

# Pediatric Bipolar Disorder (BPD)

## Agenda

- DSM-IV Diagnosis
- Controversies in Diagnosis
- Epidemiology
- Clinical Course
- Comorbidity
- Etiology
- Assessment
- Treatment

## DSM-IV Diagnosis

### DSM-IV: Manic Episode

- 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:

### Manic Episode (cont'd)

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 (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

### Manic Episode (cont'd)

- 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).

### **DSM-IV: Hypomanic Episode**

- A. A distinct period of persistently elevated, expansive, or irritable mood, lasting at least 4 days, that is clearly different from the usual nondepressed mood.
- 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:

### **Hypomanic Episode (cont'd)**

- 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 (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

### **Hypomanic Episode (cont'd)**

- 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.

### **Hypomanic Episode (cont'd)**

- 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).
  - **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.

### **DSM-IV: Mixed Episode**

- 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 one 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).

### **DSM-IV: BPD**

- **BPD-1:** Diagnosis requires at least one Manic or Mixed episode, but there may be episodes of Hypomania or Major Depression as well.
- **BPD-2:** Presence (or history) of one or more Major Depressive Episodes **AND** of at least one Hypomanic Episode **AND** there has never been a Manic Episode or a Mixed Episode.
- **BPD, NOS:** "...includes disorders with bipolar features that do not meet criteria for any specific BPD."

**DSM-IV:**  
**Cyclothymic Disorder**

- A. For at least 1 year (adults = 2 years), the presence of numerous periods with hypomanic symptoms and numerous periods with depressive symptoms that do not meet criteria for a Major Depressive Episode.
- B. During the above 1 year period, the person has not been without the symptoms in Criterion A for more than 2 months at a time.
- C. No Major Depressive Episode, Manic Episode, or Mixed Episode has been present during the first year of the disturbance.

**Cyclothymic Disorder**  
**(cont'd)**

- D. The symptoms in Criterion A are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.
- E. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism).
- F. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

**Controversies**  
**in Diagnosis of Pediatric**  
**Bipolar Disorder**

**Research**  
**Driving the Controversy**

**“National Trends in the Outpatient  
Diagnosis and Treatment of Bipolar  
Disorder in Youth”**

- Compared rates of growth between 1994-1995 and 2002-2003 in visits with a bipolar disorder diagnosis by individuals aged 0 to 19 years vs. those aged 20 years or older.

Moreno et al, Arch Gen Psychiatry, Sept. 2007; 64(9):1032-1039

**Research**  
**Driving the Controv. (cont'd)**

**“National Trends...”**

- **Results:** The estimated annual number of youth office-based visits with a diagnosis of bipolar disorder increased from 25 (1994-1995) to 1003 (2002-2003) visits per 100,000 population, and adult visits with a diagnosis of bipolar disorder increased from 905 to 1679 visits per 100,000 population during this period.

**Relevant Publications**

1. “NIMH Research Roundtable on Prepubertal BPD”, JAACAP, 8/2001
2. “Research Roundtable on Pediatric BPD-NOS”, NIMH, 9/2002
3. “Methodological Issues & Controversies in Clinical Trials with C&A Patients with BPD: Report of Consensus Conference,” J Child Adol Psychopharm, 3/2003
4. “Pediatric BPD: A Review of the Last 10 Years”, JAACAP, 9/2005.
5. “Practice Parameter for the Assessment and Treatment of Children and Adolescents With Bipolar Disorder,” JAACAP, 1/2007.

### NIMH Research Roundtable on Prepubertal BPD

“On April 27, 2000, the National Institute of Mental Health (NIMH) Developmental Psychopathology and Prevention Research Branch, in collaboration with the Child and Adolescent Treatment and Preventive Intervention Research Branch, convened a small roundtable meeting for open-ended discussion of possible approaches to outstanding issues for research on the diagnosis of prepubertal bipolar disorder.”

### NIMH Res. Roundtable on Prepub. BPD (cont'd)

Agreement on two basic definitions:

1. Phenotypes that fit DSM-IV BPD-1 and BPD-2 criteria (“narrow phenotypes”).
2. Phenotypes that encompass more heterogeneity, basically BPD-NOS, and include children who do not meet DSM-IV criteria but who are still *severely impaired by symptoms of mood instability* (“broad phenotype”).

