33. Chen MH, Pan TL, Bai YM, Huang KL, Tsai SJ, Su TP, et al. Postpartum depression and psychosis and subsequent severe mental illnesses in mothers and neurodevelopmental disorders in children: a nationwide study. J Clin Psychiatry. 2021;82:20m13735.
34. Hirshfeld-Becker DR, Biederman J, Henin A, Faraone SV, Dowd ST, De Petrillo LA, et al. Psychopathology in the young offspring of parents with bipolar disorder: a controlled pilot study. Psychiatry Res. 2006;145:155-67.
35. Turgay A. Treatment of comorbidity in conduct disorder with attention-deficit hyperactivity disorder (ADHD). Essent Psychopharmacol. 2005;6:277-90.
36. De Alwis D, Lynskey MT, Reiersen AM, Agrawal A. Attention-deficit/hyperactivity disorder subtypes and substance use and use disorders in NESARC. Addict Behav. 2014;39:1278-85.
37. Demontis D, Walters RK, Martin J, Mattheisen M, Als TD, Agerbo E, et al. Discovery of the first genome-wide significant risk loci for attention deficit/hyperactivity disorder. Nat Genet. 2019;51:63-75.
38. Faraone SV, Biederman J, Wozniak J. Examining the comorbidity between attention deficit hyperactivity disorder and bipolar I disorder: a meta-analysis of family genetic studies. Am J Psychiatry. 2012;169:1256-66.
39. Brainstorm Consortium; Anttila V, Bulik-Sullivan B, Finucane HK, Walters RK, Bras J, et al. Analysis of shared heritability in common disorders of the brain. Science. 2018;360:eaap8757.
40. Wu Y, Cao H, Baranova A, Huang H, Li S, Cai L, et al. Multi-trait analysis for genome-wide association study of five psychiatric disorders. Transl Psychiatry. 2020;10:209.
41. Cross-Disorder Group of the Psychiatric Genomics Consortium. Identification of risk loci with shared effects on five major psychiatric disorders: a genome-wide analysis. Lancet. 2013;381:1371-9.
42. Long Y, Pan N, Yu Y, Zhang S, Qin K, Chen Y, et al. Shared and distinct neurobiological bases of bipolar disorder and attention-deficit/hyperactivity disorder in children and adolescents: a comparative meta-analysis of structural abnormalities. J Am Acad Child Adolesc Psychiatry. 2023;S0890-8567:02244-X.
43. Pålsson E, Sellgren C, Rydén E, Kizza R, Pelanis A, Zetterberg H, et al. Cerebrospinal fluid monoamine metabolite profiles in bipolar disorder, ADHD, and controls. J Neural Transm (Vienna). 2017;124:1135-43.
44. Cosci F, Fava GA. Staging of mental disorders: systematic review. Psychother Psychosom. 2013;82:20-34.

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