Diagnosis & Management of Major Depression: A Review of What’s Old and New

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Why You’re Treating So Much Mental Health

59% of Psychiatrists Are Over the Age of 55

Why You’re Treating So Much Mental Health

5% of Medical Students Matched into Psychiatry in 2017

Antidepressant Prescriptions in the US 2006-2007

62% of all Antidepressants are prescribed by Primary Care Providers

Goals and Objectives

1. Define the current criteria for the diagnosis of Major Depression
2. Review current evidence based guidelines for the treatment of major depression
3. Compare and contrast unique properties of antidepressant medications
4. Discuss emerging technologies and their evidence in the treatment of depression
Diagnosis
Major Depression

Depressed mood **OR** loss of interest/pleasure in activities

+ 4 additional symptoms for 2 weeks

- Changes in appetite or weight
- Insomnia or Hypersomnia
- Psychomotor Agitation or Retardation
- Loss of Energy
- Feelings of guilt or worthlessness
- Difficulty concentration
- Recurrent thoughts of death or suicide
Specifiers in the DSM-5

- With **peripartum onset**: onset during pregnancy or within 4 weeks of delivery
- With **seasonal pattern**: clear temporal relationship between time of year and symptoms
- With **psychotic features**: psychotic only when depressed
Persistent Depressive Disorder

A. Depressed mood for most of the day, for more days than not for at least 2 years

B. 2 or more of the following while depressed
1. Poor appetite or overeating
2. Insomnia or hypersomnia
3. Low energy or fatigue
4. Low self esteem
5. Poor concentration or difficulty making decisions
6. Feelings of hopelessness

C. During this period, symptoms have
Treatment Options

- Psychotherapy
- Pharmacotherapy
- Brain Stimulation
Efficacy of Depression Treatment: Psychotherapy

• Psychotherapy is similarly efficacious to medication treatment for mild-moderate symptoms

• Therapy tends to lead to longer remission

• Interpersonal (IPT) or Cognitive Behavioral Therapy (CBT)
What is CBT?
Pharmacologic Treatment
Efficacy of Depression Treatment: Medications

- Antidepressants are generally equally effective
- About 50% of patients will have a significant response to antidepressants in 6 weeks
- Large placebo affect in antidepressant studies
### Major Classes of Antidepressants

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
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<tbody>
<tr>
<td>Monoamine Oxidase Inhibitors (MAOI)</td>
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<tr>
<td>Tricyclic Antidepressants (TCA)</td>
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Major Classes of Antidepressants

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- Tricyclic Antidepressants (TCA)
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- Serotonin-Norepinephrine Reuptake Inhibitors (SNRI)
- Serotonin Modulators
The Serotonin Hypothesis

- Depletion of serotonergic pathways plays a causal role in depression

- There are at least 15 different serotonin receptors

- Serotonin is not the only neurotransmitter involved in depression nor acted upon by antidepressants
Major Classes of Antidepressants

Tricyclic Antidepressants (TCA)
Tricyclic Antidepressants

- Amytriptylline, Nortriptyline, Doxepin
- Helpful for insomnia
- Can check blood levels
- Many off-label uses for comorbid conditions
Tricyclic Antidepressant Side Effects

- QTc prolongation
- Highly anticholinergic
- Highly antihistaminic
- Lethal in overdose
Major Classes of Antidepressants

1. Tricyclic Antidepressants (TCA)
2. Selective Serotonin Reuptake Inhibitors (SSRI)
Selective Serotonin Reuptake Inhibitors (SSRI)

- Most widely use class worldwide
- Can treat many comorbid psychiatric issues
- Easy to use and safe in overdose
<table>
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<th>Fluoxetine (Prozac)</th>
<th>Paroxetine (Paxil)</th>
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<tr>
<td>Long half-life</td>
<td>Short half-life</td>
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<tr>
<td>More activating</td>
<td>More associated with sedation, weight gain, and sexual side effects</td>
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<tr>
<td>Most used SSRI in pregnancy</td>
<td>Pregnancy class D</td>
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<td>Many drug-drug interactions</td>
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Citalopram (Celexa)

- 20mg max for adults over 60 or hepatic impairment
- Black box warning for QTc prolongation
- Few drug-drug interactions

Escitalopram (Lexapro)

- Structurally similar to citalopram
- Few drug interactions
- Narrow dosing range
Sertraline (Zoloft)

- Considered more activating
- Wide dosing range
- Potentially more GI effects
SSRI Side effects

- Weight gain
- Sedation/Insomnia
- Sexual Dysfunction
- Nausea/Diarrhea
- Hyponatremia
- Increased risk of bleeding
- Headaches
- QTC prolongation
- Increased Suicidal thoughts
- Emotional blunting
- Increased sweating
- Bruxism
Major Classes of Antidepressants

- Tricyclic Antidepressants (TCA)
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Serotonin-Norepinephrine Reuptake Inhibitors (SNRI)

