The Treatment of Mood Disorders in the Individual with IDD

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Pharmacy Alternatives

Mood Disorders

Outline of Lecture

I. Description of Mood Disorders
II. Etiological Theories Major Depression
III. Treatment Major Depression
IV. Description and Treatment of Bipolar Disorder
Suicide

- 8th leading cause of death in the U.S.
- Overwhelmingly white phenomena
- Suicide rates also quite high in Native American
- Rate of suicide is increasing in adolescents and elderly
- Males are more likely to commit suicide
- Females are more likely to attempt suicide (except China)

Mood Disorders

- Depressive Disorders
- Mania
- Bipolar Disorder

Depressive Disorders

- Major Depressive Disorder (single, recurrent)
- Major Depressive Disorder
- Dysthymic Disorder
Major Depressive Disorder:
Diagnostic Criteria

5 of following symptoms, must include one of first two, occurred almost every day for two weeks
- Depressed mood
- Pleasure or interest loss
- Appetite
- Sleep disturbance, too much or too little
- Agitation or retardation
- Fatigue
- Feelings of worthlessness or guilt
- Difficulty concentrating or deciding
- Recurrent thoughts of death

Depressive Symptoms Mnemonic:
“Space Drags”

S - Sleep disturbance
P - Pleasure/interest (lack of)
A - Agitation
C - Concentration
E - Energy (lack of)/fatigue
D - Depressed mood
R - Retardation movement
A - Appetite disturbance
G - Guilt, worthless, useless
S - Suicidal thought

Major Depression

MDD, Single episode
- Absence of mania or hypomania

MDD, Recurrent
- 2 major depression episodes, separated by at least a 2 month period with more or less normal functioning/mood
What does this look like?

• In persons with I/DD, depressed mood may be described by others as irritable, grouchy, assaultive, self-injurious behavior, spitting, yelling, swearing, property destruction or increase in ritualistic behaviors
• Facial expressions: sad, not able to show animation or smile
• Crying or if severe disease unable to cry

What does this look like?

• Neglect of personal appearance: untidy clothes, uncombed hair
• Body movements and voice: hesitant or delayed
• Poverty of speech: how long it takes and little comes out, sparse, long pauses
• Slowness of mental activity
• Anxious or agitated depression: restlessness, hand wringing, signs of tension such as scratching and picking at the skin

What does this look like?

• Pessimism
• Low self esteem
• Expecting the worst and negative expectations
• Self blame
• Difficulty in making decisions
• Body aches and pains
• Weakness and fatigue
What does this look like?

- Sleeping too much or too little
- Not wanting to eat
- Not wanting to be involved in activities or workshop
- Isolation
- Slowness of body functions such as salivation, bowel activity and menses
- Early waking and feeling of exhaustion in the morning

Dysthymic Disorder: Symptoms

A. Depressed/irritable mood
B. Presence of two of the following:
   - Appetite disturbance
   - Sleep disturbance
   - Loss of energy/fatigue
   - Poor concentration or difficulties making decisions
   - Feelings of hopelessness
C. Present for two year period (one year in children and adolescents)
D. No evidence of a Major Depressive Episode during the first two years (one year for children)
E. No manic or hypomanic episode
F. No chronic psychotic disorder
G. Not related to organic factors

Mood Disorders: Summary

**Depressive Disorders**
- Major Depressive Disorder (single, recurrent)
- [Major Depressive Disorder: Postpartum onset]**
- Dysthymic Disorder

**Bipolar Disorders**
- Bipolar I Disorder
- Bipolar II Disorder
- Cyclothymic Disorder
Mood Disorders: Prevalence

<table>
<thead>
<tr>
<th>Disorders</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Depression</td>
<td>4.9%</td>
</tr>
<tr>
<td>Dysthymia</td>
<td>3.2%</td>
</tr>
<tr>
<td>Bipolar I</td>
<td>3.7%</td>
</tr>
<tr>
<td>Bipolar II</td>
<td>3.9%</td>
</tr>
<tr>
<td>MDD (Postpartum)</td>
<td>13%</td>
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</tbody>
</table>

Major Depressive Disorder: Etiological Theories

- Biological (genetic, brain structures, neurotransmitters)
- Behavior and cognition
- Emotion
- Social and cultural factors
- Developmental factors