### NIMH Res. Roundtable on Prepub. BPD (cont'd)

**BPD-NOS:** To advance research on this non-*DSM-IV* phenotype, it was agreed in general that BPD-NOS could be used as a “working diagnosis,” as long as the children are well described (with particular attention to symptoms of ADHD, but also to symptoms of anxiety, oppositional defiant disorder [ODD], and prepubertal onset of substance use).

### NIMH Res. Roundtable on Prepub. BPD (cont'd)

Outstanding issues for the study of bipolar disorder in prepubertal children include the following:

- Describing the course of BPD-1, BPD-2, Cyclothymia, and BPD-NOS.
- Defining thresholds for and boundaries between BPD-1, BPD-2, and Cyclothymia.
- Defining occasions for combining versus separating BPD-1 and BPD-2.
- Establishing inclusion and exclusion criteria for BPD,NOS (and identifying subtypes?).

### NIMH Res. Roundtable on Pediatric BPD-NOS

“On September 9, 2002, the NIMH Developmental Psychopathology and Prevention Research Branch convened a research roundtable to focus on the pediatric Bipolar-NOS phenotype, in order to address the issue of how the heterogeneous group of children given this diagnosis should be described and studied.”

### NIMH Res. Roundtable on Ped. BPD-NOS (cont'd)

Decided to proceed with data collection from ongoing studies of BPD-NOS, using the three phenotypes described by Leibenluft et al.:

Two “intermediate phenotypes”:

- a) (Hypo)**mania NOS**: meets DSM-IV criteria except for episode duration and
- b) Irritable (hypo)**mania**: meets DSM-IV criteria, but lacks elevated or expansive mood; and

One “broad phenotype”:

- c) Severe mood and behavioral dysregulation: chronically ill, without discernible episodes.

### “Pediatric BPD: A Review of the Past 10 Years”

Endorsed the use of the above-noted diagnostic differentiation between “narrow”, “intermediate” and “broad” phenotypes, but with regard to the last two noted:

- “Additional studies are needed to determine whether these children actually have BPD, prodromal symptoms of BPD, or other psychiatric disorders accompanied by mood dysregulation or instability.”

### “Practice Parameter for the Assessment and Tx of C&A With BPD”

- “The DSM-IV criteria, including the duration criteria, should be followed when making a diagnosis of mania or hypomania in children & adolescents.”
- “BPD NOS should be used to describe youths with manic symptoms lasting hours to less than four days, or for those with chronic manic-like symptoms representing their baseline level of functioning.”
- “The diagnostic validity of BPD in young children has yet to be established. Caution must be taken before applying this diagnosis to preschool children.”

### Recent Research

“Phenomenology of Children & Adolescents with Bipolar Spectrum Disorders”

- Compared 438 kids between ages 7 & 17 with BPD-I, BPD-II, & BPD-NOS
- BPD-NOS was diagnosed IF child showed:
  - Hypomanic episode w/o any major depressive episodes
  - Manic episode that meets duration, but not symptom, criteria
  - Manic episode that meets symptom, but not duration, criteria

Axelsson et al, Arch Gen Psychiatry, Oct. 2006; 63:1139-1148

### Results:

- Frequency of diagnoses: BPD-I: 58%; BPD-NOS: 35%; BPD-II: 7%
- Youth with BPD-NOS were generally not diagnosed with BPD-I or BPD-II because they did not meet the duration criteria for a manic or hypomanic episode
- Elevated mood was present in 82% of BPD-NOS, & 92% of BPD-I

### Concept of “Severe Mood Dysregulation”

- To facilitate research on these questions, some researchers have suggested a classification system differentiating children with strictly defined DSM-IV bipolar disorder (i.e., narrow phenotype) from those with nonepisodic irritability and hyperarousal (i.e., broad phenotype).

### Proposed Dx Criteria for “SMD”

1. Aged 7–17, with the onset of symptoms before age 12.
2. Abnormal mood (specifically anger or sadness), present at least half of the day most days, and of sufficient severity to be noticeable by people in the child’s environment (e.g., parents, teachers, peers).
3. Hyperarousal, as defined by at least three of the following symptoms: insomnia, agitation, distractibility, racing thoughts or flight of ideas, pressured speech, intrusiveness.

