Overview of Psychopharmacology

Practical information for the therapist
Goals of this Lecture

• Overview of commonly used medications
• When to refer for medication evaluation
• When to contact your collaborating prescriber
• How to discuss realistic expectations of medication response with your patients
# Therapy vs. Medication

<table>
<thead>
<tr>
<th>Pro-Therapy</th>
<th>Pro-Medication</th>
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<tr>
<td>Works on long term coping skills</td>
<td>Works faster</td>
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<td>Patients are responsible for their improvements</td>
<td>More effective for certain symptoms</td>
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<td>Medication makes people less motivated to do much needed therapy</td>
<td>Can help patients become more productive in therapy</td>
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<td>Medication has side effects</td>
<td>More appropriate for certain individuals who are not good candidates for therapy</td>
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<td>Medication fosters dependency, not autonomy</td>
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You know, just 30 minutes of exercise a day can reduce depression by 50%.

Just give me the drugs!

Reduce Depression
Overview of Commonly Used Medications
Medication Types

- Antidepressant Medications
- Antianxiety Medications
- Antipsychotic Medications
- Mood Stabilizers
- Medications for ADHD
- Medications for Sleep
- Miscellaneous
Antidepressant Medications
Antidepressant Medications Subtypes

- Selective Serotonin Reuptake Inhibitor (SSRI)
- Serotonin Norepinephrine Reuptake Inhibitor (SNRI)
- Atypicals
- Alternatives
- Tricyclics and Monoamine Oxidase Inhibitors
Selective Serotonin Reuptake Inhibitors

- Fluoxetine (Prozac)
- Paroxetine (Paxil/Pexeva)
- Sertraline (Zoloft)
- Citalopram (Celexa)
- Escitalopram (Lexapro)
- Fluvoxamine (Luvox)
Multiple Uses

- Depressive disorders
- Anxiety disorders
- Eating disorders
- OCD and OCD like disorders
- PTSD
Mechanism of Action of SSRIs

How do they work in the brain?
Let’s first take a closer look....
...at the brain.
Different Neurotransmitter Pathways
This is where the focus of attention lies.
How do SSRIs work on the neurons in the brain?
Mechanism of Action

Blocks the serotonin reuptake enzyme in the synapses of neurons in the brain. This results in serotonin being less reabsorbed by the pre-synaptic neuron and thereby increases the amount of serotonin in the synaptic space.

It is unclear if this is the mechanism which actually alleviates symptoms.

There are also second messengers that are affected by this change.
Therapeutic Issues and Side Effects

- Increase in suicidal thinking in adolescents - black box warning
- Delay in therapeutic effect (2-6 weeks)
- Gastrointestinal upset
- Sexual Dysfunction
- Weight/appetite changes
- Affective blunting
- Serotonin syndrome
- Mania
- Problems in Pregnancy
- Sweating
- Yawning
SNRIs

- Venlafaxine (Effexor, Effexor XR)
- Desvenlafaxine (Pristiq)
- Duloxetine (Cymbalta)
Mechanism of SNRI
Mechanism of Action

Similar to SSRIs except they block the reuptake inhibitors for both serotonin and norepinephrine..

Result is increased serotonin and norepinephrine in the synaptic space.
How do you feel the new antidepressant combo is working?

I’ll tell ya Doc, I’ve got a splitting headache. My tongue feels like dry leather. I can’t hold anything down. I’m anxious, restless, and even lost my sex drive!

So then IT’s WORKING.

Medication Management
Atypical Antidepressants

• Bupropion (Wellbutrin, Zyban)
  – Mechanism of action is via increasing levels of norepinephrine and dopamine in the brain.
  – Used for depression, ADD and smoking cessation.
  – Not useful for anxiety in most cases
  – Useful especially for seasonal mood issues and atypical depression.
  – Used in combination with SSRIs for treatment resistance.
  – Side effects are jitteriness, activation, weight loss, insomnia, seizures
Atypical Antidepressants (cont.)

