Unpacking Bipolar Disorder

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February 8, 2011
Bipolar Disorders: Scope of the Problem

- Bipolar I and II disorders occur in up to 4% of the population \(^1,2\)
- frequently begin in the mid to late-teens \(^3,4\)
- cause chronic disability \(^5-7\)
- characterized by recurrent and chronic symptoms with associated multiple psychiatric and medical comorbid conditions \(^1,2\)
  - also excess and premature mortality and suicide \(^8-10\)
- Bipolar disorder has been listed among the top 10 causes of disability worldwide \(^7\)
  - estimated to cost about $70 billion/year in 2008 dollars \(^11,12,15\)
Bipolar Disorders: Part I

Understanding Diagnosis

Whatever goes up must come down
unless it goes into orbit
Understanding the DSM
Diagnostic and Statistical Manual, 4th Edition, Revised
Published by the American Psychiatric Association

- **Committee determined symptom criteria**
  - Based on peer reviewed literature and/or
  - Expert consensus
- **Disability or clear change from baseline lasting a week or more**
- Not accounted for by a broader category of illness or substance use
- Designed to promote inter-rater consistency and credible research comparisons
Bipolar Disorder: What is it?

- A spectrum disorder of mood and cognition that has been described for centuries
- Classification and treatments have developed mostly since the 1970’s
- Psychotic levels of mania were often described as schizophrenia before then
Diagnostic requirements

- Symptoms meet full criteria for either
  - a major depressive episode in association with hypomaniac symptoms on occasion, or
  - a manic episode
What is Hypomania?
ICD 10: F30.0 Hypomania

- A disorder characterized by a
  - persistent mild elevation of mood
  - increased energy and activity
  - may show marked feelings of well-being and both physical and mental efficiency
  - increased sociability, talkativeness, over-familiarity
  - increased sexual energy
  - decreased need for sleep
  - irritability, conceit, and boorish behaviour not accompanied by hallucinations or delusions

- does not lead to severe disruption of work or result in social rejection
DSM 4 Criteria for Hypomanic Episode

A. A distinct period of persistently elevated, expansive, or irritable mood, lasting throughout at least 4 days, that is clearly different from the usual non depressed mood.

B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

1. inflated self-esteem or grandiosity
2. decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
3. more talkative than usual or pressure to keep talking
4. flight of ideas or subjective experience that thoughts are racing
5. distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
6. increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
7. excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., the person engages in unrestrained buying sprees, sexual indiscretions, or foolish business investments)
What is Mania?
“Doc, if I were Manic, could I do this for 12 hours and still keep my appointment?”
International Classification of Diseases, 10th Edition:  
Mania without psychotic symptoms

- **F30.1** Mood is elevated out of keeping with the patient's circumstances and may vary from carefree joviality to almost uncontrollable excitement.
  - Elation is accompanied by increased energy, resulting in overactivity, pressure of speech, and a decreased need for sleep.
  - Attention cannot be sustained, and there is often marked distractibility.
  - Self-esteem is often inflated with grandiose ideas and overconfidence.
  - Loss of normal social inhibitions may result in behaviour that is reckless, foolhardy, or inappropriate to the circumstances, and out of character.
International Classification of Diseases, 10th Edition: Mania *with* psychotic symptoms

- In addition to the clinical picture described in F30.1
- delusions (usually grandiose) or hallucinations (usually of voices speaking directly to the patient) are present, or
- the excitement, excessive motor activity, and flight of ideas are so extreme that the subject is incomprehensible or inaccessible to ordinary communication.
DSM5 Draft Criteria for Manic Episode: Criteria A
(requires all three below)

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)
DSM5 Draft Criteria for Manic Episode: Criteria B
(requires three or more that represent a noticeable change)

1. inflated self-esteem or grandiosity
2. decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
3. more talkative than usual or pressure to keep talking
4. flight of ideas or subjective experience of racing thoughts
5. distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed
6. increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
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)
Hypomania & Mania: Short Version