### Dx Criteria for “SMD” (cont’d)

4. Compared to his/her peers, the child exhibits markedly increased reactivity to negative emotional stimuli that is manifest verbally or behaviorally. For example, the child responds to frustration with extended temper tantrums (inappropriate for age and/or precipitating event), verbal rages, and/or aggression toward people or property. Such events occur, on average, at least three times a week.

### Dx Criteria for “SMD” (cont’d)

5. The symptoms noted in 2–4 above are currently present and have been present for at least 12 months without any symptom-free periods exceeding two months.
6. The symptoms are severe in at least one setting (i.e., violent outbursts, assaultiveness at home, school, or with peers). In addition, there are at least mild symptoms (distractibility, intrusiveness) in a second setting.

### Dx Criteria for “SMD” (cont’d)

#### Exclusion Criteria:

1. The individual exhibits any of these cardinal bipolar symptoms:
  - Elevated or expansive mood.
  - Grandiosity or inflated self-esteem.
  - Episodically decreased need for sleep.
2. The symptoms occur in distinct periods lasting more than 4 days.
3. Meets criteria for schizophrenia, schizophreniform disorder, schizoaffective illness, PDD, or PTSD

### Dx Criteria for “SMD” (cont’d)

#### Exclusion Criteria (cont’d):

4. Meets criteria for substance use disorder in the past 3 months
5. IQ<70
6. The symptoms are due to the direct physiological effects of a drug of abuse, or to a general medical or neurological condition.

### Recent Research Comparing BPD & SMD

#### Psychophysiological:

- Subjects with severe mood dysregulation (N=21) or narrow-phenotype bipolar disorder (N=35) and comparison subjects (N=26) completed the affective Posner task, an attentional task that manipulated emotional demands and induced frustration.
- Mood response, behavior (reaction time and accuracy), and brain activity (event-related potentials) were measured.

(Rich et al, Am J Psychiatry Feb. 2007; 164:309–317)

### Recent Research Comparing BPD & SMD (cont’d)

#### Psychophysiological (cont’d):

- **Results:** The severe mood dysregulation and narrow-phenotype bipolar disorder groups both reported significantly more arousal than comparison subjects during frustration, but behavioral and psychophysiological performance differed between the patient groups (particularly when SMD was accompanied by Oppositional Defiant Disorder).

### **Recent Research** **Comparing BPD & SMD (cont'd)**

#### **Genetic:**

- Parents of youth with narrow phenotype bipolar disorder (proband N= 33, parent N=42) and youth with severe mood dysregulation (proband N=30, parent N=37) were interviewed using the Diagnostic Interview for Genetic Studies, by clinicians who were blind to the child's diagnostic status.

(Brotman et al, Am J Psychiatry, Aug. 2007, 164:1238-1241)

### **Recent Research** **Comparing BPD & SMD (cont'd)**

#### **Genetic (cont'd):**

- **Results:** Compared to parents of youth with severe mood dysregulation, parents of youth with narrow phenotype bipolar disorder were significantly more likely to be diagnosed with bipolar disorder. There were no other diagnostic differences between the two groups.

## **Epidemiology**

### **General** **Population**

- The estimated lifetime prevalence of bipolar I disorder in the general population ranges from 0.4% to 1.6%, with about 0.5% having bipolar II (American Psychiatric Association, 2000).
- The National Comorbidity Survey Replication study found the combined prevalence of bipolar I and II disorders to be 2.6% (Kessler et al., 2005).

