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Phenomenology, longitudinal course and outcome of children and adolescents with bipolar spectrum disorders

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1. Introduction

It is now well established that bipolar disorder (BP) occurs in children and adolescents ^{1, 2}. However, aspects of the phenomenology and clinical course of pediatric bipolar are controversial.

The goal of this chapter is to review the clinical characteristics, differential diagnosis, course, and prognosis of pediatric BP.

2. Clinical Characteristics

2.1. DSM-IV criteria

It is clear from the work of several groups that some children and adolescents meet the full DSM-IV criteria for BP, despite the fact that the criteria were not specifically adapted for use in the pediatric population ^{1, 3}. When examining the DSM-IV criteria for a Manic (table 1) or Hypomanic (table 2) episode, it is obvious that normal children can exhibit many of these features to some degree, especially in certain situations or environments. Therefore it is of utmost importance to evaluate whether the mood and symptoms are abnormal or clearly different from child's usual mood and behavior the given the context and the child's level of development.

The distinction between a Manic and Hypomanic Episode can be difficult, but also must be taken in a developmental context. Beyond the differences in minimum duration, Manic Episodes require marked impairment, which should be measured against what would be the expected level of functioning for a child given his/her chronological age and intellectual capabilities, in the psychosocial domains that are relevant to youth (e.g. school, family, peers,

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etc.). A Hypomanic Episode does not require impairment, although there must be an unequivocal change from usual functioning and the mood and functional changes must be observable by others. Given that lack of insight can be associated with mania or hypomania, it is imperative to obtain information from caregivers or other significant adults in the child's or adolescent's life in order to accurately assess symptoms and potential change in functioning.

2.2. Mood symptomatology

Kowatch et al., (2005) ¹ conducted a literature review and meta-analysis of seven reports describing the phenomenology of pediatric BPD. The weighted average rates of irritable mood (81%) and euphoria/elated mood (70%) found in the studies were not statistically different. However, there was statistically significant heterogeneity in the rates of irritability and euphoria/elated mood among the individual studies. For instance the rate of euphoria/elation ranged from 14% to 89%. Grandiosity was present in an average of 78% of subjects. Increased energy was on average the most common presenting symptom of mania, occurring in an average of 89% of cases across the samples. Distractibility and pressured speech were nearly equally common. Racing thoughts, decreased need for sleep, and poor judgment were all displayed by around 70% of youths with mania. Hypersexuality was significantly less common than any other symptom or associated feature of mania, and it manifested in fewer than half of all cases in all samples with relevant data. Flight of ideas was the second rarest symptoms, appearing in an average 56% of cases (table 3). These patterns of symptom presentation also appear to be consistent with recent analyses of a large group of children and adolescents with bipolar spectrum disorders ³ and a report on the phenomenology of cases with early onset BD in Europe ⁴.

Though there is less published research on the phenomenology of depression in BP youth, depressive symptoms appear to be quite common. BP youth are frequently described as having mixed states of manic and depressive symptoms or very rapid cycling between mania and depression ⁵. Rates of mixed episodes vary among different studies of bipolar youth. Some groups have reported chronic mixed state lasting years in duration and rapid cycling between mania and depression as frequently as several times per day ⁶⁻¹⁰. The issue is complicated by the fact that there are no clear boundaries that delineate a mixed state from an actual switch in episode polarity, or from mood lability and/or transient dysphoria occurring in the midst mania. It is not clear whether the reports of multiple mood cycles in a day represent periods where the child switches from meeting the full criteria of the manic syndrome to a period where they are completely depressed or whether they are manifestations of mood lability within the manic state. However, the evidence does indicate that the majority of BP youth have symptoms of depression interspersed in some manner with manic symptoms ¹¹.

Bipolar children and adolescents can have clear periods of depression that meet the full criteria for a Major Depressive Episode (MDE); over 50% of BP youth had a prior history of a MDE in a recent report ³. A major depressive episode may precede the onset of manic symptomatology, so that some children and adolescents who appear to have unipolar depression may actually have BP with depression as the initial presentation.

Psychotic symptoms are frequently present in youth with bipolar disorder. In the Kowatch meta-analysis, hallucinations and/or delusions were present in an average for 42% of BP youth; however there was substantial heterogeneity in the rates of psychosis across the different studies ¹. The presence of hallucinations or delusions in a youth should trigger careful evaluation for mood disorder, for even though pediatric BD uncommon, it has a significantly higher prevalence than early-onset schizophrenia or other potential causes of psychotic features in children.

2.3. Controversies regarding the diagnosis of pediatric BP

The diagnosis of children with BP disorder may be difficult because pediatric bipolar disorder usually manifests with rapid mood changes and therefore many children do not have the currently required DSM-IV duration of symptoms to fulfill diagnosis for bipolar I disorder or bipolar II disorder. According to McClellan et al. (2007) ⁵, the most common presentation among youth with bipolar disorder in community settings is characterized by “outbursts of mood lability, irritability, reckless behavior, and aggression”. Shifts in mood state are short-lived ¹² and irritability, rather than euphoria, tends to be the predominant and most impairing mood state ⁷. Furthermore, developmental issues influencing the clinical pictures of bipolar disorder in youths, the difficulties children and adolescents have in verbalizing their emotions, and the high rates of comorbid disorders with symptoms that overlap with bipolar disorder account for the complexity and current controversies in diagnosing children and adolescents with bipolar disorder.

One factor that may contribute to the difficulty of diagnosing BP in youth is that the most common symptoms of pediatric mania from the meta-analysis by Kowatch et al., (2005) ¹ also happen to be frequently present in other pediatric psychiatric disorders. A recent study comparing the phenomenology of bipolar disorder and ADHD found that there were no significant differences between the BP vs. the ADHD subjects in the rate of irritability (98% BP vs. 72% ADHD), accelerated speech (97% vs. 82%), distractibility (94% vs. 96%) or unusual energy (100% vs. 95%) ¹³. The lack of specificity makes it problematic to diagnose mania by simply counting the presence or absence of symptoms. Symptoms expressions concerning inflated self-esteem and increased goal-directed activity are best judged in the context of the child’s history because behaviors in isolation may be misleading and may be accounted for by the child’s cognitive, biological, or social development.

2.4. DSM vs. cardinal symptoms vs. irritability

The overlap of manic symptoms with features of other psychiatric illnesses emphasizes the diagnostic importance of symptoms that tend to be more specific to mania. Some authors have advocated that two of these mania-specific symptoms, elated/elevated mood and grandiosity, are core features of the manic syndrome so that they should be considered cardinal symptoms ^{13–15}. These two symptoms are present in most manic youth, though there was considerable heterogeneity among studies in the rates of euphoria/elation, and one of the largest studies in the analysis required the presence of either elevated mood or grandiosity as an inclusion criterion for the BP subjects. However a subsequently published large study of BP-I youth that did not require either of these symptoms, also had high rates of elated/elevated mood (86%) and grandiosity (57%) ³. Long-term longitudinal studies of youth meeting the DSM-IV criteria for mania with or without cardinal symptoms have not been completed.

Irritable mood may be a frequent presentation of manic mood disturbance, and irritability is generally accepted as one of the most impairing features of pediatric mania. Irritability can be a diagnostic feature of depression, generalized anxiety disorder, ODD, post-traumatic stress disorder, or intermittent explosive disorder, and it is a clinical feature frequently associated with conduct disorder, ADHD, Asperger’s disorder, autism, and a variety of other conditions. Irritability provides a sensitive marker for pediatric BP, but it is not specific to any particular condition ¹.

Some reports have prompted controversy by stating that chronic presentations of irritability alone, particularly when the irritability is severe and accompanied by aggression and volatility, is the primary mood disturbance in bipolar youth and that elevated or expansive mood is uncommon ^{6–8}. However the high prevalence of elated/expansive mood in most cross-sectional pediatric BP samples stands in contrast to these reports. Prospective evaluations of

the phenomenology of new manic episodes in youth have not been published, so it is difficult to assess how frequently pediatric mania presents with only irritable mood.

Children with disruptive behavior disorders (DBDs) or ADHD may also have irritability, mood lability, and episodes of anger, defined as “Severe Mood Dysregulation” (SMD) ¹⁶. These children differ from youth with BP spectrum disorder in course, response to lithium, family history, and neuroimaging ¹⁵.

