BIPOLAR DISORDER IN CHILDREN AND ADOLESCENTS

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It is now widely accepted that bipolar disorder (BD), also known as manic depressive illness, occurs in children and adolescents and the controversy has shifted from a debate about whether it can be diagnosed in youth to how it is diagnosed, how it can be distinguished from other more commonly diagnosed childhood psychiatric disorders, and how it can be treated and prevented.

Despite concerns about over-diagnosing BD, this disorder is still undiagnosed in many children.

BD-I is classified under mood disorders and characterized in its classic form by cyclic changes between mania and major depressive episodes. Other subtypes of BD include episodes of major depression with hypomania (BD-II), multiple episodes of hypomania with depressed mood but no clear episodes of major depression (cyclothymia), and sub-threshold (e.g., shorter) episodes of mania or hypomania with or without depression (BD-not otherwise specified, NOS) (for further details regarding the classification, please see the section below about subtypes of BD). There are subtle differences between the International Classification for Diseases-10 (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV), but in parallel with the majority of reports in youth, unless otherwise specified, the DSM-IV criteria (APA, 2000) will be used in this chapter when discussing BD. For the purposes of this chapter the word youth denotes children and adolescents. The goal of this chapter is to review the epidemiology, age of onset and course, subtypes, etiology, clinical presentation, differential diagnosis, and treatment of BD in children and adolescents.

EPIDEMIOLOGY

Click on the picture to access the transcripts of an interview with David Axelson MD about issues related to the rate of BD diagnosis in youth.

The prevalence of BD-I and BD spectrum disorders in adults is around 1% and 5%, respectively, and the majority of them had the onset of their mood symptoms before age 20 years (Perlis et al., 2009). In clinical populations the prevalence of BD in youth in the US has been reported between 0.6% and 15% depending on the setting, the referral source, and the methodology to ascertain BD. Recent studies especially those in the US have shown dramatic increases in recognition and rates of BD in youth over the past 20 years and some authors have questioned the possibility of over-diagnosing children with BD in the US, whereas many others have brought up the possibility of long neglecting the presence of this condition in childhood (see also Chapter E.3).

Studies suggest that it takes on average 10 years to identify and begin treatment of BD, indicating the need for timely detection and treatment of this serious illness.

A recent meta-analysis about the epidemiology of BD in youth around the world – enrolling 16,222 youth between the ages of 7 and 21 years during a period from 1985 to 2007 – reported that the overall rate of BD was 1.8% (95% CI, 1.1%–3.0%) (Van Meter et al, 2011). This meta-analysis suggested that:

- The prevalence of BD in youth is similar to the current prevalence estimates of BD in adults
- The prevalence of BD in youth is not different in the US relative to other countries (e.g., Netherlands, UK, Spain, Mexico, Ireland, and New Zealand), and
- Despite BD being diagnosed more commonly in clinical settings, the prevalence of BD in youth in the community is not increasing.

There was no significant difference in the mean rates of BD in youth between US and non-US studies, but US studies had a wider range of rates, especially when a broader definition of BD was used (Van Meter et al, 2011).

Gender and age differences in the prevalence of BD

Similar to adults, studies in clinical populations suggest that the rates of bipolar spectrum disorders in youth are equally common in males and females (Axelson et al, 2006). However, BD-II and adolescent-onset BD are more prevalent

in females (Birmaher et al, 2009b). A large epidemiological study in the US reported slightly higher rates of BD-I and D-II in female than in male adolescents (3.3% versus 2.6%, respectively) with increasing rates of BD with older ages (Merikangas et al, 2010). The meta-analysis of international BD studies concluded that BD can have its onset in childhood but prevalence was much higher during adolescence (Van Meter et al, 2011).

Early identification of BD in youth is the key not only for mood stabilization but also to enable the child to follow a normative developmental path and prevent an unrecoverable loss in the child's psychosocial development and education (Birmaher & Axelson, 2005).

Burden of the illness

The World Health Organization (WHO) indicates that BD is the 6th leading cause of disability in the world. BD in youth is now increasingly recognized as a significant public health problem that is often associated with impaired family and peer relationships, poor academic performance, high rates of chronic mood symptoms and mixed presentations, psychosis, disruptive behavior disorders, anxiety disorders, substance use disorders, medical problems (e.g., obesity, thyroid problems, diabetes), hospitalizations, and suicide attempts and completions (Diler, 2007). Moreover, youth with BD can have higher behavioral health costs and greater utilization of medical services than youth with unipolar depression or non-mood disorders. Patients with undiagnosed BD may also have higher behavioral health costs than those with diagnosed BD. Given the high rates of morbidity and mortality and the chronic course of the condition, early diagnosis and treatment in bipolar children is critical (Birmaher & Axelson, 2005; Diler, 2007).

AGE OF ONSET AND COURSE

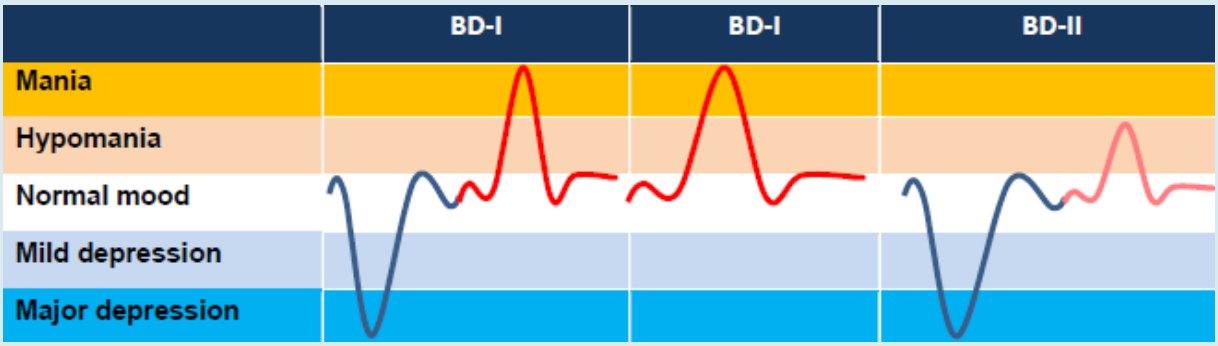
Retrospective studies in adults with BD have reported that 10%–20% had the onset before 10 years of age and up to 60% had the onset before the age of 20 (Diler, 2007; Perlis et al, 2009). BD in adults is frequently preceded by childhood disruptive behavior disorders and anxiety disorders. Early onset BD is associated with a severe course of illness and poor outcome; children with pre-pubertal onset BD are reported as approximately 2 times less likely to recover as those with post-pubertal onset BD. In addition, subjects with pre-pubertal onset BD had more chronic symptoms, spent more follow-up time with subsyndromal mood symptoms, and had more polarity changes per year than post-pubertal-onset BD subjects (Birmaher et al, 2009a; Diler, 2007).

BD in young people is an episodic illness with subsyndromal and syndromal episodes mainly with depressive and mixed symptoms and rapid mood changes.

Youth with BD show a continuum of BD symptom severity from subsyndromal to full syndromal with frequent mood fluctuations. Naturalistic and research follow-up studies have reported that 70% to 100% of youth with BD will eventually recover (e.g., no significant symptoms for 2 months) from their index episode. However, up to 80% will experience recurrences after recovery (e.g., one or more recurrences in a period of 2-5 years) despite ongoing treatment. In addition, complementary analyses indicate that the prospective course in these youth, analogous to findings reported for adults, shows mood fluctuations of varying intensities during 60%-80% of the follow-up time, particularly depressive and mixed symptoms, and frequent shifts in symptom polarity. During adolescence, there is a drastic increment in the rates of suicidal ideation and attempts and substance abuse. In addition, youth with BD shows high rates of legal, social, familial, and academic problems (Birmaher et al, 2009a; Diler, 2007).

Early age of onset, long duration, low socioeconomic status, mixed or rapid cycling episodes, psychosis, subsyndromal mood symptoms, comorbid disorders, exposure to negative life events, high expressed-emotion, and family psychopathology are associated with worse course and outcome (Birmaher et al, 2009a; Diler, 2007).

Figure E.2.1 Mood episodes in bipolar disorder-I and bipolar disorder-II



BD: bipolar disorder

DIAGNOSIS AND SUBTYPES

It is important to have a common language and use terms appropriately between professionals (and with patients and families) when describing, reporting, and monitoring mood changes in youth. According to the DSM-IV, there are four subtypes of BD: bipolar I (BD-1), bipolar II (BD-II), cyclothymia, and bipolar disorder-not otherwise specified (BD-NOS); except for the cyclothymia, their diagnostic criteria are the same for adults and children (APA, 2000).

- *BD-I* requires the current presence or history of a manic (or mixed manic) episode (please see Tables E.2.1 and E.2.2) with or without a major depressive episode. A mixed manic episode is when the child meets criteria for both mania *and* major depression during the same episode (simultaneously or in rapid sequence). To diagnose BD-I, both symptom criteria (3 or 4 symptoms in addition to elation or irritability, respectively) and duration criteria should be met in addition to the "significant functional impairment or psychosis" during mania. For the duration criteria, a manic episode should last at least seven consecutive days or an inpatient admission was required anytime during the episode.
- *BD-II* is characterized by at least one major depressive episode and at least one hypomanic episode (hypomania should last at least 4 consecutive days) (please see Table E.2.3).
- *Cyclothymia* is characterized by numerous hypomanic episodes together with numerous periods of depressed mood or loss of interest or pleasure that do not meet all the criteria for a BD or a major depressive episode (*1 year of duration of illness in youth, versus 2 years in adults, is required for the diagnosis*).
- *BD-NOS* is used when there are features of hypomanic or mixed episodes but do not meet the diagnostic criteria for any of the more specific BD subtypes. Because BD-NOS criteria are vague in DSM, researchers have developed clearer definitions to identify a BD-NOS diagnosis – such as at least a 2-day long history of hypomania, or at least 4 shorter (≥ 4 hours each) episodes of hypomania (one symptom less to meet the full symptom criteria) (Axelson et al, 2011b).