Major Depression: Genetics

**Family studies:**
- Relatives of those with a mood disorder are two to three times more likely to have a mood disorder (usually major depression)

**Twin studies:**
- If one identical twin has a mood disorder the other twin is 3 times more likely than a fraternal twin to have a mood disorder (particularly for bipolar disorder)
- Severe mood disorders may have stronger genetic contribution than less severe disorders
- Heritability rates are higher for females
Major Depression: Neurotransmitters

- Low levels of serotonin deregulates the activity of other neurotransmitters
- Permissive hypothesis

Major Depression: Endocrine System

- Elevated cortisol

Major Depression: Cognition

- Learned helplessness (Seligman)
- Negative cognitive styles (Beck)
Major Depression: Social and Cultural Factors

- Stressful life events
- Social support (marital relationship)
- Gender
- Culture (see chart)

Ethnicity and Prevalence of MDD
Percentage by Ethnicity

Adjustment Disorder with Depressed Mood

- Short-term
- Emotional or behavioral problems
- Reaction to identified stressor
Bipolar Disorders

- Bipolar I Disorder
- Bipolar II Disorder
- Cyclothymic Disorder

Bipolar Disease

Definition: a syndrome in which patients suffer from episodes of mania and depression.

In a national survey done in the year 2000 of 4192 individuals diagnosed with bipolar disease:

1/3 of respondents sought help within 1yr,
69% misdiagnosed,
4 different MDs prior to correct diagnosis

Bipolar Disease

Epidemiology:
1. Bipolar I and II disorders affect 3.7-3.9% of the US population, and in patients presenting with depression 21-49% have bipolar disorder
2. Bipolar I disorder occurs equally in men and women, while bipolar II occurs more often in women
3. although patients may present with bipolar disorder at any age, 21 is average onset, and peak is 15-24 years
### Bipolar Disease

**Pathophysiology**

1. Positive family history: 80-90% of patients
2. Imbalance of neurotransmitters, and levels fluctuate, and present differently
   - Manic episode: elevated NE
   - Depressed episode: lower NE
3. Dysregulation of **GABA** (inhibitory neurotransmitter), may lead to mania caused by unopposed excitatory neurotransmitters, like NE and DA
4. Increased levels of **Calcium** in the cerebral spinal fluid for mania, decreased for depression.

Changes in calcium levels can affect the excitability of neurons.

### Bipolar Disease

**Pathophysiology**

5. Recent research: **G Proteins** have an effect on mood stabilization because they are involved in signal transduction and activation of secondary messenger systems for neurotransmitters like DA, 5-Ht and NE
   - Hyperactive G proteins cause mood instability, therefore if normalized, mood stability occurs
   - G proteins and **Glutamate** play a role as glutamate binding to G proteins linked to NMDA receptors
   - 5Ht and NE are involved, but cycling and long term potentiation mediated by glutamate and medications that affect glutamate receptor system

### Bipolar Disease

**Psychosocial and Physical stressors**

1. Trigger early episodes of bipolar disease
2. Later episodes thought to be caused by increased sensitivity in the brain
Most frequent misdiagnosis:
- Depression (60%) 
- Anxiety disorder (26%) 
- Schizophrenia (18%) 
- Borderline or antisocial personality (17%)

Definition of Terms
- Bipolar Disease
- Bipolar I: manic depression
- Bipolar II: soft bipolar, hypomania
- Hypomania
- Mixed episodes
- Cyclothymic: mild but chronic

Bipolar Disorder

Bipolar I
- Alternation of full manic and depressive episodes
- Average onset is 18 years
- Tends to be chronic
- High risk for suicide

Bipolar II
- Alternation of Major Depression with hypomania
- Average onset is 22 years
- Tends to be chronic
- 10% progress to full bipolar I disorder
Manic Episode: Diagnostic Criteria

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood
B. Mood disturbance plus three of the following symptoms (four if the mood is only irritable):
   • Inflated self esteem or grandiosity
   • Decreased need for sleep
   • More talkative than usual or pressure to keep talking
   • Flight of ideas, or racing thoughts
   • Distractibility
   • Increase in goal directed activity
   • Excessive involvement in pleasurable activities
C. Marked impairment
D. No psychosis
E. Not organic

Characteristic Symptoms of Manic Phase of Bipolar Disease

• Symptoms should be evaluated and determined to not be due directly to one or more of the following:
  – Substance abuse
  – Medical conditions eg. Mania due to antidepressant therapy or steroid usage

Characteristics of Depressive Phase of Bipolar Disease

• Five or more symptoms present nearly every day during same 2 week period:
  – A. Depressed mood
  – B. Markedly diminished interest or pleasure
  – C. Significant change in weight or appetite
  – D. Insomnia or hypersomnia
  – E. Fatigue or loss of energy
  – F. Feeling of worthlessness or excessive or inappropriate guilt
Characteristics of Depressive Phase of Bipolar Disease

• Five or more symptoms (cont)
  – G. Decreased ability to think or concentrate, or inability to make decisions
  – H. Recurrent thought of death, or thoughts of suicide

Characteristics of Depressive Phase of Bipolar Disease

• Symptoms cause clinically significant distress or impairment in social and/or occupational functioning
• Symptoms need to be evaluated as not to be due to substance abuse or medical conditions
• Symptoms should not be better attributed to normal bereavement patterns

Hypomania: Diagnostic Criteria

• All the criteria of a Manic episode except criterion C (marked impairment)
  – A. elevated mood present for at least 4 days, with at least 3 of the same symptoms as mania
Mixed Disorder: Diagnostic Criteria

• The criteria for both mania and depression are met every day for at least one week and affects social and occupational functioning

Cyclothymia

A. For at least two years (one year for children and adolescents) presence of numerous hypomanic episodes and numerous periods with depressed mood or loss of interest or pleasure that did not meet criterion A (5 symptoms) of Major Depression
B. During a two-year period (1 year in children and teens) of disturbance, never without hypomanic or depressive symptoms for more than two months at a time
C. No evidence of MDD or Manic episode during the first two years of disturbance
D. No psychotic disorder
E. No organic cause

Brain Chemistry

• Dysfunction in norepinephrine, serotonin, dopamine, GABA neurotransmitters
• Deregulation in the adrenal, thyroid, and growth hormones
• Abnormalities in the sleep cycle and in the regulation of circadian rhythms
Psychosocial Interventions for the Optimal Management of Bipolar Disorder

- Provide psychoeducation
- Encourage participation in individual, family, group therapies and support groups
- Manage comorbid conditions
- Minimize noncompliance

The Bipolar Patient: Treatment Goals

- The best treatments result in the fewest, briefest, or mildest episodes
- Primary therapeutic objectives
  - Treat acute depression
  - Treat acute mania
  - Prevent depressive recurrence
  - Prevent manic recurrence
- Monotherapy is usually not effective for all therapeutic objectives

Multiphase Treatment Strategy
Consensus Practice Guidelines

• Acute treatment of manic, mixed, and hypomanic episodes
  – Selecting a mood stabilizer
  – Selecting adjunctive treatments for psychosis, agitation, and insomnia
  – Inadequate response to first treatment
• Acute treatment of bipolar depression
  – Selecting an overall strategy
  – Selecting specific medications
  – Inadequate response to first treatment
• Continuation and maintenance treatment
• General issues in all treatment phases

Acute Phase Treatment of Bipolar Disorder

Goals of Oral Loading

• Stabilize the patient
• Ameliorate the mood symptoms
• Ameliorate psychotic and other symptoms
• Do it as rapidly as possible
• Do it safely
• Establish a maintenance medication
Medications

Pharmacotherapeutic Options

• Mood Stabilizer Usage in Maintenance Phase of Bipolar Disease

• Mood stabilizers are the mainstay of treatment
• Recent literature has supported the use of atypical antipsychotics as monotherapy or adjunctive therapy
• Agents for the treatment of depressive episodes: emerging data for lamotrigine, quetiapine, and olanzapine-fluoxetine
Lithium
• 1950-1970’s: alters the distribution and exchange of ions involved in the process of conduction of electrical impulses in the brain
• First line treatment for acute and maintenance of mania and hypomania
• First line for the maintenance treatment of mixed episodes
• Adjunctive treatment for depressive episodes

Lithium
• Formulations:
  – A. Lithium carbonate:
    • Regular: Eskalith
    • Controlled release: Eskalith CR
    • Extended release: Lithobid
  B. Lithium citrate: Lithonate syrup

Lithium Pharmacokinetics:
a. Eliminated primarily through the kidneys
b. Changes in renal function can dramatically affect lithium levels
c. Narrow therapeutic index
d. Toxicity especially with low sodium
e. Salt (chloride, carbonate), non-sedating, prophylactic properties, inexpensive
f. Weigh effectiveness vs. side effects
Lithium

1. Therapeutic levels: 0.6 mEq/L-1.5 (2-3 300mg tabs of lithium carbonate/day)
   - Serum concentration dose 3 days after starting/changing dose
   - Levels obtained 12 hours after dose usually in am
   - fine hand tremor, thirst, nausea, excessive sweating

2. Toxic signs: diarrhea, vomiting, drowsiness, confusion, muscle weakness

3. Levels>2.0: ataxia, tinnitus, kidney dysfunction

Lithium

Clinical response:
- 1. acute mania: two weeks
- 2. depression: 4-6 weeks
- Half life 20-24 hours

Lithium

Factors that increase lithium levels:
- ACE inhibitors
- Angiotension II receptor blockers (Cozar, Diovan, etc)
- NSAIDS
- Thiazides
- Dehydration
- Renal dysfunction
- Sodium loss
- fluoxetine
Lithium
• Factors that decrease lithium levels:
  – Acetazolamide
  – Methylxanthines (theophylline, caffeine)
  – Osmotic diuretics
  – Pregnancy
  – Sodium supplements
  – Urine alkalinizers (NaCO3)

Mood Stabilizers (Divalproate)
– Very effective for mood stabilization (efficacy in both manic as well as depressive stages) and aggression
– Increases levels of GABA
– Less medication interactions than Carbamazepine
– Need to monitor liver functions and platelet counts (especially in elderly)
– May require doses higher than antiepileptic doses for good control of impulsivity/aggression (blood levels of 100-150 mcg/ml)

SE:
– Dose related side effects:
  – A. tremor and gait disturbance (back off the dose)
  – B. GI
  – C. sedation
  – D. Elevated liver enzymes

– Idiosyncratic:
  – Weight gain
  – Brittle hair
Depakene (Valproic Acid) and Depakote (Valproate)

- Pharmacokinetics
  - Depakote tablets lag in absorption (1 hr on empty stomach, up to 8 hrs w/food)
  - Depakote tablets are coated to reduce possible GI side effects (Do not crush)
  - Depakene are liquid filled capsules, and appear to have more GI side effects (TID or QID)
  - Dosage strengths: 125, 250 and 500mg tablets

Depakote sprinkles and ER formulation

- Sprinkles available in 125mg capsules that allow for smoother, extended release flow and more consistent blood levels
- Depakote ER formulated in 250 and 500mg tablets that allow for 1-2 times daily dosing minimizing side effects and allowing for a sustained release action

Carbamazepine (CBZ)

- Considered to be a 2nd line agent owing to its numerous adverse events and medication interactions
- MOA: thought to be its effects on GABA and G protein-linked second message systems
- Enzyme inducer
- Levels should be obtained 5-7 days after initial therapy. Continue levels over the next few weeks as levels will decrease due to auto-induction.
Carbamazepine (CBZ)

- Adverse events: dizziness, drowsiness, ataxia, blurred vision, diplopia, nystagmus, confusion, headache, GI, rash leukopenia, thrombocytopenia, hyponatremia, elevated liver enzymes, weight gain
- Idiosyncratic: Stevens-Johnson, liver failure, agranulocytosis, aplastic anemia
- Complete blood counts, liver function, thyroid, electrolytes at baseline and every 3-6 months

Carbatrol and Tegretol XR

- Carbatrol
  - 200mg and 300mg sustained release capsule
- Tegretol XR
  - 100, 200, and 400mg sustained release tablets
- Advantages of both
  - Ease of dosing (bid)
  - Smoother blood level
  - Less potential side effects

Lamotrigine (Lamictal)

- Indicated for bipolar disorder, primarily for depressive stage
- MOA: decrease release of glutamate and aspartate by blocking sodium channels
- More than 95% metabolized, many metabolites, some active
- Dosage form: 25, 100, 150, 200mg tabs; 2.5 and 25mg chewable tabs
Lamotrigine (Lamictal)

• Pharmacokinetics:

  – Highly affected by concomitant use of other antiseizure medications, so initial dose must be low, start slow, and titrate over several MONTHS.

  – Initial dose if on divalproex and enzyme inducers is 25mg qod.
  – If not on divalproex, but on enzyme inducer, use 50mg/day.
    » Inducers: carbamazepine, phenobarbital, phenytoin

Lamotrigine (cont)

• Maintenance dose of 100-150mg/day if on divalproex, otherwise, 300-500mg/day dosed bid

• Half-life:
  – Ave 25hrs (monotherapy)
  – Ave 14hrs (inducers)
  – Ave 27hrs (inducers & VPA)
  – Ave 70 hrs (VPA)

Lamotrigine (cont)

• Steady state: 3-15 days
• Side effects:
  – CNS: drowsiness, diplopia, dizziness, ataxia
  – Rash

• Drug interactions:
  – Carbamazepine and phenytoin decrease half-life
  – Divalproex prolongs half-life
Use of Antidepressant Medications in the Treatment of Bipolar Disease

**Tricyclic Antidepressants**

- The most widely used class of antidepressants prior to SSRI class
- More general effects on neurotransmitters, less refined
- Out of favor because overdose can be fatal
- May be prescribed when other classes have not worked

**Tricyclic Side Effects**

- Orthostatic hypotension (watch elderly)
- Weight gain
- Dry mouth
- Blurred vision
- Constipation
- Sweating
- Sexual dysfunction
### Tricyclics

- Anafranil (chlomipramine) 75-300mg
- Ascendin (amoxapine) 150-600mg
- Elavil (amitriptyline) 75-300mg
- Ludiomil (maprotiline) 75-225mg
- Norpramin (desipramine) 75-300mg
- Pamelor (nortriptyline) 50-150mg
- Sinequan (doxepin) 150-300mg
- Surmontil (trimipramine) 75-300mg
- Tofranil (imipramine) 75-300mg
- Vivactil (protriptyline) 15-60mg

### Selective Serotonin Reuptake Inhibitors (SSRIs)

- Came on the market in 1980s
- The most popular antidepressant
  - Side effects are less severe than older agents
  - Consequences of overdose are less severe
- Often first choice in antidepressant

### SSRI Usage

- Major depressive disorder
- Dysthymia
- SAD
- Mixed depression and anxiety
- Anxiety related disorders
- Premenstrual syndrome
- Eating disorders
- Some types of chronic pain
SSRIs Pharmacology

- They “clog the pump” which normally tells first neuron to pump some of the released serotonin back into the cell as a measure of checks and balances
- Therefore increased amount of serotonin hangs out in the synapse available for usage
- Takes 1-4 weeks to become effective, 4-6 weeks before true evaluation of effectiveness
- No dosage or drug changes should take place sooner than 1 month

SSRIs Side Effects

- Increased anxiety
- Fatigue
- Upset stomach
- Insomnia
- Apathy
- Lack of sexual interest
- Inability to obtain orgasm

Monitoring Medications

- Seldom if ever are blood levels necessary or recommended
- Evaluation of effectiveness based on clinical picture
- Evaluate potential side effects and make specific comment(s) on whether they appear, to what extent, and precautions taken to counter side effects
- Discuss troublesome side effects with clinition
SSRIs Side Effects

- Dizziness
- Sweating
- Tremors
- Dry mouth
- Headache
- Weight loss
- Weight gain
- Side effects worse during the first couple of weeks and diminish with time

SSRIs

- Celexa (citalopram) usual dosage 10-60mg, may have fewer interactions with other drugs, and not particularly stimulating or sedating
- Lexapro (Escitalopram) usual dosage 10-20mg, chemically similar to Celexa, may work faster

SSRI cautions

- Bipolar disease and increased activation of manic state
- Abrupt discontinuation: flu-like symptoms, vivid dreams and problems with sleep
- Black Box Warning for children and adolescents
- Avoid MAOIs
**SSRIs**

- Prozac (fluoxetine) usual dosage 10-80mg, stimulating, may cause insomnia if taken late in the day, some report increase in anxiety, least withdrawal symptoms due to liver enzyme inhibition, but more drug interactions
- Zoloft (sertraline) usual dosage 50-200mg not as stimulating or sedating