2.5. Subthreshold presentations

Some children and adolescents present in clinical and research settings with what appears to be significant manic symptomatology, but they do not meet the DSM-IV criteria for BP-I or BP-II disorders. Reasons for this include: (1) the manic symptoms are not present for sufficient time to meet the DSM-IV duration criteria for a Manic, Hypomanic or Mixed Episode; (2) the mood disturbances and symptoms do not occur in distinct episodes; (3) the potential manic symptoms are not clearly temporally associated or do not intensify with the abnormal mood; or (4) it cannot be reliably determined whether the abnormal mood and symptoms are attributable to BP or better accounted for by another psychiatric diagnosis. The diagnosis and management of these children and adolescents is controversial, though many present for mental health treatment with significant impairment and are frequently assigned a diagnosis of Bipolar Disorder Not Otherwise Specified (BP-NOS). Empirical research in subthreshold presentations of bipolarity in youth is in its early stages.

A recent multicenter study examined children and adolescents who presented with a history of clinically significant subthreshold manic symptoms. Specifically, BP-NOS patients had (a) elated mood plus two “B” mania symptoms, or irritable mood plus three “B” symptoms; (b) change in level of function associated with mood symptoms; (c) at least four hours of symptoms within 24 hours; and (d) at least four cumulative lifetime days meeting criteria. Though the subjects could have been below the DSM-IV threshold for either the number of manic symptoms or the duration of episode, the majority of these youth fulfilled the full mood and symptom 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 ³.

These cases of BP-NOS uniformly presented with histories of significant impairment and nearly all had some form of psychiatric treatment prior to assessment. There were no significant differences among the BP-I and BP-NOS groups in age of onset, duration of illness, lifetime rate of comorbid diagnoses, suicidal ideation and major depression, family history, and the types of manic symptoms that were present during the most serious lifetime episode. Compared with youth with BP-NOS, subjects with BP-I had more severe manic symptoms, greater overall functional impairment, and higher rates of hospitalization, psychosis, and suicide attempts ³. Elevated mood was present in 82% of subjects with BP-NOS and 92% of subjects with BP-I ³. A significant proportion (36%) of these youth with BP-NOS has converted to BP-II or BP-I diagnoses over an average four year follow-up period.

Bipolar disorder is more likely to present with hypomania or subthreshold manic symptoms in community settings. A large community study of adolescents found that the lifetime prevalence of bipolar disorder (primarily bipolar II disorder and cyclothymia) was approximately 1%. An additional 5.7% of the sample reported what would be categorized in the DSM-IV as BP-NOS ¹⁷. Lifetime prevalence for subsyndromal BD was approximately 5%. Less than 1% of adolescents with major depressive disorder (MDD) switched to BD by age 24. Adolescents with BD had an elevated incidence of BD from 19 to 23 years, while adolescents with subsyndromal BD exhibited elevated rates of MDD and anxiety disorders in young adulthood ¹⁸.

The diagnosis of BP-NOS was addressed in the recent American Academy of Child and Adolescent Psychiatry (AACAP) practice parameter guidelines⁵. These guidelines note that irritability and emotional reactivity are nonspecific symptoms found in multiple behavioral, affective, and developmental disorders and are therefore not diagnostic of mania. The AACAP guidelines suggest that the BD-NOS diagnosis be given to youths with either (a) manic symptoms of insufficient duration (i.e., lasting less than four days) or (b) youths with “chronic manic-like symptoms which constitute baseline functioning”⁵. However, prominent differences between these two classifications may indicate that BP-NOS, as defined by the AACAP guidelines, are clinically heterogeneous¹⁶.

2.6. Comorbid disorders

Pediatric BP is usually accompanied by other psychiatric disorders. The rates of comorbid disorders vary according to the age of the child, sample selection (clinical versus community), and the methods used to ascertain the psychiatric symptomatology². Depending on the population studied, approximately 50%-80% have ADHD, 20% to 60% disruptive behavior disorders, and 30% to 70% anxiety disorders². Beginning in adolescence, the rates of comorbid substance abuse and conduct disorder progressively increases¹. To a lesser degree, other psychiatric disorders such as obsessive compulsive disorder as well as medical conditions can accompany BP. The presence of these disorders affects the child's response to treatment and prognosis indicating the need to identify and treat these conditions¹.

Children with pediatric BD tend to have higher rates of ADHD than do adolescents with BD, whereas the latter have higher rates of substance abuse^{10, 17, 19}. Wilens et al. (2004)²⁰ found that the risk of substances abuse was 8.8 times higher in adolescent-onset BD than childhood-onset adolescent BD. As in adult BD, pediatric BD is specifically associated with panic disorder^{21, 22}. Pediatric BD can be comorbid with autistic spectrum disorders, with one report showing rates of comorbid pervasive developmental disorder to be as high as 11%²³.