• Mirtazapine (Remeron)
  – An alpha adrenergic antagonist with some antagonism of serotonin receptors
  – Also antihistaminic which leads to its side effects of weight gain and sedation

• Aripiprazole (Abilify)
  – An antipsychotic
  – Approved as an augmentation for residual depression
Atypicals (cont)

Nefazodone (Serzone)
  not often used anymore secondary to rare cases of liver failure leading to death

Trazodone
  Typically too sedating at therapeutic antidepressant doses.
  Commonly used as a non-narcotic sleep aid
  New medication Oleptra (extended release version)
Tricyclics and MAOIs

- **Tricyclics**
  - Amitriptyline (Elavil)
  - Nortriptyline (Pamelor)
  - desipramine (Norpramin)
  - clomipramine (Anafranil)
  - imipramine (Tofranil)
  - trimipramine (Surmontil)
  - Cardiac arrhythmias in overdose
  - Many side effects

- **Monoamine Oxidase Inhibitors**
  - Tranylcypromine (Parnate)
  - Phenelzine (Nardil)
  - isocarboxazid (Marplan)
  - selegiline (Eldepryl, Emsam, Zelapar)
  - Restricted diet, tyramine, hypertensive crisis
Mechanism of MAOI
Miscellaneous

- Lithium
- Stimulants
- Thyroid medication
- St johns wort
- Sam E
- Light therapy
Medications for Anxiety
Medications for Anxiety

• All SSRIs and SNRIs
  – Anxiety disorders generally require higher doses to achieve therapeutic effect
  – True to their symptoms, these patients tend to be more anxious about going on medication and are more tuned in to side effects.

• Benzodiazepines

• Other
  – Buspirone
  – Vistaril
  – Benadryl
  – Atarax
  – gabapentin
Benzodiazepines

- Alprazolam (Xanax)
- Clonazepam (Klonopin)
- Lorazepam (Ativan)
- Diazepam (Valium)
- Chlordiazepoxide (Librium)
Mechanism of Action

Benzodiazepines enhance the effect of gamma aminobutyric acid (GABA) which has an inhibitory effect on the neuron which alleviates anxiety.
Side effects and therapeutic issues of Benzodiazepines

• Addiction, tolerance, withdrawal, abuse
• Sedation
• Psychomotor slowing
• Blurred vision
• Nausea
• Dizziness
• Amnestic for events
• Paradoxical reactions especially in Axis II pathology
Other Antianxiety Medications

Buspirone (Buspar) Limited effectiveness
– Acts by having some serotonin increasing effects
– Can cause sedation

• Hydroxyzine (Vistaril, Atarax)
  – antihistaminic

• Diphenhydramine (Benadryl)
  – antihistaminic

• Gabapentin (Neurontin) inhibits the calcium channel???
Antipsychotic Medications

Typicals or First Generation Neuroleptics versus Atypicals or Second Generation Neuroleptics
Antipsychotics (cont.)

Typicals or First Generation

Older medications
Generally block Dopamine 2 (D2) receptors
Examples include:
• Haloperidol (Haldol)
• Fluphenazine (Prolixin)
• Chlorpromazine (Thorazine)
• Perphenazine (Trilafon)
• Thioridazine (Mellaril)
Antipsychotics (cont.)

• Side Effects
  – Extrapyramidal side effects
    • Akathisia
    • Dystonia
    • Parkinsonism
    • Neuroleptic Malignant Malignant Syndrome
  – Tardive Dyskinesia
  – Hyperprolactinemia
  – Anticholinergic (constipation, dry mouth, difficulty urinating, sexual dysfunction, sedation)
  – Postural hypotension
Antipsychotics (cont.)

Atypicals or Second Generation

Newer medications

Generally broader range of blockade (dopamine, serotonergic, histaminic, acetylcholinergic, alpha adrenergic)

Also used commonly for bipolar disorder for mood stabilization
Antipsychotics (cont.)

Atypicals

- Risperidone (Risperdal)
- Olanzapine (Zyprexa)
- Ziprasidone (Geodon)
- Aripiprazole (Abilify)
- Clozapine (Clozaril)
- Quetiapine (Seroquel)
- Paliperidone (Invega)
- Asenapine (Saphris)
- Iloperidone (Fanapt)
- Lurasidone (Latuda)
Antipsychotics (cont.)
Atypicals

• Side Effects
  – Similar to first generation
  – Lower incidence of extrapyramidal side effects
  – Metabolic changes
  – Some issues with QT prolongation with Geodon
  – