Recognizing Pediatric Bipolar Disorder

James Peacey, MD

Webinar | June 6, 2020
Objectives

1. Participants will have increased knowledge and confidence to identify and diagnose bipolar disorders in children and adolescents.

2. Participants will have increased knowledge and confidence to discuss the relative risks and benefits of psychotherapeutic and medication treatments for bipolar disorder with youth and their caregivers.
Disclosures

• Financial: No relevant financial conflicts exist.

• Unlabeled/unapproved uses: Off-label medication use is discussed in this presentation, and it will be highlighted when it occurs.
The diagnosis of bipolar disorder in children is a controversial topic even amongst child psychiatric specialists. This controversy makes it difficult for primary care providers to know what to do when they are wondering about bipolar disorder in their patient.

We would prefer that primary care providers would not have to struggle with this, and could refer all such patients to skilled mental health specialists to assist with diagnosis and treatment. The reality is that many primary care providers feel they do not have that option.

This guide on bipolar diagnosis and treatment aims to provide guidance to the primary care provider struggling on their own to sort out a diagnosis, or otherwise manage a bipolar disordered child in their practice.
Considering Bipolar Disorder?

Strongly consider other reasons for the symptoms such as:
- ADHD
- Conduct Disorder
- Oppositional Defiant Disorder
- Major Depression
- Early abuse or neglect in dysregulation syndromes
- "Difficult" temperament of child plus interpersonal conflicts
- Autism Spectrum Disorder, especially with oppositionality
- OCD, separation anxiety or other anxiety disorder
- Medical causes of mania (including fetal alcohol syndrome)

Safety check:
- Suicidality?
- Drug abuse?
- Current neglect/abuse?

Diagnosis:
- Does child have history of clear manic episode for >4 days?
- Does child have hospitalization for mania?
- History of psychosis or severe suicidality?
- Symptom of inappropriate euphoria/grandiosity?

Is this an "Unspecified," or "Other Specified" Bipolar Disorder?
These are the DSM-5 labels for bipolar symptoms that cause impairment, but the duration or other criteria for Bipolar I or II are not met. This "soft" criteria bipolar diagnosis in children is controversial. Most irritable, moody, irrational, hyperactive kids when evaluated more fully are found NOT to have a bipolar disorder.

More likely Bipolar spectrum if:
- Episodic patterns of changes in mood, activity and energy including elation, hyperactivity, grandiosity, hypersexuality, decreased sleep that are a departure from baseline function (not fully explained by child's response to stressor)
- Have 1st degree relative with bipolar

Treatment:
1. Consider consultation with a mental health specialist, especially if safety concerns.
2. Consider medical causes of manic symptoms like hypothyroidism, neurological dysfunction.
3. Psychosocial/behavioral intervention tailored to family, including:
   a. family psychoeducation
   b. child/family focused CBT
   c. enhancing school and community supports
   d. individual or family psychotherapy
   e. behavior management training
4. Medication trial, single agent preferred, choose among:
   a. atypical antipsychotic
   b. lithium
   c. lamotrigine (especially if bipolar depression)
   d. divalproex, carbamazepine also options, though have less evidence basis
5. Be cautious of prescribing antidepressants (manic switching risk).
6. Follow up frequently, perhaps weekly until stabilizing.
7. Ensure adequate sleep hygiene — consider sleep medications if necessary.

Treat other causes of symptoms, especially if unsure of bipolar diagnosis

If yes to any, child should see a mental health specialist to evaluate/treat Bipolar I or Bipolar II (also called "narrow phenotype" bipolar)

Less likely Bipolar spectrum if:
- Younger age (such as <10)
- Rages only after frustrations
- Symptoms only in 1 setting (i.e., home)
- High expressed emotion in household (think of ODD)

Reconsider other etiologies like ADHD, PTSD, ODD, or Disruptive Mood Dysregulation Disorder; please see Disruptive Behavior section of this guide for behavior management guidance.

Primary References:
AACAP "Practice Parameter for the Assessment and Treatment of Adolescents and Children with Bipolar Disorder" JAAACAP, 2007, 46(1), 127-125
The Bipolar Disorders

- Bipolar I Disorder
- Bipolar II Disorder
- Cyclothymic Disorder
- Substance/Medication-Induced Bipolar and Related Disorder
- Bipolar and Related Disorder Due to Another Medical Condition
- Other Specified Bipolar and Related Disorder
- Unspecified Bipolar and Related Disorder
Mania

A distinct period (at least 7 days, or less if hospitalization required) of abnormally and persistently (nearly every day, most of the day)

• elevated, expansive or irritable mood
• Increased goal-directed activity or energy
• During which, 3 of the following:
Mania Criteria cont’d