2.7. Associated Features

Psychosis appears to be associated with pediatric BD. Most research groups have found that approximately one-fifth of youths meeting diagnostic criteria for BP I will also have hallucinations or delusions during the course of a mood episode¹. The prevalence of psychotic features is lower in adolescent mania as compared with adult mania, with lower ratings on thought disorder and delusions. It is critical to pay attention to age-specific manifestation of the symptoms².

Pediatric bipolar disorder significantly affects the normal psychosocial development of the child. Youth with bipolar disorder have a high risk for suicidal behaviors and completed suicide, substance abuse as well as for behavioral, academic social, legal problems, and health utilization^{2, 3, 24}.

2.8. Differential Diagnosis

It can be difficult to diagnose pediatric BP because the variability in the clinical presentations, high comorbidity and overlap in symptom presentation with other psychiatric disorders. Depending on their level of cognitive development, children may have problems expressing or describing their symptoms. In addition, psychotropic medications used for treatment can potentially affect a child's mood and/or behavior²⁴. Use of illicit drugs or alcohol can also complicate the diagnostic picture.

In daily practice, severe behavior disruptive disorders and ADHD are the most frequent conditions that may be confused with BP. The DSM-IV diagnostic criteria for a Manic Episode overlap with that of ADHD (distractibility, motor hyperactivity, pressured speech) and ODD

(irritability/anger). In addition, youth with ADHD frequently present with mood variability, difficulty falling asleep, and engage in risk-taking or thrill-seeking behavior that could be difficult to differentiate from BP. There are some symptoms that mainly occur in BP youth and may help to differentiate between BP and these disorders, such as clinically relevant euphoria, grandiosity, significant decreased need for sleep, hypersexuality (without history of sexual abuse or exposure to sex) and hallucinations¹³. Most depressed youth seen at psychiatric clinics are experiencing their first episode of depression²⁵. Some of these subjects may develop BP, but so far it is almost impossible to know who will develop BP at the time of first assessment. Thus, a careful assessment for history of manic or hypomanic symptoms is indicated. Also, the presence of psychosis, family history of BP, and pharmacologically induced mania/hypomania may indicate an increased risk to develop BP^{26–29}.

Schizophrenia is rare in children and sometimes BP may manifest with psychosis and bizarre behavior. In older adolescents, the presence of mood-incongruent delusions and hallucinations and thought disorder can lead to the misdiagnosis of BP as schizophrenia in as many as 50% of cases^{30,31}. Therefore, mood disorders need to be ruled out in any child with psychosis.

Youth with PDD-NOS or Asperger's disorder may have mood lability, aggression, and agitation and be misdiagnosed as having BP. Substance abuse may also induce severe mood changes that may be difficult to differentiate from BP.

The use of medications such as antidepressants, stimulants or steroids may unmask or trigger manic symptomatology in a susceptible individual³². However this does not necessarily mean the child has bipolar disorder. Family history, the severity, length, and quality of manic symptomatology as well as the temporal association to changes in medication may help to differentiate between BP and agitation induced by these or other medications³³.

3. Clinical course

3.1. Recovery and recurrence

There is a consensus for definitions used to characterize the longitudinal course of BD. Recovery is defined as eight consecutive weeks without meeting any of the DSM-IV criteria for mania, hypomania, depression, or mixed affective state. Remission is defined as 2–7 weeks without meeting for any of the DSM-IV criteria for affective episodes. Relapse is defined as two consecutive weeks of DSM-IV criteria for affective episodes with clinically significant impairment (Children's Global Assessment Scale score of <60). Chronicity is defined as failure to recover from an affective episode for a period of at least 2 years. Retrospective studies³¹ and naturalistic longitudinal studies of children and adolescents with BD^{9, 17, 34–38} have reported that 40%–100% will recover in a period of 1–2 years. Of those patients who recovered, however, approximately 60%–70% showed recurrences in an average of 10–12 months².

Birmaher et al., (2006)¹¹ reported that overall 68% of subjects recovered from their index episode a median of 78 weeks after the onset of the episode. There were no significant differences in the rates of recovery among the BP-I, BP-II and BP-NOS, but subjects with BP-NOS had a significantly longer time to recovery than subjects with BP-I and BP-II (all comparisons, $p \leq .05$) (Figure 1). They reported also that overall 56% of subjects had at least 1 recurrence at a median of 61.0 weeks after recovery of the index episode. Subjects with BP-II had higher rates of recurrence than subjects with BP-NOS and subjects with BP-NOS had significantly longer time to recurrence than those with BP-I and BP-II (all comparison, $p \leq .05$) (Figure 2). In summary, subjects with BP-I and BP-II recovered from their index episode and had recurrences more frequently than those with BP-NOS. In contrast, subjects with BP-NOS had a more protracted illness, but once they recovered from their index episode, they took

a longer time to recur than those with BP-I and BP-II. On average, subjects had 1.5 syndromal recurrences per year, particularly depressive episodes.

The results for BP-I subjects are similar to those of Geller et al. (2004)⁹, who found that 70% to 100% of children and adolescents with bipolar disorder will eventually recover from their index episode over the 4-year follow-up, but of those who recover, up to 80% experience one or more recurrences in a period of 2 to 5 years. Del Bello et al. (2007)³⁸ showed that 85% had syndromic recovery in an average period of 27 weeks after the onset of their index episode when evaluated the 1-year outcome after discharge from an inpatient unit of BP I adolescents admitted for their first manic or mixed episode. However, of these subjects, about 52% had at least one syndromic recurrence 17 weeks on average after they recovered.

Several factors have been identified that may potentially affect the course and outcome of bipolar youth. DelBello et al. (2007)³⁸ report that the comorbid presence of attention deficit hyperactivity disorder (ADHD), anxiety disorders, low socioeconomic status, and poor adherence to pharmacological treatment was associated with longer time to recovery. Alcohol use disorder, lack of psychotherapy treatment and use of antidepressants were associated with shorter time to recurrence.

Preliminary analyses from the Course and Outcome of Bipolar Youth study showed that subjects with prepubertal-onset BP were approximately 2 times less likely than those with postpubertal-onset to recover³⁹. In addition, subjects with prepubertal-onset BP had more chronic symptoms, defined as percentage of follow-up time with any mood symptoms, spent more follow-up time with any mood symptoms, and had more polarity changes per year than postpubertal-onset BP subjects. Preliminary analyses showed that mixed episodes, psychosis, low socioeconomic status, comorbid ADHD, conduct anxiety, substance abuse, and family psychopathology were associated with significantly more follow-up time with syndromal and subsyndromal symptoms³⁹.

Geller et al., (2004)⁹ found that low scores on an assessment of maternal warmth was the factor with the strongest association with worse outcome and predicted faster relapse after recovery from mania. Psychosis predicted more weeks ill with mania or hypomania.

3.2. Week-to week mood symptomatology

Recent studies have shown that bipolar disorder is not only manifest by punctuated recovery and recurrences, but also by ongoing fluctuating syndromal and subsyndromal symptoms^{2, 9–11, 24}. Birmaher et al., (2006)³⁹ analyses of weekly mood symptoms showed that subjects were symptomatic approximately 60% of the follow-up time, with about 22% of the time in full syndromal episodes (Manic, Hypomanic, Mixed or Major Depressive Episodes) and 38% of the time with subsyndromal symptoms of mania and/or depression. Subjects with BP I had more syndromal manic/hypomanic and mixed episodes than those with BP-NOS, and subjects with BP-II had more syndromal and subsyndromal depression than those with BP-I and BP-NOS. In contrast, subjects with BP-NOS showed more subsyndromal symptoms. During the follow-up, subjects with all types of BP, and particularly those with BP-NOS, with early onset or psychosis showed numerous changes in symptoms and shifts of polarity.

DelBello et al., (2007)³⁸ show that during 1 year follow-up after hospitalization, bipolar disorder adolescents spent 38% of their time meeting full syndromic criteria (mainly mixed episodes), 46% of the time with subsyndromal symptoms, and 16% without symptoms.

3.3. Developmental differences in course

There are developmental differences in the course of BP between children and adults^{2, 6, 9, 10, 40, 41}. Youth with BP-I spent significantly more time symptomatic and had more mixed/

cycling and subsyndromal episodes (Figure 2, Symptomatic periods and mixed = $p < .001$; subsyndromal = $p .05$), than adults with BP-I. Moreover, BP-I youth showed significantly more polarity switches than adults with BP-I (Figure 3) (all comparisons $p < .001$). Thus, across the age span and especially in youth, BP usually follows an ongoing changeable course with patient having a wide spectrum of mood symptoms ranging from mild to severe depression, mania and/or hypomania³⁹.