Hypomania

Hypomania is described as a milder form of a manic episode. The patient should have "distinct change" from baseline functioning but "not have marked functional impairment". Sometimes patients actually like being hypomanic because they are able to do more things such as working on more projects.

Click here to view a summary of DSM diagnoses of BD based on the type of mood episode.

Subtypes of BD in youth may not be stable over time

In a 4-year follow up study, 25% percent of youth with BD-II converted to bipolar I and 45% of those with BD-NOS converted to BD-I or II (Axelson et al, 2011b).

Definition of BD-NOS for research

Based on the Course and Outcome for Bipolar Youth (COBY) study, the recommended criteria for BD-NOS in youth when DSM-IV criteria for BD-I or BD-II were not met but there was a distinct period of abnormally elevated, expansive or irritable mood are as follows (Axelson et al, 2006; Birmaher et al, 2009a):

1. Two DSM-IV manic symptoms (three if the mood is irritable only) that were clearly associated with the onset of abnormal mood
2. Clear change in functioning
3. Mood and symptom duration of a minimum of 4 hours within a 24-hour period for a day to be considered meeting diagnostic threshold; and
4. A minimum of four days (not necessarily consecutive) meeting the mood, symptom, duration and functional change criteria over the subject's lifetime, which could be two 2-day episodes or four 1-day episodes.

Table E.2.1 DSM IV criteria for manic episode[1,2] (APA, 2000)

A	A distinct period of abnormally and persistently elevated, expansive or irritable mood, lasting at least 1 week (or any duration if hospitalization is necessary)
B	During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree: 1. Inflated self-esteem or grandiosity 2. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep – it does not mean sleeping less at night and then feeling tired and napping during the day) 3. More talkative than usual or pressure to keep talking 4. Flight of ideas or subjective experience that thoughts are racing 5. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli) 6. Increase in goal-directed activity (at work, at school, or sexually) or psychomotor agitation 7. Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)
C	The symptoms do not meet criteria for a mixed episode
D	The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features
E	The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication or other treatment) or a general medical condition (e.g., hyperthyroidism)

[1]Readers may use "GRAPES(+D)" to remember the symptoms of mania: G (grandiosity), R (racing thoughts), A (activity level), P (pressured speech), E (elated mood), S (Sleeping less) +D(distractibility).

[2]Manic-like episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of bipolar-I disorder.

ETIOLOGY AND RISK FACTORS

The single best predictor of BD in youth is family history with rates of positive family history in up to 20% of cases. Twin and family studies have demonstrated that BD is largely an inherited illness with concordance between identical twins of about 70%, two to three times the rate reported for non-identical twins. Current studies have indicated that multiple genes seem responsible for BD but so far they have not being identified. You may wish to read Schulze's recent review on the topic (Schulze, 2010) or a list of potential susceptibility genes for BD.

Despite BD being largely a genetic illness, there are other important biological, social or emotional factors that can either precipitate BD or serve as

Table E.2.2 DSM IV criteria for a mixed episode[1] (APA, 2000)

A	The criteria are met both for a manic episode and for a major depressive episode (except for duration) nearly every day during at least a 1-week period.
B	The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.
C	The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment), or a general medical condition (e.g., hyperthyroidism)

[1]Mixed-like episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of bipolar-I disorder.

Note: rapid cycling refers to at least 4 episodes in the previous 12 months that meet criteria for a major depressive, manic, mixed or hypomanic episode, and the episodes are demarcated either by partial or full remission for at least 2 months or a switch to an episode of opposite polarity – e.g., major depressive episode to manic episode).

Table E.2.3 DSM IV criteria for hypomanic episode[1] (APA, 2000)

A	A distinct period of persistently elevated, expansive or irritable mood, lasting throughout at least 4 days, that is clearly different from the usual non-depressed mood.
B	During the period of mood disturbance, three (or more) of the manic symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree.
C	The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic.
D	The disturbance in mood and the change in functioning are observable by others.
E	The mood disturbance not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization, and there are no psychotic features.
F	The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication or other treatment) or a general medical condition (e.g., hyperthyroidism)

[1]Hypomanic-like episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of bipolar-II disorder.

protective factors in people who are genetically predisposed. Research and clinical experience also suggest that trauma or stressful life events can trigger an episode of BD; however, many episodes occur without an obvious cause. In brief, the etiology is multifactorial with a complex interaction between biological vulnerabilities and environmental influences (a summary of the etiology of BD can be accessed at the American Academy of Child and Adolescent Psychiatry's frequently asked questions about BD in youth).

Click on the picture to visit the AACAP's resource center to access reading materials such as "facts for families" and "frequently asked questions" and to watch two video clips: a short interview with Drs Birmaher and Kashurba and one roundtable discussion with experts (Drs Carlson, Birmaher, Kowatch, Leibenluft, and Wozniak) about diagnosis, assessment, comorbidity, natural history, treatment, and questions.

Recent advances in neuroimaging techniques such as magnetic resonance imaging (MRI) and functional MRI (fMRI) have indicated that neural circuits involved in emotion processing and regulation in BD youth are different from their healthy peers, including subcortical (e.g., amygdala) and prefrontal regions. The reduced volume of amygdala in BD adolescents compared to healthy controls is one of the most consistent neuroimaging findings in pediatric BD (Pfeifer et al, 2008). These findings suggest the possibility of a developmental delay in the gray matter of subcortical regions in BD adolescents. In addition, prefrontal cortex

continues to mature until early adulthood in healthy youth but this is possibly delayed in BD youth (Fleck et al, 2010). In parallel to MRI studies, magnetic resonance spectroscopy studies in BD youth have suggested that substances that serve as markers for neuronal integrity are affected. However, neuroimaging findings in BD youth need to be interpreted with caution because of the small samples and other confounding factors such as subjects' different mood phases (e.g., depressed, hypomanic, euthymic) and the presence of comorbid disorders and medications. Readers may wish to read Dr Mani Pavuluri's detailed presentation about brain function in youth with BD or access the National Institute of Mental Health's website for Dr Ellen Leibenluft's summary of imaging studies.

Available studies suggested that youth with BD may be impaired in their capacity to identify emotions correctly and may perceive fear or anger in emotionally neutral faces (Leibenluft & Rich, 2008). Furthermore, preliminary investigations in BD youth have found several *cognitive deficits*, such as in visuospatial memory, verbal memory, executive functions and attentional set-shifting. Improvement of the acute mood episode may accompany improvement in neurocognitive functioning (e.g., verbal and working memory); however, studies suggest that neurocognitive deficits may be independent of the BD child's mood state, can exist even when there are no signs of mania or depression, and may have lifelong implications for reduced functional ability (Pavuluri et al, 2009).

"One of the overall goals of neuroimaging is to understand what differentiates children who are at risk for BD from other children. The ultimate goal is to identify neurobiological markers (physical differences in the chemistry and structure of the brain) for BD so that we can more effectively treat those who are at risk for developing it" (DelBello). You may wish to read an interview with Melissa DelBello MD at The Balanced Mind Foundation website or click on the picture below to listen to Dr DelBello's talk about brain structures involved in BD (15:45).

COMORBIDITY

Comorbid disorders, particularly disruptive behavior disorders (30% to 70%), ADHD (50% to 80%), and anxiety disorders (30% to 70%) are very common. The prevalence of these disorders depends on the methods utilized to ascertain them and the sample studied (e.g., more frequent in clinical versus community samples), as well as according to age (in children ADHD and oppositional defiant disorder are more common while in adolescents there are more conduct and substance use disorders). The presence of comorbid disorders influences response to treatment and prognosis, indicating the need to identify and treat them effectively.

CLINICAL PRESENTATIONS

The AACAP in their practice parameter for BD recommends clinicians to follow DSM-IV, including the duration criteria (requiring an episodic change in mood lasting at least 4 days for hypomania and 7 days for mania) (McClellan et al, 2007). There is consensus among experts that children and adolescents can fulfill the strict DSM-IV criteria for BD-I and II. However, it appears that in practice in the US the majority of youth are diagnosed with BD-NOS because they do not meet the time requirement for BD-I or II (Axelson et al, 2011b).

Below we will review key issues about making an accurate diagnosis of BD in youth such as the requirement of clearly identifying mood episodes (e.g., episodicity), the role of cardinal symptoms, irritability, subthreshold presentations, bipolar depression, and preadolescence and preschool presentations.

Click on the picture to hear Dr Kiki Chang's talk about comorbidity in BD youth (7:34)

Episodicity

Similar to adults with BP, for pediatric BD, taking into account the emotional and cognitive developmental stage of the child, the DSM-IV criteria for

manic, mixed, or hypomanic episode require a *distinct* period of abnormal mood and accompanying symptoms. Despite suggestions by some investigators that episodicity is not needed to diagnose pediatric BD, most researchers, clinicians, and the AACAP guidelines (McClellan et al, 2007) recommend that episodicity is required to diagnose BD in youth. In fact, it is suggested to focus on determining the presence of mood episodes first and then ascertain the extent to which DSM manic or hypomanic symptoms are present during an identifiable time frame.

Cardinal symptoms

In contrast to the current DSM criteria for a manic episode (Table E.2.1), to be more specific and avoid misdiagnosing BD in youth, few investigators have suggested that elated mood and grandiosity must be present to diagnose pediatric BD (Geller et al, 2002). A meta-analysis of pediatric BD, showed that elation and grandiosity are present in 70% and 78%, respectively, of youth diagnosed with BD (Kowatch et al, 2005). However, some youth may have BD without elation and grandiosity and there is considerable heterogeneity among studies in the rates of these symptoms, perhaps reflecting the different origin and age of the samples, and disparate methodologies and interpretation of symptoms. It is important to consider the difficulty identifying elation and grandiosity, especially in younger children, and we will review the developmental issues below under the preschool presentations.

Irritability

Irritability is a very common symptom in BD youth (Kowatch et al, 2005) and the DSM-IV criteria for a manic episode explicitly allows for the presence of irritable mood alone to satisfy the "A" criterion, though it qualifies this by requiring an additional symptom criterion. In other words, four or more manic symptoms should accompany irritability during the same time frame (clustering) of the mood episode. In addition, in order to be counted as a symptom of a manic episode – although not every researcher in the BD field agree with this – irritability needs to be episodic, even if the child has preexisting irritability (e.g., worsening of irritability during the manic episode when other comorbid disorders exist such as anxiety disorders, ADHD, or ODD) (Leibenluft & Rich, 2008). Furthermore, irritability rarely occurs in manic youth without elation.

It is important to consider that irritability is also part of the DSM-IV diagnostic criteria for other disorders, such as oppositional defiant disorder, major depression, generalized anxiety, and post-traumatic stress disorders, and is frequently present in youth with other psychiatric diagnoses such as ADHD and pervasive developmental disorders. Therefore, irritability has low specificity for BD – analogous to fever or pain in physical illnesses that suggests that "something is wrong" (Kowatch et al, 2005). On the other hand, absence of episodic irritability may decrease the likelihood of a BD diagnosis. It has been argued that the severity and duration of irritability (the "super-angry/grouchy/cranky-type" of irritability), but not the "mad/cranky" or oppositional defiant-type irritability (Mick et al, 2005) are important clinical factors when assessing subjects with BD.

Chronic irritability was associated with ADHD, oppositional defiant disorder, and major depressive disorder rather than BD. Episodic irritability was associated with increased risk to develop BD and anxiety (Leibenluft et al, 2006)

In contrast to episodic irritability, chronic presence of this symptom has been recently conceptualized as the core feature of a new diagnostic category proposed for DSM-5 (also known as disruptive mood dysregulation disorder, temper dysregulation disorder with dysphoria, and severe mood dysregulation)

(see Chapter E.3). Interested readers may wish to visit the DSM-5 website for the most recent updates and refer to the articles by Leibenluft (2011) and Axelson et al (2011a) that argue for and against introducing disruptive mood dysregulation disorder as a new diagnostic category.

Subthreshold presentations

The assessment and diagnosis of subthreshold presentations of BD in children and adolescents is controversial. The COBY study is the first report on the systematic assessment and comparison of children and adolescents with bipolar spectrum disorders (BD-I, II, and NOS) (Axelson et al, 2011b; Birmaher et al, 2009a). The results suggest that the majority of youth with BD-NOS fulfilled the mood and symptoms criteria for mania and/or hypomania, but did not meet the 4-day duration criteria for a hypomanic episode or the 7-day duration criteria for a manic/mixed episode. In parallel, the AACAP also defined BD-NOS as manic symptoms that cause impairment but are not present for long enough to meet the DSM-IV duration requirement for a manic, hypomanic or mixed episode (McClellan et al, 2007).

BD-NOS in youth is not a mild or "soft" BD phenotype with less impairment but may developmentally exist on a continuum with BD-I (Axelson et al, 2011b).

Follow-up studies (Birmaher et al, 2009a; DelBello et al, 2007) have shown that the most common presentation of BD is subsyndromal, particularly with mixed and depressive symptomatology. For example, the COBY study showed that, during 60% of the four years of follow-up, children and adolescents with BD experienced syndromal and subsyndromal mood symptoms and 40% of the mood symptoms were subsyndromal (Birmaher et al, 2009a). Furthermore, subsyndromal symptoms were accompanied by significant psychosocial difficulties and increased risk for suicidality, legal problems and substance abuse. In addition, about 50% of youth with the COBY definition of BD-NOS converted into BD-I or II, especially if they had a family history of mania or hypomania (Axelson et al, 2011b). The above findings indicate the need for early recognition and treatment of subsyndromal symptomatology (Birmaher et al, 2009a; DelBello et al, 2007).

About 50% of the youth with BD-NOS, particularly those with a family history of mania or hypomania, converted into BD-I or II during follow up (Axelson et al, 2011b).

Bipolar depression

Similar to adults, depressive episodes are reported to be the most common (in both frequency and duration) manifestation of BD in children and adolescents (Birmaher et al, 2009a). However, depression is commonly underdiagnosed. In addition to the different treatment interventions for bipolar and unipolar depression (please see treatment section below), bipolar depression is associated with increased risk for psychosocial impairment and suicide than unipolar depression (Wozniak et al, 2004). Therefore, early identification and treatment of bipolar depression is of vital importance. Moreover, depressed youth with psychosis, pharmacologically induced mania/hypomania, and family history of BD may be at high risk of developing BD (Diler, 2007).

Depression is usually the first mood episode observed in many youth with BD; however, a diagnosis of BD cannot be made before a history or presence of mania/hypomania. Careful assessment of current and past symptoms of mania/hypomania is necessary for all youth, especially in those who present with depression.

It is very important to conduct a comprehensive assessment of depressive symptoms for diagnostic clarification. A history of a major depressive episode is needed when making BD-II diagnosis (major depressive episode plus at least one hypomanic episode) but the full DSM-IV criteria for BD-II does not appear to be common in youth with BD, specifically in research and outpatient settings (Axelson et al, 2011b). The evidence indicates that the majority of youth with BD have symptoms of depression interspersed with manic symptoms but it is important to consider that DSM-IV criteria for a mixed episode require that

criteria for both a manic episode and a major depressive episode are met nearly every day during at least a 1-week period.

Preadolescence and preschool presentations

It is reported that mood lability (e.g., rapid mood fluctuations with several mood states within a brief period of time which appears internally driven without regard to environmental circumstances) and irritability/anger, are more characteristic of childhood-onset rather than adolescent-onset mania (Birmaher et al, 2009c). Adolescents with BD, relative to children with BD, show more adult-like manic symptoms (e.g., more typical and severe manic and depressive symptomatology) (Birmaher et al, 2009c).

In comparison with adolescent-onset BD, childhood-onset BD manifest itself with more subsyndromal presentations, rapid mood changes and not well defined grandiose ideation. Also, children with BD have a higher familial loading for mood disorders and a different pattern of comorbid disorders than adolescent-onset BD. In contrast, adolescent-onset BD is associated with more severe and more "classic" (e.g., adult-like) mood symptomatology (Birmaher et al, 2009c).

Given the emotional and cognitive developmental stage of preschool children (three to seven years of age), questions have been raised regarding the validity of manic symptoms such as grandiosity and elation at this age. Similarly, the AACAP guidelines suggest that clinicians should be cautious when making a diagnosis of BD in children younger than six years (McClellan et al, 2007). There are few studies suggesting that preschool children may have BD (Luby et al, 2008). In these studies, irritability was more common but grandiosity and elation were suggested as helpful in preschool children when differentiating BD from other disorders such as major depressive disorder and disruptive behavior disorder (Luby et al, 2008).

DIFFERENTIAL DIAGNOSIS

It is very important for clinicians to have a good knowledge of normative cognitive, behavioral, and emotional development and cultural norms so that they can be determine whether a certain behavior is expected or pathological during the child's present stage of development. It is often difficult to diagnose BD in youth given the variability in the clinical presentation, high comorbidity, overlap in symptom presentation with other psychiatric disorders, the effects of development on symptom expression, children's difficulties in verbalizing their symptoms, and the potential effect of medication on the child's mood (Birmaher & Axelson, 2005). Presence of past and current mania/hypomania should be a routine aspect of every child psychiatric assessment, considering the high comorbidity and symptom overlap of BD with a wide range of clinical presentations such as anxiety, pervasive developmental, eating, impulse control, disruptive behavior (including conduct disorder and oppositional defiant disorder), psychotic, substance abuse disorders, ADHD, and physical and sexual abuse.

Clinicians should carefully observe whether the symptoms of the comorbid disorder disappear or persist while children with BD are euthymic and whether symptoms associated with BD worsen during the mood episode.

Clinicians must be cautious about attributing symptoms to mania or hypomania unless they show a clear temporal association with the abnormally elevated, expansive and/or irritable mood. For example, substance use can complicate the clinical picture of BD, but the essential feature of a drug-induced mood disorder is the onset of symptoms in the context of drug use, intoxication, or withdrawal. Both substance use and BD can also co-exist (e.g., dual diagnosis); however, mood symptoms that start before or persist longer than a month after cessation of drug use can be considered as the primary mood disorder (APA, 2000). Furthermore, chronic symptoms such as hyperactivity or distractibility should not generally be considered evidence of mania unless they clearly increase with the onset of an episode of abnormal mood. Prolonged presentations of non-

specific manic-like symptoms that do not change in overall intensity should raise the possibility of an alternative diagnosis (Birmaher & Axelson, 2005).

The presence of psychotic symptoms calls for differential diagnoses with other disorders that may present with psychosis such as schizophrenia. In that case, onset is usually insidious and patients lack the engaging quality associated with mania. The following characteristics would favor a BD diagnosis:

- Good affective contact
- Transient rather than persistent incoherence and poverty of content
- Good response to treatment with mood stabilizers, and
- Family history of BD.

However, the first episode of mania can present with severe thought disorder and hallucinations making the differential diagnosis between schizophrenia and BD difficult. In these cases the careful and continuous follow-up of the case will help to clarify the diagnosis (Diler, 2007).

Bipolar disorder versus disruptive behavior disorder

- If the behavior problems only occur while the child is in the midst of an episode of mania or depression, and the behavior problems disappear when the mood symptoms improve, the diagnoses of oppositional or conduct disorder should not be made.
- If a child has "off and on" oppositional or conduct symptoms or these symptoms only appear when the child has mood problems, the diagnosis of BD (or other disorders such as recurrent unipolar depression or substance abuse) should be considered.
- If the child had oppositional behaviors before the onset of the mood disorders, both diagnoses may be given.
- If a child has severe behavior problems that are not responding to treatment, consider the possibility of a mood disorder (bipolar and non-bipolar depressions), other psychiatric disorder (e.g., ADHD, substance abuse), and/or exposure to stressors.
- If a child has behavior problems and a family history of bipolar, consider the possibility that the child has a mood disorder (unipolar major depression or BD disorder).
- If a child has behavior problems and is having hallucinations and delusions consider the possibility of BD disorder. Also consider the possibility of schizophrenia, use of illicit drugs/alcohol, or medical/neurological conditions.

