Antidepressant Medication Strategies – We’ve Come a Long Way… or Have We?

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Who Writes Prescriptions for Psychotropic Medications

<table>
<thead>
<tr>
<th>Class of Medications</th>
<th>Psychiatrists (%)</th>
<th>Non-psychiatric M. D. s (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipsychotics</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>21</td>
<td>79</td>
</tr>
<tr>
<td>Antianxiety</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>Hypnotics</td>
<td>11</td>
<td>89</td>
</tr>
<tr>
<td>Lithium</td>
<td>62</td>
<td>38</td>
</tr>
</tbody>
</table>

Biological Psychiatry
Neurotransmitters

**Norepinephrine**
- Adrenaline for the brain
- Secreted by adrenal glands in response to stress or arousal
- Regulates the fight-or-flight response

**Serotonin**
- Regulates mood, anxiety, pain
- Affects appetite, sleep, sexual functioning
- Neurotransmitter most often linked to the management of depression
**Dopamine**
- Influences emotional behavior and cognition
- Regulates motor activity
- The pleasure principle’s best friend

**Unipolar Depression**

**Etiology**
- Think of depression not as a diagnosis, but as a cluster of symptoms with many possible influences.
- Its cause is likely on a much deeper molecular level.
- For treatment purposes, focus more on its influences.
Possible Influences on Clinical Depression

- Reactive
- Biological
- Medical
- Medication induced
- Hormonal
- Substance abuse

How Antidepressants Work

Structure of a Neuron

Chemical Events Occurring at the Level of the Synapse
As I See It

- Response to antidepressants begins to manifest within a week of treatment initiation
- 30% of antidepressant users achieve sustained, measurable symptom remission
- The improvement curve is more substantial for those with severe melancholic depression
- It’s difficult to measure AD improvement in mild to moderate depression. Increasingly prescribed for the wrong symptom set
- Depression as a clinical condition has become diluted
- The more frequently clients are seen, the better they do
- Two most reliable predictors of treatment response: initial improvement, family history

Contemporary Antidepressants

- Cyclics
- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin and norepinephrine reuptake inhibitors (SNRIs)
- Norepinephrine reuptake inhibitors (NRIs)
- The Other Category

Cyclic Antidepressants

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>Elavil</td>
</tr>
<tr>
<td>Amoxapine</td>
<td>Asendin</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Anafranil</td>
</tr>
<tr>
<td>Desipramine</td>
<td>Norpramin, Pertofrane</td>
</tr>
<tr>
<td>Doxepin</td>
<td>Sinequan, Adapin</td>
</tr>
<tr>
<td>Imipramine</td>
<td>Tofranil</td>
</tr>
<tr>
<td>Maprotiline</td>
<td>Ludional</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>Pamelor, Aventyl</td>
</tr>
<tr>
<td>Protriptyline</td>
<td>Vivactil</td>
</tr>
<tr>
<td>Trazadone</td>
<td>Desyrel</td>
</tr>
<tr>
<td>Trimipramine</td>
<td>Surmontil</td>
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</tbody>
</table>
Selective Serotonin Reuptake Inhibitors (SSRIs)

As a Class:
- 70% of all new antidepressant Rx are for an SSRI
- Better tolerated
- Advantage of once-a-day dosing
- Much safer in overdose
- Antianxiety agents as well as antidepressants
- All of the SSRIs are equally effective
- Similar side effects, similar actions
- Approved indications: MDD, OCD, GAD, PTSD, Social Anxiety disorder, PMDD
- All SSRIs are available in generic

Prozac (fluoxetine)
- Energizing
- Half-life of 7 days
- Prone to cause anxiety, agitation, irritability
- Interaction with other medications potentially significant
**Zoloft (sertraline)**

- Neither too sedating nor too energizing
- 50% of the drug excreted by the body in one (1) day
- Stable blood levels achieved within one week
- Minimal interaction with other medications

**Paxil (paroxetine)**

- Antianxiety benefit
- Unpleasant withdrawal symptoms upon abrupt discontinuation
- High discontinuation rates
- Highest rate of sexual side effects
- Most weight gain among SSRIs
- Concern regarding use in pregnancy

**Celexa (citalopram)**

- Slightly more sedating than activating
- May cause slightly less sexual dysfunction compared to other SSRIs
- Minimal interactions with other medications
Lexapro (escitalopram)

- “S” (active) isomer of Celexa (citalopram)
- 10mg of Lexapro daily comparable to 40mg Celexa daily
- Well-respected, independent reviews: NO real difference between Lexapro and Celexa

Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)

Effexor (venlafaxine)

- “Prozac with a punch”
- Dose-response curve
- Cumbersome to use
- Risk of hypertension at doses greater than 225mg per day
- Available in extended-release
- Generically available
Cymbalta (duloxetine)

- Dual indications for depression and diabetic neuropathy
- Does not demonstrate any advantage over Effexor
- Unlike Effexor, liver toxicity is a problem
- Significant nausea
- Direct-to-consumer ads focus more on pain management

Pristiq (desvenlafaxine)

- TV Ad was a bit creepy
- No dose-response curve
- Unlikely to interact with other medications metabolized by the liver
- Active metabolite of Effexor
- “Patent extender” for Effexor XR
- More nausea than Effexor

A Couple of Others
**Wellbutrin (bupropion)**

- Dopamine and norepinephrine reuptake inhibitor
- Activating like Prozac
- Few, if any, sexual side effects, no weight gain
- Seizure risk at doses greater than 400mg/day; avoid in ETOH withdrawal
- Marketed as Zyban for the treatment of smoking cessation

**Remeron (mirtazapine)**

- Increases hypersomnia
- Marked sedation and weight gain, highest among ADs

**Viibryd (vilazodone)**

- Blockbuster AD waiting to happen?
- Combines the actions of SSRIs with the actions of Buspar by “massaging” serotonin receptors
- Dual-action effect on serotonin
- Minimal weight gain; fewer sexual side effects?
### Side Effects

<table>
<thead>
<tr>
<th>Side Effects</th>
<th>Prozac</th>
<th>Paxil</th>
<th>Zoloft</th>
<th>Celexa</th>
<th>Effexor</th>
<th>Lexapro</th>
<th>Wellbutrin</th>
<th>Cymbalta</th>
<th>Pristiq</th>
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</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>None</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
</tr>
<tr>
<td>Sedation</td>
<td>Lower</td>
<td>Higher</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
</tr>
<tr>
<td>Insomnia</td>
<td>None</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
</tr>
<tr>
<td>Nausea</td>
<td>None</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
</tr>
<tr>
<td>Sexual Dysfunction</td>
<td>None</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
</tr>
</tbody>
</table>

riages in blue.

⊕ No one AD or AD class consistently out performs another
⊕ Side effects are different among ADs
⊕ Different actions don’t predict treatment response

It makes sense for many clients to choose their own initial antidepressant based on acceptable side effects

"I'll have to get Dr. Clark to reduce the dosage of the mood-stabilizer."
Alternative Medications for the Treatment of Depression

Herbals are NOT FDA Regulated!!

St. John’s Wort
(hypericum perforatum)

⊕ One of the most effective herbals for the treatment of mild depression
⊕ Usual adult dose is 900mg. per day
⊕ Similar in action to the SSRIs, referred to as “nature’s Prozac”
⊕ Should not be used in combination with SSRIs
⊕ Should be avoided by pregnant women – possible teratogen
⊕ Decreases the efficacy of contraceptives
⊕ High incidence of drug/drug interactions
⊕ Common side effect is photosensitivity

Omega-3 fatty acids

⊕ Well established in improving nerve conduction
⊕ Anti inflammatory and cardiac benefits
⊕ Studies demonstrate a correlation between low levels of omega-3s and depression
⊕ Results promising as a treatment for depression
⊕ How we get them
If Depression Persists, Then What?

Strategies for Combating Treatment Resistant Depression

⊕ Re-examine the diagnosis
⊕ Monitor dosage
⊕ Monitor compliance

Also

⊕ AUGMENT
  ○ Add Lithium
  ○ Add a stimulant
  ○ Add an atypical antipsychotic (Zypraxa, Seroquel, Geodon, Abilify)
  ○ Add thyroid, methylfolate, Sam-e
  ○ Combine antidepressants
    ■ SSRIs + Wellbutrin
    ■ Effexor + Wellbutrin
    ■ Cymbalba + Wellbutrin
    Mechanical is next in line
Dosage Range Chart - Antidepressants

<table>
<thead>
<tr>
<th>BRAND NAME</th>
<th>GENERIC NAME</th>
<th>CLASS</th>
<th>DAILY DOSAGE RANGE *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anafranil</td>
<td>clomipramine</td>
<td>cyclic</td>
<td>150 mg - 250mg</td>
</tr>
<tr>
<td>Aplenzin</td>
<td>bupropion (Hbr)</td>
<td>cyclic</td>
<td>174mg – 522mg</td>
</tr>
<tr>
<td>Celexa</td>
<td>citalopram</td>
<td>SSRI</td>
<td>20 mg - 80 mg</td>
</tr>
<tr>
<td>Cymbalta</td>
<td>duloxetine</td>
<td>SNRI</td>
<td>20 mg - 80 mg</td>
</tr>
<tr>
<td>Disyrel</td>
<td>trazodone</td>
<td>cyclic</td>
<td>150 mg - 400 mg</td>
</tr>
<tr>
<td>Effexor</td>
<td>venlafaxine</td>
<td>SNRI</td>
<td>75 mg - 350 mg</td>
</tr>
<tr>
<td>Effexor XR</td>
<td>venlafaxine XR</td>
<td>SNRI</td>
<td>75 mg - 350 mg</td>
</tr>
<tr>
<td>Elavil</td>
<td>amitriptyline</td>
<td>cyclic</td>
<td>100 mg - 300 mg</td>
</tr>
<tr>
<td>Emsam (patch)</td>
<td>selegiline</td>
<td>MAOI</td>
<td>6 mg - 12 mg</td>
</tr>
<tr>
<td>Lexapro</td>
<td>escitalopram</td>
<td>SSRI</td>
<td>10 mg - 40 mg</td>
</tr>
<tr>
<td>Luvox</td>
<td>fluvoxamine</td>
<td>SSRI</td>
<td>100 mg - 400 mg</td>
</tr>
<tr>
<td>Nardil</td>
<td>phenelzine</td>
<td>MAOI</td>
<td>45 mg - 60 mg</td>
</tr>
<tr>
<td>Norpramin</td>
<td>desipramine</td>
<td>cyclic</td>
<td>150 mg - 300 mg</td>
</tr>
<tr>
<td>Pamelor</td>
<td>nortriptyline</td>
<td>Cyclic</td>
<td>75 mg - 150 mg</td>
</tr>
<tr>
<td>Parnate</td>
<td>tranylcypromine</td>
<td>MAOI</td>
<td>20 mg - 60 mg</td>
</tr>
<tr>
<td>Paxil</td>
<td>paroxetine</td>
<td>SSRI</td>
<td>20 mg - 50 mg</td>
</tr>
<tr>
<td>Prozac</td>
<td>fluoxetine</td>
<td>SSRI</td>
<td>20 mg - 80 mg</td>
</tr>
<tr>
<td>Remeron</td>
<td>mirtazapine</td>
<td>atypical</td>
<td>15 mg - 45 mg</td>
</tr>
<tr>
<td>Sarafem</td>
<td>fluoxetine</td>
<td>SSRI</td>
<td>20 mg - 80 mg</td>
</tr>
<tr>
<td>Sinequan</td>
<td>doxepin</td>
<td>cyclic</td>
<td>150 mg - 300 mg</td>
</tr>
<tr>
<td>Strattera</td>
<td>atomoxetine</td>
<td>NRI</td>
<td>10mg- 40mg</td>
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<tr>
<td>Symbyax</td>
<td>olanzapine/fluoxetine</td>
<td>atypical</td>
<td>60 mg – 120 mg</td>
</tr>
<tr>
<td>Tofranil</td>
<td>imipramine</td>
<td>cyclic</td>
<td>150 mg - 300 mg</td>
</tr>
<tr>
<td>Viibryd</td>
<td>vilazodone</td>
<td>cyclic</td>
<td>10mg – 40mg</td>
</tr>
<tr>
<td>Wellbutrin SR</td>
<td>bupropion SR</td>
<td>atypical</td>
<td>150 mg – 300mg</td>
</tr>
<tr>
<td>Wellbutrin LA</td>
<td>bupropion LA</td>
<td>atypical</td>
<td>150 mg – 300mg</td>
</tr>
<tr>
<td>Zoloft</td>
<td>sertraline</td>
<td>SSRI</td>
<td>50 mg - 200 mg</td>
</tr>
</tbody>
</table>

* Suggested adult dose

Note: Dosage ranges may vary depending on source, and may vary according to age.

You’d Want To Know…

① The antidepressant vs. placebo response will rage on
② With AD treatment, there is no right way, or wrong way, only possibilities
③ Length of treatment is highly debatable due to “poop out”
④ Reasonable expectations: meds won’t change behavior
⑤ Tedious process
⑥ Thou shall not give up!
THANK YOU!

Joe Wegmann, PD, LCSW