Bipolar Depression & OCD

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Learning objectives

At the end of this session, participants will be able to:

• Review the diagnosis of Bipolar Disorder and it’s epidemiology

• Management of BP Depression.

• Diagnose OCD with increased confidence.

• Choose evidence-based pharmacotherapies to help patients with Bipolar Disorder & OCD.

• Utilize behavioural interventions to help manage OCD.
Faculty/Presenter Disclosure

• Faculty: Dr. Nik Grujich
• Relationships with commercial interests:
  – Grants/Research Support: Nil
  – Speakers Bureau/Honoraria: Sunovion, Pfizer
  – Consulting Fees: Nil
Case
Normal Life
Mood Episodes

Mood
Mood Episodes

Mood

Mania

Depression
Mood Episodes

- Mania
- Depression
- Hypomania
Mixed Features Specifier
Epidemiology

• Life time prevalence:
  – BP-1 = 0.87%
  – BP-2 = 0.67%

• Age of onset: 25 years (teens – thirty's)
  – In atypical presentations, consider organic causes (eg onset after age 50).
Course of Bipolar Disorder

• 80-90% of individuals have recurrences

• Average lifetime # of episodes = 9
  • 4 episodes/10 years
Course Of Illness

• Highly variable
  – Good interepisode recovery
  – 60% BP 1 will have chronic difficulties b/w episodes

• Poor response to treatment
  • Non-adherence
  • SUD
  • Comorbid illness (eg personality disorder, SUD, Anxiety)

Time Spent in Different Phases of Bipolar Illness

146 BD-I patients followed 12.8 years

- Asymptomatic: 53%
- Depressed: 32%
- Manic/hypomanic: 9%
- Cycling/mixed: 6%

86 BD-II patients followed 13.4 years

- Asymptomatic: 46%
- Depressed: 50%
- Manic/hypomanic: 2%
- Cycling/mixed: 1%

% Weeks

Importance of Early Diagnosis & Tx

• More episodes, more likely chance of relapse and longer duration and more severe episodes

Neuroprogressive Disease

• Reduction in grey and white matter volume.
• Worsening cognitive impairment.
• Decrease in inter-episodic recovery and functioning.
• Higher rate and severity of relapse.
• Reduced rate of treatment response to both pharmacotherapy and psychotherapy.

More episodes ➔ Neuroprogression

Revolving Door = Vicious Cycle

Delay in treating first episode

Treatment response but subsequent poor adherence to treatment

Progression to chronic illness and/or treatment resistance

Relapse & need to re-establish treatment
Screening For BP

• Complete a careful psychiatric history including:
  – FHx of first-degree relatives.
  – Attention paid to any suspected periods of increased activity, irritability, or other change in behaviours.
  – Collateral information*.

• Serial monitoring of symptoms (mood charting)

• Validated instrument such as the MDQ

THE MOOD DISORDER QUESTIONNAIRE

Instructions: Please answer each question to the best of your ability.

1. Has there ever been a period of time when you were not your usual self and...

   YES | NO
   --- | ---
   ...you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?
   ...you were so irritable that you shouted at people or started fights or arguments?
   ...you felt much more self-confident than usual?
   ...you got much less sleep than usual and found you didn’t really miss it?
   ...you were much more talkative or spoke much faster than usual?
   ...thoughts raced through your head or you couldn’t slow your mind down?
   ...you were so easily distracted by things around you that you had trouble concentrating or staying on track?
   ...you had much more energy than usual?
   ...you were much more active or did many more things than usual?
   ...you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?
   ...you were much more interested in sex than usual?
   ...you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?
   ...spending money got you or your family into trouble?

2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time?

3. How much of a problem did any of these cause you – like being unable to work, having family, money or legal troubles, getting into arguments or fights?
   Please circle one response only.
   No Problem | Minor Problem | Moderate Problem | Serious Problem

4. Have any of your blood relatives (i.e. children, siblings, parents, grandparents, aunts, uncles) had manic-depressive illness or bipolar disorder?

5. Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?

If the patient answers:

1. “Yes” to seven or more of the 13 items in question number 1;
   AND

2. “Yes” to question number 2;
   AND

3. “Moderate” or “Serious” to question number 3;

© 2006 by The University of Texas Medical Branch. Reprinted with permission. This instrument is designed for screening purposes only and is not to be used as a diagnostic tool.
When to Suspect Bipolar Disorder?

• 15% of depressed patients have bipolar disorder

• At risk:
  – Antidepressant-induced irritability, manic symptoms or rapid cycling.
  – Family history of BD.
  – Postpartum depression or psychosis.
  – Depression with psychotic features.
  – Brief, highly recurrent depressive episodes (>5).
  – Earlier age of illness onset (<25 years).

Treatment

1. Pharmacotherapy

2. Psychosocial (all equal efficacy, all effective as adjuncts to pharmacotherapy)
   - CBT
   - Psycho education
   - IPSRT (Interpersonal Social rhythm therapy)

PsycHoEd During Maintenance Treatment

![Graph showing time to recurrence (months) for patients in treatment and control groups. The x-axis represents time in months (6, 12, 18, 24), and the y-axis represents patients in percentage (%). The treatment group is shown in red and the control group in blue. The graph includes data for 120 patients (n=120) with p<0.003.]

Colom F. Arch Gen Psychiatry 2003;60:402-407.
PsychoEd To The Patient & Family

• Early detection of depression and mania.
• Stress management.
• Diminish the effects of stigma and denial of the illness.
• Tips on enhancing medication adherence and developing healthy lifestyles:
  – Minimizing the use of alcohol, tobacco, drugs, stimulants such as caffeine.
  – Getting regular exercise.
  – Regulating sleep and wake times.

• Peer support, individual therapy, group therapy all have evidence.

Before We Get Started

- History
  - Medical comorbidities, smoking, ETOH use, drugs, pregnancy status, family hx of CVD

- Investigations
  - Waist circumference, weight and BMI
  - BP

**TABLE 23** Baseline laboratory investigations in patients with bipolar disorder

<table>
<thead>
<tr>
<th>Investigation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
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<tr>
<td>Fasting glucose</td>
</tr>
<tr>
<td>Fasting lipid profile (TC, vLDL, LDL, HDL, TG)</td>
</tr>
<tr>
<td>Platelets</td>
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<tr>
<td>Electrolytes and calcium</td>
</tr>
<tr>
<td>Liver enzymes</td>
</tr>
<tr>
<td>Serum bilirubin</td>
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<tr>
<td>Prothrombin time and partial thromboplastin time</td>
</tr>
<tr>
<td>Urinalysis</td>
</tr>
<tr>
<td>Urine toxicology for substance use</td>
</tr>
<tr>
<td>Serum creatinine</td>
</tr>
<tr>
<td>eGFR</td>
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<tr>
<td>24h creatinine clearance (if history of renal disease)</td>
</tr>
<tr>
<td>Thyroid-stimulating hormone</td>
</tr>
<tr>
<td>Electrocardiogram (&gt;40 years or if indicated)</td>
</tr>
<tr>
<td>Pregnancy test (if relevant)</td>
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<tr>
<td>Prolactin</td>
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</tbody>
</table>

CBC, complete blood count; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride; vLDL, very low density lipoprotein (Adapted from Yatham et al. 2006).