- Too energetic, talkative, impulsive, intrusive, gregarious, grandiose, boorish
  - Clear change from baseline
  - Creates significant problems with relationships, work/school, health
  - Lasts days or weeks
  - Not caused by drugs or medical illness

- If hallucinating, delusional, incomprehensible or hospitalized, then it’s mania
Manic illness in adolescents

- Grandiosity
- Hyper-sexuality
- Sleeplessness
Children and teens having a manic episode may

- Feel very happy or act silly in a way that’s unusual
- Have a very short temper
- Talk really fast about a lot of different things
- Have trouble sleeping but not feel tired
- Have trouble staying focused
- Talk and think about sex more often
- Do risky things
Manic symptoms during a first depressive episode

SLIDE 8
Symptoms of Mania During an Index Bipolar Depressive Episode in the NIMH STEP-BD

31% had no manic symptoms. Neither elation nor grandiosity was elevated.

NIMH STEP-BD = National Institute of Mental Health Systematic Treatment Enhancement Program for Bipolar Disorder.

What is Major Depression?
DSM 4 Symptoms of Major Depression

(need 5+ symptoms lasting more often than not for 2+ weeks)

A) Depressed mood or

B) Loss of interest or pleasure

- Change in appetite
- Change in weight
- Insomnia or hypersomnia
- Irritability
- Poor concentration
- Low energy
- Loss of libido
- Feelings of worthlessness
- Hopelessness/suicidal thinking/plan/intent/act
DSM5 Draft Criteria for Depressive Episode: Criteria A
requires five+ observable symptoms occurring more often than not over 2+ weeks including
1) depressed mood or
2) loss of pleasure or interest

1. Depressed mood
   ▪ **Note:** In children and adolescents, can be irritable mood.
2. Markedly diminished interest or pleasure
3. Significant weight loss or weight gain
   ▪ **Note:** In children, consider failure to make expected weight gain
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue or loss of energy
7. Feelings of worthlessness or excessive or inappropriate guilt
8. Diminished ability to think or concentrate, or indecisiveness
9. Recurrent thoughts of death or suicide (ask about plans)
Children and teens having a depressive episode may

- Feel very sad
- Complain about pain a lot, like stomachaches and headaches
- Sleep too little or too much
- Feel guilty and worthless
- Eat too little or too much
- Have little energy and no interest in fun activities
- Think about death or suicide
ICD 10 - Grading depression

- **F32.0** Two or three of the above symptoms are usually present. The patient is usually distressed by these but will probably be able to continue with most activities.

- **F32.1 Moderate depressive episode** Four or more of the above symptoms are usually present and the patient is likely to have great difficulty in continuing with ordinary activities.

- **F32.2 Severe depressive episode without psychotic symptoms** An episode of depression in which several of the above symptoms are marked and distressing, typically loss of self-esteem and ideas of worthlessness or guilt. Suicidal thoughts and acts are common and a number of "somatic" symptoms are usually present.
  - Agitated depression
  - Major depression
  - Vital depression
  - Single episode without psychotic symptoms

- **F32.3 Severe depressive episode with psychotic symptoms** An episode of depression as described in F32.2, but with the presence of hallucinations, delusions, psychomotor retardation, or stupor so severe that ordinary social activities are impossible; there may be danger to life from suicide, dehydration, or starvation. The hallucinations and delusions may or may not be mood-congruent. Single episodes of:
  - Major depression with psychotic symptoms
  - Psychogenic depressive psychosis
  - Psychotic depression
  - Reactive depressive psychosis
Other problems children and teens with bipolar disorder may have:

- Substance abuse
- ADD/ADHD
- Anxiety disorders (separation anxiety etc)
  - Children with both types of disorders may need to go to the hospital more often than other people with bipolar disorder.
- Medical illnesses
  - delirium, thyroid, steroids, tumors
- Trauma
  - disasters, severe losses, abuse
Mood Disorders Not Currently Listed in DSM-IV

- **Mixed Anxiety Depression**
- **Mixed Features Specifier**
- **Premenstrual Dysphoric Disorder**
Proposed Diagnostic Criteria for Mixed Anxiety Depression

- Three or four of the symptoms of **Major Depression** must include depressed mood and/or anhedonia, and accompanied by anxious distress.
  - Must have lasted at least 2 weeks
  - No other DSM diagnosis of anxiety or depression present
  - Both occurring at the same time

- **Anxious distress** is defined as having two or more of the following symptoms:
  - Irrational worry, preoccupation with unpleasant worries, having trouble relaxing, motor tension, fear that something awful may happen
Mixed Features Specifier (cont.)

B. If predominantly Depressed, full criteria are met for a Major Depressive Episode (see Criteria for Major Depressive Episode), and at least 3 of the following symptoms are present nearly every day during the episode.

- Elevated, expansive mood
- Inflated self-esteem or grandiosity
- More talkative than usual or pressure to keep talking
- Flight of ideas or subjective experience that thoughts are racing
- Increase in energy or goal directed activity (either socially, at work or school, or sexually)
- Increased or 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).
- Decreased need for sleep (feeling rested despite sleeping less than usual (to be contrasted from insomnia))

C. Mixed symptoms are observable by others and represent a change from the person’s usual behavior.

D. For those who meet full episode criteria for both Mania and Depression simultaneously, they should be labeled as having a Manic Episode, with mixed features, due to the marked impairment and clinical severity of full mania.

E. The mixed symptom specifier can apply to depressive episodes experienced in Major Depressive Disorder, Bipolar I and Bipolar II disorders.

F. The mixed symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment).
**SLIDE 1**

**DSM-IV Mixed Episode**

- Mood Elevation, Irritability, or Depression

<table>
<thead>
<tr>
<th>Manic Symptoms</th>
<th>Depressive Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distractibility</td>
<td>Sleep increase or decrease</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Interest diminished</td>
</tr>
<tr>
<td>Grandiosity</td>
<td>Guilt/low self-esteem</td>
</tr>
<tr>
<td>Flight of ideas/racing thoughts</td>
<td>Energy loss</td>
</tr>
<tr>
<td>Activity increase</td>
<td>Concentration poor</td>
</tr>
<tr>
<td>Speech increase</td>
<td>Appetite increase or decrease</td>
</tr>
<tr>
<td>Thoughtlessness</td>
<td>Psychomotor agitation/retardation</td>
</tr>
<tr>
<td>Suicidality</td>
<td></td>
</tr>
</tbody>
</table>
SLIDE 3

Bipolar Symptoms Usually Accompany Bipolar Depressive Episodes: Number of DSM-IV Manic Symptoms During an Index Episode of Bipolar Depression in STEP-BD (N=1,380)⁴

<table>
<thead>
<tr>
<th>Number of DSM-IV Manic Symptoms</th>
<th>Percent of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>31.2%</td>
</tr>
<tr>
<td>1</td>
<td>54.0%</td>
</tr>
<tr>
<td>2</td>
<td>14.8%</td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
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<tr>
<td>5</td>
<td></td>
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<tr>
<td>6</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; STEP-BD=Systematic Treatment Enhancement Program for Bipolar Disorder.
Premenstrual Dysphoric Disorder (PMDD)

A. In most menstrual cycles during the past year, five (or more) of the following symptoms occurred during the final week before the onset of menses, started to improve within a few days after the onset of menses, and were minimal or absent in the week postmenses, with at least one of the symptoms being either (1), (2), (3), or (4):

1. markedly depressed mood, hopelessness, or self-deprecating thoughts
2. marked anxiety, tension, feelings of being "keyed up," or "on edge"
3. marked affective lability
4. marked irritability or anger or increased interpersonal conflicts
5. decreased interest in usual activities (work, school, friends, hobbies)
6. subjective sense of difficulty in concentration
7. lethargy, easy fatigability, or marked lack of energy
8. marked change in appetite, overeating, or specific food cravings
9. hypersomnia or insomnia
10. a subjective sense of being overwhelmed or out of control
11. other physical symptoms such as breast tenderness or swelling, joint or muscle pain, a sensation of "bloating," weight gain
Bipolar Disorders: Part II

Differential Diagnosis

What else could it be?
DSM 4: What else could be going on?