1. Inflated self-esteem or grandiosity
2. Decreased need for sleep
3. More talkative or pressured speech
4. Flight of ideas or racing thoughts
5. Distractibility
6. Increased goal directed goal-directed activity or psychomotor agitation
7. Excessive involvement in activities that have a high potential for painful consequences (spending sprees, sexual indiscretions, foolish business investments)
   • Marked impairment, hospitalization required or psychotic features
   • Criteria are met if symptoms continue after the effects of a mood-elevating substance would have dissipated.
Hypomanic Episode

A distinct period (at least 4 days) of abnormally and persistently (nearly every day, most of the day)

- Same criteria set as for manic episode
- Distinct change in functioning observable by others – not severe enough to cause marked impairment
Major Depressive Episode

Two week period with 5 of 9:

1. Depressed mood (sad, empty, hopeless, irritable in children and adolescents)
2. Markedly diminished interest in pleasure in activities
3. +/- weight or appetite
4. +/- sleep
5. Psychomotor agitation or retardation
6. Fatigue or loss of energy
7. Feelings of worthlessness/guilt
8. Diminished ability to think or concentrate or indecisiveness
9. Recurrent thoughts of death/suicide
The Bipolar Disorders

• Bipolar I Disorder – One lifetime manic episode necessary and sufficient for diagnosis. Additional episodes including major depressive episode and hypomanic episodes are typical

• Bipolar II Disorder – Hypomanic Episode and Major Depressive Episode

• Cyclothymic Disorder – 2 years (1 year for children and adolescents) of numerous periods of hypomania and depression symptoms >50% of time.
Other Bipolar Disorders

A prominent and persistent period of abnormally elevated, expansive or irritable mood and abnormally increased activity or energy that predominates the clinical picture.

- Substance/Medication-Induced Bipolar and Related Disorder
- Bipolar and Related Disorder Due to Another Medical Condition

Symptoms characteristic of a bipolar and related disorder that cause clinically significant distress or impairment...but do not meet the full criteria...

- Other Specified Bipolar and Related Disorder
- Unspecified Bipolar and Related Disorder
Specifiers

• With anxious distress – experience of increased energy is not always pleasant
• With mixed features – simultaneous symptoms of mania and depression or “ultrarapid cycling”
• With rapid cycling – 4 mood episodes in 12 months
Differential Diagnosis and Comorbidities

<table>
<thead>
<tr>
<th>Strongly consider other reasons for the symptoms such as:</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD</td>
</tr>
<tr>
<td>Conduct Disorder</td>
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<tr>
<td>Oppositional Defiant Disorder</td>
</tr>
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Treat other causes of symptoms, especially if unsure of bipolar diagnosis
ADHD Symptom Overlap

1. Inflated self-esteem or grandiosity
2. Decreased need for sleep*
3. More talkative or pressured speech**
4. Flight of ideas or racing thoughts*
5. Distractibility**
6. Increased goal directed goal-directed activity or psychomotor agitation**
7. Excessive involvement in activities that have a high potential for painful consequences (spending sprees, sexual indiscretions, foolish business investments)
Trauma Symptom Overlap

Marked alterations in arousal and reactivity:
1. Irritable* behavior and angry outbursts
2. Reckless* and self-destructive behavior
3. Hypervigilence
4. Exaggerated startle response
5. Problems with concentration*
6. Sleep disturbance*

Intrusion symptoms and dissociation may resemble psychosis
Irritability in the DSM-5

Diagnostic Criteria Regardless of Age
• Manic Episode
• Generalized Anxiety Disorder
• Posttraumatic Stress Disorder

Child Specific Diagnostic Criteria
• Major Depressive Disorder
• Oppositional Defiant Disorder
• Disruptive Mood Dysregulation Disorder

Associated Feature
• Attention-Deficit/Hyperactivity Disorder
• Autism Spectrum Disorder
Activation on Antidepressants

- Activation represents a hyperarousal event that is typically characterized by specific symptoms including an increase in activity, impulsivity, disinhibition, restlessness and insomnia.

- May be related to increased suicidal ideation

- More likely with younger age and ADHD diagnosis

- May be hard to distinguish from medication-induced bipolar disorder

Data from National Comorbidity Survey Adolescent Supplement (NCS–A)
Past Year Prevalence of Major Depressive Episode Among U.S. Adolescents (2017)

Data Courtesy of SAMHSA

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Race/Ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>13.3</td>
<td>13.8</td>
</tr>
<tr>
<td>Female</td>
<td>20.0</td>
<td>14.0</td>
</tr>
<tr>
<td>Male</td>
<td>6.8</td>
<td>9.5</td>
</tr>
<tr>
<td>12</td>
<td>4.8</td>
<td>11.3</td>
</tr>
<tr>
<td>13</td>
<td>8.8</td>
<td>16.3</td>
</tr>
<tr>
<td>14</td>
<td>11.8</td>
<td>16.9</td>
</tr>
<tr>
<td>15</td>
<td>17.2</td>
<td>16.9</td>
</tr>
<tr>
<td>16</td>
<td>16.9</td>
<td>16.9</td>
</tr>
<tr>
<td>17</td>
<td>18.5</td>
<td>16.9</td>
</tr>
</tbody>
</table>

