Bipolar Disorder in Late Life

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Disclosures

We have no disclosures to be made.

Who is in the audience?

Psychiatric Provider? Primary Care Provider? Other?
Older-Age Bipolar Disorder (OABD) = patients ≥50 years

Age of onset of bipolar disorder

Onset over age 50 is about 5 – 10% of individuals with bipolar disorder.

Age at diagnosis – is it the same disorder?

New-onset mania >50 years: Often associated with vascular changes or other brain pathology.

Family history of affective disorder is common.

New-onset mania <50 years: No specific pattern noted.

Family history of affective disorder is uncommon.
As the population ages . . .

The percent of bipolar patients who are over age 60 grows

- Currently about 25% of patients with bipolar disorder are > 60 years old. By 2030 this will be 50%.

Some more numbers...

- In psychiatric outpatients, prevalence of late-life mania is 0.6%.
  In psychiatric inpatients units it is 6%.
- Patients with bipolar disorder tend to die young.
  Most cases of OABD (70-95%) represent cases with onset age <50.
- Men with bipolar disorder die younger.
  Geriatric bipolar patients are predominantly female, 69% women.
  Younger bipolar adults, ratio of females to males was approximately 1:1.

Bipolar disorder is characterized by episodes of

- Major depression
- Mania
- Hypomania
Major Depressive Episode – DSM 5 Diagnostic Criteria

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from the person’s usual behavior:

1.心境低落(或不耐烦，烦躁)
2.精力下降或易疲劳
3.睡眠障碍
4.食欲或体重变化
5.自我评价下降或自责
6.去活动减少(或不能集中精力)
7.思维迟缓或减慢
8.想死或自杀念头

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

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

D. The disturbance in mood and the change in functioning are observable by others.

E. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the individual when not symptomatic.

F. The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization. If there are psychotic features, the episode is, by definition, a manic episode.

G. Note:
- Do not include symptoms that can clearly be attributed to another medical condition.
- The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- The episode is not attributable to the physiological effects of a substance or another medical condition.

Hypomanic Episode

A. Distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least 4 consecutive days and present most of the day, nearly every day.

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:

1. More talkative than usual or pressure to keep talking.
2. Increased goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation.
3. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.
4. Flight of ideas or subjective experience that thoughts are racing.
5. Inflated self-esteem or grandiosity.
6. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep).
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).
8. Excessive goal-directed activity, purposeless non-goal-directed activity, or psychomotor agitation.
9. In children, consider failure to make expected weight gain.
10. In children and adolescents, can be irritable mood.

Manic Episode

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:

1. Irresistible goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation.
2. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.
3. More talkative than usual or pressure to keep talking.
4. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep).
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Note:
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- The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- The episode is not attributable to the physiological effects of a substance or another medical condition.
Is it bipolar disorder?

The prevalence of misdiagnosis is high (48%-61%) in bipolar disorder. Misclassification decreases with age, but is still substantial.

What does mania look like in Old Age Bipolar Disorder (OABD)?

Hyperactivity  Aggression  Insomnia  Cognitive impairment

Comorbid general medical illnesses  more common
Hypersomnia  less common
Comorbid anxiety and substance use disorders  less common

Differential Diagnosis of OABD

Unipolar depression disorder
Schizophreniform disorder bipolar type
Schizophrenia
Other neurodevelopmental disorder (demented)
Othetum
Drug and substance disorder due to another medical condition
Unspecified mood disorder due to another medical condition
Substance-related disorder
### Medical causes of mania

#### Neurologic
- Dementia
- Head injury
- CNS tumor
- Multiple sclerosis
- Stroke
- Epilepsy
- Wilson’s disease

#### Toxic
- Medications
- Corticosteroids
- Amphetamines
- Other sympathomimetics
- L-DOPA
- Other substances

#### Infectious
- HIV
- Syphilis
- Lyme disease
- Viral encephalitis

#### Endocrine
- Hypo-or hyperthyroidism
- Hypercortisolism

#### Sleep Apnea

#### Vitamin B12 Deficiency

### Cognitive dysfunction in OABD

Cognitive dysfunction found in > 30% of people with OABD.

- Does BD cause neuroprogression? CONTROVERSIAL
- Cognitive outcomes are worse in early onset bipolar disorder
- Some neurodegenerative disorders (Frontal-Temporal Dementia) may resemble OABD, leading to misdiagnosis.

### What to do?
1) Protect from CV risk factors.
2) Avoid medications that worsen cognition (e.g. benzodiazepines and anticholinergic drugs).