Mood Disorders
- Mood Episodes: Major Depressive Episode | Hypomanic Episode | Manic Episode | Mixed Episode
- Depressive Disorders: Dysthymic Disorder | Major Depressive Disorder: Single Episode | Recurrent
- Bipolar Disorders: Bipolar I Disorder | Bipolar II Disorder | Cyclothymic Disorder | Bipolar Disorder NOS 296.80
- Mood Disorder Due to a General Medical Condition with: Depressive Features | Manic Features | Mixed Features
- Substance-Induced Mood Disorder
- Mood Disorder NOS (296.90)

Anxiety Disorders: Acute Stress Disorder | Agoraphobia Without History of Panic Disorder | Anxiety Disorder Due to General Medical Condition | Generalized Anxiety Disorder | Obsessive-Compulsive Disorder | Panic Disorder With Agoraphobia | Panic Disorder Without Agoraphobia | Posttraumatic Stress Disorder | Specific Phobia | Social Phobia | Substance-Induced Anxiety Disorder | Anxiety Disorder NOS (300.00)

Somatoform Disorders: Body Dysmorphic Disorder | Conversion Disorder | Hypochondriasis | Pain Disorder | Somatization Disorder | Undifferentiated Somatoform Disorder | Somatoform Disorder NOS (300.81)

Factitious Disorders: Psychological | Physical | Combined | Factitious Disorder NOS (300.19)

Dissociative Disorders: Dissociative Amnesia | Depersonalization Disorder | Dissociative Fugue | Dissociative Identity Disorder | Dissociative Disorder NOS (300.15)
Trauma

- The great impersonator among mood disorders
  - Create open, no-fault alliances
  - Piece together a careful history
  - Be sure your client stays in charge of therapy focus, pace and content
  - If all else fails, slow it down
    - better too slow than too fast
Prevalence of civilian trauma and posttraumatic stress disorder in a representative national sample of women

Lifetime exposure to any type of traumatic event was 69%

Exposure to crimes that included sexual or aggravated assault or homicide of a close relative or friend occurred among 36%

Prevalence of PTSD was 12.3% lifetime and 4.6% within prior 6 months

The rate of PTSD was significantly higher among crime vs noncrime victims (25.8% vs 9.4%).

History of incidents that included direct threat to life or receipt of injury was a risk factor for PTSD.

-- Resnick, Heidi S.; Kilpatrick, Dean G.; Dansky, Bonnie S.; Saunders, Benjamin E.; Best, Connie L.

Journal of Consulting and Clinical Psychology, Vol 61(6), Dec 1993, 984-991
The number of American adults who abuse alcohol or are alcohol dependent rose from 13.8 million (7.41 percent) in 1991-1992 to 17.6 million (8.46 percent) in 2001-2002, according to results from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a study directed by the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

The NESARC study -- a representative survey of the U.S. civilian noninstitutionalized population aged 18 years and older - showed that the rate of alcohol abuse increased from 3.03 to 4.65 percent across the decade while the rate of alcohol dependence, commonly known as alcoholism, declined from 4.38 to 3.81 percent.
SLIDE 7
Lifetime Prevalence of Alcohol Abuse or Dependence: High Degree of Association With Bipolar Disorder