## Hierarchical Rankings of First and Second Line Treatments Recommended for Management of Acute Bipolar I Depression

### ACUTE DEPRESSION

<table>
<thead>
<tr>
<th>First Line Treatments</th>
<th>LEVEL OF EVIDENCE OF PHASE OF TREATMENT</th>
<th>CONSIDERATIONS FOR TREATMENT SELECTION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acute Depression</td>
<td>Maintenance</td>
</tr>
<tr>
<td>Quetiapine</td>
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<tr>
<td>Lurasidone + Li/DVP</td>
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<td>Lithium</td>
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<tr>
<td>Lamotrigine</td>
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<td>Lurasidone (adj)</td>
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<tr>
<td>Lamotrigine (adj)</td>
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<tr>
<td>Divalproex</td>
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<tr>
<td>SSRIs/bupropion (adj.)</td>
<td></td>
<td>n.d.</td>
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<tr>
<td>ECT</td>
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<tr>
<td>Cariprazine</td>
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<tr>
<td>Olanzapine-fluoxetine</td>
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<table>
<thead>
<tr>
<th>Second Line Treatments</th>
<th>LEVEL OF EVIDENCE OF PHASE OF TREATMENT</th>
<th>CONSIDERATIONS FOR TREATMENT SELECTION</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>

### LEVEL OF EVIDENCE OF PHASE OF TREATMENT
- Level 1 evidence
- Level 2 evidence
- Level 3 evidence
- Level 4 evidence
- Level 1 negative evidence
- Level 2 negative evidence
- Level 3 negative evidence
- Level 4 negative evidence
- n.d.: no data
- #: limited impact on treatment selection
- 1: trend for superiority on the primary efficacy measure, hence the lower rating
- 2: Effective in those with an index episode of depression
- 3: Negative data from the trial is likely due to methodological issues, rating based on expert opinion
- 4: Divalproex and carbamazepine should be used with caution in women of child bearing age
- DVP: divalproex
- ECT: electroconvulsive therapy
- Li: lithium
- SSRIs: serotonin reuptake inhibitors
SUNOVION ANNOUNCES HEALTH CANADA APPROVAL OF LATUDA® (LURASIDONE HCL) TO TREAT ADOLESCENTS (13 TO 17 YEARS OF AGE) WITH BIPOLAR DEPRESSION

Friday, April 20, 2018 11:34 am EDT

MARLBOROUGH, Mass.--(BUSINESS WIRE)--Sunovion Pharmaceuticals Inc. (Sunovion) today announced that Health Canada has approved the Supplemental New Drug Submission (SNDS) that expands the use of Latuda® (lurasidone HCl) to include the acute management of depressive episodes associated with bipolar I disorder in adolescents (13 to 17 years of age).

LATUDA is currently indicated in Canada for the management of the manifestations of schizophrenia in adults and adolescents (15 to 17 years of age) and the acute management of depressive episodes associated with bipolar I disorder in adults.

“Given the enormous burden of depression symptoms, and the high rates of suicidality among youth with bipolar disorder, there is an urgent need for treatments that are supported by gold-standard evidence,” said Benjamin Goldstein, M.D., Ph.D., FRCPC, Director of the Centre for Youth Bipolar Disorder at Sunnybrook Health Sciences Centre, and Professor of Psychiatry and Pharmacology at the University of Toronto, Ontario. “LATUDA is a new, effective and generally well-tolerated treatment option for adolescents with bipolar depression, and is a first-line treatment in recent international treatment guidelines. Having evidence-based treatments for bipolar depression in adolescent patients is critically important for the Canadian mental health community.”
How To Choose A Treatment?

- Lamotrigine
- Quetiapine
- Lithium
- Lurasidone
Numbers needed to harm for pooled short-term weight gain with SGAs vs PBO

De Hert M et al. CNS Drugs 2012;26:733–59.

ARI, aripiprazole; ASE, asenapine; ILO, iloperidone; LUR, lurasidone; OLA, olanzapine; PALI, paliperidone; PBO, placebo; QUE, quetiapine; RIS, risperidone; SGA, second generation antipsychotic; ZIP, ziprasidone.
# Monitoring