### Medical comorbidities in OABD

Death occurs an average of 10 years earlier in bipolar patients than in the general population.
Cerebrovascular risk in OABD

Silent cerebral infarctions
• present in over ½ of patients with OABD

Risk Factors
• Smoking
• Obesity
• Lack of Exercise

Treatment of OABD

Drug response in bipolar disorder is variable
• Not everyone responds in the same way to the same drug
  (What works for one person might not work for another)

Medical comorbidity can limit the treatment options for OABD because of
• Drug tolerability
• Drug-drug interactions
• Drug-disease interactions
• Altered metabolism
FDA approved medication for Management of Acute Mania and Hypomania

First line - Lithium, Valproate, Olanzapine, Quetiapine

Lithium compared with divalproex, the results indicate that the benefit of each drug is substantial and generally comparable.

Lithium and Divalproex in the Treatment of Mania in Older Patients With Bipolar Disorder: A Randomized Double-Blind Controlled Trial

Points to remember which one to choose from
- past response to medications
- psychotic symptoms
- side effect profiles
- comorbid general medical conditions
- potential for drug-drug interactions
- patient preference, and cost

50-80% of older adults with mania will respond to a first-line treatment

Lithium

Start low and go slow in DABO

Baseline monitoring: CBC, CMP, TSH, EKG

Starting dose 120 mg, One to two times daily

- Increase as tolerated every 1-3 days. Half life longer in older patients
- Rarely 900 mg daily will be required.

Lithium levels are determined by 12-hour serum trough level that should be drawn five to seven days after each dose increase.

Serum concentrations, from the International Society for Bipolar Disorders consensus practice guidelines for maintenance treatment in bipolar disorder (2012) and are based upon age:
- Patients 60 to 79 years old - 0.4 to 0.8 mEq/L (0.4 to 0.8 mmol/L)
- Patients 80 years and older - 0.4 to 0.7 mEq/L (0.4 to 0.7 mmol/L)

Lithium (Doesn’t bind to proteins, Excreted in Kidneys, not metabolized)

Effective for
- Bipolar Mania
- Bipolar Depression
- Bipolar Maintenance Treatment

Risks/Side effects
- Nausea/vomiting
- Sedation
- Weight gain
- Numb
- Hypothyroidism (15% female and 4% male)
- Nephrogenic Diabetes insipidus - Polyuria and Polydipsia – Ultimate renal failure if not treated.
-Bradycardia, AV block - check EKG before starting
- Neurological: Confusion, ataxia, Stupor, Coma and even death in case of toxicity

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Lithium and renal risk in OABD

- Co-prescription with ACE inhibitors
- Co-channel blockers
- Diuretics-HCTZ, Loop

Increasing lithium levels
Worsening renal function

Co-morbid
- Diabetes
- Hypertension
- Age-related renal decline

Inadequate lithium monitoring

Anti-epileptic drugs for OABD

For acute mania
- Carbamazepine
- Valproate
- (Gabapentin)

For bipolar maintenance treatment
- Lamotrigine (Avoid using with valproate)
- Valproate

For bipolar depression
- Lamotrigine (Off label use)


Valproate - 1

Start low and go slow in OABD
- Start at 125 to 500mg/day and increase slowly every one to five days.
- With 24 hour extended-release preparations, blood level checks after 18-24hrs later, prior to next dose. Bioavailability is 30% less with ER formulations.
- Serum level of 65 to 100 mcg/ml recommended (mean serum concentration 74 mcg/ml per GERi-BD), although some elderly patients will not tolerate the higher ranges.
- The half-life and free-plasma fraction of valproate may increase with age.

Target dose- 500 to 1500 mg/ day. (Mean dose 1200mg/day per GERi-BD)

Elderly patients may tolerate Depakote over Depakote ER due to less cognitive and renal side effects.
Valproate - 2

Baseline monitoring: CBC (White count and Platelets), BMP, LFTs, Lipase (if suspected acute abdominal pain) and wt.

Common side effects in older geriatric bipolar
• gastrointestinal distress,
• sedation,
• weight gain and hand tremor

Other Side Effects to know:
• Neutropenia,
• Thrombocytopenia,
• Pancreatitis,
• PCOS - Polycystic Ovarian syndrome
• Decreased LFTs - liver failure if untreated
• Hair loss and
• Neural Tube Defect in Pregnancy (Less likely with Elderly)

Valproate in OABD (3)

Drug-drug interactions
• Aspirin
• Warfarin
• Digitoxin
• Phenytoin
• Lamotrigine - valproate decreases clearance

Ammonia levels can become elevated, even with normal valproate levels.