**Serotonin / Norepinephrine Reuptake Inhibitors (SNRIs)**

- Cymbalta (duloxetine) usual dosage 30-120mg, although seldom effective >60mg, often used for pain
- Effexor (venlafaxine) usual dosage 75-375mg may have quicker action so good for severe depression, fewer drug interactions than most, may increase blood pressure in higher dosages
- Effexor XR as above

**SSRIs**

- Luvox (fluoxamine) usual dosage 50-300mg, generally more sedating than the others, the first to be approved for OCD
- Paxil (paroxetine) usual dosage 20-60mg somewhat sedating, more drug interactions, weight gain, an more pronounced withdrawal symptoms
- Paxil CR usual dosage 12.5-62.5mg
Serotonin-2 antagonists
Reuptake Inhibitors (SARIs)

• Desyrel (trazadone) usual dosage 150-400mg sedating side effects, used mostly along with other antidepressants as a sleep aid
• Serzone (naftazodone) usual dosage 100-600mg may be sedating and help with anxiety 1 case liver failure resulting in death / transplant 250,000-300,000pt yrs, avoid if active liver disease

Noradrenergic / specific Serotonergic antidepressant (NaSSA)

• Enhances the release of norepinephrine and serotonin while blocking certain serotonin receptors
• Remeron (mitrazapine) usual dosage 15-45mg help when insomnia is a problem, may cause weight gain

Norepinephrine / Dopamine Reuptake Inhibitor (NDRI)

• Welbutrin (buproprion) usual dosage 150-450mg less likely to cause weight gain or sexual dysfunction, may initially increase anxiety, not for those with seizures
• Welbutrin SR (2 x daily dosing)
• Welbutrin XL (1 x daily dosing)
MAO Inhibitors

- First antidepressants marketed
- Discovered in the 1950’s serendipidously by chemist looking for treatment for TB

MAO Pharmacology

- Monoamine: neurotransmitters
- Oxidase: enzyme that breaks down monoamines
- MAO inhibitors: destroy this enzyme
- Allow for increased amount of neurotransmitters
- Work on norepinephrine, dopamine and serotonin

MAO I side effects

- Dangerous sudden increase in blood pressure which may lead to death, cerebral hemorrhage
- Avoid tyramine, which also increases blood pressure
- Tyramine is a natural substance found in the body and food products, tyramine forms as proteins break down as they age
Foods with Tyramine

- Aged sausages
- Beer
- Red wine
- Avocados
- Aged cheese
- Smoked fish
- Soy products

Drug Interactions

- Other antidepressants
- Most drugs for colds and asthma
- Drugs for the treatment of diabetes
- Blood pressure medications
- Some pain killers

Predictors for Potential Need for Combination Therapy

- Mania
- Mixed states
- Rapid cycling
- Psychosis
- Severity of disease
- Increasing age
- Prior hospitalization
- Depressive component
Continuation and Maintenance Phase
Treatment of Bipolar Disorder

Continuation Phase: Mania
• Continue successful acute therapies at full dose
  – To maintain effective serum levels
  – To allow patient to tolerate medication
• Average mania lasts 19 weeks

Maintenance Phase: General Principles
• Continue treatments that worked acutely—mood stabilizers
• If patient has significant history of depression
  – Consider adding lithium
  – Use an antidepressant as a second-line option
• Taper antipsychotic medications
  – If patient is left on antipsychotic, consider an atypical antipsychotic over conventional ones
• Use of Anxiolytics in the Treatment of Bipolar Disease

Anxiolytic Medications

• Benzodiazepines: Use for rapid symptom relief for the shortest duration possible
• Example: lorazepam

Management of Psychotic Symptoms Use of Antipsychotics in Bipolar Disorder
Conventional (Typical) vs Atypical Antipsychotics

Conventional
- Introduced in 1950s & 1960s
- Dopamine-receptor blockade
- Examples
  - Haloperidol
  - Thioridazine
  - Chlorpromazine

Atypical
- Introduced in the 1990s
- Dopamine and serotonin receptor blockade
- Examples
  - Clozapine
  - Risperidone
  - Olanzapine
  - Quetiapine
  - Ziprasidone
  - Aripiprazole