Early-onset BD may be a particularly severe form of the illness. BD disrupts a child's developmental trajectory, limiting his or her ability to achieve critical developmental milestones that has a lasting impact on their functioning into adulthood. Bipolar adults with onset in childhood or adolescence have higher rates of manic and depressive episodes, comorbid psychiatric disorders and spend less time in a euthymic (normal) mood state as compared to those with adult-onset⁴². Children and adolescents with BD have phenotypic features that are associated with poor prognosis in adults with BD, including high rates of mixed depressive and manic symptomatology, psychosis and long periods of subsyndromal mood symptoms³⁹. Given the severity of illness, identifying and treating bipolar disorder in children is extremely important, particularly since recent large studies indicate that between $\frac{1}{3}$ – $\frac{1}{2}$ of bipolar adults recall the onset of their symptoms during childhood or adolescence^{42, 43}.

3.4. Rate of conversion between BP-I, BP-II and BP-NOS

Birmaher et al., (2006)¹¹ reported that approximately 20% of subjects who had an intake diagnosis of BP-II converted into BP I. About 25% of the BP-NOS subjects converted to either BP-I or II over an average of 2 years of follow-up. Factors associated with conversion included female sex and longer duration of illness. The rates of conversion from BP-II to BP-I found in children³⁹ is higher than the cumulative rate of conversion reported in than adult literature⁴⁴, possibly suggesting that BP-II is less developmentally stable in the pediatric age group. However it is currently unknown how many of the youth with BP-NOS will eventually become bipolar adults or which subthreshold presentations predict development of BP-I or BP-II disorder versus those that are not truly bipolar²⁴.

3.5. Consequences

The enduring and rapid changeability of symptoms in children and adolescents with BP are occurring early in life and at crucial stages of their lives. This can deprive them of the opportunity for normal emotional, cognitive, and social development^{2, 6, 9, 10, 17, 18, 36, 45–47}. The pediatric prospective naturalistic studies as well as retrospective reports^{36, 48–53} have showed high rate of hospitalizations and health service utilization, psychosis, suicide attempts and completions, switch from BP-NOS to BP-I or II and from BP-II to BP-I, substance abuse, unemployment, legal problems and poor psychosocial functioning. The ongoing BP symptoms also have negative impact in the family, marital, and sibling relationships as well as the family economics. The considerable impairment in psychosocial functioning reported in these studies is not only due to the fact that most of them were carried out in clinical samples, because similar findings have been reported BP adolescents never referred for treatment^{17, 18}.

Functional impairment—Pediatric BD is associated with aggressive behavior, attention problems anxious and depressed symptoms delinquent behavior, social problems withdrawal, and thought problems^{54–56}. Geller et al. (2002)⁵⁷ reported that more than half of youths diagnosed with BD had poor social skills, had no friends, and were teased by other children. They have poor relationships with siblings and conflictual relationship with their parents. Specifically, there was a high degree of hostility and low warmth in maternal-child relationships, poor agreement between parents on child-rearing practices, and minimal

problem-solving skills. Parent and child reported elevated novelty-seeking traits in pediatric BD compared with those with ADHD and healthy controls⁵⁸. Onset of bipolar illness in adolescence negatively impacts on the teenager's ability to function effectively in the school environment⁵⁹. Additional studies are required to clarify whether social skill deficits are related to BD, comorbid disorders, family psychopathology, or demographic factors, and the interactions among these variables.

Suicidality: Longitudinal follow-up indicates that through age 18 years, 44% of cases with bipolar diagnoses (excluding BP-NOS) attempted suicide, versus 22% of cases with major depressive disorder, 18% of BP-NOS cases, and only 1% of cases with no diagnosis⁶⁰. BP was associated with the highest rates of suicidal ideation (72% of cases, versus 52% of major depressive disorder, 41% of core positive bipolar NOS, and 6% of participants with no diagnosis), as well as younger age at first attempt (mean of 13.3 years), higher rates of multiple attempts (88% of cases), and significantly greater medical lethality of attempts⁶⁰.