Bipolar disorder versus attention deficit hyperactive disorder (ADHD)

Suspect the presence of bipolar disorder in a child with ADHD if:

- The "ADHD" symptoms appeared later in life (e.g., at age 10 years old or older)
- The symptoms of "ADHD" appeared abruptly in an otherwise healthy child
- The ADHD symptoms were responding to stimulants and now are not
- The "ADHD" symptoms come and go and tend to occur with mood changes
- A child with ADHD:
  - Begins to have periods of exaggerated elation, grandiosity, depression, no need for sleep, inappropriate sexual behaviors
  - Has recurrent severe mood swings, temper outbursts, or rages
  - Has hallucinations and/or delusions
  - Has a strong family history of BD in his or her family, particularly if the child is not responding to appropriate ADHD treatments.

ASSESSMENT

Psychiatric Interviews

It is important to evaluate **F**requency, **I**ntensity, **N**umber, and **D**uration (FIND) when assessing mood episodes. The most widely used interviews in BD studies are conducted with two similar instruments: the Kiddie Schedule for Affective Disorders and Schizophrenia for school age children, Present and Lifetime version (K-SADS-PL) (free of charge) and the Washington University KSADS (WASH-U-KSADS). However, these interviews are lengthy, time-consuming, mainly used for research purposes, and require training of interviewers. Thus, symptom checklists based on DSM criteria are useful.

Clinician-based rating scales

Two clinician-based rating scales are currently used for the assessment of manic symptoms and their severity in youth, the Young Mania Rating Scale (YMRS; Young et al, 1978) and the K-SADS Mania Rating Scale, derived by Axelson and his colleagues from the K-SADS-P mania module (KSADS-MRS) (free of charge).

Youth, parent, and teacher rating scales

There are suggestions that parental reports are more effective in identifying mania than youth or teacher reports. The General Behavior Inventory (GBI; Youngstrom et al, 2008), the parent version of the Young Mania Rating Scale (P-YMRS) (available for free), the parent version of the Mood Disorder Questionnaire (MDQ), and more recently the Child Mania Rating Scale for Parents about their children (CMRS-P) (Pavuluri et al, 2006) have been shown to have appropriate psychometric properties and be useful for the screening of BD symptoms in youth.

The parent version of the Mood Disorder Questionnaire (Wagner et al, 2006) has the easiest reading level and most translations, but it is no longer in the public domain (its self-rating version for adolescents is available). The Parent General Behavior Inventory GBI-10 (Youngstrom et al, 2008) has the most research data, is sensitive to treatment effects, but has the most difficult reading level (may be available from the author, Eric Youngstrom). It has been suggested that the Child Mania Rating Scale for Parents (CMRS -10; Henry et al, 2008) is the most specific instrument for screening for BD in youth and has a teacher version (may be available from the author, Mani Pavuluri). Interested readers can refer to Youngstrom et al (2005a) for a study comparing instruments for mania.

Other parent-report instruments have been used to screen for BD in youth such as the Child Behavior Checklist (CBCL), but these instruments are not specific or useful for *ruling in* mania (Diler et al, 2009). On the other hand the CBCL or its subscales (e.g., sum of its Aggression, Attention, and Anxiety/Depression subscales – called CBCL-dysregulation profile, formerly called bipolar profile, see also Chapter E.3) may reflect symptom severity, comorbidity, or functional impairment among BD youth (Diler et al, 2009). Low scores in this profile (e.g., externalizing problems) may be helpful in *ruling out* mania (or any psychopathology) (Diler et al, 2007; Youngstrom et al, 2005b).

Mood time-lines and diaries

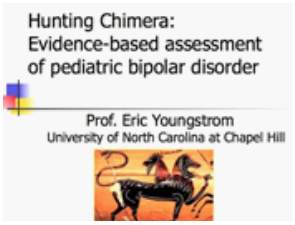
Mood time-lines or diaries and using school years, birthdays and holidays as anchors are very helpful in the assessment and monitoring of mood symptoms and episodes. These instruments can help children, parents and clinicians to visualize the course of their mood and identify events that may have triggered depression, hypomania/mania, irritability, and sleep problems, and to examine response to treatment. Many of these instruments use colors or ratings (e.g., from 0-10) to chart daily changes in mood along with concurrent stressors, illnesses and treatments. We include in Appendix E.2.1 a sample mood assessment and monitoring tool, the Mood & Energy Thermometer, which we developed at the inpatient child and adolescent bipolar services, University of Pittsburgh. Readers can also visit http://www.manicdepressive.org/images/moodchart.pdf and http://www.dbsalliance.org/pdfs/calendarforweb.pdf for other instruments for mood charting.

Mood time lines (mood monitoring) instruments should be user (child)-friendly and can be modified (according to the child's age, culture and interests) to increase compliance.

Other areas for assessment

Psychosocial functioning

It is imperative to obtain information from multiple sources such as caregivers, teachers or other significant adults in the young person's life in order to accurately assess potential change in functioning, which should be measured against what would be the expected level of functioning (e.g., school, family, peers, etc.) for a child in that culture, chronological age and intellectual capabilities.



Click on the picture to hear Dr Youngstrom's 45-minute presentation on the assessment of BD in youth at the New York University Child Study Center's grand rounds.

Level of care

Clinicians should also evaluate the appropriate intensity and restrictiveness of care (e.g., outpatient treatment versus inpatient or partial hospitalization). Decisions about level of care will depend on factors such as severity of mood symptoms, presence of suicidal or homicidal ideation (and risk for lethality), psychosis, substance dependence, agitation, child's (and parents') adherence to treatment, parental psychopathology, and family environment.

Medical conditions

The presence of medical conditions that may trigger or worsen mood symptoms should be assessed. At the present time no biological or imaging tests are clinically available for the diagnosis of BD; however, thyroid function (e.g., TSH), whole blood count, B12, folate, and iron levels can be obtained when a first mood episode of BD is identified (please see below for additional laboratory tests recommended before or during medication treatment). More detailed organic work-up may be required if a first episode psychosis is considered in the differential diagnosis (please see Chapter H.5).

Team approach

Psychiatrists, psychologists, behavioral and developmental pediatricians, social workers, school counselors and teachers, and many other professionals who are involved in treating the child should work together as a team so optimal care can be attained in the medical, educational, family, and social domains. It is very important to consider the parents, the child, and the school as a part of this team and include them in decision making.

TREATMENT

The treatment of BD has 3 stages: (1) acute, (2) continuation and (3) maintenance. The goal of the acute stage is to control or ameliorate the acute symptoms that are affecting the child's psychosocial functioning and well-being or endangering the child's life. Continuation treatment is required to consolidate the response during the acute phase and avoid new episodes or recurrences. The choice of pharmacological, psychosocial, or combined (pharmacological and psychosocial) treatment for each of these stages depends on the severity, phase of the illness, subtype of BD, chronicity, comorbid disorders, child's age, family and

patient preference and expectations, availability of skilled psychotherapists, family and environmental circumstances, and family psychopathology.

A balanced daily schedule maintained through practical lifestyle habits, such as regular sleep patterns and consistent daily routines may improve BD symptoms while irregular sleep patterns may induce mood episodes.

Psychoeducation

Psychoeducation and support start during the assessment stage and are always indicated at any stage of treatment. Family members and the patient should be educated about the causes, symptoms, course, different treatments of BD, and the risks associated with each treatment option, as opposed to no treatment at all. The patient and family should be equipped for what is likely to be a recurrent and often chronic illness with frequent fluctuations in the child's mood, and be aware of the importance of good adherence to treatment. A great deal of time is needed to discuss with these families the need for medication and accompanying psychological treatment. It is critical to help parents understand that the negativity and rapid mood swings are not a reflection of oppositionality in misbehaving children. In addition, restoration of hope and reversal of demoralization for the child and their parents, and case management (e.g., negotiation with school and parents about reasonable expectations) may be necessary (Birmaher & Axelson, 2005).

To assist with psychoeducation, dedicated associations and several other websites and books are available including: Depression and Bipolar Support Alliance (DBSA)'s Guide for BD; NIMH parent guide for BD; and against stigma.

Sleep hygiene and routine are important, especially in view of sleep deprivation leading to worsening of mood symptoms (see Table E.2.4). Ensuring a stable circadian rhythm is needed to have a positive effect on physiology and daily functioning.

Acute treatment

In this chapter, the word mood stabilizer refers to lithium and anticonvulsants such as valproate, carbamazepine, oxcarbazepine, topiramate, and lamotrigine as well as second-generation antipsychotics (SGAs) such as risperidone, aripiprazole, quetiapine, olanzapine, and ziprasidone.

When planning treatment in each phase, it is very important to take into account quality of life issues for youth with BD that would consider:

- Cultural differences and expectations
- Meaningful relationships with family, peers, mentors, coaches, and teachers
- Optimal academic performance
- Optimal occupational performance as it pertains to endeavors such as music, art, dance, athletics
- Other personally rewarding areas from which the youth derives a sense of competency, mastery, and pleasure.

Most of the current evidence about effectiveness of treatment is derived from open-label, retrospective analyses, case reports, and acute randomized controlled trials (RCTs) and are summarized in more detail in the treatment guidelines for children with BD (McClellan et al, 2007) and a meta-analysis of the existing pharmacological treatments for youth with BD (Liu et al, 2011). There are very few studies targeting prepubertal children (Geller et al, 2012), bipolar depression and the treatment of BD in the context of comorbid disorders such as anxiety and ADHD.

