2013 Update: Treatment of Bipolar Disorder

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Diagnosing Bipolar Disorder

- Continues to be difficult
- DSM5
- Mood Disorder Questionnaire/Structured Clinical Interview
- Psychogenomics
- Cerebral Blood Flow 2013: ??

Increasing Diagnostic Accuracy

- A novel brain scanning method that measures cerebral blood flow may help distinguish between bipolar disorder and depression early, new research suggests.
- A small study of 54 adult women used a new imaging method called arterial spin labeling (ASL) to measure blood flow in subdivisions of the anterior cingulate cortex (ACC), brain regions that are associated with depression.
- Using this measure resulted in an 81% accuracy rate in identifying which of the participants had unipolar depression and which had bipolar depression.
Increased mortality

- 6,587,036 Swedish adults, including 6618 with bipolar disorder.
- 2-fold increased mortality risk
- Women with bipolar disorder died 9.0 years earlier
- Men with bipolar disorder died 8.5 years earlier
- Men and women with bipolar disorder had an increased risk for death from ischemic heart disease, diabetes, COPD, and influenza and pneumonia.
- Influenza and pneumonia (3.7-fold for women; 4.4-fold for men)
- Diabetes (3.6-fold for women; 2.6-fold for men)
- COPD (2.9-fold for women; 2.6-fold for men)

Bipolar disorder was strongly associated with increased mortality from suicide, with a 10-fold increased risk.
New Advances: Lithium

- Clearly neuroprotective
- 10 year prospective study, a minimum of 5 manic episodes
- Non-lithium group had smaller hippocampal volumes than control participants or the patients in the lithium group
- Lithium-treated hippocampal volumes were comparable to healthy control participants, significantly larger than those of the non-lithium patients
- Very few patients on long term lithium develop Alzheimer's
- Clearly suicide protective
- Meta analysis of 48 RCT, 6684 patients
- Unipolar
- Bipolar
- Long term maintenance with risk

Evidenced Based Treatment

- Lithium
- Anticonvulsants
  - Lamotrigine
  - Valproic Acid/Divalproex sodium
  - Carbamazepine/Ox
- Atypical Antipsychotics
Lithium

- Best Candidates
  - Clear euphoric mania, non-rapid cycling, clear family history, prominent suicidality, hepatic compromised

- Monitoring
  - Cr, eGFR, TSH baseline & q 6 months
  - EKG only if cardiac history (sinus node dysfunction)
  - Lithium level
    - 1-2 weeks, 1-2 months, then q 6months and q dose change, symptomatic
  - Check if change in use NSAIDs, ace inhib, diuretics, caffeine
  - 12 hour draw

Lithium Adverse Effects

- Nausea/Vomiting/GI distress
  - Take with food, Use CR
  - Use CR formulations

- Fine Tremor
  - Propranolol 10-20 mg bid to tid

- Polyuria
  - Reassure, Vary dosing

- Weight Gain

- Cognitive Fuzziness
  - Check TSH

Dosing

- Initial dosing 300 mg bid to 450 CR bid / 900CR HS
- Level at 12 hours after 1-2 weeks .5/.8 to 1.2
- Dosing is linear to blood level
- Educate about TOXIC symptoms
  - Nausea, vomiting, diarrhea, tremor worsening
Lamotrigine

- **Best Candidates**
  - Many depressive episodes, substance abuse, rapid cycling, obesity, DM, anxiety disorders
- **No lab monitoring**
- **Adverse Side Effects**
  - Minimal if any weight gain, cognitive changes
  - Lengthy titration, not suitable for acute mania
  - Risk of Stevens Johnson syndrome- rash assess
  - Caution w/psoriasis

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Lamotrigine

- Write directions
- Start the titration while using acute agent concomitantly, then taper out the acute agent
- Use slower titration if on VPA
  - Faster than regular titration if on carbamazepine
  - Regular Titration: 25 mg for 2 weeks, then 50 for 2 weeks, then 100 mg.
  - Increase dosage in 2 week intervals.
  - Hold at 100-200 to assess efficacy, titrate up to 400 mg.

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Valproic acid (VPA)

- **Best Candidates**
  - Patients with rapid cycling, substance abuse, can use loading dose (20mg/kg), less $$
- **Monitoring**
  - CBC, CMP, blood level q dose change
- **Adverse Effects**
  - Teratogenic (Document)
  - Weight gain, hematological, hepatic impairment, alopecia, increase plasma ammonia
  - Contraindicated w/history of pancreatitis
Valproic Acid Pearls

- Useful agent in aggression, intermittent explosive disorder
- Multivitamin w/B complex, selenium & zinc helps prevent & decrease hair loss
- If mood continues unstable, increase dose to blood level above 80 at 12 hour draw
- Bioavailability of ER formulation is approximately 75% of regular formulation
- ASA increases blood level

Effective Dosing

- Check level 12 hours p dose
- VPA- 80-100
- Lithium- 0.8- 1.0
- Carbamazepine- 8-12
- THINK ON/OFF SWITCH
- Lamotrigine (up to 400 mg) (+ atypical/Li)
- Avoid leaving your patient unprotected

Atypical Agents

- Best candidates
  - Need rapid treatment
  - with psychosis
  - is a treatment of choice for pregnancy and lactation
- Monitoring
  - Metabolics (lipids, glu, weight, waist circum)
- Adverse Effects
  - Weight gain, dizziness, EPS, dry mouth, sedation & activation, differential metabolic impact
Antipsychotics

- Check metabolics!
  - Fasting glu monthly, then quarterly
  - Lipids (fasting) quarterly, then semiannual

- Assess for:
  - Dystonia = (teeth grinding, jaw, arms stiff, leg kicking)
  - Akathisia = (pacing, subjective restlessness, agitation)
  - TD = (nonpatterned tongue, mouth, hand movements)

Use lowest effective dose, but often needs higher dosing

Mapping out Metabolic Impact

<table>
<thead>
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<th>High</th>
<th>Moderate</th>
<th>Low</th>
<th>Lowest</th>
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<tbody>
<tr>
<td>Olanzapine</td>
<td>Quetiapine</td>
<td>Aripiprazole</td>
<td>Lurasidone</td>
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<tr>
<td>Clozapine</td>
<td>Risperidone</td>
<td>Ziprasidone</td>
<td>Asenapine</td>
</tr>
</tbody>
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Atypical Pearls

- Olanzapine good “rescue drug”
- Decide which agent based on side effects desired
- Generally new agents (lurasidone, asenapine) require trial of risperidone for insurance to cover
- Atypical at low dose can augment other agent
Carbamazepine/Ox

- Second line (third line?)
- Similar to valproic acid with less weight gain
- Check labs
  - More concerns with WBC suppression/platelets
  - No labs needed with oxcarbazepine
- CLONAZEPAM
- Augmentation role for mood stability

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So what about depression in patients with bipolar disorder??

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Bipolar patients, on mood stabilizers, now depressed: antidepressants versus placebo

Santucci G et al, New England Journal of Medicine, April 2001
10th International BD Congress

- Antidepressants NEVER as monotherapy
- May be used ONLY in patients with bipolar disorder in a depressive episode IF
  - Has shown to be effective in the past
  - Has not caused rapid switch to mania/hypomania
- Use as maintenance ONLY if patient becomes depressed when agent is discontinued

Effective Strategies: Bipolar Depression

1. Optimize dosage of the mood stabilizer
   - VPA > 80; Lithium > .8 at 12 hour draw
   - Lamotrigine up to 400 mg
2. Add psychosocial interventions
3. Address specific symptoms (sleep, anxiety)
4. Add an atypical agent
5. Add a second other mood stabilizer
6. For "pure" depressive episode, add a non-TCA antidepressant if worked in past and did not make manic

Improving Adherence & Outcomes

- 1/3 of patients choose to change/not take medication
- Today outweighs Longterm Benefit
- Understanding Patient’s Etiological Understanding
- Speaking the Language
- Provide More Information about Medications
- Offer Choices - including psychological treatments
- Provide more Emotional Support
- Increase Stability in Health Care Professional Relationships

Susanne Gibson, Sarah L. Brand, Sarah Burt, Zoe V R Baden, Ouli Bensen
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