

Assessment and Management of Bipolar Disorder

Samar McCutcheon, MD
Clinical Assistant Professor
Department of Psychiatry
The Ohio State University Wexner Medical Center

Objectives

- Establish criteria for bipolar spectrum disorders
- Formulating an accurate diagnosis
- Review approaches to treatment

Why talk about Bipolar Disorder?

- 12th most common disabling condition
- 10 year lag in diagnosis and treatment
- *Potential* risk of using unopposed antidepressants
- Loss of healthy life years
- Increased risk for premature death

Definitions

- *Episodic* mood disorder characterized by mania, hypomania and/or depression
- Subtypes:
 - Bipolar I Disorder: mania
 - +/- hypomania and depressive episodes
 - Bipolar II Disorder: hypomania + depressive episode
 - No manic episodes
 - Other Specified Bipolar Disorder/Unspecified Bipolar Disorder

DSM-5 Criteria: Mania

- A) Distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least 1 week and present most of the day, nearly every day (*or any duration if hospitalization is necessary*)
- B) During the period of mood disturbance and increased energy or activity, three (or more) of the following symptoms (four if the mood is only irritable) are present to a significant degree and represent a noticeable change from usual behavior:

DSM-5 Criteria: Mania

- 1) Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed
- 2) Excessive involvement in activities that have a high potential for painful consequences (e.g. buying sprees, sexual indiscretions)- Impulsivity
- 3) Inflated self-esteem or Grandiosity

DSM-5 Criteria: Mania

- 4) Flight of ideas or subjective experience that thoughts are racing
- 5) Increase in goal-directed Activity (either socially, at work or school, or sexually) or psychomotor agitation (i.e., purposeless non-goal-directed activity)
- 6) Decreased need for Sleep (e.g. feels rested after only three hours of sleep)
- 7) More Talkative than usual or pressure to keep talking

DSM-5 Criteria: Mania

- C) The mood disturbance is sufficiently severe to cause *marked impairment in social or occupational functioning* OR to necessitate *hospitalization* to prevent harm to self or others OR there are *psychotic features*
- D) The episode is not attributable to the physiological effects of a substance or another medical condition

⇒ New disclaimer allows for diagnosis for antidepressant induced mania if the symptoms “persist beyond the physiological effect of that treatment”

DSM-5 Criteria: Hypomania

How does it compare to mania?

- Different in **DURATION** and **INTENSITY**

⇒ Time criteria: 4 days instead of 1 week

⇒ “Unequivocal change in functioning” but no marked impairment in functioning, no hospitalization and no psychotic features

DSM-5 Criteria: Depression

A) Five (or more) symptoms in a 2 week period with at least 1 of the symptoms being depressed mood or loss of interest/pleasure

1. Depressed mood
2. Sleep- Insomnia or hypersomnia
3. Diminished interest or pleasure in all or almost all activities
4. Feelings of worthlessness or excessive or inappropriate guilt
5. Fatigue or loss of energy

DSM-5 Criteria: Depression

6. Diminished ability to concentrate or indecisiveness
7. Significant weight loss when not dieting or weight gain (5% change in body weight) or a decrease or increase in appetite nearly every day
8. Psychomotor agitation or retardation observable by others
9. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or plan for committing suicide

DSM-5 Criteria: Depression

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

C) Symptoms are not attributable to the effects of a substance or to another medical condition

DSM-5 Episode Specifiers

Specifiers describing the clinical status of the current/most recent episode

- -Mild, Moderate, Severe, In Partial Remission, In Full Remission

Specifiers describing features of the current episode

- -With Anxious Distress
- **-With Mixed Features**
- **-With Rapid Cycling**
- -With Melancholic Features
- -With Atypical Features
- -With Mood-congruent Psychotic Features
- -With Mood-incongruent Psychotic Features
- -With Catatonia
- **-With Peripartum Onset**
- -With Seasonal Pattern

Key Clinical Features

- **Bipolar II disorder can cause more long term impairment**
- **In both Bipolar I and II, depressive episodes are most common and often hardest to treat**
- **With psychotic features, delusions are more common than hallucinations**
 - **Persecutory, sexual, religious, political**

Assessment of the Patient

Clinical Case:

John is a 23 year old male who is a newly established patient in the clinic and presents with report severe depression. On quick review of “SIGECAPS,” he is positive for all symptoms except suicidality. He has no previous mental health diagnoses on chart review.