In order to avoid unnecessarily high dosages and increase the risk of side effects and poor adherence to treatment, unless the child is too agitated, acutely suicidal, and/or psychotic , it is recommended *to start at low dosages and increase them slowly according to response and side effects.* In general, and until further studies show otherwise, dosage of anticonvulsants and SGAs as well as the target blood level for lithium and some of the anticonvulsants are similar to those used in adults with BD. However, it is possible that children and adolescents may need lithium blood concentration close to 1 mEq/dl (Geller et al, 2012), because it seems that relative to adults, children and adolescents have lower ratios of brain-to-serum lithium concentration (Birmaher & Axelson, 2005).

Table E.2.4 Sleep hygiene. Tips from the American Sleep Association.

Maintain a regular sleep routine

- Go to bed at the same time. Wake up at the same time. Ideally, your schedule will remain the same (+/- 20 minutes) every night of the week.

Avoid naps if possible

- Naps decrease the "sleep debt" that is so necessary for easy sleep onset.
- Each of us needs a certain amount of sleep per 24-hour period. We need that amount, and we don't need more than that.
- When we take naps, it decreases the amount of sleep that we need the next night – which may cause sleep fragmentation and difficulty initiating sleep, and may lead to insomnia.

Don't stay in bed awake for more than 5-10 minutes.

- If you find your mind racing, or worrying about not being able to sleep during the middle of the night, get out of bed, and sit in a chair in the dark. Do your mind racing in the chair until you are sleepy, then return to bed. No TV or internet during these periods! That will just stimulate you more than desired.
- If this happens several times during the night, that is OK. Just maintain your regular wake time, and try to avoid naps.

Don't watch TV or read in bed.

- When you watch TV or read in bed, you associate the bed with wakefulness.
- The bed is reserved for two things – sleep and hanky panky.

Do not drink caffeine

- The effects of caffeine may last for several hours after ingestion. Caffeine can fragment sleep, and cause difficulty initiating sleep. If you drink caffeine, use it only before noon.
- Remember that soda and tea contain caffeine as well.

Avoid inappropriate substances that interfere with sleep

- Cigarettes, alcohol, and over-the-counter medications may cause fragmented sleep.

Exercise regularly

- Exercise before 2 pm every day. Exercise promotes continuous sleep.
- Avoid rigorous exercise before bedtime. Rigorous exercise circulates endorphins into the body which may cause difficulty initiating sleep.

Have a quiet, comfortable bedroom

- Set your bedroom thermostat at a comfortable temperature. Generally, a little cooler is better than a little warmer.
- Turn off the TV and other extraneous noise that may disrupt sleep. Background "white noise" like a fan is OK.
- If your pets awaken you, keep them outside the bedroom.
- Your bedroom should be dark. Turn off bright lights.

If you are a "clock watcher" at night, hide the clock.

Have a comfortable pre-bedtime routine

- A warm bath, shower
- Meditation, or quiet time

PHARMACOTHERAPY

Interested readers may visit the US clinical trials website and search for ongoing studies of BD in youth.

Acute manic and mixed episodes

Available studies (e.g., 16 open label and 9 double-blind with more than 1200 youth participants) suggest that monotherapy with lithium, valproate or carbamazepine are comparable in treating non-psychotic mania/mixed episodes (the oxcarbazepine RCT was negative), with manic symptoms response ranging from 23% to 55% (41% in open-label and 40% in double-blind studies) (Liu et al, 2011). Lithium was the first medication to be approved by the US Federal Drug Administration (FDA) for the treatment of mania in youth ages 12–17 years. A recent large RCT in manic or mixed BD-I children and adolescents reported 35.6% response rate with lithium; not different from the 24% response rate with divalproex sodium (Geller et al, 2012).

Recent studies (e.g., 11 open-label and 9 double-blind studies with more than 1500 youth) have suggested that the SGAs may be more efficacious than the traditional mood stabilizers (e.g., lithium and anticonvulsants) with responses for mania/mixed symptoms ranging from 33% to 75% (53% in open-label and 66% in double-blind studies) and appear to yield a quicker response (Liu et al, 2011). A recent RCT in manic and mixed children and adolescents with BD-I reported significantly higher response rate with risperidone (68.5%) than with lithium (35.6%) and divalproex sodium (24%) (Geller et al, 2012). However, risperidone was associated with more side effects (please see below the section on monitoring pharmacotherapy and clinical concerns). The US FDA has approved several SGAs for the acute treatment of manic/mixed episodes in in children and adolescents: risperidone for 10–17 year olds, olanzapine for 13–17 year olds, aripiprazole for 10–17 year olds, and quetiapine for 10–17 year olds.

Clinicians should be aware of available mood stabilizers in their country or state and the requirements and limitations in prescribing them.

Partial or non-responders

Monotherapy is recommended as first step intervention; however, for subjects who do not respond to monotherapy or who do not tolerate medication side effects, clinicians can try to *remove* potential *mood destabilizing* medications (e.g., antidepressants), *optimize* current treatment, *switch* to a different treatment – with one of the mood stabilizers not previously tried – or *combine* with other treatment options. While the ideal is to use the lowest possible dose of one single medication to decrease adverse side effects, most patients may require higher doses to stabilize manic, hypomanic, mixed or depressive symptoms. In addition, several studies have used short-term adjuvant medications or rescue paradigms during the acute phase of the illness because patients receiving mood stabilizer monotherapy without rescue medications had high drop-out rates due to lack of efficacy (Liu et al, 2011). For example, lorazepam and clonazepam sometimes are used briefly for the management of acute agitation or insomnia (Birmaher & Axelson, 2005), but clinicians should be aware of the possibility of behavioral disinhibition caused by these medications in some children. Despite absence of research to support its efficacy or establish the dose range, youth with BD (after trying sleep hygiene recommendations) may benefit from melatonin (starting with a low dose and not exceeding 6-9 mg/day according to the clinical experience on our adolescent inpatient unit) to help with sleep phase problems and difficulty falling asleep. For combined medication treatment, combining two mood stabilizers with different mechanisms of action (e.g., lithium and an anticonvulsant) or adding a SGA (to

If a child does not respond to treatment at any stage, factors associated with non-response need to be considered, such as:

- Misdiagnosis
- Poor adherence to treatment
- Presence of comorbid psychiatric and medical conditions, and
- Ongoing exposure to negative events (family conflict, abuse, etc.).

lithium or an anticonvulsant) may be superior to mood a stabilizer alone for the acute treatment of manic/mixed episodes, with responses ranging between 60% and 90% (Liu et al, 2011).

Acute hypomania

There are no studies in children and adolescents that specifically address the treatment of hypomania. Therefore, until research is available, for those youth whose hypomanic symptoms that significantly impair their functioning, similar treatments to those described for mania are recommended.

Acute bipolar depression

Youth with BD spend substantial amounts of time suffering from syndromal or subsyndromal depressive symptoms that significantly impair their functioning and increase their risk for suicide; however, there are few studies in youth with bipolar depression. There is one small RCT with quetiapine in youth with BD-I that reported a 71% response rate, which was not superior to placebo (DelBello et al, 2009). Two open-label studies in depressed BD youth reported response rates of 48% with lithium alone in BD-I (Patel et al, 2006) and 84% with lamotrigine (adjunct or monotherapy) in BD-I, BD-II and NOS (Chang et al, 2006). Few of the open-label studies in the treatment of mania assessed improvement in depression and response rates for depressive symptoms ranged from 35% to 60% for SGAs (aripiprazole, olanzapine, risperidone, and ziprasidone), 43% for carbamazepine, and 40% with omega-3 fatty acids (Liu et al, 2011).

Clinicians may consider starting treatment with psychosocial interventions such as cognitive behavior therapy or family focused psychotherapy, especially for mild to moderate depressions. Although response to medication in youth versus adults with bipolar depression may be different, it is important to briefly review available studies in adults. Quetiapine monotherapy and the combination of olanzapine and fluoxetine in acute treatment and lamotrigine in maintenance treatment of bipolar depression in adults are efficacious (Nivoli et al, 2011). Other options suggested for the acute treatment of adults with bipolar depression include monotherapy with lamotrigine, valproate, and the combination of an anticonvulsant or SGA with an antidepressant (a serotonin reuptake inhibitor (SSRI) or bupropion). These medications may be helpful in youth as well, but RCTs are needed to confirm these findings.

There are other interventions that can be considered. However, in addition to the efficacy of these interventions in youth with BD, the safety should be further investigated including risk for manic switch. An open-label study with omega-3 fatty acids showed minimum to modest improvement in depressive symptoms in manic youth (Wozniak et al, 2007) with good tolerance. For subjects with recurrent seasonal depression, light therapy may be considered. Transcranial magnetic stimulation (TMS) is suggested as a treatment option for unipolar depression in a few small studies in youth, but it needs to be evaluated further (Birmaher & Axelson, 2005).

Treatment of comorbid conditions

BD in youth usually presents with comorbid conditions that may worsen the prognosis of BD. In general, before treating the comorbid disorder(s), it is recommended to first stabilize the symptoms of BD especially if the child's

comorbid symptoms (e.g., ADHD, behavior problems) appear to be secondary to the mood disorder (mania, depression, or both) (Birmaher & Axelson, 2005). If the comorbid conditions cannot be attributed to BD or do not improve after the symptoms of mania/hypomania subside, treatment for both the BD and the comorbid conditions is indicated, especially if youth with BD have comorbid substance use. If available, psychosocial treatments should be tried before adding new medications. It is recommended to use the best available medications and psychosocial treatments for each specific comorbid disorder; however, treatment for each comorbid disorder should begin sequentially. Sometimes the use of medications for BD may also improve the other medical or psychiatric disorder (Birmaher & Axelson, 2005; McClellan et al, 2007). Amphetamine salts and atomoxetine are medication options for ADHD after stabilizing the mood in youth with BD.

It is very important to pay a close attention to patients' own description of what the important side effects are and what the side effects mean to them. For example, a patient may become noncompliant with lithium (without telling the doctor), because of weight gain, acne or tremor.

Monitoring pharmacotherapy and clinical concerns

Because all psychotropic medications are associated with important adverse effects, a careful risk-benefit analysis is needed (and should be discussed with the parents and youth) when initiating pharmacologic treatment; these side effects are reviewed below.

The list of prescription drugs that interact with psychotropic medications is long and should be checked prior to prescribing any new medication. There are several websites (e.g., Medscape Reference) and smart phone applications (e.g., Micromedex Drug Information by Thomson Reuters or Medscape) that provide updated drug to drug interactions to minimize dangerous complications.

A pregnancy test should be performed in all post-menarchal females at baseline and whenever pregnancy is a possibility during follow-up. Urine drug screen may be ordered in adolescents at baseline and then as necessary. Height and weight (e.g., body mass index; BMI), vital signs, and waist circumference should be recorded at each visit. Laboratory tests are not a replacement for clinical evaluation (e.g., physical exam and family history of cardiac, diabetes, and thyroid diseases) and it is important to review signs and symptoms of potential adverse events with patients and their families as well as emphasize the need to contact the prescribing physician if these symptoms (e.g., rash with lamotrigine and other anticonvulsants) occur. Table E.2.5 summarizes common side effects from mood stabilizers and gives general monitoring guidelines based on recommendations from FDA package inserts and clinical practice from our clinic and research center. We discuss below side effects of lithium, anticonvulsants and SGAs.

Click on the picture to visit the US FDA website to view updated information about the safety of psychotropic medications.

Lithium and anticonvulsant mood stabilizers

- *Lithium* has a low therapeutic index (blood levels between 0.6 and 1.2 mEq/L) and severe toxicity can cause permanent renal and neurological damage as well as death. Tolerability varies among patients and some individuals may suffer side effects at lower blood levels although signs and symptoms of toxicity usually do not appear until blood levels are above 1.5 mEq/L. Patient and parents should be informed about clinical symptoms of lithium toxicity (e.g., dizziness, clumsiness, unsteady gait, slurred speech, coarse tremors, abdominal pain, vomiting, sedation, confusion and blurred vision). If a patient has difficulty taking fluids or has excessive fluid loss (e.g., due to nausea, vomiting, diarrhea, febrile illness), lithium doses should be

Table E.2.5 Side effects of mood stabilizers and routine laboratory monitoring before and during pharmacotherapy (Birmaher & Axelson, 2005).

	Common	Uncommon	Rare	Baseline tests	Follow-up tests	Test frequency	Comments
Lithium	• Polyuria • Polydipsia • Tremor • Weight gain • Nausea Diarrhea • Hypothyroidism • Cognitive dulling • Sedation, • Leukocytosis	• New onset or exacerbation of acne or psoriasis • Bradycardia • Hair loss • ECG changes (T-wave flattening)	• Kidney, brain damage and death (due to acute toxicity) • Decreased renal function • Pseudotumor cerebri • Extrapyramidal symptoms • Movement abnormalities • Nystagmus • Seizures • Hyperparathyroidism • Sinus node dysfunction • Arrhythmias	• BUN • Creatinine • Urinalysis • TSH, Free T4 • CBC • Electrolytes • Calcium, Albumin • Weight	• Lithium level • BUN • Creatinine • Urinalysis • Calcium • Albumin • Weight	• Each[1] dose change & every 3-6 months and PRN • Every 3-6 months	24-hour urine for protein and creatinine clearance if proteinuria, marked polyuria or change in serum creatinine
Valproate	• Weight gain • Tremor • Nausea • Diarrhea • Cognitive dulling • Sedation, fatigue • Ataxia • Dizziness	• Serum transaminase elevation • Alopecia • Elevated testosterone • Polycystic ovary syndrome • Rash • Hair loss	• Hepatic failure • Thrombocytopenia • Pancreatitis • Severe dermatological reactions • Myelosuppression • Anticonvulsant hypersensitivity syndrome	• CBC with differential & platelet count • AST, ALT • Lipase • Weight • Menstrual history	• Divalproex level • Platelet Count • AST, ALT • Weight • Menstrual history	• Each[1] dose change and PRN • Every 2weeks x2, then q • every month x2, then every 3-6 months	Risk of hepatic failure is highest in first 6 months of treatment Repeat lipase if pancreatitis suspected

BMI: body max index; BUN: blood urea nitrogen; TSH: thyroid stimulating hormone; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CBC: complete blood count; HDL: high density lipoprotein; LDL: low density lipoprotein; AIMS: Abnormal Involuntary Movement Scale; PRN: as needed.
[1]Initially, regular blood tests are required to check serum level. Once a desired and stable level is achieved, the other tests are to check serum levels and other parameters (e.g., renal and thyroid function).

Table E.2.5 (Continuation)

	Common	Uncommon	Rare	Baseline tests	Follow-up tests	Test frequency	Comments
Carbamazepine	• Nausea, vomiting • Clumsiness, dizziness • Nystagmus • Sedation • Blurred vision, diplopia, photosensitivity • Cognitive dulling • Ataxia • CYP450 enzyme-induction (increased clearance of drugs metabolized by hepatic cytochrome system, including oral contraceptives)	• Hyponatremia • Rash • Confusion • Leukopenia	• Serious dermatological reactions • Agranulocytosis • Aplastic anemia • Atrioventricular block, arrhythmias • Hepatitis • Renal dysfunction • Anticonvulsant hypersensitivity syndrome	• CBC with differential & platelet count • AST, ALT • Sodium	• Carbamazepine level • CBC with differential & platelet count • AST, ALT • Sodium	• 1 & 3-4 weeks[1] after dose change and PRN • With blood levels after dose change and then every 3-4 months	Check labs if unexplained fever, sore throat, lymphadenopathy or severe fatigue
Lamotrigine	• Dizziness • Ataxia • Headache • Tremor • Blurred vision, diplopia,	• Rash • Nausea, vomiting • Ataxia • Cognitive dulling • Confusion	• Serious dermatological reactions • Anemia • Anticonvulsant hypersensitivity syndrome	• CBC with differential & platelet count • AST, ALT	• Lamotrigine level is not suggested but may guide treatment • CBC with differential & platelet count • AST, ALT	• Every 3-6 months	Clear instruction should be given about how to avoid skin rash (e.g., avoiding sun burn, not changing lotion, shampoo, or detergent) and when/ how to reach doctor when rash occurs

BMI: body max index; BUN: blood urea nitrogen; TSH: thyroid stimulating hormone; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CBC: complete blood count; HDL: high density lipoprotein; LDL: low density lipoprotein; AIMS: Abnormal Involuntary Movement Scale; PRN: as needed.
[1]Initially, regular blood tests are required to check serum level. Once a desired and stable level is achieved, the other tests are to check serum levels and other parameters (e.g., renal and thyroid function).

Table E.2.5 (continuation)

	Common	Uncommon	Rare	Baseline tests	Follow-up tests	Test frequency	Comments
Antipsychotics	• Weight gain • Postural hypotension • Extrapyramidal symptoms • Dizziness • Sedation	• Hyperglycemia, hypercholesterolemia, increased triglycerides, diabetes • Hyperprolactinemia • Rash • Photosensitivity • Nausea, diarrhea, dyspepsia, constipation • Elevated serum transaminases • Urinary difficulties • Sexual dysfunction • Cognitive dulling	• Tardive dyskinesia • Neuroleptic malignant syndrome • Seizure • Hepatic failure	• Glucose • Triglycerides, total cholesterol,HDL, LDL • AIMS • Height, weight, BMI, waist circumference • EKG (for ziprasidone)	• Glucose • Triglycerides, total cholesterol,HDL, LDL • AIMS • Other tests as necessary (e.g., EKG) • Height, weight, BMI, waist circumference	• Every 3-6 months and PRN	

BMI: body max index; BUN: blood urea nitrogen; TSH: thyroid stimulating hormone; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CBC: complete blood count; HDL: high density lipoprotein; LDL: low density lipoprotein; AIMS: Abnormal Involuntary Movement Scale; PRN: as needed.

Click on the picture to view Stephen Fry-The Secret Life of The Manic Depressive, a 60 minute documentary.

reduced or temporarily held until regular fluid intake is resumed. If other symptoms of lithium toxicity occur in addition to gastrointestinal distress, referral for immediate evaluation is necessary (Birmaher & Axelson, 2005). Blood levels should be obtained as early as 4-5 days after each dose increase, and immediately if clinical symptoms of toxicity occur. In addition, other baseline laboratory tests such as those for thyroid and kidney functioning are necessary at baseline and during follow up (see Table E.2.5). Patients should be encouraged to maintain adequate hydration during vigorous exercise or on hot days and to avoid major changes in salt, caffeine or fluid intake. Also, they must notify physicians and pharmacists that they are taking lithium and not take substances that interact with lithium. Common medications, including non-prescription ones, and substances that can elevate lithium levels include most non-steroidal anti-inflammatory drugs (acetaminophen does not), alcohol and marijuana. Caffeine tends to lower lithium levels (Birmaher & Axelson, 2005).

The US FDA issued a warning in 2008 about the risk for suicidality associated with use of *anticonvulsant medications* (Arana et al, 2010). Although some studies do not report an increased suicide risk with anticonvulsants, patients (and families) should be informed about this risk and closely monitored. Anticonvulsant mood stabilizers have neurological, cognitive, and gastrointestinal side effects (see Table E.2.5) that can usually be managed by dose adjustments. Dose increases should be gradual and periodic blood tests are often suggested (see Table E.2.5) in order to monitor the blood level for many of them and for rare but serious side effects (e.g., hepatic failure, pancreatitis, thrombocytopenia). It is very important that patients and family members are aware of the initial symptoms of these side effects and how to contact the doctor if they occur. On the other hand, it is controversial as to whether this reduces the risk of serious adverse events.

