



A latent class analysis of parental bipolar disorder: Examining associations with offspring psychopathology



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ABSTRACT

Bipolar disorder (BD) is highly heterogeneous, and course variations are associated with patient outcomes. This diagnostic complexity challenges identification of patients in greatest need of intervention. Additionally, course variations have implications for offspring risk. First, latent class analysis (LCA) categorized parents with BD based on salient illness characteristics: BD type, onset age, polarity of index episode, pole of majority of episodes, rapid cycling, psychosis, anxiety comorbidity, and substance dependence. Fit indices favored three parental classes with some substantively meaningful patterns. Two classes, labeled “Earlier-Onset Bipolar-I” (EO-I) and “Earlier-Onset Bipolar-II” (EO-II), comprised parents who had a mean onset age in mid-adolescence, with EO-I primarily BD-I parents and EO-II entirely BD-II parents. The third class, labeled “Later-Onset BD” (LO) had an average onset age in adulthood. Classes also varied on probability of anxiety comorbidity, substance dependence, psychosis, rapid cycling, and pole of majority of episodes. Second, we examined rates of disorders in offspring (ages 4–33, $M_{age}=13.46$) based on parental latent class membership. Differences emerged for offspring anxiety disorders only such that offspring of EO-I and EO-II parents had higher rates, compared to offspring of LO parents, particularly for daughters. Findings may enhance understanding of BD and its nosology

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1. Introduction

Bipolar disorder (BD) is a chronic illness characterized by high rates of relapse and recurrence (Harrow et al., 1990), and patients experience psychosocial impairment that often persists between episodes and impacts essentially all areas of functioning (Coryell et al., 1993; Yatham et al., 2004). However, BD is also a complex and heterogeneous disorder, with profound variations in the severity, length, and number of manic/hypomanic and depressive episodes and patterns of comorbidity (Akiskal et al., 2000). Further, course variations can lead to more or less favorable patient outcomes, psychosocial impairment, and stress (Bauer et al., 2001). Given these variations in BD course and characteristics, current diagnostic systems do not provide for the identification of which patients may be in greatest need of intervention and support (Ghaemi et al., 2008). Uncovering this information would assist in the prevention of long-term maladaptive patient outcomes.

Additionally, this information would inform targeted intervention for offspring of parents with BD (OPBD), as parental illness course may have implications for both environmental and genetic offspring risk.

1.1. Bipolar disorder characteristics

Past research has identified a number of specific BD course variants that may be linked with greater illness severity and poorer functional outcome (Treuer and Tohen, 2010). These include the indicators in current classification systems, such as BD type, rapid cycling, and psychosis. For example, although bipolar I disorder (BD-I) and bipolar II disorder (BD-II), are operationalized to differ only by mania severity, BD types also may have different profiles in terms of chronicity, comorbidity, and clinical features. Specifically, although BD-I may be a more severe form of the disorder (e.g., presence of psychosis, more acute impairment), BD-II is generally more chronic, with higher rates of depression, episode switching, and anxiety comorbidity (Vieta et al., 1997; Judd et al., 2003a; 2003b). The presence of rapid cycling is also linked with greater illness severity, suicide risk, and treatment failure (Coryell et al., 2003; Kupka et al., 2003;

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Tondo et al., 2003). Psychotic symptoms are associated with BD episode severity, higher hospitalization rates, and poorer treatment response (van Rossum et al., 2008; Ozyildirim et al., 2010). In fact, in addition to BD type, research suggests that rapid cycling and psychotic features may be markers of particular BD subtypes (Bauer et al., 1994; Potash et al., 2001).

Other factors, not in the current nosology, are also associated with BD severity and functional outcome, including onset age, comorbidity, and characteristics associated with episode polarity. For example, onset age has shown inverse associations with episode length and recurrence and impairment in functioning (Benazzi, 2009; Perlis et al., 2009). These differences in clinical expression and outcome between earlier and later onset BD, along with data indicating different patterns of familial risk between the groups (Somanath et al., 2002), has led researchers to suggest that onset age could be a valid alternative to polarity for classifying BD (Schurhoff et al., 2000; Benazzi, 2009). In terms of comorbidity, both anxiety and substance use disorders are linked with BD severity (e.g., suicidality, hospitalization), chronicity, poor treatment outcome, and impaired functioning (Cassidy et al., 2001; Simon et al., 2004; Gaudiano and Miller, 2005; Goldstein and Levitt, 2008; Mazza et al., 2009; Sala et al., 2012). Although anxiety and substance use disorders tend to overlap with one another in BD patients, the disorders have different patterns of associations with BD course and may uniquely contribute to severity and outcome (Simon et al., 2004; Bauer et al., 2005).

Finally, evidence suggests that characteristics associated with episode polarity may impact severity and outcome. Studies show that BD course is predominantly characterized by episodes of the same polarity, and there may be important clinical differences in severity and chronicity between patients with predominantly manic versus depressive episodes (Colom et al., 2006; Rosa et al., 2008). BD course also may be associated with the polarity of the index episode, such that, compared to patients with manic episode onset, those who have an initial depressive episode have more chronic illness course, more suicidality, later onset, fewer hospitalizations, and fewer psychotic symptoms (Daban et al., 2006). Polarity at onset may be a familial feature, such that relatives have the same episode type at onset (Kassem et al., 2006), suggesting that this feature may delineate different BD subtypes.

1.2. Associations with offspring outcomes

Although abundant literature has identified illness characteristics associated with poorer outcomes in BD patients, few studies have examined specifically the impact of these characteristics on offspring. High-risk research has instead largely compared psychopathology rates in OPBD versus offspring of parents without BD, without examining parental illness characteristics as moderators of risk. Such research overwhelmingly shows that OPBD are at increased risk for a variety of psychiatric disorders themselves (Lapalme et al., 1997; DelBello and Geller, 2001; Birmaher et al., 2009). However, given the heterogeneity of BD, offspring living with BD parents may have vastly different experiences, including variable levels of stress and unpredictability. Additionally, offspring might be at higher genetic risk of certain types of psychopathology depending on parental BD course characteristics.

Grigoriu-Serbanescu et al. (1989) found that the presence and severity of any diagnosis in 72 OPBD was associated with parents' illness severity, number of manic/mixed episodes, and onset age. More recently, in 50 OPBD, Garcia-Amador et al. (2013) found that, when BD parents had a lifetime history of psychotic symptoms or BD-II, offspring were more likely to exhibit psychopathology. Two additional studies point to the role of parental BD onset age in increasing risk for offspring mood disorders (depression and BD), specifically (Chang et al., 2000; Oquendo et al., 2013). However,

Goldstein et al. (2010) failed to find any relationship between parental illness characteristics (BD type, rapid cycling, onset age, suicidality, psychosis, comorbidity) and the presence of offspring BD. These discrepancies, and the fact that many of the studies were limited by small offspring sample sizes, warrant replication in a larger sample that examines a range of offspring disorders. Additionally, rather than examining correlations between individual parental illness characteristics and offspring psychopathology, it may be important to instead evaluate relationships with empirically derived patterns of parental BD course.

Taken together, the above research suggests that a number of BD characteristics—some within and some outside of the current nosology—predict severity and outcome. However, given that these course characteristics are interrelated, determining which particular indicators may be driving associations with patient outcomes proves challenging. Past studies have largely examined these features in isolation, rather than examining if and how certain factors “hang together,” which may provide insight into understanding course patterns. Additionally, some studies suggest relationships between parental BD course characteristics and offspring psychopathology, although this literature is sparse. The current study used latent class analysis (LCA) as a novel method of categorizing parents with BD based on salient characteristics of illness course. Given our relatively small sample size of parents, this approach was used in an exploratory fashion to generate hypotheses regarding course patterns. Next, we examined links between these parental latent classes and offspring emotional and behavioral disorders to investigate whether patterns of parental course may be linked with offspring risk for certain types of psychopathology. Finally, we examined offspring sex differences in the above relationships.

2. Methods

The investigation combined data from two studies examining BD patients receiving treatment at Massachusetts General Hospital (MGH) psychiatry units and their offspring (Henin et al., 2005). Parents were informed of the study via advertisements in waiting rooms and letters to clinicians, and contacted the study coordinators if interested in participating. Study coordinators then administered a screening questionnaire to confirm parental BD diagnosis. Next, structured diagnostic interviews, administered by trained interviewers, evaluated potential participants and their offspring. Parents with a positive BD diagnosis were included. MGH Subcommittee for Human Studies approved all procedures. Parents provided informed consent for participation, and offspring provided assent. Participants were compensated for their involvement.

Parent and offspring diagnostic interviews were conducted by master- and bachelor-level diagnosticians who were extensively trained and supervised in interview procedures and diagnostic criteria. Diagnosticians discussed each interview with experienced, board-certified child and adult psychiatrists and licensed psychologists for review and to resolve diagnostic uncertainties. Kappa coefficients of agreement were computed by having experienced, board certified child and adult psychiatrists and licensed clinical psychologists diagnose subjects from audio taped interviews. Based on 500 assessments from interviews of children and adults, the median kappa coefficient was 0.98. Kappa coefficients for individual diagnoses included: attention deficit/hyperactivity disorder (ADHD; 0.88), conduct disorder (CD; 1.0), oppositional defiant disorder (ODD; 0.90), depression (1.0), mania (0.95), separation anxiety (1.0), agoraphobia (1.0), panic disorder (0.95), obsessive compulsive disorder (OCD; 1.0), generalized anxiety disorder (GAD; 0.95), specific phobia (0.95), posttraumatic

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