Bipolar Disorder: Diagnosis and Management

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Objectives

- Know the epidemiology of bipolar disorder

- Diagnose bipolar disorder and know when and how to rule out medical causes

- Initiate first line pharmacologic treatment for different phases of bipolar disorder

- Refer patients with bipolar disorder when appropriate
Major Depressive Episode

<table>
<thead>
<tr>
<th>S</th>
<th>Sleep changes (increase or decrease)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>loss of Interest</td>
</tr>
<tr>
<td>G</td>
<td>excessive feelings of Guilt</td>
</tr>
<tr>
<td>E</td>
<td>loss of Energy</td>
</tr>
<tr>
<td>C</td>
<td>difficulty Concentrating</td>
</tr>
<tr>
<td>A</td>
<td>changes in Appetite (increase or decrease)</td>
</tr>
<tr>
<td>P</td>
<td>Psychomotor slowing or agitation</td>
</tr>
<tr>
<td>S</td>
<td>Suicidal thoughts</td>
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2 weeks or more of **depressed mood or loss of interest in pleasurable activities** with 5 or more symptoms.
Manic Episode

One week or more of elevated or irritable mood and increased energy and at least 3 of the following

D = Distractibility
I = Irresponsibility and erratic uninhibited behavior
G = Grandiosity
F = Flight of ideas
A = Increased goal-directed activity
S = Decreased need for sleep
T = Talkativeness
Other possible signs of mania

- Increased religious preoccupation
- Increased sexual behavior
- Intrusive behavior
- Labile or rapidly shifting mood or affect
- Poor insight
- Psychotic features: delusions and hallucinations
Hypomaniac Episodes

- Less severe
- No psychosis
- Not severely impairing
- Does not require hospitalization
- May be as short as only 4 days
Mixed Episodes

- Some people may meet criteria for either a depressive or manic episode but simultaneously have several features of the other.

- For example, a person may meet criteria for depression but have decreased need for sleep, racing thoughts, and engage in high-risk activities, such as spending sprees or sexual affairs.
Bipolar Disorder Spectrum

- Bipolar I: major depressive and manic episodes
- Bipolar II: major depressive and hypomanic episodes
- Cyclothymic Disorder: mild depressive and hypomanic episodes

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*Manning JS, Ahmed S, McGuire HC, Hay DP. Mood Disorders in Family Practice: Beyond Unipolarity to Bipolarity Prim Care Companion J Clin Psychiatry*
Psychotic Mood Episodes

- Usually mood congruent
- Typically occur in more severe episodes
- May result in misdiagnosis and schizophrenia
Epidemiology

- Bipolar I prevalence approximately 0.5-1%
- Bipolar II prevalence as high as 5%
- Family history is a significant risk factor

Epidemiology

- Age of onset usually around age 18-25
- May take years to be properly diagnosed
- Late onset may be an indication of another diagnosis or medical condition

From: Prevalence and Correlates of Bipolar Spectrum Disorder in the World Mental Health Survey Initiative

Cumulative age-at-onset distributions of bipolar disorder type I (BP-I), bipolar disorder type II (BP-II), and subthreshold bipolar disorder (BP) among respondents projected to develop these disorders in their lifetime.
Suicide Risk

- Suicide risk is 6-15% (up to 15-20x greater than general population)

- Risk factors:
  - History of suicide attempts
  - Family history of suicide
  - Substance abuse
  - Anxiety
  - More severe depression
  - Higher impulsivity
More than 90% of people who have a manic episode go on to have additional mood episodes.

Depressive episodes often follow resolution of manic episodes.

Most people experience more time in depressive episode than manic.
Differential Diagnosis

- Unipolar depression
- Schizoaffective Disorder or Schizophrenia
- Anxiety
- ADHD
- Personality Disorders
- Dementia
- Substance induced mood disorders
- Medical conditions
Diagnostic Challenges

- Poor insight
  - Manic/hypomanic patients often don’t see symptoms as a problem
  - Often unable to accurately report symptoms even after episode

- Depressive episodes more common
  - Treating bipolar as unipolar likely to be ineffective

- Co-morbid substance abuse
# Medical Conditions and Substances

<table>
<thead>
<tr>
<th>Depression</th>
<th>Mania</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endocrine</strong>: Hypothyroidism, Hypoparathyroidism, Cushing’s disease, Addison’s disease, Diabetes</td>
<td><strong>Endocrine</strong>: Cushing’s disease</td>
</tr>
<tr>
<td><strong>Rheum</strong>: Rheumatoid Arthritis, Lupus</td>
<td><strong>Neuro</strong>: Multiple sclerosis, Brain injury or CVA, especially frontal lobe</td>
</tr>
<tr>
<td><strong>Neuro</strong>: Multiple Sclerosis, Parkinson’s disease, brain injury or CVA</td>
<td><strong>Substances</strong>: cocaine, stimulants, steroids</td>
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<tr>
<td><strong>Cardiovascular</strong>: CHF, CAD</td>
<td></td>
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<tr>
<td><strong>Malignancies</strong>: pancreatic and GI</td>
<td></td>
</tr>
<tr>
<td><strong>Substances</strong>: alcohol, benzos, interferon, steroids, cocaine or stimulant withdrawal</td>
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Treating acute mania/hypomania

- Assess for suicidality, aggression, psychosis or dangerous behavior and consider psychiatric hospitalization or referral to psychiatrist
- Stop antidepressants
- Assess compliance and drug levels if available and optimize dose
- Begin monotherapy or combination therapy with a first line mood stabilizing agent
- If already optimized on a first line agent, add another first line agent

Mood Stabilizers

First line

- Lithium
- Divalproex
- Atypical Antipsychotics: Olanzapine, Quetiapine, Risperidone, Paliperidone, Aripiprazole, Asenapine

Combination therapy: Lithium or divalproex + atypical antipsychotic
Mood Stabilizers

Second line and third line
- Carbamazepine, oxcarbazepine, ECT, typical antipsychotics (haloperidol, chlorpromazine), clozapine

Not recommended: gabapentin, topiramate, lamotrigine
Lithium

- Benefits: strong evidence of efficacy in all phases of bipolar disorder, neuroprotective, decreases suicide risk

- Dosing:
  - Start 300-600mg TID (immediate release) or 900-1800mg qhs (extended release)
  - Target blood level: 0.6-1.2 (lower in geriatric population)
    - Trough level 4-5 days after last dose adjustment

- Drug interactions: NSAIDS, ACE inhibitors, diuretics

- Toxicity: GI side effects, tremor, altered mental status, muscle weakness, ataxia, blurred vision, tinnitus
Lithium

- Contraindications: Use with caution (if at all) in renal insufficiency, cardiovascular disease, dehydration

- Adverse Effects:
  - nephrotoxicity
  - diabetes insipidus
  - hypothyroidism
  - cardiovascular effects (bradycardia, brugada syndrome, sinus node dysfunction)
  - Common side effects: tremor, nausea/vomiting, weight gain, hair loss, acne
Divalproex Sodium

- **Benefits**: rapidly effective in acute mania, mixed episodes and maintenance phase, less toxicity than lithium

- **Dosing**:
  - Start 250mg TID (delayed release or valproic acid), 750mg qhs or 20mg/kg (extended release)
  - Lower and slower in geriatrics
  - Target blood level: 50-125mcg/ml

- **Drug interactions**: Warfarin, other AEDs (carbamazepine, lamotrigine, phenytoin), antipsychotics (olanzapine, risperidone), antibiotics (meropenem)
Divalproex Sodium

- Contraindications: liver dysfunction, pregnancy

- Adverse Effects:
  - Hepatic failure or mild to moderate elevation of LFTs
  - Hyperammonemia +/- encephalopathy
  - Pancreatitis
  - Neural tube defects in pregnancy
  - Thrombocytopenia or myelodysplasia
  - Suicidal thoughts
  - Common side effects: nausea, vomiting, diarrhea, sedation, weight gain, dizziness, HA, tremor
Atypical Antipsychotics

- **Benefits**: No blood levels, less toxicity, long acting injectable formulations (risperidone, paliperidone, aripiprazole)

- **Dosing**:
  - Olanzapine: 10mg qhs, titrate up to 20mg/day
  - Risperidone: 2mg qhs, titrate up to 6mg/day
  - Quetiapine: 50mg BID (immediate) or 300mg qhs, titrate quickly to 400-800mg
  - Aripiprazole: 15mg daily, titrate up to 30mg/day
  - Ziprasidone: 40mg BID, up to 80mg BID
  - Paliperidone: 6mg daily, up to 12mg/day
Atypical Antipsychotics

- Contraindications: Use with caution in obese or diabetic

- Adverse Effects:
  - Weight gain, metabolic syndrome (greatest with olanzapine, least with aripiprazole)
  - Extrapyramidal symptoms (greatest with risperidone, least with quetiapine or clozapine)
  - Sedation (greatest with quetiapine, least with aripiprazole)
  - QTc prolongation (greatest with ziprasidone, least with aripiprazole)
  - Increased mortality in dementia (all)
  - GI side effects
Management of an acute depressive episode

- Assess for suicidality/self-harm, ability to function and adhere to treatment plan and consider psychiatric hospitalization or referral to psychiatrist

- Begin one or more first line agents

- If on a first line agent, compliant and dose optimized, then add or switch to another first line agent or combination
Management of acute depressive episode

First line

- Monotherapy: lithium, lamotrigine, quetiapine

- Combination therapy: SSRI + lithium or divalproex or olanzapine, lithium + divalproex, bupropion + lithium or divalproex
Management of acute depressive episode

Second line

- Monotherapy: divalproex, lurasidone (atypical antipsychotic)
- Combination: SSRI + quetiapine, lithium or divalproex + lamotrigine, lithium or divalproex + lurasidone, lithium or divalproex + SNRI

Not recommended: aripiprazole, ziprasidone, gabapentin
Antidepressants

- May lead to manic switch
- SSRIs have good efficacy and favorable side effect profile
  - GI side effects, sexual side effects, HA, hyponatremia
- Bupropion
  - Fewer sexual side effects than SSRIs but more likely to cause agitation or worsening psychosis
- SNRIs may have higher rate of switching
- Tricyclic antidepressants effective but have narrow therapeutic window, cardiac and anticholinergic side effects
Lamotrigine

- Benefits: efficacy in bipolar depression/maintenance, particularly preventing depressive episodes

- Dosing: 25mg/day, double dose every 2 weeks until 200mg
  - Double doses if using enzyme inducing AEDs (carbamazepine)
  - Half doses if using divalproex
Lamotrigine

- **Contraindications:** Use with caution in renal insufficiency

- **Adverse Effects:**
  - Rash, including Steven Johnson’s, erythema multiforma
  - Blood dyscrasias
  - Suicidality
  - Liver failure
  - Common side effects: GI side effects, dizziness
Maintenance therapy

- First Line Pharmacotherapy: lithium, lamotrigine (mostly in bipolar II), divalproex, olanzapine, quetiapine, long acting risperidone, aripiprazole, atypical antipsychotic + lithium or divalproex

- Improve Adherence
  - Psychoeducation
  - Family involvement
  - Monitoring of side effects

- Refer for psychotherapy
  - CBT, family therapy, interpersonal and social rhythm therapy
Non-medication Interventions

- Promote good sleep
- Develop consistent routine
- Engage in calm interactions and avoid intense emotions
- Recognize early signs
- Family involvement
Crisis

- Allegheny re:solve (888) 796-8226
- Armstrong/Indiana: (877) 333-2470
- Beaver: (800) 400-6180, press 1
- Blair: (814) 889-2141
- Butler: (800) 292-3866
- Cambria: (877) 268-9463
- Erie: (800) 300-9558
- Fayette: (724) 437-1003
- Greene: (800) 417-9460
- Lawrence: (724) 652-9036
- Mercer: (724) 662-2227
- Somerset: (866) 611-6467
- Venango: (814) 432-9111
- Washington: (877) 225-3567
- Westmoreland: (800) 836-6010
- National Suicide Prevention Lifeline: 1-800-273-TALK (8255)
- National Hopeline Network: 1-800-SUICIDE (800-784-2433)
- Emergency: 911
References