Substance abuse and behavior problems: Comorbid substance use disorder (SUD) are common among adults with BP, and are associated with markedly increased burden of illness across multiple domains. Epidemiologic and clinical studies demonstrate that youth-onset BP confers even greater risk of SUD in comparison to adult-onset BP. Recent studies of youth with BP have not identified childhood SUD; however the prevalence escalates during adolescence, with estimates ranging from 16–39%. SUD among adolescence with BP is associated with suicide attempts, legal problems, pregnancy, and abortion⁶¹. Several studies suggest that substance use disorders are more common among youth with BP than among healthy and psychiatric controls. Wilens et al., (1999)⁶² found that the prevalence of SUD was significantly higher among subjects with BP compared to those without BP. The increased prevalence of SUD among youth with BP remained significant after controlling for conduct disorder^{20, 62}.

4. Future directions for research

Despite the growing evidence that the consequences of BP arising during childhood can be devastating, with high rates of mixed and cycling presentations, substance abuse, suicidal risk, and social, family, vocational, and academic impairment^{2, 11}, the long-term course of BP in youth has been insufficiently studied. Extensive follow-up time is needed to evaluate the continuity of BP symptoms from childhood to adulthood. Finally, studies should evaluate and analyze the positive or negative contributions to the child's outcome of factors such as the child's emotional and cognitive development, social and coping skills, circadian/social rhythms, and the child's home and community environment. Regarding this last factor, important issues such as parental lifetime and current psychopathology, support, exposure to negative life events should be considered.

5. Summary

Though findings vary somewhat among different research groups, there are several unique features that have been consistently demonstrated in studies of the phenomenology and course of pediatric BD: (1) high rates of elevated, expansive or elated mood; (2) prominent irritability; (3) prolonged mood episodes characterized by significant periods of subsyndromal symptomatology; (4) depressive symptoms interspersed with manic or hypomanic symptoms; (5) high rates of comorbid psychiatric disorders, especially ADHD, other disruptive behavior disorders and anxiety disorders; (6) high rates of substance use disorders in older adolescents with BP; and (7) high rates of psychotic symptoms, suicide attempts and significant functional impairment. These features emphasize the need for early recognition and treatment of children and adolescents with bipolar disorder to ameliorate ongoing syndromal and subsyndromal

symptoms and to reduce or prevent the serious psychosocial morbidity that usually accompanies this illness.

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Figure 1. Comparison of weekly symptoms status between youth with BP-I, II and NOS (From Birmaher et al, 2006³⁹)

A comparison of the weekly symptoms status of youth with bipolar I disorder, bipolar II disorders, and not otherwise specified. The weekly symptoms status is the percentage of follow-up weeks that were asymptomatic or symptomatic in different mood categories.

Figure 2. Weekly symptoms status. Comparison between youth with BP-I vs. adults with BP-I
(From Birmaher et al, 2006³⁹)

A weekly symptoms status comparison between youth and adults with bipolar I disorder. The weekly symptom status is the percentage of follow-up weeks that were asymptomatic or symptomatic in different mood categories; $p = .05$; $p \leq .001$.

Figure 3. Change in polarity. Comparison between youth with BP-I vs. adults with BP-I (From Birmaher et al, 2006³⁹)

A comparison of the change in polarity between youth and adults with bipolar I disorder. The change in polarity is the switch between depression and mania/hypomania or vice versa with or without intervening weeks in asymptomatic status. All comparisons are significant at $p < .001$

Table 1
DSM-IV Criteria for a Manic Episode

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- A.** A distinct period of abnormally and persistently elevated, expansive, or irritable mood for 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)
 - 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 (either socially, at work or school, or sexually) or psychomotor agitation
 - 7.** excessive involvement in pleasurable activities that have a high potential for painful consequences (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).
-

Note: 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.

Table 2
DSM-IV Criteria for a Hypomanic Episode

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A.	A distinct period of persistently elevated, expansive, or irritable mood, lasting throughout at least 4 days, that is clearly different from the usual nondepressed mood.
B.	Same as B criterion for Manic Episode.
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 episode is 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).
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Note: 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.

Table 3Symptoms of Mania from Meta-analysis of Pediatric BP studies (From Kowatch et al, 2005 ¹)

Symptom	Weighted Rate	95% Confidence Interval
Increased energy	89%	76 – 96%
Distractibility	84%	71 – 92%
Pressured speech	82%	69 – 90%
Irritability	81%	55 – 94%
Grandiosity	78%	67 – 85%
Racing thoughts	74%	51 – 88%
Decreased need for sleep	72%	53 – 86%
Euphoria/elation	70%	45 – 87%
Poor judgment	69%	38 – 89%
Flight of ideas	56%	46 – 66%
Hypersexuality	38%	31 – 45%