

Supplementary Material S1: Systematic search protocol

Written based on the WHO Review Protocol Template, 2011

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

1. Background: Bipolar disorder (BD) is a mental disease defined by the occurrence of mood change episodes known as depression and mania. Studies have shown that this condition can be related to attention deficit hyperactivity disorder (ADHD), a mental disorder characterized by psychomotor agitation and distractibility, symptoms that are also commonly present in BD patients. Therefore, the aim of this systematic review is to investigate if bipolar parents might have an increased rate of having ADHD offspring.
2. Objective: This review outcome is to evaluate if current literature findings support evidence of a higher risk of parents with bipolar disorder having offspring with ADHD.
3. Review Question (Population Intervention Comparison Outcome)
Population: genitors with bipolar disorder and included their offspring
Intervention: analyze the risk of ADHD heritability
Comparison: a comparison group was preferable, but not mandatory
Outcome: ADHD psychopathology in offspring

Evidence Gathering and Study Selection: PubMed, SciELO, PsycINFO and Cochrane databases will be searched. Full search terms for each database and results found per database are listed in the Appendix 2.

Reference Searches: Bibliographies of papers deemed eligible for this review will be hand searched to identify any additional eligible references, which will then be screened for title, abstract or full text as appropriate.

4. Eligibility Criteria
The results of these searches will be combined and deduped using Rayyan. They will then be screened for title and abstract, and then full text using the following eligibility criteria.
 - i) Type of study included: any
 - ii) Types of participants: Genitors with bipolar disorder, which included an offspring
 - iii) Types of outcome measures: behavior, neurodevelopment or psychopathology in offspring were reported
5. Exclusion Criteria
Reviews, studies that did not report original data, studies with an animal model, and in vitro studies will be excluded.
6. Data extraction
Data extracted will include: Title, name of the first author, year of publication, parent age, parent gender, offspring gender, offspring age, parent use of substance, parent disease time, current parent mood episode, offspring grade and parent comorbidities.
7. Data Synthesis
Narrative synthesis is planned. The systematic review will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). We anticipate that there will be limited scope for meta-analysis because of the possible heterogeneity of the results.
8. Dissemination
A manuscript will be prepared for submission to a peer reviewed journal in the neuroscience field.

9. Results

The quality appraisal of the 23 studies is summarized in Supplementary Table S1. The overall average stars achieved through the 23 included studies was 7.0 stars (range = 3–9), which is considered as moderate quality.

Supplementary Material S2: Search terms

PubMed:

("Bipolar Disorder"[MeSH] OR "bipolar disorder") AND (offspring*[tiab] OR progen*[tiab] OR parent*[tiab] OR herit*[tiab] OR inherit*[tiab] OR "family history" OR "familial history") AND ("Attention Deficit Disorder with Hyperactivity"[MeSH] OR "ADHD")

SciELO, Cochrane and PsycInfo:

("Bipolar Disorder" OR "manic depression" OR "bipolar affective disorder") AND (children OR descendants OR parents OR genetic OR inheritance OR "family background" OR "family history") AND ("Attention Deficit Hyperactivity Disorder" OR "ADHD" OR "hyperactivity disorder" OR "attention deficit disorder").

Supplementary Table S1 - Quality score

Case control studies

Authors	Is the case definition adequate?	Representativeness of the cases	Selection of controls	Definition of controls	Comparability	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate
Birmaher B [2022]	*		*	*	**	*	*	*
Propper L [2021]	*	*	*	*	**	*		*
Teh Y et al [2021]		*	*	*	**		*	*
Goetz M et al [2017]	*	*	*	*	**	*	*	*
Neslihan Inal-Eiroglu F et al [2008]	*	*		*			*	*
Sanchez-Gistau V [2015]	*	*	*	*	**	*	*	
Axelson D et al [2015]	*	*	*	*	**	*	*	*
Garcia-Amador M et al [2012]	*	*	*	*	*		*	*
Singh MK et al [2008]	*	*	*	*	*	*	*	
Birmaher B et al [2021]	*	*	*	*		*	*	
Sparks GM et al [2013]	*	*	*	*	**	*	*	
Oquendo MA et al [2013]	*	*		*	**	*	*	
Birmaher B et al [2010]	*	*	*	*	**	*	*	
Palacio-Ortiz JD et al [2017]	*	*	*	*	**	*	*	
Findling RL et al [2005]				*	**	*	*	
Parvaresh N et al [2010]	*	*	*	*			*	*
Hirshfeld-Becker DR et al [2006]	*	*	*	*	**	*	*	*

Cross-sectional studies

Authors	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of exposure	Comparability	Assessment of the outcome	Statistical test
Chang KD et al [2000]		*	*	*		**	
Zappitelli MC et al [2011]				*		**	

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Cohorts

Authors	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start	Comparability	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow up of cohorts
Solberg BS et al [2021]	*	*			*	*	*	
Duffy A et al [2007]	*	*	*	*		*	*	*
Liang CS et al [2023]	*	*		*	**	*	*	
Chen MH et al [2021]	*	*	*	*	**		*	*