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

DSM 5

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
    - Hyperverbal 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
    - Hyperverbal or pressured speech
    - Flight of Ideas or subjective racing thoughts
    - Distractiblity
    - 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

Increases Lithium

- Thiazide diuretics
- Furosemide
- Caffeine via diuresis
- ACEIs
- ARBs
- NSAIDs (except sulindac)
- Reduced sodium intake

Decreases Lithium

- Increased sodium intake
- Sodium bicarbonate antacids
- Theophylline
- Verapamil
- Osmotic diuretics

Other

- Carbamazepine
- Methyldopa
- MAOIs
- Diltiazem
- Verapamil
- SSRIs
- Antipsychotics

Antiepileptic

- Valproate
  - Established efficacy: acute manic episodes and in maintenance for those patient whose acute episode responded to valproate
  - Adverse effects: weight gain, hepatoxicity, 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

Adverse Event	Aripiprazole	Clozapine	Olanzapine	Quetiapine	Risperidone	Ziprasidone
Anticholinergic effects	+	++++	+++	+	+	+
EPS	+	-	+	-	++	+
Hyperglycemia	+	++++	+++	++	+	-
Hyperlipidemia	+	++++	+++	++	+	-
Hyperprolactinemia	+	+	+	+	+++	+
NMS	+	+	+	+	+	+
Orthostatic Hypotension	+	+++++	+	+++	++	+
QTc prolongation	-	++	++	++	++	+++
Sedation	+	++++	+++	+++	++	+
Tardive dyskinesia	-	-	+	-	+	+
Weight gain	-	++++	+++	++	++	-

Antidepressants

- Clear evidence that antidepressants should be 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?