(Image of bar chart showing the prevalence rates for different demographics.)
Prepubertal MDD – under 3% with even sex ratio

**Comorbidity**
ADHD 40-90%
ODD or Conduct Disorder 30-76%
Substance Use Disorders 30-40%
Anxiety Disorders 36%
History of Controversy

- Do chronically irritable/explosive children have an early-onset variant of Bipolar Disorder? New diagnosis of Disruptive Mood Dysregulation Disorder (DMDD) with DSM-5 in 2013

- Do teenagers who start staying out late, become involved in sexual activity and are irritable at home have mania?

- Is early onset bipolar disorder rare or is timely diagnosis in children and adolescents rare?
Safety check: 
- Suicidality?
- Drug abuse?
- Current neglect/abuse?

Diagnosis:
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Maybe:

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Reconsider other etiologies like ADHD, PTSD, ODD, or Disruptive Mood Dysregulation Disorder: please see Disruptive Behavior section of this guide for behavior management guidance.
Clinical Interview

- Increased goal directed activity
- Decreased need for sleep and increased energy
- Flight of ideas and distractibility
- Grandiosity
- Hypersexuality
Rating Scales

- Mood Disorder Questionnaire (MDQ)
- Young Mania Rating Scale, Parent Version (P-YMRS)
- General Behavior Inventory (GBI, PGBI-10M)
- Child Mania Rating Scale, Parent Version (CMRS-P)
Treatment:

1. Consider consultation with a mental health specialist, especially if safety concerns.
2. Consider medical causes of manic symptoms like hyperthyroidism, neurological dysfunction.
3. Psychosocial/behavioral intervention tailored to family, including:
   a. family psychoeducation
   b. child/family focused CBT
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4. Medication trial, single agent preferred, choose among:
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   b. lithium
   c. lamotrigine (especially if bipolar depression)
   d. divalproex, carbamazepine also options, though have less evidence basis
5. Be cautious of prescribing antidepressants (manic switching risk).
6. Follow up frequently, perhaps weekly until stabilizing.
7. Ensure adequate sleep hygiene — consider sleep medications if necessary.
Evidence Based Therapies

• Child- and Family-Focused Cognitive-Behavioral Therapy (CFF-CBT)

• Family-Focused Therapy (FFT)

• Social Rhythm Therapy (SRT)

• Dialectical Behavior Therapy (DBT) – Emphasis on emotion regulation and suicide prevention
Elements of Effective Therapies

- Patient education
- Good sleep hygiene and enhanced circadian rhythms
- Stress reduction, skill development
- Substance abuse prevention
- Managing suicide risk
- Focus on treatment adherence (loss of hypomania)
- Family conflict reduction
Evidence base on bipolar medications is for narrow phenotype, or classic Bipolar I or II. Broad phenotype, or Bipolar Not Elsewhere Classified has not been well researched in children.
Why treat other/comorbid disorders first?

• Medication treatments for ADHD, anxiety and depression have strong evidence base and are safe.

• Medication treatments for bipolar disorder are often higher risk with greater monitoring burden
# Atypical Antipsychotics

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosage Form</th>
<th>Usual Starting Dose</th>
<th>Sedation</th>
<th>Weight Gain</th>
<th>EPS (stiff muscles)</th>
<th>Bipolar (+) child RCT evidence?</th>
<th>FDA bipolar approved?</th>
<th>Editorial Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risperidone (Risperdal)</td>
<td>0.25, 0.5, 1, 2, 3, 4mg/ml</td>
<td>0.25mg QHS</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Yes</td>
<td>Yes (Age ≥10)</td>
<td>Generic forms. More dystonia risk than rest</td>
</tr>
<tr>
<td>Aripiprazole (Abilify)</td>
<td>2, 5, 10, 15, 25, 30mg/ml</td>
<td>2mg QD</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>Yes</td>
<td>Yes (Age ≥10)</td>
<td>Generic forms. Long 1/2 life, can take weeks to build effect, more weight gain than for adults</td>
</tr>
<tr>
<td>Quetiapine (Seroquel)</td>
<td>25, 50, 100, 200, 300, 400mg</td>
<td>25mg BID</td>
<td>++</td>
<td>+</td>
<td>+/-</td>
<td>Yes</td>
<td>Yes (Age ≥10)</td>
<td>Generic forms. Pills larger, could be hard for kids to swallow.</td>
</tr>
<tr>
<td>Ziprasidone (Geodon)</td>
<td>20, 40, 60, 80mg</td>
<td>20mg BID</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>Yes</td>
<td>No</td>
<td>Generic forms. Greater risk of QT lengthen, EKG check</td>
</tr>
<tr>
<td>Olanzapine (Zyprexa)</td>
<td>2.5, 5, 7.5, 10, 15, 20mg</td>
<td>2.5 mg QHS</td>
<td>++</td>
<td>++</td>
<td>+/-</td>
<td>Yes</td>
<td>Yes (Age ≥13)</td>
<td>Generic forms. Greatest risk of weight gain, increased cholesterol</td>
</tr>
<tr>
<td>Asenapine (Saphris)</td>
<td>Sublingual 2.5, 5, 10mg</td>
<td>2.5 mg SL BID</td>
<td>++</td>
<td>+/-</td>
<td>+/-</td>
<td>Yes</td>
<td>Yes (Age ≥10)</td>
<td>Oral paresthesias, must dissolve in mouth</td>
</tr>
<tr>
<td>Lurasidone (Latuda)</td>
<td>20, 40, 60, 80, 120mg</td>
<td>20 mg QD</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>Yes</td>
<td>Yes (Age ≥10)</td>
<td>Take with food</td>
</tr>
</tbody>
</table>
Lurasidone (Latuda)

