Mood Stabilizers

Bipolar Disorder (Manic Depressive Disorder)

- Characterized by alternating periods of mania, depression, and normal mood.

- Manic Symptoms
  - Unlimited physical and psychological energy.
  - Delusional feelings of self-worth that may reach level of psychosis.
  - Heightened emotional reactivity.
  - Incoherent thought processes.

- Approximately 4% of population will show at least one episode of mania.

3 diagnostic forms of bipolar disorder.

- Bipolar I – Episodes of mania and depression severe enough to seriously disrupt functioning or require hospitalization.
- Bipolar II – Less severe mania (hypomania) alternating with depression
- Cyclothymia – Alternating elation and depressed mood not meeting criteria for mania or MDD.

Subclassifications

- Rapid Cycling
- Mixed Mania
Pharmacotherapy for bipolar disorder

- Characteristics of the ideal “mood stabilizer”.
  - Treats both depression and mania.
  - Doesn’t induce depression or mania.
  - Suitable as a prophylactic to prevent recurrence of symptoms.
    - No “cure” for bipolar disorder.

Lithium Salt (e.g. LiCO₃)

- Oldest effective approach (1970s).
- Still considered the “gold-standard”.

**Mechanism of action of Li⁺ still unclear.**

- Newer theory: Effects on second-messenger pathways?
  - Neuroprotective effects?
- Effects on ion channels to inhibit cellular activity?
  - eg. VG Na⁺ channels?

Side-effects of Lithium contribute to narrow therapeutic window and patient noncompliance.

- Gastrointestinal – Nausea, vomiting, diarrhea.
- Neurological – Headache, muscle tremor, lethargy, blunted cognition, slurred speech.
- Dermatological – Skin rash and acne.
- Weight gain
- Teratogenicity
- Toxic levels can cause seizures, confusion, irregular heartbeat, coma, death.
  - Very important to monitor Li⁺ blood levels.
• Li+ eliminated **only** by renal excretion.
• Reduced renal functioning can lead to toxicity.
• Reduced Na+ intake can interfere with excretion and lead to toxicity.

**Alternatives to Lithium**
• Anticonvulsants
  • E.g., Divalproex (*Depakote*)
  • Used alone or in combination with Li+.
  • More effective than Li+ for acute mania and rapid-cycling.
  • Similar side-effects as Li+ but less severe.

**Atypical Antipsychotics**
• Use of *Typical* antipsychotics actually predates Li+.
  • Wasn’t very effective and caused EPS.

• Atypical Antipsychotics are effective (more for mania) with no EPS.
  • Olanzapine (*Zyprexa*) most common.
  • Used alone or in combination with other drugs.

**Antidepressants**
• Most commonly SSRIs, bupropion, or venlafaxine.
• Used during depressive phase only…
  …or as a prophylactic in combination with an antimania drug.
  • *Symbyax* (olanzapine + fluoxetine).
• CAUTION: May induce mania or rapid cycling.
• Anti-anxiety medications (benzodiazepines) used in combination with mood stabilizers.
  • E.g., Diazepam (*Valium*)
• Omega 3 fatty acids (herbal remedy).

The most effective treatment for bipolar seems to be a combination of pharmacotherapy and psychotherapy.

• Psychotherapy useful for:
  • Medication compliance.
  • Psychological issues associated with the disorder (e.g., interpersonal, self esteem, occupational, etc…).
  • Recognition of the disorder as a disease.