### **Child &** **Adolescent**

- Only one community study (Lewinsohn, 1995) has looked at rates of bipolar spectrum disorders in older adolescents (14-18 years)
  - Lifetime prevalence = 1% (but only 0.1% with mania)
  - 5.7% had "distinct period of abnormally & persistently elevated, expansive, or irritable mood" that did not meet BPD DSM-IV criteria

## **Clinical Course**

## Definitions

- **Recovery:** Eight consecutive weeks without meeting DSM-IV criteria for mania, hypomania, depression, or mixed state
- **Remission:** Two to seven weeks without meeting DSM-IV criteria for affective episodes
- **Relapse:** Two consecutive weeks of DSM-IV criteria for an affective episode, with significant impairment
- **Chronicity:** Failure to recover from an affective episode for at least two years

## Studies

Several retrospective & naturalistic longitudinal studies of children & adolescents with BPD show:

- 40-100% recover from the index episode in 1 to 2 years
- Of those, 60-70% relapse in an average of 10 to 12 months

## Studies (cont'd)

Recent studies show the inadequacy of the conceptualization of BPD as episodes of illness punctuating sustained symptom-free periods:

- At follow-up interviews adolescents showed syndromal or subsyndromal BPD symptoms nearly 70% of the time.
- A 4-year follow-up study showed “polarity switches” 1.1 times/year, on average.

## Studies (cont'd)

Studies attempting to define the course of BPD-NOS show a poorer prognosis:

- Longer time to recovery than other BPD diagnoses
- Shorter time to relapse
- About 25% converted to BPD-1 or BPD-2

## Studies (cont'd)

While evidence is not yet sufficient to indicate that pediatric BPD is continuous with adult BPD, studies show:

- Psychotic adolescent-onset mania is very similar to adult BPD
- Retrospective studies of adult BPD report 30% had onset under 13 YO & 40% had onset at 13 to 18 YO
- 20-30% of depressed children eventually develop BPD

## Recent Research

“Twelve-Month Outcome of Adolescents With Bipolar Disorder Following First Hospitalization for a Manic or Mixed Episode”

- Naturalistic study of 71 bipolar adolescents, recruited during their first hospitalization for a manic or mixed episode.
- They were evaluated using diagnostic, symptomatic, and functional assessments, & then were evaluated at 1, 4, 8, & 12 months to assess syndromic, symptomatic, and functional outcomes.

(DelBello et al. Am J Psychiatry, Apr. 2007; 164:582–590)

## Results

- **Pharmacological Treatment Adherence**
  - Full adherence: 35%;
  - Partial adherence: 42%;
  - Nonadherence: 23%
- **Syndromic recovery & recurrence**
  - Defined as no longer meeting criteria for Dx (but still symptomatic)
  - Sixty (85%) adolescents had syndromic recovery during the year after hospitalization.
  - Thirty-one (52%) of the 60 adolescents who had syndromic recovery had at least one syndromic recurrence within the year.

## Results (cont'd)

- **Symptomatic recovery**
  - Defined as mild or no residual symptoms
  - Twenty-eight (39%) adolescents achieved symptomatic recovery.
- **Functional recovery**
  - Defined as achieving functional level equal to or better than premorbid psychosocial functioning in the four major areas of functioning measured (role performance, interpersonal relationships, recreational enjoyment, and sexual activity)
  - Twenty-eight (39%) adolescents achieved functional recovery.

## Results (cont'd)

- “However, only 20% of bipolar adolescents experienced all three types of recovery, indicating that most bipolar adolescents continued to have impairment in at least one domain and emphasizing the importance of assessing symptomatic and functional outcomes in bipolar youth.”

## **Comorbidity**

## Comorbidity

- **Limited agreement re: rates of comorbid disorders, but studies suggest:**
  - ADHD: 11 to 75% (children > adolescents)
  - ODD: 46.4 to 75%
  - CD: 5.6 to 37%
  - Anxiety D/O: 12.5 to 56% (esp. panic)
  - SUD: 0 to 40% (adolescents > children)
  - PDD (esp. Asperger's): 11%

## **Etiology**

## Etiology

- Twin, adoption, & family studies have established heritability in adult BPD, i.e.:
  - Monozygotic twins = 70% concordance
  - Dizygotic twins = 30% concordance
- Similar studies are lacking in pediatric BPD, but what has been done certainly *suggests* heritability

## Family Studies in Peds BPD

- “Top-down” studies (examining offspring of parents with BPD):
  - 1997 meta-analysis (Lapalme et al) reported offspring of parents with BPD, compared of offspring of parents without psychiatric disorder, have:
    - 2.7x greater risk of any psychiatric disorder,
    - And 4.0x greater risk of mood disorder