Percent (%)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP I</td>
<td>46.2</td>
</tr>
<tr>
<td>BP II</td>
<td>39.2</td>
</tr>
<tr>
<td>SZ</td>
<td>33.7</td>
</tr>
<tr>
<td>PD</td>
<td>28.7</td>
</tr>
<tr>
<td>OCD</td>
<td>24.0</td>
</tr>
<tr>
<td>DYS</td>
<td>21.0</td>
</tr>
<tr>
<td>MDD</td>
<td>16.5</td>
</tr>
<tr>
<td>Gen Pop</td>
<td>13.8</td>
</tr>
</tbody>
</table>

BP = bipolar disorder; SZ = schizophrenia; PD = panic disorder; OCD = obsessive-compulsive disorder; DYS = dyslipidemia; MDD = major depressive disorder; Gen Pop = general population.
Bipolar Disorders: Part III

What causes bipolar moodswings?
Bipolar Disorder: Causes
Causes of Bipolarity

- A 2000 study in the American Journal of Psychiatry reported "in those with bipolar disorder, two major areas of the brain contain 30 percent more cells that send signals to other brain cells." This report theorizes that "the extra signal-sending cells may lead to a kind of overstimulation, which makes sense considering the symptoms of bipolar disorder(1).

- **Twin studies:** if one twin has a mood disorder, an identical twin is about three times more likely than a fraternal twin to have a mood disorder as well(2).

- In bipolar disorder specifically, the concordance rate (when both twins have the disorder) is 80 percent for identical twins, as compared to only 16 percent for fraternal twins(2).

- **Stressful life events** can lead to the onset of symptoms in bipolar disorder. However, once the disorder is triggered and progresses, "it seems to develop a life of its own."
Causes (continued)

- "Diathesis-Stress Model"
  - Underlying genetic vulnerability
    - (parent, twin)
  - Environmental stressors
    - Disasters, civic traumas, interpersonal traumas
  - Medical stressors
    - Severe illness, chronic illness
  - Chemical stressors
    - Narcotics, psychosis-inducing drugs, toxins
A bipolar blood test? Yes

A total of 10 candidate genes survived the screenings. Five came from the selection in the highmood, or manic population: Atxn1, EdnRb, Edg2, Fzd3, and Mbp. Five came from the selection in the low-mood, or depressive population: Erbb3, FGfr1, Mag, Pmp22, and Ugt8.

What do these gene sequences do? This is probably the most biologically interesting aspect of the work, and it is easily the most opaque.

Some of the gene sequences are involved in the normal myelination of neurons. These included the sequences Edg2, Mag, Mbp, Pmp22, and Ugt8.

Several of these are involved in growth factor signaling: Erbb3, FGfr1, Fzd3, Igfbp6, and Ptprm.

What does the isolation of these sequences mean to our biological understanding of mood disorders? Not much, unfortunately.
Shrinkage of dendritic spines associated with long-term depression of hippocampal synapses


Zhou Q, Homma KJ, Poo MM.
Division of Neurobiology, Department of Molecular and Cell Biology, Helen Will Neuroscience Institute, University of California, Berkeley, Berkeley, CA 94720, USA.

Abstract
Activity-induced modification of neuronal connections is essential for the development of the nervous system and may also underlie learning and memory functions of mature brain. Previous studies have shown an increase in dendritic spine density and/or enlargement of spines after the induction of long-term potentiation (LTP). Using two-photon time-lapse imaging of dendritic spines in acute hippocampal slices from neonatal rats, we found that the induction of long-term depression (LTD) by low-frequency stimulation is accompanied by a marked shrinkage of spines, which can be reversed by subsequent high-frequency stimulation that induces LTP. The spine shrinkage requires activation of NMDA receptors and calcineurin, similar to that for LTD. However, spine shrinkage is mediated by cofilin, but not by protein phosphatase 1 (PP1), which is essential for LTD, suggesting that different downstream pathways are involved in spine shrinkage and LTD. This activity-induced spine shrinkage may contribute to activity-dependent elimination of synaptic connections.
SPECT scan of woman with bipolar disorder
SPECT scan of woman with depression and anxiety
Tickets, please

Intermission
Relapse prevention

Education should be provided to the patient and family regarding the impact of:

- Noncompliance with medications
- Recognition of emergent relapse symptoms
- Sleep deprivation, substance abuse
- Stress reduction
- Promotion of stable social and sleep habits, especially for adolescents

Social and family functioning

- Bipolar disorder significantly affects
  - Social
  - Family
  - Academic
  - Developmental functioning

- Helpful Efforts:
  - Education about bipolar disorder and comorbidities
  - Individual medication and psychotherapy
  - Family therapy
  - Support groups
  - Incorporate cultural values and perspectives

Third Grade Quiz

The importance of accurate communication
Academic and occupational functioning

The educational needs of youths with bipolar disorder must be adequately addressed to help promote longterm academic growth, especially given the high rates of comorbid disruptive behavior disorders.

School consultation
Individual educational plan
Day treatment or partial hospitalization programs
For older teenagers, vocational training and occupational support

Community consultation

- Consultation may be needed
  - juvenile justice
  - social welfare programs
- Intensive community-based services to maintain them at home
- Foster care or residential services
- Community support and advocacy programs
Researchers randomly assigned participants to receive either a short-term collaborative care intervention or one of three longer-term intensive therapies that have been shown to help stabilize bipolar symptoms—cognitive-behavioral therapy (CBT), interpersonal and social rhythm therapy (IPSRT), or family-focused treatment (FFT). Collaborative care was considered the “control” intervention.
STEP-BD: What do the results mean for people with bipolar depression and the doctors who provide care for them?

- **A.** This one-year study showed that, in conjunction with adequate mood stabilizing medications, intensive psychotherapy is more effective in helping people recover from a depressive episode, and stay well over a one-year period, than a brief collaborative care treatment. All three types of intensive psychosocial treatments had comparable benefits.

- Overall, *psychotherapy appears to be a vital part of the effort to stabilize episodes of depression in bipolar illness*.
Case example # 1

- Jeanine is a 17yo high school senior who came in reluctantly during winter break at her mother’s insistence, because her grades had plummeted and she was no longer going out with her friends.

- She was way more irritable than usual and had been slamming her door closed on her parents and younger brother.
Mood screen results

- Positive for
  - Low energy, poor appetite, irritability, poor concentration, feelings of hopelessness, and periods ~ twice a month of very high energy for parts of a day

- Family history: paternal uncle – bipolar, successful on meds; father – depression, mild; mother – occ panic; maternal grandmother – Alzheimer’s
Diagnosis: possible Bipolar II vs. Major Depression, recurrent

- Does not meet full criteria for a hypomanic episode
- May well respond to medication for bipolar
Treatment

- Education about depression vs bipolar
- Query successful treatments for any family member
- Trial of antidepressant if high side energy not too disabling
- If high side energy is disabling, then trial of lamotrigine or antidepressant + lithium or depakote or oxcarbazepine
- Follow-up within 2 to 2½ weeks
The Antidepressants

- Tricyclics
- Tetracyclics
- SSRIs
- SNRIs
- Atypical antipsychotics (for psychotic depressions)
CONCLUSIONS: Mood stabilisers are moderately efficacious for acute bipolar depression. Extant studies are few and limited by high rates of discontinuation and short duration. Further study of existing and novel agents is required.
### Mood Stabilizer Safety and Tolerability

<table>
<thead>
<tr>
<th>Lithium</th>
<th>Valproate</th>
<th>Carbamazepine</th>
<th>Lamotrigine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>Gastrointestinal</td>
<td>Gastrointestinal</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>Weight gain</td>
<td>Weight gain</td>
<td>Rash</td>
<td>Rash</td>
</tr>
<tr>
<td>Neurotoxicity</td>
<td>Tremor</td>
<td>Neurotoxicity</td>
<td>Headache</td>
</tr>
<tr>
<td>Renal toxicity</td>
<td>Hepatotoxicity</td>
<td>Hepatotoxicity</td>
<td>Dizziness</td>
</tr>
<tr>
<td>Thyroid toxicity</td>
<td>Thrombocytopenia</td>
<td>Thyroid changes</td>
<td>Pruritus</td>
</tr>
<tr>
<td>Hair Loss</td>
<td>Hair Loss</td>
<td>Blood dyscrasias</td>
<td>Dream abnormality</td>
</tr>
<tr>
<td>Cardiac toxicity</td>
<td>Pancreatitis</td>
<td>Cardiac toxicity</td>
<td></td>
</tr>
<tr>
<td>Acne, psoriasis</td>
<td>PCOS</td>
<td>Hyponatremia</td>
<td></td>
</tr>
<tr>
<td>Teratogen</td>
<td>Teratogen</td>
<td>Teratogen</td>
<td>Teratogen</td>
</tr>
<tr>
<td>Suicidality (?)</td>
<td>Suicidality (?)</td>
<td>Suicidality (?)</td>
<td></td>
</tr>
</tbody>
</table>

Red boxes indicate boxed warning in prescribing information.

(?) = recent alert. PCOS = polycystic ovary syndrome. All mood stabilizers have at least one boxed warning.
The Mood Stabilizers

- **Lithium** *(the best for those with stable water balance)*
- **The anticonvulsants** *(best for rapid cycling moods)*
  - Depakote *(works well - too much weight gain for most patients)*
  - Lamictal* *(for predominant depression with minimal elevations)*
  - Trileptal* *(good all-purpose mood stabilizer)*
  - Gabapentin *(well tolerated – helpful as second agent)*
- **The atypical antipsychotics**
  - Olanzapine* *(effective for psychosis & sedation - very sedating)*
  - Quetiapine* *(good anxiolytic at lower doses)*
  - Risperidone* *(~ avoids weight gain)*
  - Ziprazidone *(well tolerated – doesn’t work all that well)*
  - Aripiprazole* *(well tolerated – doesn’t always work)*

* My usual choices
Bipolar Disorders: Part V

Co-Morbidity
Suicide Risk for Bipolar Disorders

Take home message: Lithium works

- RESULTS: Data from 34 reported studies involved 42 groups with lithium maintenance averaging 3.36 years, and 25 groups without lithium followed for 5.88 years, representing 16,221 patients in a total experience of 64,233 person-years.

- Risks for all suicidal acts/100 person-years averaged 3.10 without lithium versus 0.210 during treatment (93% difference) versus approximately 0.315 for the general population. A 14-fold increase

- For attempts, corresponding rates were 4.65 versus 0.312 (14-fold increase), and for completed suicides, 0.942 versus 0.174 (5-fold increase).

- Subjects with bipolar versus various recurrent major affective disorders showed similar benefits (95% vs. 91% sparing of all suicidal acts).

- Risk reductions for unipolar depressive, bipolar II, and bipolar I cases ranked 100%, 82%, and 67%. Suicide risk without lithium tended to increase from 1970 to 2002, with no loss of effectiveness of lithium treatment.

Suicide among children and young people

In 2007, suicide was the third leading cause of death for young people ages 15 to 24.¹

Children ages 10 to 14 — 0.9 per 100,000
Adolescents ages 15 to 19 — 6.9 per 100,000
Young adults ages 20 to 24 — 12.7 per 100,000

As in the general population, young people were much more likely to use firearms, suffocation, and poisoning than other methods of suicide, overall.

Children were dramatically more likely to use suffocation.¹

Gender differences:
Males 15-19 – 5 times more likely
Males 20-24 – 6 times more likely
SLIDE 1
Common Medical Conditions in Patients with Bipolar Disorder

- Hypertension: 35%
- Dyslipidemia: 25%
- Alcohol Use d/o: 25%
- Diabetes: 17%
- Low Back Pain: 15%
- Arthritis: 15%
- IHD: 11%
- COPD: 11%
- Cocaine use d/o: 10%
- Hepatitis C: 6%

IHD = ischemic heart disease; COPD = chronic obstructive pulmonary disease.

