Diagnosis and Treatment of Bipolar Disorder

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Points to Cover

• What is the defining characteristic of Bipolar Disorder?
• Bipolar I vs. Bipolar II
• Strategies for the treatment of Mania, Hypomania, and Mixed Episodes
• Strategies for the treatment of Bipolar Depression
What is Bipolar?

- Newer term for Manic Depression
- Mood disorder characterized by acute exacerbations of mania, hypomania, and depression.
- Familial illness
- Significant morbidity and mortality
Clinical Picture

- Lifetime prevalence of 2-5%
- Age of onset: 10-20% before 10 years of age; up to 60% before age 20.
- Gender difference: equally common in males and females
- Course of illness: chronic and recurrent
- Risk factors: increased 8-10 fold in first-degree relatives of bipolar adults relative to community samples.
  - Offspring of parents with bipolar are also at high risk to develop depression, anxiety, ADHD, and behavioral problems.
- Diagnostic challenge
DSM-V Criteria

Manic Episode

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood, and abnormally and persistently increased goal-directed activity or energy lasting at least one week (or any duration if hospitalization is necessary)

B. Three or more of the following symptoms (for if the mood is only irritable) are present to a significant degree and represent a noticeable change from usual behavior:
   1. Inflated self-esteem or grandiosity
   2. Decreased need for sleep
   3. More talkative than usual, or pressure to keep talking
   4. Flight of ideas, or subjective experience that thoughts are racing
   5. Distractibility, as reported or observed
   6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (i.e. purposeless, non-goal-directed activity)
   7. Excessive involvement in activities that have a high potential for painful consequences (e.g. engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

C. Marked Impairment in social or occupational functioning, or need to hospitalize, or presence of psychotic features.
DSM-V Criteria

D. The episode is not attributable to the physiological effects of a substance (e.g. drug of abuse, a medication, other treatment) or to another medical condition.

- Mnemonic: GRAPES(+D)
  - G: Grandiosity
  - R: Racing thoughts
  - A: Activity level
  - P: Pressured speech
  - E: Elevated mood
  - S: Sleeping less
  - D: Distractibility
# DSM-V Criteria

## Table 2 – Mania and hypomania diagnostic criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Mania&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Hypomania&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum timeframe for diagnosis</td>
<td>1 week</td>
<td>4 days</td>
</tr>
<tr>
<td>Number of symptoms for diagnosis</td>
<td>At least 3</td>
<td>At least 3</td>
</tr>
<tr>
<td>Grandiosity</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Decreased need for sleep</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>More talkative</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Flight of ideas</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Distractibility</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Increased goal-directed activity</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Risky behavior</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Marked impairment of social/occupational functioning</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Psychotic features</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>May require hospitalization</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<sup>a</sup> More severe.

<sup>b</sup> Less severe.

Adapted from DSM-5.
Major Depressive Episode

- **A.** Five or more of the following symptoms have been present during the same two week period and represent a change from previous functioning, at least one of the symptoms is either depressed mood or loss of interest/pleasure.
  - 1. Depressed mood, as indicated by either subjective report or observations by others.
  - 2. Markedly diminished interest or pleasure in almost all activities (as indicated either by subjective accounts or observation).
  - 3. Significant weight loss or gain, or increase or decrease in appetite. (Also, failure to make expected weight gain in children).
  - 4. Insomnia or hypersomnia.
  - 5. Psychomotor agitation or retardation (observable by others).
  - 6. Fatigue or loss of energy.
  - 7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional).
  - 8. Diminished ability to think or concentrate, or indecisiveness (either by subjective account or observed by others).
  - 9. Recurrent thoughts of death, recurrent suicidal ideation with or without specific plan, or a suicide attempt.


- **B.** Symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

- **C.** The episode is not due to the physiological effects of substance or another medical condition.
Assessment

- HPI (identify manic or depressive episodes first)
- Drug use history, family/genetic history, medical conditions, medications
- Collateral info – Family Members
- Screening Tools – MDQ (Mood Disorder Questionnaire); score 7 and above → confirms
# Mood Disorder Questionnaire (MDQ)

**Name:** ___________________________  **Date:** ___________________________

**Instructions:** Check (○) the answer that best applies to you. Please answer each question as best you can.

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Has there ever been a period of time when you were not your usual self and...</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...you were so irritable that you shouted at people or started fights or arguments?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...you felt much more self-confident than usual?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...you got much less sleep than usual and found you didn’t really miss it?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...you were much more talkative or spoke faster than usual?</td>
<td></td>
<td></td>
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<tr>
<td>...thoughts raced through your head or you couldn’t slow your mind down?</td>
<td></td>
<td></td>
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<tr>
<td>...you were so easily distracted by things around you that you had trouble concentrating or staying on track?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...you had much more energy than usual?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...you were much more active or did many more things than usual?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...you were much more interested in sex than usual?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...spending money got you or your family in trouble?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time? Please check 1 response only.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. How much of a problem did any of these cause you — like being able to work; having family, money, or legal troubles; getting into arguments or fights? Please check 1 response only.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No problem</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>4. Have any of your blood relatives (e.g., children, siblings, parents, grandparents, aunts, uncles) had manic-depressive illness or bipolar disorder?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This questionnaire should be used as a starting point. It is not a substitute for a full medical evaluation. Bipolar disorder is a complex illness, and an accurate, thorough diagnosis can only be made through a personal evaluation by your doctor.

For Bipolar I diagnosis – one needs a manic episode ± hypomanic or depressive episodes
For Bipolar 2 diagnosis – one needs a hypomanic episode and a depressive episode.
*Mixed Episodes/Rapid Cycling
Distinguishing Bipolar Depression from MDD

- Family history of bipolar disorder
- Earlier onset of illness
- Antidepressant misadventures (mood switches)
- Reverse neurovegetative symptoms (hypersomnia and increased appetite)
- History of postpartum depression
- Psychotic features
- Mixed episode presentations
- History of suicide attempts
- Mood reactivity
Differential Diagnosis

- Schizophrenia
- Schizoaffective Disorder
- Cyclothymic Disorder
- Major Depressive Disorder
- Substances (Methamphetamine, cocaine)
- Medications (Steroids, etc.)
- Medical Conditions (Hyperthyroidism, MS)
- ADHD / Borderline Personality Disorder
Treatment Options

Management of Mania and Hypomania

- Assess need for hospitalization
- For mild to moderate manic or mixed episodes and hypomania - first line monotherapies are
  - Lithium
  - Valproate
  - Second-generation antipsychotics
  - These could also be used in various combinations (e.g. lithium or valproate with antipsychotic)
<table>
<thead>
<tr>
<th>Drug</th>
<th>Bipolar mania</th>
<th>Usual dose range (mg)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>A, A</td>
<td>600-2400</td>
<td>Usual therapeutic serum range: 0.8-1.2 mEq/L for acute mania; teratogenic potential; requires ongoing monitoring of weight, renal and thyroid function</td>
</tr>
<tr>
<td>Divalproex</td>
<td>A</td>
<td>750-2000</td>
<td>Usual therapeutic serum range: 50-125 µg/L for acute mania; teratogenic potential; requires ongoing monitoring of weight, CBC count, LFTs, and menstrual history</td>
</tr>
<tr>
<td>Divalproex ER</td>
<td>A, B</td>
<td>750-2000</td>
<td>Usual therapeutic serum range: 85-125 µg/L for acute mania; teratogenic potential; requires ongoing monitoring of weight, CBC count, LFTs and menstrual history</td>
</tr>
<tr>
<td>Carbamazepine XR</td>
<td>A, B</td>
<td>800-1600</td>
<td>Possible therapeutic serum range: 4-12 µg/mL; requires ongoing monitoring of weight, CBC count, LFTs, electrolytes; several AEs; teratogenic potential and drug-interaction issues limit usefulness</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>A</td>
<td>200-800</td>
<td>Approval not based on present-day FDA criteria</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>A, B, C, D</td>
<td>5-20</td>
<td>Sedation; cardiometabolic AEs</td>
</tr>
<tr>
<td>Risperidone</td>
<td>A, B, C</td>
<td>1-6</td>
<td>Neuromotor AEs; hyperprolactinemia</td>
</tr>
<tr>
<td>Risperidone LAI</td>
<td>A, A, C</td>
<td>25-50</td>
<td>May resolve absorption and adherence issues; may be used as monotherapy or in combination with lithium or divalproex; hyperprolactinemia</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>A, C, D</td>
<td>400-800</td>
<td>Sedation and cardiometabolic AEs</td>
</tr>
<tr>
<td>Quetiapine XR</td>
<td>A, B, C</td>
<td>400-800</td>
<td>Sedation and cardiometabolic AEs</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>A, B</td>
<td>80-800</td>
<td>Cardiometabolic risks reduced</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>A, B, C, D, E</td>
<td>5-30</td>
<td>Agitation/anxiety; akathisia; cardiometabolic risks reduced</td>
</tr>
<tr>
<td>Asenapine</td>
<td>A, B, C</td>
<td>10-20</td>
<td>Sublingual formulation only</td>
</tr>
</tbody>
</table>

A, monotherapy; B, mixed states; C, adjunct to lithium or valproate; D, pediatric/adolescent; E, acute parenteral.

CBC, complete blood cell; LFT, liver function test; ER, extended release; XR, extended release; AEs, adverse effects; LAI, long-acting injectable.

*Every 2 weeks.*
Treatment Recommendations

- Second-line therapy for Mania and Hypomania
  - Other anticonvulsants, like carbamazepine and oxcarbazepine, with or without an antipsychotic
- Blood levels for anticonvulsants
- Maintenance treatment
  - Same medications can be continued
  - Long-acting injectables of second-generation antipsychotics
  - Clozapine and ECT
- Psychotherapy (CBT, family focus therapy, psychoeducation, interpersonal therapy)
Treatment Options for Bipolar Depression

- The three FDA-approved Acute Bipolar Depression therapies
  - Olanzapine – Fluoxetine combination
  - Quetiapine monotherapy ± lithium or valproate
  - Lurazidone as monotherapy or ± lithium or valproate

- Other treatment options or strategies: lithium, valproate, carbamazepine, ECT, antidepressants (controversial)

- Antidepressants – avoid in Bipolar I patients, those with mixed episodes or rapid cyclers, those with comorbid substance abuse, and should only be considered after better supported approaches prove insufficient and only in combination with a mood stabilizer

- FDA-Approved Medication for Maintenance
  - Lamictal
Future Directions

Studies in the Pipeline

- Genetic and neuroimaging findings
- Immune System
- The role of oxidative stress
- Dopamine and glutamate systems
- Disruptions in biological rhythms
References

- Baldassaro, Claudia; Chengappa MD, Roy; and Perlis, Roy. *Managing Bipolar Mania*.
Post-Test Questions

- True or False:
  1. The presence of mania or hypomania is the defining characteristic of bipolar disorder.
  2. Bipolar I disorder distinguishes itself from Bipolar II by meeting the criteria for a full manic episode.
  3. Bipolar II must meet criteria for both hypomanic and depressive episodes.
  4. Lithium, valproate, and second-generation antipsychotics, in monotherapy or in various combinations, can be used to treat mania, hypomania, and mixed episodes.
  5. There are only four FDA-approved medications for treatment of bipolar depression.