- Duloxetine, Venlafaxine, Desvenlafaxine
- Inhibit the reuptake of serotonin and norepinephrine
- Chronic pain/fibromyalgia indications
- Safe in Overdose
Venlafaxine (Effexor)

- NE effect at doses greater than 150mg
- Can increase blood pressure
- Comes in IR and XR formulations
- Notorious discontinuation effect

Duloxetine (Cymbalta)

- Also has indications for diabetic nerve pain and fibromyalgia
SNRI Side Effects

• Largely same side effects of SSRIs
• Perhaps less sexual side effects than SSRIs
• More likely to have discontinuation syndrome
Buproprion (Wellbutrin)

- Increases Dopamine and NE
- No sexual side effects
- Contraindicated in eating disorders and seizure disorders
- Very stimulating and not useful for anxiety

Mirtazapine (Remeron)

- A2 antagonist -> increased SE and NE
- Rarely causes sexual side effects
- Associated with increased sedation and weight gain
- May also decrease nausea
Major Classes of Antidepressants

- Tricyclic Antidepressants (TCA)
- Selective Serotonin Reuptake Inhibitors (SSRI)
- Serotonin-Norepinephrine Reuptake Inhibitors (SNRI)
- Serotonin Modulators
Serotonin Modulators: Vilazodone (Viibryd)

- Dosing (10-40mg)*
- Inhibits presynaptic reuptake of serotonin
- Partial agonist at postsynaptic serotonin 5-HT1A receptors
- Little to no effect on: QTc, blood pressure, body weight, or sexual function

*Must be taken with food, no need for renal adjustment
Serotonin Modulators: Vorioxetine (Trintellex)

- Dosing (10-20mg)*
- Inhibits serotonin reuptake and is an agonist and antagonist at several serotonin receptors
- Long half-life
- No need for renal dosing
- Little to no effect on: vitals, weight, QTc
- Low risk of sexual side effects but probably underreported

*Dose is decreased when taken with 2D6 inhibitor (bupropion)
What About Ketamine?
Improvements in Pharmacotherapy: Gene Guided Therapy

A patient’s DNA is used to tailor treatment to specific patients
**Patient, Sample**  
DOB: 7/22/1984  
Order Number: 9904  
Report Date: 1/6/2016  
Clinician: Sample Clinician  
Reference: 1456CIP

# ANTIDEPRESSANTS

## USE AS DIRECTED
- desvenlafaxine (Pristiq®)
- levomilnacipran (Fetzima®)
- vilazodone (Viibryd®)

## MODERATE GENE-DRUG INTERACTION
- trazodone (Desyrel®) 1
- venlafaxine (Effexor®) 1
- selegiline (Emsam®) 2
- fluoxetine (Prozac®) 1.4
- citalopram (Celexa®) 3.4
- escitalopram (Lexapro®) 3.4
- sertraline (Zoloft®) 3.4

## SIGNIFICANT GENE-DRUG INTERACTION
- bupropion (Wellbutrin®) 1.6
- mirtazapine (Remeron®) 1.6
- amitriptyline (Elavil®) 3.8
- clomipramine (Anafranil®) 1.6,8
- desipramine (Norpramin®) 1.6,8
- doxepin (Sinequan®) 1.6,8
- duloxetine (Cymbalta®) 1.6,8
- imipramine (Tofranil®) 1.6,8
- nortriptyline (Pamelor®) 1.6,8
- vortioxetine (Brintellix®) 1.6,8
- fluvoxamine (Luvox®) 1.4,6,8
- paroxetine (Paxil®) 1.4,6,8
Improvements in Treatment: Gene Guided Therapy

• Early studies show improvement in:
  – Response rates
  – Symptom scores
  – Medication costs
  – Healthcare utilization costs
Improvements in Treatment: Gene Guided Therapy

- Most of the available data is industry sponsored

- Cost effectiveness and long term effects remain a question
Brain Stimulation
Electroconvulsive Therapy

• Highest rate of remission and response of all depression treatments
• 70% of patients show improvement in symptoms
• Generally safe but it can be hard to reassure patients
Improvements in Treatment: Brain Stimulation
Improvements in Treatment: Brain Stimulation

• Transcranial Magnetic Stimulation (TMS)
  – Noninvasive way to stimulate portions of the brain thought to be affected by depression
  – Meta-analyses generally indicate a significant improvement in depression symptoms with moderate effect size

Slotema et al. J Clin Psychiatry 2010
Improvements in Treatment: Brain Stimulation

• Transcranial Magnetic Stimulation (TMS)
  – Generally considered safe
  – Less systemic side effects than oral medication
  – Used primarily in individuals who have failed a medication
  – Longevity of improvement remains unclear
Take-Home Points

• No major changes in diagnosis
• Consider new oral agents for those concerned about metabolic or sexual side effects or with renal impairment
• TMS is a evidence based alternative to medications and ECT
Additional Resources

- Stahl’s Prescribers Guide for quick reference for psychopharmacology

- American Psychiatric Association (APA) Treatment Guidelines (available for free online)
Questions?