



## Research paper

## Longitudinal course and characteristics of cyclothymic disorder in youth



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## ABSTRACT

**Objectives:** Epidemiological studies suggest that cyclothymic disorder is the most prevalent subtype of bipolar disorder (BD). However, it is rarely diagnosed, especially in youth. This may be because it can be difficult to ascertain whether a youth meets diagnostic criteria. Clearer, easy-to-apply criteria could reduce misdiagnosis. The objective of this study was to determine whether proposed research diagnostic criteria for cyclothymic disorder (RDCyc), based on DSM-5 criteria, could be quantified and validated in youth.

**Methods:** Participants from the Longitudinal Assessment of Manic Symptoms (LAMS) study were recruited based on symptoms of mania and followed prospectively. RDCyc criteria were: 1) At least one core symptom each of mania and depression; 2) one additional symptom of mania and of depression; 3) persistence over two consecutive six-month periods, and 4) impairment. Exclusionary criteria were having a [hypo]manic or depressive episode. Outcomes at the two-year follow-up were compared between RDCyc youth and other diagnostic groups (BD I/II, BD NOS/non-RDCyc cyclothymic disorder, disruptive behavior disorders [DBD], depression).

**Results:** Thirty-seven youth met RDCyc criteria. There were no consistent differences between the RDCyc youth and youth with other BD subtypes ( $p$ s=0.001–0.960, with all-but-one  $p$  value > 0.02). RDCyc youth had higher depression ( $p < 0.0005$ ) and mania scores ( $p=0.001$ ), lower functioning ( $p=0.012$ ), and higher suicide risk than DBD youth ( $p=0.001$ ). They had higher mania scores than depressed youth ( $p=0.018$ ).

**Limitations:** The majority of youth in the sample were recruited due to elevated symptoms of mania, which may limit the generalizability of the results. Youth were followed for two years, which may not be long enough to determine whether or not they will eventually develop a manic or depressive episode.

**Conclusions:** Applying RDCyc criteria identified youth who were similar to others with BD and were more impaired than those with DBD. Using these criteria could reduce misdiagnosis and increase our understanding of this prevalent, but largely ignored, diagnosis.

Mood lability and irritability are common among youth with mental health problems, and there has been debate about how best to classify these symptoms (Geller et al., 2002; Leibenluft and Stoddard, 2013; Vidal-Ribas et al., 2016). Cyclothymic disorder – a chronic form of bipolar disorder, characterized by less extreme mood states – could be one valid diagnostic “home” for some of these cases. However, despite the fact that cyclothymic disorder has been listed in the DSM since its third revision (American Psychiatric Association, 1980), and epidemiological studies suggest that it is one of the most prevalent mood

disorders (Van Meter et al., 2011a, 2012b), it is very rarely diagnosed – particularly in young people (Van Meter and Youngstrom, 2012; Youngstrom et al., 2005). Studies of youth who do not meet criteria for bipolar I or II are almost always labeled bipolar disorder not otherwise specified, or BP-NOS (or, in the DSM-5 nomenclature, other specified bipolar disorder – for the purposes of brevity and clarity, we will use the term “BP-NOS” in this paper to refer to those youth who have a bipolar spectrum disorder that does not meet criteria for bipolar I, bipolar II, or cyclothymic disorder).

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One reason posed for the mismatch between epidemiological data, which suggest that cyclothymic disorder is prevalent, and the low/nonexistent rate of clinical or research diagnoses, is that the criteria are too vague and difficult to ascertain with any degree of accuracy, particularly in clinical settings where time and resources are limited. Given the degree of specificity (i.e., must have both hypomanic and depressive symptoms for at least one year, without *ever* having met criteria for a hypomanic, manic, or depressive episode) and the need for long-term (one year+) retrospective recall (American Psychiatric Association, 2013), accurately making this diagnosis requires a lot of attention to detail from clinicians and informants. Consequently, other diagnostic categories (e.g., BP-NOS) tend to be used instead (Jensen-Doss et al., 2014; Youngstrom, 2009). An accurate diagnosis can make a significant difference in the outcomes a young person can achieve by guiding personalized, evidence-based intervention. Currently, because the diagnosis of cyclothymic disorder is so rarely made, we know little about how – or if – its course and treatment response differ from other childhood disorders. And, because youth who meet criteria for cyclothymic disorder are often misdiagnosed, our information about the diagnostic groups to which they are usually (incorrectly) assigned is also imperfect (Van Meter and Youngstrom, 2012).

We do not yet have clear longitudinal data demonstrating whether cyclothymic disorder and BP-NOS share similar trajectories over time. What we do know is that the diagnostic criteria for cyclothymic disorder require chronicity of symptoms, whereas, in some cases, BP-NOS is diagnosed due to brevity of symptoms (Axelson et al., 2006). Further, we know that some youth with mood symptoms that do not meet criteria for bipolar I or bipolar II (i.e., cyclothymic disorder and BP-NOS) tend to get better over time, while others get worse, and some stay about the same (Birmaher et al., 2009, 2014; Cicero et al., 2009); without distinguishing cyclothymic disorder for BP-NOS in these studies, the inferences we can make are limited.

Being able to predict the expected trajectory of a youth with significant mood problems is valuable; youth with bipolar disorder usually require pharmacological intervention to manage their symptoms, but the medications prescribed can have significant side effects (Lauxen Peruzzolo et al., 2013). However, some youth who experience significant mood lability may outgrow it (Birmaher et al., 2009; Cicero et al., 2009); if we were able to predict these cases, a more conservative approach to treatment could be taken.

With more systematically-defined groups, the process of diagnostic validation – including treatment response and long-term outcome (Robins and Guze, 1970) can gain stronger footing. The primary objective of the present study was to determine whether a research operational definition based on the DSM-5 criteria for cyclothymic disorder could be quantified and validated in a sample of youth. The Research Diagnostic Criteria (RDC) were originally developed to improve reliability of psychiatric diagnoses (Ghaemi et al., 2008; Perugi et al., 2015; Spitzer et al., 1978). Our goal is consistent with objective of improving reliability; by clearly quantifying criteria for cyclothymic disorder and making the criteria easier to apply, researchers and clinicians may be able to diagnose youth with chronic mood lability more accurately and reliably. With more accurate diagnoses, we gain an opportunity to fill the gap in our understanding of the phenomenology and trajectory of cyclothymic disorder in youth.

We hypothesized the RDCyc group and youth with other DSM-IV bipolar diagnoses would endorse similar mood symptom severity, impairment, and family characteristics, consistent with their inclusion on the bipolar spectrum, and that there would be more severe mood symptoms and impairment in the RDC group than in youth with non-mood, disruptive behavior disorders. In addition to experiencing symptoms consistent with a bipolar presentation, we expected youth with an RDC diagnosis of cyclothymic disorder to have a positive family history of mental illness (Van Meter et al., 2012a, 2011b). Related, we expected caregivers for youth with cyclothymic disorder to report high stress and burden related to caregiving, particularly in light of the fact

that they might be coping with their own symptoms (Perez Algorta et al., 2015).

Data from the Longitudinal Assessment of Manic Symptoms study (LAMS; Findling, 2010; Findling et al., 2013) were well-suited for this study: The majority of participants were recruited based on elevated scores on a parent-rated measure of manic symptoms, resulting in a sample of youth at elevated risk for having or developing a bipolar spectrum disorder, including cyclothymic disorder. Youth in the study were assessed at six-month intervals for at least two years, allowing for the one year duration criteria of cyclothymic disorder to be evaluated without relying solely on retrospective report.

## 1. Method

### 1.1. Participants

Participants, aged 6–12 years, from nine clinics located among four universities enrolled in a longitudinal study of youth with elevated symptoms of mania (Horwitz, 2010). The majority of youth ( $N=621$ ) had scores above 12 on the Parent General Behavior Inventory 10 Item Mania scale (PGBI-10 M; Youngstrom et al., 2008); a demographically matched sample of 86 youth with PGBI-10 M scores below 11 were also enrolled. Participants completed evaluations every six months to assess for changes in mood or other symptoms. The present study includes data collected through the two-year follow-up, at which time retention was strong (94%).

### 1.2. Measures

**KSADS-PL-W** (Findling et al., 2010; Geller et al., 1996; Kaufman et al., 1997) was administered by a trained interviewer to youth and their parent/caregiver separately. Reliability for the KSADS items used to evaluate symptom and impairment criteria for the RDCyc diagnosis (detailed below) had Cronbach's alphas ranging from 0.93 (baseline, six-month, and 18-month time points) to 0.94 (12-month and 24-month time points). Inter-rater reliability for K-SADS diagnoses was good,  $K=0.82$  (Findling et al., 2010) in the present study. In addition to informing diagnoses, the KSADS assessed for suicidal ideation and behavior.

**Treatment** with medication was assessed using the parent report version of the Service Assessment for Children and Adolescents (SACA; Horwitz et al., 2001; Kowatch et al., 2013; Stiffman et al., 2000), which inquires about the child's history of mental health services use. For this study, we examined medications the child was taking between the 18- and 24-month follow-ups. Additionally, youth engagement with psychosocial services (therapy, counseling) was measured at baseline.

The **Family History Screen** (FHS; Milne et al., 2009) assessed the presence of mental illness among members of a family. Diagnoses were based on the presence of specific symptoms; for example, bipolar disorder was assessed by asking whether the parent has experienced “extreme, elated mood,” plus at least three other symptoms of mania. For purposes of this study, we evaluated presence/absence of bipolar disorder and of *any* psychiatric illness in the youth's biological mother or father.

The **Children's Depression Rating Scale-Revised** (CDRS-R; Poznanski et al., 1984) is a 17-item clinician-rated instrument for measuring severity of depression in children. We compared youths' 24-month follow-up scores; Cronbach's alpha in the present sample was .85.

The **Young Mania Rating Scale** (YMRS; Young et al., 1978) is an 11-item, clinician-rated measure of the severity of a child's manic symptoms. In the present study we assessed youths' 24-month follow-up scores, Cronbach's alpha was .78.

The **Child's Global Assessment Scale** (C-GAS; Shaffer et al., 1983) is a clinician-rated measure of youth overall functioning. In this study, we used current C-GAS scores from the 24-month follow-up.

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