

Treating Bipolar Spectrum Disorder

Jonathan Bolton MD
Center for Rural and Community Behavioral Health
University of New Mexico

Topics

- What are the Bipolar Disorder-spectrum disorders?
- How to treat mania/hypomania:
 - Anti-manic treatments
 - ‘Mood stabilizing treatments
- How to treat (bipolar) depression

Hypomania

- A. Abnormally/persistently elevated, expansive, irritable mood and abnormally/persistently increased activity/energy
Lasting ≥ 4 days
- B. ≥ 3 manic symptoms (\geq if mood is irritable only)
- C. Not characteristic of person; observable to others
- D. Not severe enough to require hospitalization; no psychotic features

Mania

A. Expansive-Euphoric-Elevated/Irritable mood.

Lasting \geq 1 week

B. \geq 3 (or \geq 4 if mood is only irritable)

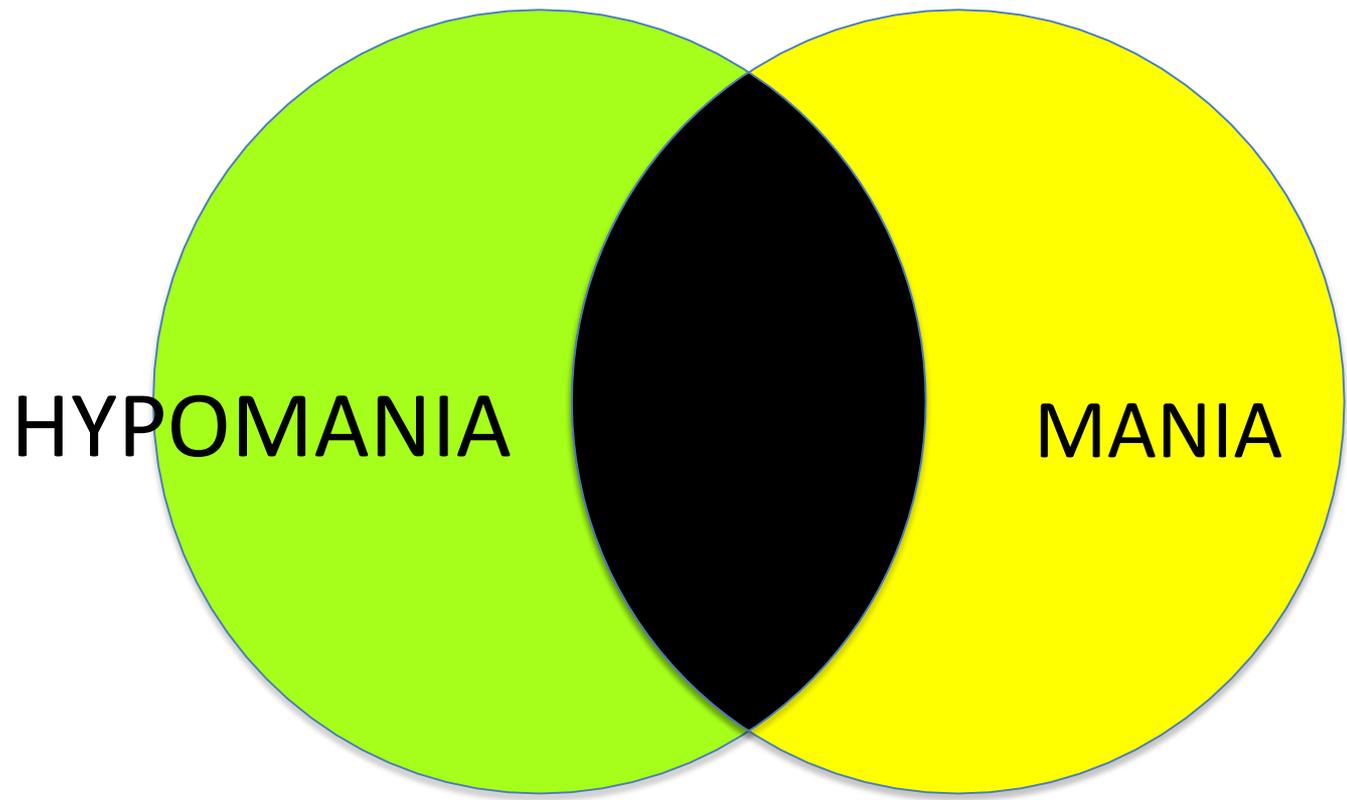
- grandiosity
- decreased need for sleep
- more talkative
- flight of Ideas
- distractibility
- increased goal-directed activity/psychomotor agitation
- excessive involvement in risky behaviors.

Specifiers

- With anxious distress
- With mixed features
- With rapid cycling
- With melancholic features
- With atypical features
- With psychotic features
- Mood congruent
- Mood incongruent
- With catatonia
- With peripartum onset
- With seasonal pattern

Bipolar Spectrum Disorders

- Bipolar I
- Bipolar II
- Cyclothymic Disorder
- Substance/Medication-induced Bipolar and Related Disorder
- Bipolar and Related Disorder due to another Medical Condition
- Other Specified Bipolar and Related Disorder
- Unspecified Bipolar and Related Disorder



HYPOMANIA

MANIA

BIPOLAR II

BIPOLAR I

Anti-Manic Treatments

- Lithium
- Anticonvulsants
 - Valproate/Depakote
 - Carbamazepine/Tegretol
 - Lamotrigine/Lamictal
- Antipsychotics
 - Quetiapine/Seroquel
 - Risperidone/Risperdal
 - Olanzapine/Zyprexa

'Mood Stabilizers': Prophylaxis

- Lithium
- Lamotrigine

Anti-Depressants (Bipolar)

- Lamotrigine/Lamictal
- Olanzapine/Zyprexa + Fluoxetine/Prozac (Symbyax)
- Quetiapine/Seroquel
- Bupropion/Wellbutrin

Treating Bipolar Depression

- Caution: Switching and destabilization
 - Avoid long half-life antidepressants
 - Consider using a ‘mood stabilizer’ with an antidepressant
 - Avoid sedating antidepressants (eg Trazodone)
- Lamotrigine/Lamictal
- Quetiapine/Seroquel
- Olanzapine/Zyprexa + Fluoxetine/Prozac (Symbyax)

Lithium

- Naturally occurring ion
- Discovered in 1949. Introduced to US in 1969
- Four uses:
 1. Antimanic
 2. Mood stabilizer (Prophylactic)
 3. Modify episodic symptoms
 4. Enhance antidepressants
- Better for euphoric mania (than rapid cycling, psychotic or mixed mania)

Lithium

- Formulations
 - Lithium carbonate
 - Regular
 - Sustained release
 - Lithium citrate
 - Liquid preparation
- Time to effect: 7-14 days
- Therapeutic window:
 - Maintenance: 0.6-1.2 mEq/L
 - Acute: ≤ 1.5 mEq/L

Lithium—Side Effects/Cautions

- Weight gain
- Impaired cognition/memory
- Tremor
- Poor coordination
- GI distress
- Hypothyroidism
- Polydipsia, polyuria
- EKG changes
- Pregnancy: Ebstein's anomaly

Drug-Drug:

- Li—NSAIDs
- Li—Loop Diuretics

Quiz 1

Lithium is the best available treatment for which form of mania?

1. Elated
2. Dysphoric
3. Mixed
4. Rapid Cycling

Quiz 2

Which labs do you not need to periodically monitor when prescribing lithium?

- A. TSH
- B. Serum Creatinine
- C. Liver function tests

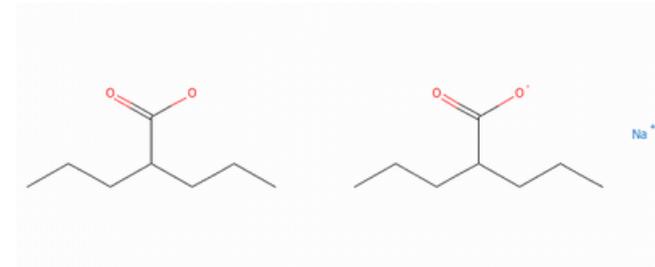
Anticonvulsants

- Valproate/Depakote
- Carbamazepine/Tegretol
- Lamotrigine/Lamictal

- Oxcarbazepine/Trileptal
- Gabapentin/Neurontin

Valproate

- Better in rapid cycling and mixed mania
- Approved for acute mania: 1994
- Formulations
 - Immediate release
 - Valproic Acid/Depakene
 - Delayed release
 - Divalproex/Depakote
 - Extended release
 - Divalproex/Depakote ER