Atypical antipsychotics

For acute mania
• Olanzapine
• Quetiapine
• Aripiprazole
• Risperidone
• Ziprasidone
• Asenapine
• Cariprazine (FDA approved for mixed episodes as well)
• Clozapine - not FDA approved

For bipolar maintenance treatment
• Aripiprazole
• Olanzapine
• Risperidone
• Quetiapine
• Ziprasidone

For bipolar depression
• Olanzapine + fluoxetine
• Quetiapine
• Lurasidone
• Cariprazine
Atypical antipsychotic challenges in OABD

Many carry ↑ risk for metabolic syndrome.
Some carry risk of extrapyramidal or Parkinson-like effects.
Check EKG prior to starting

Comparative Efficacy between various agents:

- Lithium may be less effective than olanzapine or risperidone for reducing acute mania in patients with bipolar disorder. Cochrane Database Syst Rev 2019 Jun 1;6:CD004048
- Lithium might be more effective than lamotrigine and appears similar to carbamazepine and valproate for improving acute mania in patients with bipolar disorder. Cochrane Database Syst Rev 2019 Jun 1;6:CD004048
- Olanzapine and valproate may be similarly effective for patients with bipolar disorder. JAMA Psychiatry 2013 Aug;70(8):903-10
- Antipsychotics such as haloperidol, risperidone, or olanzapine may be more effective than mood stabilizers in patients with acute mania. Lancet 2011 Oct 8;378(9799):1306
- Aripiprazole may not be more effective than haloperidol or lithium for patients with acute manic or mixed episodes. Cochrane Database Syst Rev 2013 Dec 17;(12):CD005000
- Quetiapine and lithium appear similarly effective for improving symptoms, but quetiapine may have greater adverse effects in patients with bipolar I or II disorder. J Clin Psychiatry 2016 Jan;77(1):90
- Second-generation antipsychotics may be more effective than mood stabilizers for acute mania. J Affect Disord 2011 Nov;134(1-3):14

Combination Antipsychotic and Mood Stabilizer

- Considered an alternative first-line option to monotherapy with either mood stabilizer or an antipsychotic by Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 recommendations
- May have faster onset of response than monotherapy. Lancet 2016 Apr 9;387(10027):1561-72
- May be more effective in reducing symptoms than single agent alone. Am Fam Physician. 2012 Mar 1;85(5):483-93full-text
- Can be used for patients with mania who are not adequately improving on lithium or valproate alone. Aust N Z J Psychiatry 2015 Dec;49(12):1215
Some Studies with information on combination use.

- Ziprasidone to lithium or divalproex may not be associated with improved response in patients with acute mania. Randomized trial: J Clin Psychiatry 2012 Nov;73(11):1412

- Addition of aripiprazole to lithium or valproate may improve mania symptoms. Randomized trial

- Addition of divalproex to lithium or valproate may improve symptoms of 4 weeks in manic patients not adequately responding to lithium or valproate alone. Randomized trial

- Either risperidone or haloperidol may improve short-term response in acute mania when added to mood stabilizer (lithium or valproate). Randomized trial

- Olanzapine plus divalproex appears more effective than divalproex alone for reduction of manic and depressive symptoms in patients with bipolar I disorder with mixed episodes. Randomized trial: J Clin Psychiatry 2009 Nov;70(11):1540

Electroconvulsive Therapy (ECT)

Can be an excellent option for OABD

[Link](https://youtu.be/-T0mwzXHgvI) | can stop at 1:12min.

Psychosocial interventions

- Helping Older People Experience Success (HOPES)
  - Skills training
  - Improved social skills
  - Community functioning
  - Self-efficacy
  - Attendance

- Medication adherence skills training (MAST-ED)
  - Improved medication adherence
  - Depression
  - Quality of life

Take home points

National Institute for Health and Care Excellence (NICE) 2020 recommendations for use of psychotropic medication in patients ≥ 65 years old, consider

- lower doses of medications
- increased risk of drug interactions
- Assessing and managing comorbidities
- increased risk of detriment to cognitive function and mobility with anticholinergic medication or drugs with anticholinergic mechanisms

Patients ≥ 65 years old may be more likely to have rapid cycling, fewer suicide attempts, and less manic and psychotic symptoms

Remember: antipsychotics are associated with increased risk of stroke, and greater rate of cognitive decline and mortality in patients with dementia

Cautions while using antipsychotics due to risk of exacerbating or causing SIAD or hyponatremia

References - 1


References - 2