- *Valproate* has been associated with polycystic ovarian syndrome and baseline menstrual history and a gynecological consultation of any female who develops significant changes in her menstrual cycle and/or hirsutism while on this medication is required.
- *Carbamazepine* induces the metabolism of other medications (e.g., oral contraceptives) as well as its own through cytochrome P450 1A2 and 3A4 isoenzymes and may decrease the blood level and reduce its own and other medications' effectiveness.
- *Oxcarbazepine*, 10-keto analogue of carbamazepine, may not induce hepatic enzymes and does not require blood monitoring, but may cause similar side effects to carbamazepine such as dizziness, nausea, somnolence, diplopia, fatigue, and rash.
- *Lamotrigine* is usually well tolerated with relatively lower risk for weight gain and sedation. However, particularly when the dose is increased rapidly, it may cause serious dermatological reactions such as Stevens-Johnson syndrome or toxic epidermal necrolysis. Unless a new rash is clearly attributable to another cause (e.g., contact dermatitis) other than lamotrigine, treatment should be suspended immediately. Also, lamotrigine should be reinitiated from the starting dose of 12.5 mg/day or 25 mg/day if it is held or stopped for five days or more. The rate of serious dermatological reactions may be

reduced by current dosing recommendations (prescribing small doses with a gradual escalation, e.g., 25 mg/day in ≥ 12 year olds with increases of 25 mg every two weeks given twice a day until 100 mg/day is reached). The dose of lamotrigine should be halved if combined with valproate. It may take six to eight weeks to increase the dose of lamotrigine to a therapeutic level because of this slow titration schedule making it difficult to use in acute treatment settings (e.g., inpatient care).

- Weight loss has been reported with *topiramate* when combined with an SGA (e.g., to counterbalance the weight gain side effect of SGA mood stabilizers); however, similar to the concerns with valproate, topiramate may cause significant cognitive difficulties. Please see below for adjunct topiramate use target weight gain or metabolic side effects.

The common side effects of SGAs are listed in Table E.2.5, but clinical experience suggests that there may be differences among them, such as on extrapyramidal symptoms, prolactinemia, sedation, orthostatic hypotension/dizziness, drowsiness/tiredness, and weight gain. However, these side effects can be caused to a greater or lesser extent by any of the SGAs. The metabolic effects (e.g., increased weight, glucose and lipids) of SGAs are of substantial concern, especially when used in youth over extended periods of time. Interested readers can refer to the Correll et al's reviews that suggested greater weight gain in youth relative to adults and in youth on an SGA and mood stabilizer combination (Correll et al, 2010). It is recommended to (1) measure the child's body mass index and waist circumference (e.g., at baseline and at weeks 4, 8, and 12) and (2) fasting plasma glucose and lipids (e.g., at baseline, 3 months and then annually and whenever clinical symptoms indicate) while taking these medications (see Table E.2.6). Practical monitoring tables are available at this website.

If a patient exhibits significant weight gain, a more thorough investigation of metabolic status and a re-evaluation of the risk-benefit ratio of continuing with the current SGA are indicated. As mentioned above, consultation with a pediatrician and a nutritionist and referral to a weight management clinic

Table E.2 6 Parameters in monitoring second-generation antipsychotic use.

Parameter	At the beginning				Quarterly	Annually	Every 5 Years
	Baseline	4 weeks	8 weeks	12 weeks			
Personal history	✓						
Family history	✓						
Weight (BMI)	✓	✓	✓	✓	✓		
Waist circumference	✓				✓		
Blood pressure	✓			✓		✓	
Fasting blood glucose	✓			✓		✓	
Fasting lipid profile	✓			✓			✓

is necessary before considering adjunct medications to reduce weight gain or risk for metabolic syndrome; however, available data suggest that adjunct topiramate and metformin may be helpful in some adolescents (Morrison et al, 2002; Praharaj et al, 2011). In addition, although infrequently, SGAs can cause extrapyramidal symptoms, tardive dyskinesia and neuroleptic malignant syndrome and the youth needs to be evaluated at baseline and routinely for abnormal involuntary movements. Baseline EKG is not a routine test but may be necessary to rule out cardiac problems including QTc prolongation if there is history of cardiac problems in the child or family or if ziprasidone or concomitant stimulant use is considered.

- *Antidepressants.* Selective serotonin reuptake inhibitors (SSRIs) may be helpful for the treatment of bipolar depression, but some may experience a manic switch. SSRIs or other antidepressants can trigger mania, hypomania, mixed episodes or rapid cycling, particularly when used without a concomitant mood stabilizer. Families and youth should be informed about risks versus benefits of using antidepressants (including increased risk for suicide with antidepressants). Additionally, close attention should be paid to a possible increase or onset of agitation and serotonin syndrome (especially when combined with lithium). A safety plan, which would include how to manage these risks, should be discussed with the youth and the family and, if indicated, the SSRI or other antidepressant should be started in small doses, after stabilization of manic or hypomanic symptoms with mood stabilizers (Birmaher & Axelson, 2005).

PSYCHOSOCIAL TREATMENTS

Supportive psychotherapy is necessary for all youth with BD and their families. Specific psychosocial treatments have also been developed to help with psychoeducation, manage acute manic and depressive symptoms, improve coping skills and adherence to treatment, and manage comorbid conditions. In addition, this may help to prevent recurrences (see section on continuation and maintenance treatment below). Parents should be engaged in their child's therapy and, if necessary, referred for treatment themselves (Birmaher and Axelson, 2005). Psychosocial treatments, which have been found efficacious in the management of comorbid conditions such as oppositional behaviors, substance abuse, and anxiety disorder, are indicated before initiating pharmacotherapy for these comorbid conditions.

Thus far, there are five lines of overlapping psychosocial therapies for BD youth and their families, designed to fit specific age groups and methods of intervention:

- *Child and Family Focused Cognitive Behavior Therapy (CFF-CBT)* was specifically designed for 8-18 year olds with BD (West et al, 2007). In addition to focusing on the identified child, CFF-CBT includes intensive work with parents to support them in developing an effective parenting style and to meet their own therapeutic needs. It integrates the principles of reward-based CBT with interpersonal psychotherapy, with an emphasis on empathic validation. CFF-CBT consists of 12, 60-minute sessions that are

delivered weekly over 3 months. The intervention is designed to be employed across multiple domains – individual, family, peers and school – to address the impact of BD on the child's psychosocial context. The key components of CFF-CBT are conceptualized by the acronym RAINBOW:

- **R**outine
- **A**ffect regulation
- **I** can do it
- **N**o negative thoughts and live in the now
- **B**e a good friend/balanced lifestyle for parent
- **O**h–how can we solve this problem, and
- **W**ays to get support.

- Fristad (2006) has developed *Multi-family Psychoeducation Groups (MFPG) and Individual Family Psychoeducation (IFP)* as adjunctive treatments for bipolar and depressive spectrum youth. This method has a heavy emphasis on psychoeducation around the role of medications and coping strategies. The goals are to increase knowledge and understanding of BD and its treatment, improve management of its symptoms and associated conditions, improve communication and problem-solving skills, and increase the child and family's sense of support in dealing with BD. The current IFP treatment protocol consists of 24, 50-minute individual sessions, 20 of which are manual-driven and four are to be used for crisis management or additional practice (Fristad, 2006).

- Miklowitz et al (2011) developed a manualized version of *Family Focused Therapy (FFT) specifically for adolescents with BD (FFT-A)* that has the primary goal of reducing symptoms through increased awareness of how to cope with the disorder, decreasing levels of familial expressed emotion, and improving family problem-solving and communication skills. FFT-A reduces the symptoms of BD through three treatment components: psychoeducation, communication enhancement training, and problem-solving skills training. In a 2-year randomized control trial, compared to an enhanced treatment group, adolescents who received FFT-A had shorter times to recovery from depression, spent less time in depressive episodes, and reported lower depression scores over the study period (Miklowitz et al., 2011).

- Goldstein et al (2007) adapted *Dialectical Behavior Therapy (DBT)* for the treatment of adolescents. DBT is a psychotherapy initially designed for adults with borderline personality disorder focusing on mindfulness, distress tolerance, emotion regulation, and interpersonal effectiveness. The adapted intervention consists of six months of weekly 60-minute psychotherapy sessions followed by another six months of bimonthly sessions. A one-year open study in youth with BD suggests decreased suicidality, non-suicidal self-injury, emotional dysregulation, and depression symptoms after DBT.

- Hlastala et al (2010) adapted *Interpersonal and Social Rhythm Therapy (IPSRT)* for adolescents with BD. They suggested that psychosocial stressors precipitate or exacerbate bipolar episodes through their ability to disrupt social and sleep routines. The emphasis of IPSRT is on addressing interpersonal functioning deficits and managing affective symptoms to reduce their negative influence

on psychosocial functioning. A pilot study consisted of 16 to 18 sessions over 20 weeks and reported significant improvements in manic, depressive, and general psychiatric symptoms.

Continuation and maintenance treatments

In order to prevent relapses and recurrences, unless there are side effects, all medications that helped during the acute phase need to be continued for at least 6-12 months. Severe and recurrent episodes may require longer term treatment. Lithium, lamotrigine (especially for depression), SGAs and, to a lesser extent, valproate are efficacious compared to placebo for the prevention of new episodes in adults with BD. Studies in youth with BD suggest that lithium and divalproex are similarly effective.

The optimal duration of psychosocial treatment for pediatric BD has not been established; however, continuing psychosocial interventions for subthreshold symptoms may be helpful (Miklowitz et al, 2011). It is reasonable to provide ongoing psychosocial support, crisis management and therapy booster sessions as appropriate (Birmaher & Axelson, 2005).

