Treating
Bipolar Spectrum Disorder

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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 (>= 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
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
- Buproprion/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
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, Buproprion, 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. Carbamazpine—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 dyssomnian
• 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