Bipolar Disorders

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Bipolar Disorders and Treatment

- Epidemiology and Impact
  - module 2 session 1 “overview of mood disorders”
- Diagnostic Criteria of Bipolar Disorders
- Medications Used in Bipolar Disorders
- Episode Specific Treatment Strategies
Bipolar Disorders

- Bipolar I Disorder
- Bipolar II Disorder
- Cyclothymic Disorder
- Substance or Medication Induced Bipolar Disorder
  - module 2 session 4
- Bipolar Disorder Due to Another Medical Condition
  - module 2 session 4
Diagnostic Criteria
Manic Episode

- 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 1 week and present most of the day, nearly every day.

- During the period of mood disturbance and increased energy or activity, three or more of the following symptoms are present to a significant degree and represent a noticeable change from usual behavior.
  - If the mood state is irritable then four symptoms are required.
    - Inflated self-esteem or grandiosity
    - Decreased need for sleep
    - Hypervocal or pressured speech
    - Flight of Ideas or subjective racing thoughts
    - Distractiblity
    - Increased goal-directed activity or psychomotor agitation
    - High risk activities
Hypomanic Episode

- 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 4 days and present most of the day, nearly every day.

- During the period of mood disturbance and increased energy or activity, three or more of the following symptoms are present to a significant degree and represent a noticeable change from usual behavior.
  - If the mood state is irritable then four symptoms are required.
    - Inflated self-esteem or grandiosity
    - Decreased need for sleep
    - Hypervocal or pressured speech
    - Flight of Ideas or subjective racing thoughts
    - Distractibility
    - Increased goal-directed activity or psychomotor agitation
    - High risk activities

- The episode is not severe enough to cause marked impairment in school or occupational functioning or necessitate hospitalization. If there are psychotic features, the episode is, by definition, manic.
Bipolar I Disorder

- Criteria have been met for at least one manic episode.
- The occurrence of the manic episode is not better explained by schizoaffective disorder.
- Diagnostic coding: type of current or most recent episode, severity, presence of psychotic features, and remission status.
Bipolar II Disorder

- Criteria have been met for at least one hypomanic episode and at least one depressive episode.
- There has never been a manic episode.
- The occurrence of the hypomanic and depressive episodes are not better explained by schizoaffective disorder.
- The symptoms of depression or the unpredictability caused by frequent alternation between periods of depression and hypomania causes clinically significant distress or impairment.

- Diagnostic coding: type of current or most recent episode, severity, presence of psychotic features, and remission status.
Cyclothymic Disorder

- For at least 2 years there have been numerous periods with hypomanic symptoms that do not meet criteria for a hypomanic episode and numerous periods with depressive symptoms that do not meet criteria for a major depressive episode.

- During the above 2-year periods, the hypomanic and depressive periods have been present for at least half the time and the individual has not been without the symptoms for more than 2 months at time.

- Criteria for a major depressive disorder, manic, or hypomanic episode have never been met.
Specifiers

- Manic or hypomanic episode, with mixed features:
  - Full criteria are met for a manic or hypomanic episode and at least three depressive symptoms are present during the majority of days of the current manic or hypomanic episode.

- Depressive episode, with mixed features:
  - Full criteria are met for a depressive episode and at least three manic or hypomanic symptoms are present during the majority of days of the current manic or hypomanic episode.

- For individuals whose symptoms meet full episode criteria for both mania and depression simultaneously, the diagnosis should be manic episode, with mixed features.
Specifiers

- Rapid cycling:
  - Presence of at least four mood episodes in the previous 12 months that meet criteria for manic, hypomanic, or depressive episode.
    - Episodes are demarcated by either partial or full remission of at least 2 months or a switch to an episode of the opposite polarity.
    - Except for the fact that they occur more frequently, the episodes that occur in rapid-cycling pattern are no different from those that occur in a non-rapid-cycling pattern.
Specifiers

- Anxious distress
- Melancholic features
- Atypical features
- Psychotic features
- Catatonia
- Seasonal pattern
Pharmacotherapy
Lithium

Established efficacy: acute mania and prevention of both mania and depression (although more effective in prevention of mania, NNT 8 vs 39).

- Lithium toxicity: confusion, ataxia, seizure, coma
- Adverse effects: hypothyroidism, polyuria, polydipsia, leukocytosis, dermatologic disorders, cognitive impairment, diabetes insipidus, renal complications, teratogenic (pregnancy category D), weight gain
- Serum concentration:
  - 0.8 -1.2: therapeutic goal for mania, 5 days after dose change
  - 1.2-1.5: warning for potential serious toxicity
  - 1.6-2.5: serious, but not considered life-threatening
  - >2.5: severe toxicity, medical emergency
- Monitoring:
  - Baseline: BMP, thyroid profile, pregnancy test
  - Annual: BMP, thyroid profile, CBC
# Lithium Drug Interactions

<table>
<thead>
<tr>
<th>Increases Lithium</th>
<th>Decreases Lithium</th>
<th>Other</th>
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<tbody>
<tr>
<td>• Thiazide diuretics</td>
<td>• Increased sodium intake</td>
<td>• Carbamazepine</td>
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<tr>
<td>• Furosemide</td>
<td>• Sodium bicarbonate antacids</td>
<td>• Methyldopa</td>
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<td>• Caffeine via diuresis</td>
<td>• Theophylline</td>
<td>• MAOIs</td>
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<td>• ACEIs</td>
<td>• Verapamil</td>
<td>• Diltiazem</td>
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<tr>
<td>• ARBs</td>
<td>• Osmotic diuretics</td>
<td>• Verapamil</td>
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<tr>
<td>• NSAIDs (except sulindac)</td>
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<td>• SSRIs</td>
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<td>• Reduced sodium intake</td>
<td></td>
<td>• Antipsychotics</td>
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</tbody>
</table>
Antiepileptic

- **Valproate**
  - Established efficacy: acute manic episodes and in maintenance for those patients whose acute episode responded to valproate
  - Adverse effects: weight gain, hepatotoxicity, hyperammonemia, thrombocytopenia, teratogenic (pregnancy category D)
  - Monitoring:
    - Baseline: CBC, LFT (also obtain at 1 and 3 months)
    - Annual: serum concentration, CBC, LFT, and electrolytes
    - Serum concentration: 50-125 mcg/ml, one week after dose change

- **Topiramate**
  - Ineffective treatment in acute mania, insufficient evidence in acute depression and maintenance treatments
Antiepileptic

- Carbamazepine
  - Established efficacy: acute manic episodes
  - Auto-induction of cytochrome P450 system
  - Adverse effects: ataxia, agranulocytosis, aplastic anemia, AV block, SIADH, Stephens-Johnson, thrombocytopenia
  - Serum concentration: 4-12 mcg/ml, every 2 weeks for 3 months
  - Monitoring
    - Baseline: CBC, LFT (at 1 and 3 months)
    - Annual: serum concentration, CBC, LFT, electrolytes

- Oxcarbazepine
  - Keto derivative of carbamazepine; does not require monitoring, less cytochrome p450 induction
  - Adverse effects: ataxia, agranulocytosis, aplastic anemia, AV block, SIADH, Stephens-Johnson, thrombocytopenia
Antiepileptic

- Lamotrigine
  - Established efficacy: adjunctive treatment in depressive episode and prevention of both mania and depression (although more effective in prevention of depression, NNT 11 vs 22)
  - Should not be used as monotherapy for acute mania.
  - Adverse effects: headache, cognitive impairment, Stephens-Johnson Syndrome (requires slow titration)
  - Pregnancy category C

- Gabapentin
  - Ineffective for acute mania and acute depression, no studies regarding maintenance
Antipsychotic

- First generation antipsychotic: efficacy in acute mania (anecdotal evidence of induced depression)
  - Haldol
  - Chlorpromazine

- Second generation antipsychotic: monotherapy or adjunctive therapy (combination use with lithium or antiepileptics produces a 20% increased response rate)
  - Olanzapine
  - Quetiapine
  - Ziprasidone
  - Risperidone
  - Aripiprazole
  - Lurasidone
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<th>Adverse Event</th>
<th>Aripiprazole</th>
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Antidepressants

- Clear evidence that antidepressants should not be used in acute manic episodes, monotherapy in depressive episodes, or monotherapy in maintenance treatment.

- There is some controversy when using antidepressants as adjunctive therapy in bipolar depression.
  - If used in this fashion, it is necessary to have lithium, valproate, or an atypical antipsychotic (preferably olanzapine or quetiapine) at a therapeutic level prior to initiation.
ECT

- Considered for manic patients who are severely ill or whose mania is treatment resistant, and patients with severe mania during pregnancy.
- ECT for bipolar disorder is indicated as the primary therapy in the following:
  - Psychotic symptoms
  - Catatonia
  - Severe suicidality
Episode Specific Treatments
- **Mania or Hypomania**
  - Lithium, valproate, carbamazepine, aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone
    - Chlorpromazine, FDA approved in 1973

- **Depression**
  - Quetiapine, lurasidone, or olanzapine/fluoxetine combination
    - Lithium with adjunctive lamotrigine

- **Mixed Episodes**
  - Carbamazepine, aripiprazole, olanzapine, risperidone, or ziprasidone
    - Valproate

- **Maintenance**
  - Monotherapies: lithium, lamotrigine, olanzapine, aripiprazole, and long-acting injectable risperidone
  - Combinations: quetiapine, ziprasidone, and long-acting injectable risperidone with lithium or valproate
Psychosocial Interventions
Psychoeducation

- Patient should receive psychoeducation that emphasizes:
  - The importance of active involvement in their treatment
  - The nature and course of their bipolar illness
  - The potential benefit and adverse effects of treatment options
  - The recognition of early signs of relapse
  - Behavioral interventions that can lessen the likelihood of relapse including careful attention to sleep regulation and avoidance of substance misuse.

- With the patient’s permission, family members or significant others should be involved in the psychoeducation process.

- A structured group format in providing psychoeducation and care management for patients with clinically significant mood symptoms should be considered.
Psychotherapy

- Cognitive Behavioral Therapy
- Interpersonal and Social Rhythm Therapy
- Family Therapy
Questions?