



## Review

## Comorbidity in pediatric bipolar disorder: Prevalence, clinical impact, etiology and treatment

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## ABSTRACT

**Background:** Research on pediatric bipolar disorder (PBD) is providing a plethora of empirical findings regarding its comorbidity. We addressed this question through a systematic review concerning the prevalence, clinical impact, etiology and treatment of main comorbid disorders involved.

**Method:** A comprehensive database search was performed from 1990 to August 2014. Overall, 167 studies fulfilled the inclusion criteria.

**Results:** Bipolar youth tend to suffer from comorbid disorders, with highest weighted mean prevalence rate arising from anxiety disorders (54%), followed by attention deficit hyperactivity disorder (ADHD) (48%), disruptive behavior disorders (31%), and substance use disorders (SUD) (31%). Furthermore, evidence indicates that ADHD and anxiety disorders negatively affect the symptomatology, neurocognitive profile, clinical course and the global functioning of PBD. Likewise, several theories have been posited to explain comorbidity rates in PBD, specifically common risk factors, one disorder being a risk factor for the other and nosological artefacts. Lastly, randomized controlled trials highlight a stronger therapeutic response to stimulants and atomoxetine (vs. placebo) as adjunctive interventions for comorbid ADHD symptoms. In addition, research focused on the treatment of other comorbid disorders postulates some benefits from mood stabilizers and/or SGA.

**Limitations:** Epidemiologic follow-up studies are needed to avoid the risk of nosological artefacts. Likewise, more research is needed on pervasive developmental disorders and anxiety disorders, especially regarding their etiology and treatment.

**Conclusions:** Psychiatric comorbidity is highly prevalent and is associated with a deleterious clinical effect on pediatric bipolarity. Different etiological pathways may explain the presence of these comorbid disorders among bipolar youth. Standardized treatments are providing ongoing data regarding their effectiveness for these comorbidities among bipolar youth.

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**1. Introduction**

Pediatric bipolar disorder (PBD) is a mental disorder affecting roughly 2% of youth under the age of 18 (Merikangas et al., 2011; Van Meter et al., 2011). Likewise, for 55–60% of adults with bipolar disorder (ABD), the pathology begins in childhood and adolescence (Perlis et al., 2004) with displays of subthreshold forms or prodromal signs of the disorder (Correll et al., 2014; Shaw et al., 2005; Youngstrom et al., 2005).

Unlike adult bipolar disorder, PBD phenotype may be somewhat similar to other childhood-related disorders such as disruptive behavior disorder (DBD), attention deficit hyperactivity disorder (ADHD), severe mood dysregulation disorder (SMD) and/or pervasive developmental disorder (PDD). Failure to discriminate PBD from these pathologies may lead to inadequate diagnosis and treatment, which largely hampers a sound prognosis into adulthood (Spencer et al., 2001). Given this, several systematic reviews have been undertaken to distinguish PBD from other types of childhood mental disorders, which have provided evidence regarding this major concern (Dickstein and Leibenluft, 2012; Galanter and Leibenluft, 2008; Giedd, 2000; Kim and Miklowitz, 2002; Skirrow et al., 2012; Sood et al., 2005).

Beyond differential diagnoses, these related disorders may also be comorbid conditions in bipolar youth. In fact, research on comorbidity has already emerged with a plethora of findings over the last fifteen years (Wilens et al., 2003). Because comorbidity in juvenile bipolarity tends to be the rule rather than the exception, identifying and managing these comorbid mental disorders should be a clinical target of clinicians and researchers interested in PBD (Tramontina et al., 2003). Moreover, improving their diagnosis and treatment may ultimately lead to a better prognosis for juvenile bipolarity (Joshi et al., 2010a). Hence, efforts should be made to address this topic. To date, there is only a previous comprehensive review on this issue (Joshi and Wilens, 2009). Since this prior systematic review has included results from limited time periods, we considered the need to subsume new findings into an up-to-date review embracing latest results from comorbidity of PDD, ADHD, DBD (conduct disorder and/or oppositional defiant disorder), anxiety disorders and substance use disorders (SUD). Particularly, we sought to

elucidate four issues, namely: (i) What is the lifetime prevalence of these comorbid mental disorders in PBD?. (ii) To what extent do these comorbid disorders modulate the PBD profile?. (iii) Which etiological pathways may account for comorbidity in PBD?. (iv) Which treatments have been proven to be effective in diminishing the symptomatology of these comorbid disorders?

**2. Method**

*2.1. Search strategy*

A literature search was carried out on the PsycINFO and PubMed databases from 1990 to August 2014. The terms employed included indexing terms (e.g., MeSH) and free texts: [(comorbidity OR anxiety disorder OR panic disorder OR PTSD OR OCD OR conduct disorder OR disruptive behavior disorder OR ADHD OR hyperactivity OR autism OR pervasive developmental disorder OR substance use disorder OR cannabis) AND (youth OR pediatric OR child OR adolescent OR juvenile) AND (bipolar disorder)].

*2.2. Selection criteria*

Inclusion criteria included young people: (i) aged 4–18 who were (ii) diagnosed with bipolar disorder and comorbid childhood mental disorders according to DSM-III-R (APA, 1987) or DSM-IV criteria (APA, 1994). Thus, 167 manuscripts fulfilled the inclusion criteria. Nine of them were partial reviews and another was a full review. The remaining texts were original papers.

*2.3. Data extraction*

The following variables were recorded for all the manuscripts: (i) type of methodology (cross-sectional vs. prospective study); (ii) primary ascertainment diagnosis (PBD vs. comorbid diagnosis); (iii) comparative procedure (post-hoc analysis vs. case-control studies; and iv) outcome measures (prevalence, common and

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