CULTURAL PERSPECTIVES

Many professionals do not have access to *non-English scientific literature* and we largely don't know how BD in youth is diagnosed and treated around the world (Diler, 2007). Historically, several factors have made the accurate diagnosis of bipolar disorder in childhood difficult, including lack of awareness, diagnostic confusion, clinical bias against the diagnosis of mania in children, a low base rate of the disorder, symptom overlap between BD and other more prevalent childhood-onset psychiatric disorders, developmental constraints, and variability in clinical presentation. *Stigma* is still a big problem for mental disorders and BD is not an exception. Many clinicians around the world still remain skeptical about persistent non-episodic manic symptoms, ultra-rapid mood cycling, and BD diagnosis in preschool children (Diler, 2007). However, a recent meta-analysis of international epidemiological studies suggest that rates of BD in youth are similar in US and non-US studies (Van Meter et al, 2011).

In 1959, Shingawa described mania in youth in Japan as "Tendencies of hypomania, rash and frivolous words and behavior, appearance of problem behavior, and change from introversion to extroversion during periods of remission, lead on to ultimate transition into a positive personality exhibiting activeness, cheerfulness, and extroversion as a new stable personality upon cessation of the biphasic fluctuations."

Only a few countries around the world have *formal training* in child psychiatry and these countries, including the US, have a shortage of child psychiatrists (e.g., there are around 150 doctors trained in child psychology and psychiatry in China and 100 in Japan as of 2007). In addition, other mental health professionals such social workers, nurses, and case workers are lacking in many countries (Diler, 2007).

The use of different *classification systems* may have clinical implications also. Clinicians that prefer using the ICD tend to give one diagnosis whereas multiple comorbid diagnosis, especially in youth with BD, is almost the rule when using the DSM. Despite few exceptions (e.g., the Chinese Classification of Psychiatric Disorders), most clinicians and researchers around the world use the DSM not the ICD classification system when making BD diagnosis in children, but we still don't know if the expression of some manic symptoms is different or if some symptoms are presented more or less often in some cultures (Diler, 2007).

There are case reports or studies of BD in youth around the world dating back to the 1900s. Case series of adolescent onset BD appeared in the local psychiatric literature more than 100 years ago in China. Also, in the 1950s, several case reports

of children and adolescents with BD appeared in the Japanese literature, including a 10-year old child who received ECT for depression and mania (Diler, 2007). However, in many countries, research in BD followed the influx of this diagnosis in the US. These studies were initially case reports, but publications now include epidemiologic surveys (Van Meter et al., 2011) (see also Aditya Sharma's map), high-risk offspring studies, and biological (e.g., genetic, neuroimaging) studies that report findings similar to those in the US (Diler, 2007). However, in contrast to US studies, researchers in India were able to study young people with BD who had never been on medication and they usually have relatively lower rates of ADHD comorbidity. Similar to the US, the course of BD is characterised by high rates of recovery followed by relapses (Diler, 2007).

Some countries report *non-traditional treatment approaches* for youth with BD. For example, the first step in the treatment of youth with mood disorder (or BD) in China is normalizing the child's social environment, regulating the balance between active exercise/playing and mental stimulation (e.g., reducing the overstimulation from TV, movies, and video games), providing freshly prepared food (limiting the intake of sugar, dairy, cymene salicylic food and food preservatives) and supplements of zinc and iron. Some clinics in China may use psychiatric medications while others may administer acupuncture, plaster therapy, and herbals. The studies on juvenile BD from India are mostly from the National Institute of Mental Health and Neurosciences in Bangalore. The practice is to always admit children with their caregivers who stay with the children during the entire period of hospitalization. Research and data from around the world would definitely progress or even challenge our understanding of pediatric BD and help us integrate better cultural/regional aspects of this condition (Diler, 2007).

CONCLUSION

Despite the controversies, it is clear that, taking into account the developmental stage of the child, it is possible to diagnose BD in children and adolescents. However, it is true that the diagnosis of this illness is cumbersome, especially in children. Pediatric BD is associated with severe psychosocial consequences for children and the adolescents, stressing the need for prompt identification and treatment.

BD in youth is not limited to a few countries but a global problem. We encourage clinicians around world to share their experiences through case reports or clinical studies that will help to incorporate cultural aspects of the clinical presentation of this debilitating condition. Compared to 15-20 years ago, we now know more about effective methods to screen and diagnose this condition and have more research data to guide pharmacologic as well as psychosocial interventions; however, most of the treatment studies focus on the acute treatment of manic/mixed presentations and more studies are needed of the acute treatment of bipolar depression and comorbid conditions such as ADHD and anxiety disorders. We also need to learn more about the treatment of subsyndromal presentations and prevention of recurrences. High risk studies are important to identify early presentations that can guide prevention efforts. Preliminary studies that have investigated disease- and treatment-specific bio-markers are promising but future longitudinal biological studies with larger samples are needed to better understand the core pathophysiological processes underlying BD in youth.

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Appendix E.2.1

Name:

MOOD and ENERGY THERMOMETER

Please circle one or more of the below numbers FROM EACH COLUMN that reflects your mood & energy levels eflecting your day. You can circle more than one number if your mood/energy changes during the day.

ELEVATED / UP

+10 SUPER ELEVATED
Have constant excitement and feel super happy, and have no control over self & cannot be calmed down at all & cannot function at all & someone needs to be present to monitor safety.

+9 EXTREMELY ELEVATED
Have extreme excitement and feel extremely happy, non-stop giggling & laughing, and cannot control self & cannot be calmed down & function poorly

+8 SEVERELY ELEVATED-almost all day

+7 SEVERELY ELEVATED- less than 50% of the day
Feel very happy & giggling & laughing, and can control self only briefly & very difficult to calm down & don't function well.

+6 MODERATELY ELEVATED-almost all day

+5 MODERATELY ELEVATED- less than 50% of the day
Feel cheerful/optimistic much more than usual/baseline (out of proportion) & some difficulty to control self & some difficulty to calm down & don't function as good as before.

+4 MILDLY ELEVATED-almost all day

+3 MILDLY ELEVATED-less than 50% of the day
Feel cheerful and optimistic more than usual/baseline & others may notice it, but can calm down & function ok.

+2 SLIGHTLY ELEVATED-almost all day long

+1 SLIGHTLY ELEVATED- less than 50% of the day
Feel a little bit more cheerful and optimistic, but others don't notice & function ok

+10 SUPER ENERGETIC
Have constant motor excitement, non-stop moving around, and cannot control self & cannot slow down at all & cannot function at all & someone needs to be present to monitor safety.

+9 EXTREMELY ENERGETIC
Have motor excitement, non-stop moving around, and cannot control self & cannot slow down & function poorly.

+8 SEVERELY ENERGETIC -almost all day

+7 SEVERELY ENERGETIC- less than 50% of the day
Have excessive energy & constantly moving and pacing about, and can control energy only briefly & very difficult to slow down & don't function well.

+6 MODERATELY ENERGETIC -almost all day

+5 MODERATELY ENERGETIC-less than 50% of the day
Feel energetic and hyper much more than usual/baseline (out of proportion) & restless/pace & some difficulty to control energy & some difficulty to slow down & don't function as good as before.

+4 MILDLY ENERGETIC-almost all day

+3 MILDLY ENERGETIC-less than 50% of the day
Feel energetic and hyper more than usual/baseline & others may notice it, but can easily slow down & function ok.

+2 SLIGHTLY MORE ENERGY-almost all day long

+1 SLIGHTLY MORE ENERGY-less than 50% of the day
Feel a little bit more energetic than usual, but others don't notice a change & function ok.

OK MOOD | **OK ENERGY**

DEPRESSED / DOWN

-1 SLIGHTLY DOWN- less than 50% of the day
Feel a little depressed and cheerless, but others don't notice a change & function ok

-2 SLIGHTLY DOWN-almost all day

-3 MILDLY DOWN - less than 50% of the day
Feel depressed and cheerless more than usual & enjoying things and having fun is somewhat difficult & others may notice a change, but can brighten up & function ok.

-4 MILDLY DOWN -almost all day

-5 MODERATELY DOWN - less than 50% of the day
Feel depressed and cheerless (out of proportion) much more than usual & enjoying things and having fun is more difficult & some difficulty to brighten up & don't function as good as before.

-6 MODERATELY DOWN -almost all day

-7 SEVERELY DOWN- less than 50% of the day
Feel very depressed & cheerless & gloomy, and don't enjoy things and don't feel like having fun & very difficult to brighten up & don't function well.

-8 SEVERELY DOWN -almost all day

-9 EXTREMELY DOWN (life is not worth living)
Have extreme depression and feel very miserable, have psychic pain ("I cannot stand it"), and cannot control self & cannot be down & function poorly.

-10 AT THE LOWEST POINT
Have constant painful sadness and feel very numb & empty & don't want to live & cannot function at all & someone needs to be present to monitor safety.

-1 SLIGHTLY TIRED- less than 50% of the day
Feel a little bit tired, but others don't notice a change & function ok.

-2 SLIGHTLY TIRED-almost all day

-3 MILDLY TIRED-less than 50% of the day
Feel more tired and less active than usual/baseline & others may notice it, but can be active during the day & function ok.

-4 MILDLY TIRED-almost all day

-5 MODERATELY TIRED-less than 50% of the day
Feel very tired & slowed down than usual/baseline (out of proportion) & have considerably less energy to do things & less active & spend more time than usual to rest & don't function as good as before.

-6 MODERATELY TIRED-almost all day

-7 SEVERELY TIRED- less than 50% of the day
Have excessive tiredness & very difficult to move around & spend very long time to rest & physical activity is limited to few & don't function well.

-8 SEVERELY TIRED-almost all day

-9 EXTREMELY TIRED
Feel like drained and worn out & almost no physical activity and cannot move around & function poorly.

-10 NO ENERGY AT ALL
Have constant motor retardation, and cannot move arms or legs & cannot function at all & someone needs to be present to monitor safety.

DAILY SCHEDULE…

TODAY.. What time did you

a. wake up? _____

b. have breakfast? _____

c. have dinner? _____

Diler RS. Mood and Energy Thermometer. Child and Adolescent Bipolar Services (CABS)-2009 Western Psychiatric Institute and Clinic, Pittsburgh, PA.