Valproate--Dosing

- Loading dose
 - 20-30 mg/kg/d
- Serum concentration: 50-110 micrograms/mL

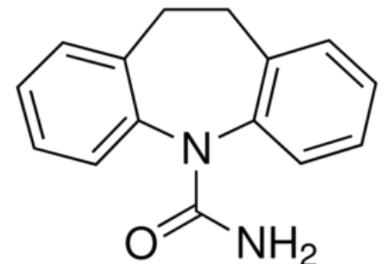
Valproate—Side Effects/Cautions

- Cognitive dulling, sedation, ataxia
- GI distress
- Polycystic Ovarian syndrome
- Weight gain
- Dyscrasias: thrombocytopenia
- Hepatotoxicity
- Pancreatitis
- Hair loss, kinky hair

- Spina Bifida, cleft palate

Carbamazepine/Tegretol

- More effective for mixed mania
- Dosing:
 - Starting dose: 200 mg bid
 - Target serum concentration: 12 micrograms/mL
 - Recheck levels (auto-induction of enzymes)
- Drug-Drug issues:
 - OCP, Bupropriion, alprazolam

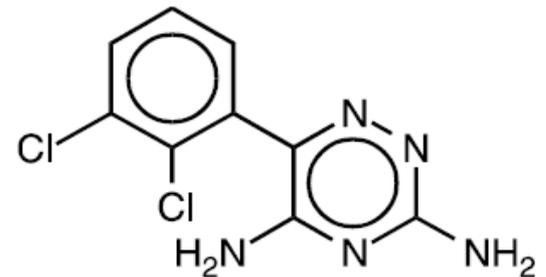


Carbamazepine—Side Effects/Cautions

- Dermatological
 - Rash: 10-15% (severe form = Stevens-Johnson Syndrome)
- Hematological
 - Agranulocytosis
 - Aplastic anemia
 - Thrombocytopenia

Lamotrigine/Lamictal

- Mood stabilizer
- Better at preventing depression
- May be effective against rapid cycling/mixed mania
- No switching
- Cautions:
 - Rash:
 - Serious 1/1000 adults, 1/100 children
 - Stevens-Johnson syndrome



Lamotrigine--Dosing

- 25 mg/d for first week
- Increase by 25 mg per week
- Target dose: 200 mg/d

- If discontinuing, should taper

- Drug—Drug interactions
 - Valproate: increases Lamotrigine concentration
 - Carbamazepine: decreases Lamotrigine concentration

Antipsychotics

- Antimanic; Antidepressant; mood stabilizer
- Not associated with switching

- Olanzapine/Zyprexa
- Quetiapine/Seroquel
- Risperidone/Risperdal

Quiz 3

Which drug-drug interactions are not relevant to treating Bipolar Disorder:

- A. Lithium—NSAIDS (eg ibuprofen, Naprosyn)
- B. Lithium—loop/thiazide diuretics (eg HCTZ)
- C. Carbamazepine—Valproic Acid
- D. Carbamazepine—Oral Contraceptives
- E. Valproic acid—Lamotrigine
- F. Valproic acid—Grapefruit juice

Bipolar Disorder--Strategy

- Control the crisis: Antimanics
- Prevent recurrence: Mood stabilizers
- Treat the depression
 - Caution re ‘switching’ and destabilizing
- Treat associated anxiety and dyssomnia
- Treat comorbid conditions: substance abuse, panic

Quiz 4

Which medication is not effective for Bipolar Depression?

- A. Quetiapine/Seroquel
- B. Lamotrigine/Lamictal
- C. Olanzapine/Zyprexa + Fluoxetine/Prozac
- D. Topiramate/Topomax

Psychotherapy and Bipolar Disorder

- Sense of self
- Shame
- Self-care
- Suicidality