<table>
<thead>
<tr>
<th>Modifiable Risk Factors</th>
<th>Schizophrenia</th>
<th>Bipolar Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>45–55%, 1.5–2 x RR</td>
<td>21–49%, 1–2 x RR</td>
</tr>
<tr>
<td>Smoking</td>
<td>50–80%, 2–3 x RR</td>
<td>54–68%, 2–3 x RR</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10–15%, 2 x RR</td>
<td>8–17%, 2 x RR</td>
</tr>
<tr>
<td>Hypertension</td>
<td>19–58%, 2–3 x RR</td>
<td>35–39%, 2 x RR</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>25%, ≤5 x RR</td>
<td>23%, ≤5 x RR</td>
</tr>
</tbody>
</table>
Twenty percent of hospital admissions are due to drug adverse events
SLIDE 1

Comorbidity Rates of Major Depressive Disorder/Dysthymia and Adult ADHD

Primary Diagnostic Group

- ADHD 18.6%
- ADHD 12.8%
- Major Depression 9.4%
- Dysthymia 22.6%

ADHD=attention-deficit/hyperactivity disorder.
Bipolar Disorders: Part VI

Case discussion
Case question

- I have a client in her late 30s, she had two suicidal attempts in her teens. She was not diagnosed with BD until 7 years ago. The previous diagnosis was depression. She exhibits symptoms of anxiety, some panic reactions, depression and rage episodes. She is on Depakote (1000mg) and Welbutrin extended release (300mg) now. She would like to know what interventions or alternative therapies will be helpful to her besides medication.
Depression vs Bipolar II

- How can we tell the difference between depression and Bipolar disorder II? What are the consequences of a mis-diagnosis in regard to the treatment? I have a client told me that he was treated for depression and has a hard time and almost committed suicide. Later on he was diagnosed of bipolar disorder and was helped by medication.
Trauma and Moodswings

- Traumatic stress is a subjective experience
  - Overwhelmed by fear of death, severe pain, humiliation
  - Intentional assault much worse than accidental injury of the same severity
  - Prior trauma predisposes to heightened distress
  - Trauma leads to irritability, panic, emotional collapse, flashbacks, and subsequent intrusive fears and disability
- These experiences can create major moodiness
- Physical self-harm can effectively displace terrorized feelings for short periods of time, as can suicidal thinking
Getting Started
Establishing your alliance for healing

- How can I help you?
  - 15-20 minutes to elicit your client’s story
- What will change if we are successful?
- How will you know when we have finished our work together?
- What ideas do you have about what will help?
- What has helped at least on occasion?
Mood symptoms to watch for

- Childhood tantrums lasting over half hour
- Childhood statements about wanting to die
- Difficult to soothe
- Resistant to being held or cuddled
- Chronically irritable or moody
- Childhood depression
- Soaks up more than half a mother’s energy
Follow-up Strategies

- Help parents/partners see the necessity to care well for themselves first
- Solve the empty-jar depletion of family energy
- It takes a village to scaffold bipolar behaviors
- Help the family create a treatment team
Bipolar over the lifespan

- Life-long illness requires constant care
  - “I have a bipolar illness which I cannot control by myself”
  - Medication
  - Family support
  - Community support

- Many successful professionals – healthy personalities

- Many severely disabled – overwhelmed by symptoms they cannot control
Stable is a place where horses live
Hypomanics build houses in the sky

Manics live in them

Psychiatrists collect the rent
Some Baggage You Just Can’t Lose At The Airport
You appear to have a bipolar disorder.
GREAT TRUTHS ABOUT LIFE
THAT LITTLE CHILDREN HAVE
LEARNED
Bipolar Disorder

National Institute of Mental Health
Resources

- The Greg Montgomery Story (NFL punter with bipolar disorder) [http://vimeo.com/18105537](http://vimeo.com/18105537)

- National Institutes of Mental Health brochures: