What is Type II Bipolar Disorder?

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## Dr. Jeffrey Rakofsky,
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<table>
<thead>
<tr>
<th>External Industry Relationships *</th>
<th>Company Name(s)</th>
<th>Role</th>
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<tbody>
<tr>
<td>Equity, stock, or options in biomedical industry companies or publishers**</td>
<td>None</td>
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<tr>
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<tr>
<td>Royalties from Emory or from external entity</td>
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</tr>
<tr>
<td>Industry funds to Emory for my research</td>
<td>Novartis, AstraZeneca</td>
<td>Principal Investigator</td>
</tr>
<tr>
<td>Other</td>
<td>None</td>
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*Consulting, scientific advisory board, industry-sponsored CME, expert witness for company, FDA representative for company, publishing contract, etc.  
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Learning Objectives

1. To understand the diagnostic criteria for Bipolar Disorder type II

2. To become familiar with demographic and clinical findings associated with Bipolar Disorder type II

3. To become familiar with treatment options for Bipolar Disorder type II
Bipolar Disorder

- Mood disorder characterized by recurrent manic, hypomanic, depressive and mixed episodes
- Affects close to 5% of the population
- Significant morbidity and mortality
Catherine Zeta-Jones has Bipolar II
Bipolar Diagnosis Rules:

• 1 or more manic episodes = Bipolar Type I

• 1 or more hypomanic episodes + 1 or more Depressive episodes = Bipolar Type II
What is a Manic Episode?

• A period of elevated, euphoric or irritable mood lasting at least one week

• 3 (or 4, if mood is irritable) symptoms characterized by accelerated cognitive and behavioral activity which occur simultaneously with the mood change. (DIGFAST)

• Must cause severe impairment
D.I.G.F.A.S.T.

- D-Distractibility
- I-Insomnia (decreased need for sleep)
- G-Grandiosity
- F-Fast (racing) thoughts/flight of ideas
- A-Activities (increased, goal directed)
- S-Speech (overtalkative)
- T-Thoughtless (reckless-impulsive) behaviors
What is a Hypomanic Episode?

• A period of elevated, euphoric or irritable mood lasting at least four days

• 3 (or 4, if mood is irritable) symptoms characterized by accelerated cognitive and behavioral activity which occur simultaneously with the mood change. (DIGFAST)

• Must NOT cause severe impairment
What is a Depressive Episode?

• A period of sad mood or loss of interest in most things all day long, nearly every day for at least two weeks.

• 4 symptoms characterized by decelerated cognitive and behavioral activity.

• Must cause impairment
S.I.G.E.C.A.P.S.

- S-Sleep changes (usually increased)
- I-Loss of interest
- G-guilty feelings/worthlessness
- E-Energy low
- C-Concentration
- A-Appetite changes (usually increased)
- P-Psychomotor changes (usually retardation)
- S-Suicidal ideation or recurrent thoughts of death
Bipolar Diagnosis Rules:

- 1 or more manic episodes = Bipolar Type I
- 1 or more hypomanic episodes + 1 or more Depressive episodes = Bipolar Type II
Lifetime Bipolar Prevalence Rates

- Type II = 1.1%
- Type I = 1%
- Subthreshold BPD = 2.4%

Merikangas et al., Archives of General Psychiatry, 2007; 64:543.
## 1-3 days vs. 4 days?

**Zurich Cohort Study: Validators of Episode Length of Hypomania**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Hypomanic 1-3 days</th>
<th>Hypomanic 4+ days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of Onset (median)</td>
<td>n/a</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Fam Hx of Mania</td>
<td>4.2</td>
<td>8.7</td>
<td>16.5</td>
</tr>
<tr>
<td>Fam Hx of Depression</td>
<td>30</td>
<td>50</td>
<td>48.9</td>
</tr>
<tr>
<td>Suicide Attempts</td>
<td>2.2</td>
<td>16.7</td>
<td>8.4</td>
</tr>
<tr>
<td>Hypomonic days per yr*</td>
<td>n/a</td>
<td>31.6</td>
<td>59.3</td>
</tr>
<tr>
<td>Depressive days per yr</td>
<td>n/a</td>
<td>73.0</td>
<td>68.9</td>
</tr>
</tbody>
</table>

Angst et al., *J Affective Disorders*, 2003; 73:133.

### 2-6 days vs. ≥ 7 days hypomania: no difference in course, demographics, age at onset, clinical presentation or severity, family hx of mood disorders, or comorbid anxiety/substance use disorders

Judd et al., *Arch Gen Psy*, 2003; 60:261.
Gender Distribution

- Type II
  (1:2)

- Type I
  (1:1)

Bipolar II Symptom Burden

- Patients spend more than half the follow up time symptomatically ill—mostly depressed

Percent of weeks spent in different mood states

- Asymptomatic: 46.1%
- Pure depression: 50.3%
- Pure mania/hypomania: 1.3%
- Cycling/mixed symptoms: 2.3%

Judd et al., Archives of Gen Psych, 2003; 60:261
Bipolar I Symptom Burden

- Patients spend much less time depressed than Type II patients and more time manic/hypomanic

Percent of weeks spent in different mood states:

- Asymptomatic: 52.7%
- Pure depression: 9.3%
- Pure mania/hypomania: 5.9%
- Cycling/mixed symptoms: 31.9%