• Should be taken with food (350 calories)

• Approved for treatment of depressed phase

• Akathisia is common side effect
Monitoring for all atypical antipsychotics:

1. Weight checks and fasting glucose/lipid panel roughly every 6 months.

2. If weight gain is severe, will need to change treatments.

3. AIMS exam at baseline and Q6months due to risk of tardive dyskinesia that increases with duration of use.

4. Review neuroleptic malignant syndrome risk before starting medication.

5. Discuss dystonia risk, and explain the use of diphenhydramine if needed as antidote.
## Other Medication Options

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Bipolar (+) RCT evidence in kids</th>
<th>FDA bipolar approved children?</th>
<th>Monitoring</th>
<th>Editorial Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>Yes</td>
<td>Yes (Age ≥7)</td>
<td>Baseline EKG, BUN/creat, TSH, CBC. Lithium level after 5 days. Q3month Lithium level. Q6mo TSH,BUN/creatinine CBC level checks needed</td>
<td>Sedating, weight gain, renal and thyroid toxicity. If dehydration can get acute toxicity. Reduces suicide risk though an overdose can be fatal</td>
</tr>
<tr>
<td>Valproate</td>
<td>No</td>
<td>No</td>
<td>CBC, LFT at baseline, in 3 month, then Q6-month. VPA level checks needed</td>
<td>Weight gain, sedation, rare severe toxicity of liver, ↓platelets ↓WBC, risk of polycystic ovarian syndrome</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>No</td>
<td>No</td>
<td>CBC, LFT at baseline, then every 3-6 months. CBZ level checks needed</td>
<td>Aplasia and rash risk. Oxcarbazepine bipolar trial with kids had negative results</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>No</td>
<td>No</td>
<td>CBC, LFT at baseline, in 2-4 weeks, then Q6-month. Monitor for rash</td>
<td>Stevens-Johnson rash risk requires slow titration, adult studies support use for bipolar depression</td>
</tr>
</tbody>
</table>
Targeted Treatment

- Mania and mixed episodes – Atypical antipsychotics (except lurasidone), Lithium
- Bipolar Depression – Lurasidone, Olanzapine+Fluoxetine, Quetiapine*
- Maintenance (episode prevention) – Lithium, Lamotrigine*
Lithium

- Toxicity and side effects typically dose (blood level) related. Acute treatment 0.8-1.2 mEq/L, maintenance 0.4-0.8 mEq/L (10-14 hour trough)
- Typical dosing 900 to 1800 mg/day
- GI upset common – controlled release formulations and slow titration help
- No NSAIDs
- Polyuria
- May need to supplement thyroid
- Tends to increase WBC counts
Lamotrigine

Follow recommended titration to minimize risk of Stevens-Johnson Syndrome

- For adults: 25 mg x 2 weeks, 50 mg x 2 weeks, 100 mg x 1 week, then 200 mg target dose

- Repeat titration after period off lamotrigine

- Stop for rash – unfortunately, benign rashes are not uncommon
Treating Comorbid Symptoms

• Anxiety – rule out residual mania or medication side effect.

• ADHD – Stimulants usually not destabilizing, but watch for worsening sleep. Atomoxetine can precipitate mania. Guanfacine and clonidine are usually well tolerated.

• Antidepressants – try to avoid, especially without concurrent mood stabilizer.

• Addition of fluoxetine will increase levels of aripiprazole and risperidone.
Course of Illness

• Children and adolescents may have prodromal symptoms for years before onset of mania.

• Major depressive episodes may precede first mania/hypomania.

• A substantial proportion (25%-30%) of youth with bipolar I or II disorder maintain euthymic states over extended periods of follow-up.