**ONGOING METABOLIC MONITORING FORM FOR PATIENTS ON ATYPICAL ANTIPSYCHOTICS AND MOOD STABILIZERS**

<table>
<thead>
<tr>
<th>Currently on medication at 1st assessment:</th>
<th>Antipsychotic/Mood Stabilizer:</th>
<th>Date (DD/MM/YY):</th>
<th>Dose:</th>
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<th>Sex: Male □ Female □ Height (cm):</th>
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<th>Examination Measurements – Monthly from 1st assessment</th>
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<td>Weight (kg)</td>
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<td>Waist Circumference (cm)</td>
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<td>Blood Pressure (mmHg)</td>
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<tr>
<th>Laboratory Investigations – Every 3 months from 1st assessment</th>
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<td>Date</td>
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<th>1st Assessment (DD/MM/YY)</th>
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<td>Fasting Lipid Profile</td>
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<tr>
<th>If on Lithium – Every 3 months from 1st assessment</th>
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<tbody>
<tr>
<td>Lithium Level</td>
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<table>
<thead>
<tr>
<th>O – Ordered</th>
<th>R - Reviewed</th>
<th>O</th>
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<th>NOTES</th>
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<thead>
<tr>
<th>If on Valproate or Carbamazepine – Every 3 months from 1st assessment</th>
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<tbody>
<tr>
<td>V.A. or CBZ Level</td>
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</tbody>
</table>
Dosing

- Onset of action for BP depression tx is typically 2 weeks.
  - Except for Lamotrigine due to slow titration (SJS)
- Lamotrigine 200 – 400 mg PO BID/QHS
- Quetiapine 300 – 600 mg PO QHS
- Lithium (dose ?) ---- > 0.8 and 1.2 meq/L
- Lurasidone 20 – 60 mg PO qSupper (>350 cal)

Lurasidone Bipolar Depression

Dosing starts at 20 mg once daily and may be increased up to 120 mg once daily as needed.

- Recommended starting dose for monotherapy and adjunctive therapy: 20 mg/day
- No initial dose titration required
- Maximum recommended dose: 120 mg/day
- Should be taken with food (at least 350 calories)
- In the monotherapy study, the higher dose range (80-120 mg/day) did not provide additional efficacy, on average, compared to the lower dose range (20-60 mg/day)

Pills shown are not actual size.
Questions
Obsessive Compulsive Disorder

1. Obsessions
   • Persistent unwanted thoughts or images
   • Intrusive, uncontrollable/excessive
   • Provoke anxiety

2. Compulsions
   • Repetitive behaviours or mental acts
   • Preformed in response to an obsession
   • Intended to reduce discomfort or prevent feared event

3. Severity
   • Symptoms occupy > 1hr / day, or,
   • Marked distress & functionally impairing
OCD Themes

• Contamination

• Doubt/Harm

• Intrusive thoughts

• Symmetry / Counting / “Just right”
OCD Themes

• Contamination

• Doubt/Harm

• Intrusive thoughts

• Symmetry / Counting / “Just right”
OCD Themes

- Contamination
- Doubt/Harm
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- Symmetry / Counting / “Just right”
OCD Themes

• Contamination

• Doubt/Harm

• Intrusive thoughts

• Symmetry / Counting / “Just right”
Bipolar & OCD

- 20% of patients with BP have OCD.
- OCD tends to be present/worse in depressive phase of illness.

J Affect Disord. 2014 Sep;166:258-63.
Treatment of OCD in Bipolar

• Mood stabilization should be the primary goal in treating BD-OCD patients.

• Addition of SRI agents seems unnecessary in most cases, although it may be needed in a minority of BD patients with refractory OCD.

• If antidepressants are used, clinical experience suggests that SSRIs are preferred, but because of the potential risk of manic switch clinicians need to optimize prophylactic antimanic agents before initiation.

J Affect Disord. 2014 Sep;166:258-63.
## OCD Treatment

**Table 27**

Recommendations for pharmacotherapy for OCD

<table>
<thead>
<tr>
<th>Level</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line</td>
<td>Escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline</td>
</tr>
<tr>
<td>Second-line</td>
<td>Citalopram, clomipramine, mirtazapine, venlafaxine XR</td>
</tr>
<tr>
<td>Third-line</td>
<td>IV citalopram, IV clomipramine, duloxetine, phenelzine, tramadol,</td>
</tr>
<tr>
<td></td>
<td>tranylcypromine</td>
</tr>
<tr>
<td>Adjunctive</td>
<td>First-line: aripiprazole, risperidone</td>
</tr>
<tr>
<td>therapy</td>
<td>Second-line: memantine, quetiapine, topiramate</td>
</tr>
<tr>
<td></td>
<td>Third-line: amisulpride, celecoxib, citalopram, granisetron, haloperidol, IV ketamine, mirtazapine, N-acetylcysteine, olanzapine, ondansetron, pindolol, pregabalin, riluzole, ziprasidone</td>
</tr>
<tr>
<td></td>
<td><strong>Not recommended</strong>: buspirone, clonazepam, lithium, morphine</td>
</tr>
<tr>
<td>Not</td>
<td>Clonazepam, clonidine, desipramine</td>
</tr>
<tr>
<td>recommended</td>
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</tr>
</tbody>
</table>

*IV = intravenous; XR = extended release.*
### OCD Treatment

#### Table 27

Recommendations for pharmacotherapy for OCD

<table>
<thead>
<tr>
<th>Classification</th>
<th>Medications</th>
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<tbody>
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</table>

Not recommended: Clonazepam, clonidine, desipramine

IV = intravenous; XR = extended release.
Treatment of OCD in Bipolar
Treatment of OCD in Bipolar

Alternatives ???
Therapy for OCD
Therapy for OCD

![Graph showing the increase in anxiety over time after a trigger event.](image-url)
Therapy for OCD

Anxiety vs. Time

- 0% Anxiety
- 100% Anxiety

Uncomfortable
Therapy for OCD

Anxiety

Time

Compulsion

0%

100%
Therapy for OCD

![Graph showing the effect of therapy on anxiety levels over time. The graph indicates a decrease in anxiety after the therapy, labeled as 'Compulsion'.]
Therapy for OCD
Therapy for OCD

![Graph showing the increase in anxiety over time. The x-axis represents time, and the y-axis represents anxiety. The graph shows a significant increase in anxiety with time.](image)
Therapy for OCD

Exposure – Response Prevention
Therapy for OCD

Exposure – Response Prevention

Anxiety

0%

100%

Time
Therapy for OCD

Anxiety decreases with subsequent exposures = HABITUATION
## Therapy for OCD

### Exposure Hierarchy

Create a list of anxiety-producing situations, beginning with the most distressing, and ending with the least distressing. Rank how distressing each item is on a scale of 1 to 10.

<table>
<thead>
<tr>
<th>Anxiety, Obsession, or Compulsion Trigger</th>
<th>Distress Level (1 – 10)</th>
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Alternatives for Refractory OCD

• Deep brain stimulation (DBS)
• Repetitive transcutaneous magnetic stimulation (rTMS)
Summary

- Bipolar Disorder is a chronic illness.
- Good evidence to support life long treatment.
- Mixed symptomatology is common.

- OCD is highly comorbid with BP.
- OCD typically responds to BP treatment.
- Consider non-SRI medications (glutamatergic drugs).
- Always consider (and employ) CBT for OCD!
Age of Onset of Bipolar Disorder

Goodwin & Jamison, 1990 (N = 1368)
Bipolar and Suicide

- Bipolar Disorder has among the highest rates of suicide among treatment Patients
  - A = Men
  - B = Women

Nordentoft, M. et al. Arch Gen Psychiatry 2011;68
Importance of Treatment

• >70% of suicide deaths and suicide attempts in patients with BD occur during depressed phase.

• Depressive episodes with mixed features are a particularly dangerous period for suicide attempts or death.

# Recent Guidelines Recommendations for First-line Therapies for Bipolar 1 Depression

<table>
<thead>
<tr>
<th></th>
<th>Florida Medicaid (USA) 2015</th>
<th>RANZCP Australia/New-Zealand 2015</th>
<th>BAP (UK) 2016</th>
<th>CINP (Intl) 2017</th>
<th>CANMAT/ISBD (Canada/Intl) 2018</th>
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