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Special review article

Can unipolar and bipolar pediatric major depression be differentiated from each other? A systematic review of cross-sectional studies examining differences in unipolar and bipolar depression

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ABSTRACT

Introduction: While pediatric mania and depression can be distinguished from each other, differentiating between unipolar major depressive disorder (unipolar MDD) and bipolar major depression (bipolar MDD) poses unique clinical and therapeutic challenges. Our aim was to examine the current body of knowledge on whether unipolar MDD and bipolar MDD in youth could be distinguished from one another in terms of clinical features and correlates.
Methods: A systematic literature search was conducted on studies assessing the clinical characteristics and correlates of unipolar MDD and bipolar MDD in youth.
Results: Four scientific papers that met our priori inclusion and exclusion criteria were identified. These papers reported that bipolar MDD is distinct from unipolar MDD in its higher levels of depression severity, associated impairment, psychiatric co-morbidity with oppositional defiant disorder, conduct disorder and anxiety disorders, and family history of mood and disruptive behavior disorders in first-degree relatives.
Limitations: Though we examined a sizeable and diverse sample, we were only able to identify four cross sectional informative studies in our review. Therefore, our conclusions should be viewed as preliminary.
Conclusions: These findings can aid clinicians in differentiating the two forms of MDD in youth.

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1. Introduction

Pediatric major depressive disorder (MDD) is a prevalent disorder in youth estimated to afflict up to 25% of youth in the U.S. (Lewinsohn et al., 1998). This disorder is associated with very high levels of morbidity, distress, and disability affecting all aspects of the afflicted child's life, including increased risk for psychiatric hospitalizations, substance use disorders, family dysfunction, distress, and deficits in both educational and work performance (Carlson and Kashani, 1988; Lewinsohn et al., 2000). MDD is also a major risk for suicide and suicide remains the second most common cause of death in youth, second only to accidents (Nock et al., 2013). The Center for Disease Control (CDC) considers pediatric MDD a major public health concern (Centers for Disease Control, 2012) and documents that even minor symptoms of MDD dramatically increase the risk for suicidal behavior, supporting efforts aimed at the identification and treatment of pediatric MDD.

However, a major problem in the diagnosis and management of pediatric MDD is distinguishing children afflicted with bipolar forms of MDD from those with unipolar forms of the disorder. The literature suggests that up to 30% of youth presenting to clinical practice with prototypical symptoms of MDD have already experienced symptoms of mania or hypomania (bipolar MDD) (Geller et al., 1994). While antidepressants remain the mainstay of treatment for MDD, a major concern in treating children with an antidepressant is the risk of pharmacologically inducing manic symptoms, psychomotor agitation and mixed states, and increasing the risk for suicidal behaviors (Faedda et al., 2004; Akiskal and Benazzi, 2005; Baldessarini et al., 2005), a risk that is particularly concerning in children with bipolar MDD. Because the literature suggests that a substantial minority of pediatric patients who present with symptoms of MDD actually have bipolar MDD, identifying which children have histories of mania or hypomania is a difficult endeavor that further complicates treatment decisions. This state of affairs supports the need for efforts at identifying bipolar from unipolar forms of MDD in clinical and research settings.

The authors of this paper recently conducted a literature review examining which clinical correlates are most predictive of ultimate manic switches in children initially presenting with depressive episodes (Uchida et al., 2014). In their systematic literature review, the authors elucidated that manic switches in pediatric depression can be predicted by several risk factors, including positive family history of mood disorders, emotional and behavioral dysregulation, subthreshold mania, and psychosis. Because of the greater morbidity associated with bipolar MDD as described above, being able to cross-sectionally distinguish bipolar MDD from unipolar MDD is of paramount importance. As such, the main aim of this study was to investigate the current body of knowledge on whether unipolar and bipolar forms of pediatric MDD could be differentiated from one another. To this end, we conducted a systematic review of the extant literature addressing this important issue. To the best of our knowledge this is the first investigation of this topic.

2. Methods

2.1. Literature review

We performed a literature search through PubMed utilizing the following search algorithm: (bipolar depression OR bipolar disorder) AND (unipolar depression OR major depressive disorder) AND (predictor OR prodrome OR risk factors OR comparison OR switch OR conversion) AND (child* OR adolesc* OR youth). References were also reviewed and added if applicable to search criteria.

2.2. Selection criteria

We included only original studies that specifically evaluated the differences in the clinical features and correlates between unipolar and bipolar MDD in youth. We implemented the following inclusion criteria: (1) original research, (2) has operationalized assessment of major depressive disorder and bipolar disorder, (3) documents comparison between unipolar and bipolar MDD, (4) subjects are limited to children of under the age of 18, and (5) a cross-sectional examination. Articles were excluded if (1) they did not differentiate symptomatic pictures of unipolar from bipolar MDD, (2) the study had a prospective design examining the risk factors of manic switching, or (3) not available in the English language.

Two psychiatrists and a research assistant screened the articles for relevance by examining the abstracts, and two psychiatrists and a research assistant reviewed the identified relevant articles in full text to evaluate their eligibility.

2.3. Data extraction

The following variables were extracted: study sample size, proband age range, and characteristics that differentiated subjects with unipolar and bipolar MDD.

2.4. Qualitative analysis

We reviewed the included articles, extracting the relevant details. We also performed a qualitative analysis of the methods and results with particular note to characteristics that differentiated subjects with unipolar and bipolar MDD.

3. Results

Fig. 1 provides the results of the identification of the articles. From the initial database search, 752 papers were identified and screened by 2 of the authors (MU and GS). After the initial screening, 45 articles were found to be relevant and the full text of each was carefully examined. Of these, 41 studies were excluded due to either 1) failure to report on the difference between the clinical correlates of