Judd et al., *Archives of Gen Psych*, 2002; 59:530
Bipolar Patients Often Miss Work

% of patients with work absenteeism > 1 yr

Ruggiero et al., *J of Affective Disorders*, 2007; 104:53
Bipolar II Patients Have Worse Health-Related Quality of Life

Medical Outcomes Study 36-Item-Short-Form Health Survey Scores

Maina et al., J Clinical Psychiatry, 2007; 68:207
Bipolar I and II Patients Experience Problems with Cognition

- Executive Function and Verbal memory
- May be worse for Type I
- Independent of mood state

Bipolar II Demonstrates Diagnostic Stability Over 5 years

<table>
<thead>
<tr>
<th></th>
<th>Non-Bipolar</th>
<th>Bipolar II</th>
<th>Bipolar I</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=442)</td>
<td>(N=64)</td>
<td>(N=53)</td>
</tr>
<tr>
<td># with at least 1 Manic Episode</td>
<td>4.3%</td>
<td>10.9%</td>
<td>60.4%</td>
</tr>
<tr>
<td># with at least 1 Hypomanic Episode</td>
<td>8.4%</td>
<td>40.6%</td>
<td>54.7%</td>
</tr>
</tbody>
</table>

Coryell et al., *Psychological Medicine*, 1989;19:129
## Bipolar II Breeds True

### Morbid Risk For Diagnosis Among 1st Degree Family Members

<table>
<thead>
<tr>
<th>Proband Diagnosis</th>
<th>Bipolar I</th>
<th>Bipolar II</th>
<th>Non-Bipolar</th>
</tr>
</thead>
</table>
| Bipolar I
N=82             | 2.9       | 2.5*       | 22.7        |
| Bipolar II
N=33             | 0.9       | 9.8        | 21.4        |
| Non-Bipolar
N=212             | 0.2       | 2.6*       | 29.4        |

* P < 0.01 compared to relatives of BD II probands

# Lifetime Comorbidities

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Bipolar I</th>
<th>Bipolar II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Substance Abuse-Dependence(^1)</td>
<td>57.8%</td>
<td>38.9%</td>
</tr>
<tr>
<td>Any Anxiety Disorder(^2)</td>
<td>52.8%</td>
<td>46.1%</td>
</tr>
<tr>
<td>Any Eating Disorder(^3)</td>
<td>14.5%</td>
<td>13.7%</td>
</tr>
<tr>
<td>Migraines(^4)</td>
<td>19.2%</td>
<td>34.8(^*)</td>
</tr>
</tbody>
</table>

\(^*\) P < 0.05

\(^1\) Chengappa et al., *Bipolar Disorders*, 2000; 2:191
\(^2\) Simon et al., *Am J Psychiatry*, 2004; 161:2222
\(^3\) McElory et al., *J Affective Disorders*, 2011; 128:191
\(^4\) Ortiz et al., *Bipolar Disorders*, 2010; 12:397
Suicide Rates

- **Attempts**
  - Type II = 32.4%
  - Type I = 36.3%

- **Completions**
  - Diagnoses of Victims

- Bipolar II: 53%
- Bipolar I: 46%
- Non-bipolar depression: 1%

Novick et al., *Bipolar Disorders*, 2010; 12:1

Rihmer et al., *J of Affective Disorders*, 1990; 18:221
## Treatment Options...

<table>
<thead>
<tr>
<th>Medication</th>
<th>Evidence</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quetiapine</td>
<td>1. Pooled data from 2 large studies: ++</td>
<td>Consider as 1&lt;sup&gt;st&lt;/sup&gt; line</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>1. BD II study: -</td>
<td>Consider as 2&lt;sup&gt;nd&lt;/sup&gt; line</td>
</tr>
<tr>
<td></td>
<td>2. Meta-regression: +</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Combination: +</td>
<td></td>
</tr>
<tr>
<td>Lithium</td>
<td>1. Open-label trial: ++</td>
<td>Consider as 2&lt;sup&gt;nd&lt;/sup&gt; line</td>
</tr>
<tr>
<td></td>
<td>2. Historical clinical experience: +</td>
<td></td>
</tr>
<tr>
<td>Antidepressants</td>
<td>1. Open-label, BD II: +</td>
<td>Consider as 2&lt;sup&gt;nd&lt;/sup&gt; line</td>
</tr>
<tr>
<td></td>
<td>2. Combination study: -</td>
<td></td>
</tr>
<tr>
<td>Pramipexole</td>
<td>1. Small study in BD II: +</td>
<td>Consider as 2&lt;sup&gt;nd&lt;/sup&gt; line</td>
</tr>
<tr>
<td>Valproate</td>
<td>1. Small study: not evaluated</td>
<td>Inadequate data</td>
</tr>
<tr>
<td>Modafanil</td>
<td>1. Combination study: +/-</td>
<td>Inadequate data</td>
</tr>
<tr>
<td>Omega-3 Fatty Acids</td>
<td>1. 2 large trials: +/-</td>
<td>Inadequate data</td>
</tr>
</tbody>
</table>

Conclusions

• Bipolar II differs from Bipolar I clinically, genetically, and demographically

• Bipolar II may be equally impairing as Bipolar I

• More Bipolar II specific treatments are needed
Questions?

Call 404-778-MOOD to learn more about our clinical trials!