Typical agents
- Effective for the symptoms of hallucinations, abnormal thoughts, bizarre behavior, hostility, etc
- Untoward CNS effects
  - EPS
  - Tardive dyskinesia
- Sedation
- Impairment of cognitive function

Atypical agents
- Effective for all before mentioned symptoms as well as withdrawal, antisocial behavior, blunted affect, poor grooming and hygiene, etc
- Atypical agents associated with less EPS, TD
- Switch to newer agents due to increased coverage of symptom relief, side effect profile
Side Effect Considerations of Atypical Antipsychotics

- Sedation
- Orthostasis, esp upon arising
- EPS and TD
- Anticholinergic
- Gait disturbance
- Metabolic abnormalities
- Cerebrovascular adverse events: stroke, TIA
- QT prolongation

Antipsychotics

- Abilify (aripiprazole) 5-10mg, start at 2mg and increase to 5mg then 10mg, then 15 or 20mg as needed
- Adjunctive treatment for major depressive disorder
- Has minimal tendency to cause weight gain, metabolic side effects, sedation or movement disorders
- Side effects and drug interactions: see atypical antipsychotics

Antipsychotics

- Geodon (Ziprazadone) indicated for Bipolar I disease, as well as manic, mixed episodes
- May be used as monotherapy or as adjunctive therapy with VPA or Lithium
- Watch QT prolongation
# Antipsychotics

- **Larasidone (Latuda)**
  - Indicated for Bipolar I disorder, acute depressive
  - 20-120mg/day
  - Used as monotherapy or as adjunctive with VPA or Lithium
  - >80mg/day rarely more effective as monotherapy
  - Give with food

- **Olanzapine (Zyprexa)**
  - Indicated for Bipolar I Disorder, manic/mixed as either monotherapy or as an adjunct with VPA or Lithium
  - Indicated for agitation associated with Bipolar I Disorder
  - Indicated acute depressive episodes of Bipolar I Disorder
  - Indicated for acute treatment resistant major depressive disorder

- **Quetiapine (Seroquel)**
  - Indicated for manic phase of Bipolar I Disorder
  - Indicated for acute depressive phase of Bipolar I Disorder
  - Somnolence: give majority of dose later in day
Antipsychotics

• Asenapine (Saphris)
• Indicated for acute manic and mixed episodes of Bipolar I Disorder as either monotherapy or adjunctive with VPA or Lithium
• SL dosing, do not cut/crush/chew

Medical Management

• Use of atypicals over typical antipsychotics is justified based on effectiveness and side effect profile
• Weigh options and consider each patient as individual
• Start low, adjust slowly, consider dosage adjustment over time

Medical Management

• Polypharmacy not normally indicated
• Treat side effects as they occur
• If unmanageable side effects occur, consider switch to alternative agent
• Use antidepressants with caution
• May trigger manic phase of bipolar disease

Algorithms for Treatment of Bipolar Disorder

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<thead>
<tr>
<th>Psychiatric Condition</th>
<th>Preferred Medications</th>
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<tbody>
<tr>
<td>Bipolar, manic episode</td>
<td>VPA, Lithium, aripiprazole, quetiapine, risperidone, ziprazadone</td>
</tr>
<tr>
<td>Rapid cycling</td>
<td>VPA, aripiprazole, quetiapine, risperidone, ziprazadone</td>
</tr>
<tr>
<td>Divalproex/valproic acid</td>
<td></td>
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<tr>
<td>Bipolar, mixed/dysphoric episode</td>
<td></td>
</tr>
<tr>
<td>Bipolar, depressive episode</td>
<td>Lithium or divalproex, lamotrigine + anti-manic</td>
</tr>
<tr>
<td>Acute depressive disorder</td>
<td>Lamotrigine + anti-manic</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>Atypical antipsychotic</td>
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Summary
• Maximize standard mood stabilizers, including combination
• Utilize anxiolytic/hypnotics, atypical neuroleptics, and novel anticonvulsants as mood stabilizers for adjunctive therapy
• Brief, acute intermittent antidepressant treatment
• Address psychoeducational needs
• Consider possible clinical improvement and side effect reduction with long acting products
• Questions?