Assessment of the Patient

Routine history should assess for:

- Depression
- Mania
- Hypomania
- Suicidal thoughts, behaviors or plan
- Risk factors for suicide attempts
- Psychotic features
- Co-morbidities

Assessment of the Patient

- Obtain collateral from the family
 - Don't forget, insight is often impaired during manic episodes
 - Ask about family history (again)

Assessment of the Patient

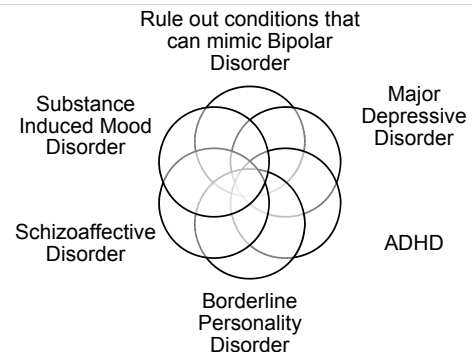
- Consider secondary (medical) causes of mania
 - **Drug abuse:** amphetamines, cocaine, MDMA, bath salts
 - **Medications:** amantadine, L-Dopa, captopril, corticosteroids, baclofen, cimetidine, antidepressants
 - **Infectious:** HIV, neurosyphilis
 - **Neurologic:** complex partial seizures, MS, TBI, Huntington's, tumors, frontotemporal dementia
 - **Systemic conditions:** B12 & niacin deficiencies, hyperthyroidism, Cushing's disease

Assessment of the Patient

- Should you use a bipolar screening tool?
 - **Mood Disorder Questionnaire**
 - Identifies ~ 67% of bipolar patients
 - False positive rate is ~ 20%
 - Less likely to catch Bipolar II diagnosis (sensitivity of 39%)
 - Strength is in specificity (approximately 90%)

Zimmerman 2012

Assessment of the Patient



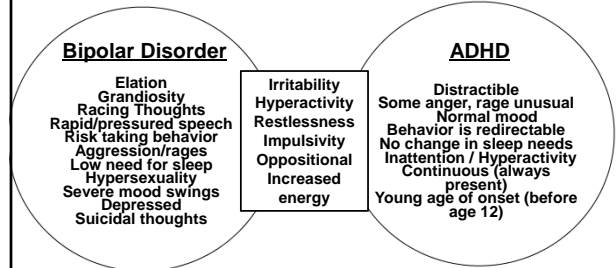
Assessment of the Patient

History features suggestive of Bipolar Disorder rather than Major Depressive Disorder

- Early age at onset
- Early depressive episodes
- Multiple recurrences of depressive episodes
- Poor antidepressant response history
- Positive family history of bipolar disorder
- Psychotic symptoms (particularly postpartum)
- Presence of co-morbid diagnoses
 - Anxiety disorder, Substance use disorders, Personality disorders

Moreno 2012

Assessment of the Patient



Assessment of the Patient

Ruling out Borderline Personality Disorder

- Prominence of *mood swings* that are much shorter duration than in bipolar disorder
- Clear inciting environmental triggers before episodes
- Underlying presence of unstable interpersonal relationships, chronic feelings of emptiness and efforts to avoid abandonment

Assessment of the Patient

Ruling out Schizoaffective Disorder:

Look for the presence of psychotic symptoms at baseline (in the absence of a current mood episode)

Ruling out Substance Induced Mood Disorder:

Screen for historical or ongoing substance use

Assessment of the Patient

- Special populations:
 - Rapid cycling
 - At least four mood episodes of a mood disturbance in the previous 12 months
 - *Has a poorer prognosis*
 - Risk factors: thyroid disorder, female sex, Bipolar II Disorder

Assessment of the Patient

- Special populations:
 - Pregnant women
 - Risk of postpartum psychosis
 - 0.1% in the general population
 - 26% in patients with bipolar disorder
 - 57% in patients with previous postpartum psychosis
 - Potential dangers to mom and baby

Assessment of the Patient

Comorbidity is the rule

- Anxiety Disorders (63%)
- Substance use disorders (40-60%)
- Personality Disorders (51%)
- ADHD (20-30%)
- Eating disorders (14%)
- Cardiovascular problems
- Type 2 diabetes mellitus and endocrine disorders
- Migraines and neurological conditions

Merikangas, 2007 Kilbourne, 2004

Assessment of the Patient

History from patient, John, reveals:

- 2 previous episodes of increased energy and activity, decreased need for sleep, pressured speech and elevated mood lasting for at least a week
- Age at onset of depressive episodes: 14
- No previous response to trials of fluoxetine or sertraline at therapeutic doses
- Collateral history from mom indicates she and her sister have a diagnosis of bipolar disorder



Assessment of the Patient:

- John's diagnosis is:
 - Bipolar I disorder, most recent episode depressed, severe, without psychotic features



Bipolar Disorder and Suicide

- 10-15% of patients with bipolar disorder die by suicide
- 2 major risk factors
 - History of attempted suicide
 - Hopelessness
- Up to 27% of patients with bipolar disorder have attempted suicide at least once

Hawton 2009

Bipolar Disorder and Suicide

- Risk factors:
 - Being single
 - History of abuse
 - Early age of onset of bipolar disorder
 - Increasing severity of episodes
 - Presence of comorbidities
 - Family history of death by suicide

Hawton 2009

Bipolar Disorder and Violence

- Elevated risk of perpetrating violent behavior—possibly related to presence of comorbidities:
 - Substance use disorders and intermittent explosive disorder
 - National registry study found violent crime risk in bipolar disorder to be 8% as compared to 4% in matched population controls
- Legal Issues:
 - Of those with a manic episode over the past 3 years, 11% had been arrested

Fazel 2010

McCabe 2013

Bipolar Disorder and Cognition

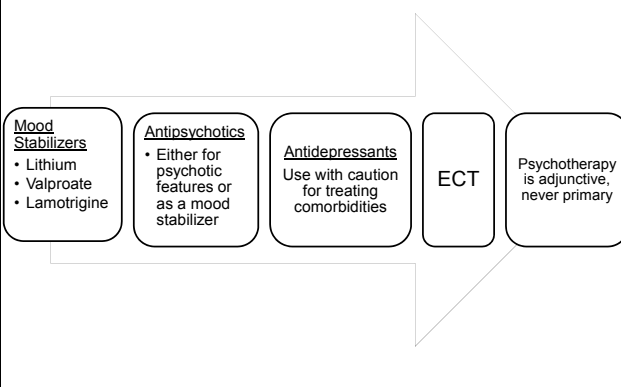
- Cognitive effects of Bipolar Disorder
 - Impairment in:
 - Attention
 - Verbal memory
 - Executive function
 - Information processing speed
 - Deficits seen during euthymia as well as acute mood episodes
 - Occur in both Bipolar I and II disorders

Bora 2009

Considerations for Referral to Psychiatry

- Impulsive and potentially dangerous behavior
- Functional impairment
- Multiple failed medication trials
- Recurrence of mood episodes

Treatment of Bipolar Disorder



STEP-BD

- Included “real world” patients with comorbidities
- Collected DNA from 2,300 patients
- 2 pathways- Best Practices and Randomized Care
- 50+ studies resulting from data analysis
- Adding an antidepressant to bipolar patients on a mood stabilizer is no more effective than placebo
- Antidepressant use can worsen rapid cycling in bipolar patient
- Average number of co-occurring medical illnesses ranged from 2.4-3.4

Treatment Options

Lithium

- Typical dosing: 900-1200mg divided BID
- Side effect profile
 - Sedation and weight gain common
 - Long term risk of damage to kidneys and/or thyroid
- Monitoring?
 - Every 6 months- chem6, thyroid function and lithium level. Monitor weight and BMI.
 - Target blood level of 0.6-1.2
- Generic? YES
- Unique Features: efficacy in reducing suicidal ideation; narrow therapeutic index; fetal risks; renally excreted

Treatment Options

Valproate

- Typical dosing: 20mg/kg
- Side effect profile
 - Sedation and weight gain common
 - Risk of necrotic pancreatitis or fulminant hepatic failure
- Monitoring?
 - Every 6 months- CBC with diff, LFTs, valproate level. Monitor weight/BMI.
 - Target level of 80-120
- Generic? YES
- Unique Features: fetal risks

Treatment Options

Lamotrigine

- Typical dosing: 50-200mg
- Side effect profile
 - Sedation and weight gain unusual
- Additional Monitoring?
 - Rash (Stevens-Johnson syndrome)
- Generic? YES
- Unique Features: requires slow titration; well tolerated; no routine labs required

Treatment Options

- Monitoring antipsychotics
 - Before initiation:
 - Weight/BMI, waist circumference, blood pressure
 - Personal and family history of diabetes, obesity, dyslipidemia, hypertension and cardiovascular disease
 - CMP, CBC, TSH
 - EKG
 - During treatment:
 - At 3 months: HbA1c, lipids
 - Biannually: abnormal involuntary movement scale (AIMS)
 - Annually: HbA1c, CMP
 - As clinically indicated: EKG, CBC, lipids

Treatment Options

- **Class Risks of Antipsychotics**
 - Neuroleptic malignant syndrome
 - Acute dystonias
 - Akathisia
 - Parkinsonism
 - Tardive dyskinesia
 - QTc prolongation
 - Metabolic syndrome

Treatment Options

Quetiapine

- Typical dosing: 300-600mg daily
- Side effect profile
 - Anticholinergic effects: Moderate
 - Orthostatic effects: Moderate
 - Weight gain: Moderate
 - Lipids: Moderate
 - Diabetes risk: Low/Moderate
- Additional Monitoring? Consider thyroid monitoring
- Generic? YES
- Unique Features: indication for bipolar depression; less likely to lower seizure threshold

Treatment Options

Lurasidone

- Typical dosing: 20-120mg daily
- Side effect profile
 - Anticholinergic effects: Very Low
 - Orthostatic effects: Low
 - Weight gain: Very Low
 - Lipids: Very Low
 - Diabetes: Very Low
- Additional Monitoring? Prolactin as clinically indicated
- Generic? NO
- Unique Features: indication for bipolar depression; must take with food (350 calories)

Treatment Options

Olanzapine

- Typical dosing: 5-20mg daily
- Side effect profile
 - Anticholinergic effects: Moderate
 - Orthostatic effects: Low/Moderate
 - Weight gain: High
 - Lipids: High
 - Diabetes: High
- Additional Monitoring? Prolactin as clinically indicated
- Generic? YES
- Unique Features: lower likelihood of prolonging QTc

Treatment Approaches- Mania

Hypomania or mild/moderate mania:

- **First line:** monotherapy with an antipsychotic
- Can use benzodiazepines as adjunct for insomnia/agitation

Severe mania:

- **CONSIDER HOSPITALIZATION**
- **First line:** Lithium + an antipsychotic
- **Second line:** Valproate + an antipsychotic

Other considerations:

- **Electroconvulsive Therapy (ECT)**
- Generally safe and effective
- Requires between 6-20 treatments

Treatment Approaches- Bipolar Depression

Treat Depression Aggressively!

HOSPITALIZATION FOR SAFETY CONCERNS

First line:

- Lithium
- Lurasidone or quetiapine

Second line:

- Lamotrigine
- Fluoxetine/olanzapine
- ECT

Treatment Approaches

Maintenance therapy

- Recommended for ALL patients
- Usually consists of the same regimen that treated an acute episode
- **Most evidence for:**
 - Lithium
 - Valproate
 - Lamotrigine
 - Quetiapine
 - Lithium + an antipsychotic
 - Valproate + an antipsychotic

Treatment Approaches

- **Therapy:**
- **Group Psychoeducation; Cognitive Behavioral Therapy; Family education**
 - **Psychotherapy Key Features:**
- 1. **Psychoeducation: importance of identifying early symptoms and of medication compliance**
- 2. **Stress reduction: teaching patients how to cope**
- 3. **Improving interpersonal and behavioral issues**
- **Support Groups:**
 - **National Alliance on Mental Illness (NAMI)**
 - **Depression and Bipolar Support Alliance**

Treatment Approaches

- Treating John's Depression:
 - Given no acute safety concerns, no need for inpatient hospitalization
 - Discussed options of lurasidone, quetapine or lithium
 - John selects quetapine
 - Obtain lipid profile, HbA1c, CMP, CBC, TSH
 - Obtain weight/BMI and family medical hx
 - Start at 25mg QHS, increasing dose every 2-3 days with target dose around 300mg



Research considerations

- Cariprazine
 - Atypical antipsychotic with possible use in bipolar depression
- Omega 3 fatty acids
 - 1 gram daily
- Ketamine
 - NMDA receptor antagonist: dissociative anesthetic
- Modafinil/Armodafinil
 - Mechanism unknown
- Repetitive Transcranial Magnetic Stimulation (rTMS)
 - Stimulates left prefrontal cortex

Oldani, 2014

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