## Family Studies in Peds BPD (cont'd)

- “Top-down” studies, continued:
  - One of the largest offspring studies (n=72 offspring, 1989) reported:
    - 60% of offspring of BPD parents vs. 25% of offspring of normal parents show psychopathology
    - Esp. disruptive behavior disorders & depression
  - Two recent U.S. studies showed 14 to 50% incidence of BPD in offspring of parents with BPD
    - BUT a Dutch study showed only 2.8% incidence

## Family Studies in Peds BPD (cont'd)

- “Bottom-up” studies (estimating prevalence of BPD among relatives of children with BPD):
  - Several studies show strong link between early age of BPD onset &:
    - Risk of BPD among first degree relatives, compared with relatives of youth with schizophrenia, MDD, & normal controls, &
    - Greater familial loading of BPD

## Family Studies in Peds BPD (cont'd)

- “Bottom-up” studies, continued:
  - Relatives of adolescents with subsyndromal BPD have increased family history of BPD (similar to those with full syndrome BPD)
  - Relatives of youth with comorbid BPD & ADHD have 5x greater rate of BPD than relatives of youth with ADHD alone

## **Assessment**

### Components of a Comprehensive Evaluation

- Interview at least the child & one parent
  - Discrepancies are common
  - Esp. re: euphoria, suicidality, psychotic Sx
- School input can be important
  - “Tie-breaker” re: symptoms
  - Symptoms in more than one setting
  - To track progress
- Develop a timeline to establish onset, offset, and duration of symptoms
  - Ask about symptoms relative to birthdays, holidays, grades, etc.

### Evaluation Components (cont'd)

- Cross-sectional documentation of current symptoms
- Functioning at home, school & with peers
  - Worst, best & current functioning
- Medical history
- History of medication &/or substance use
- Family history
  - Ideally a three generation genogram
- Consider need for psychoeducational testing once mood is stable

### Family Considerations

- Essential in gathering adequate information to make diagnosis
- Be alert to possibility of untreated or undiagnosed mood disorders in immediate family members
- Need to educate re: impact of BPD on child & family...

### **Treatment**

### Interventions

- Psycho-education
- Medication
- Treatment of Comorbid Disorders
- Psychosocial Interventions

### Psycho-education

- Help child & family make sense of the illness
- Understand the role of medications (what they can & cannot do)
- Help parents eliminate their own unhelpful cognitions
- Enhance child & family’s skills & coping strategies for dealing with the illness

## Medication

- Very few prospective studies on efficacy & safety of meds in treatment of pediatric BPD
- Lithium is the only FDA approved medication for pediatric BPD, & it is only approved for those > 13 YO
- Most medication studies on treatment of pediatric BPD published thus far are open trials

## Medication (cont'd)

- Summary of published findings:
  - Second-generation antipsychotics (SGAs) & mood stabilizers appear to be effective acute treatments
  - Combined mood stabilizers & stimulants appear promising for comorbid BPD & ADHD
  - Preliminary study of maintenance with mood stabilizer monotherapy showed less than a 4 month median survival in 18 month follow-up

## Medication (cont'd)

- For proposed medication algorithms for pediatric BPD, with & without psychotic features, see:
  - “Treatment Guidelines for Children and Adolescents With Bipolar Disorder”, JAACAP, 44:3, March 2005:213–235
- “Practice Parameter for the Assessment and Treatment of Children and Adolescents With Bipolar Disorder” published in JAACAP January 2007.

## Treatment of Comorbid Disorders

- Stabilize BPD symptoms first
- If the symptoms of the comorbid condition(s) are negatively affecting the child's functioning, then treatment is warranted, as follows:
  - Treat comorbid disorders sequentially
  - Treat with psychosocial interventions only, where possible (i.e., CBT for anxiety)
  - Introduce new medications one at a time

## Psychosocial Interventions

- To date, there are no empirically validated psychosocial treatments for BPD adolescents, but there have been some promising preliminary studies:
  - Pavuluri et al. (2004) treated school-age BP children by combining components of family-focused therapy (FFT) and CBT.
  - Fristad et al. (2002) used manual-driven, adjunctive, multiple family group therapy for 8 to 12 year-olds
  - Miklowitz et al. (2004) demonstrated the feasibility of delivering a developmentally modified version of FFT for BP adolescents.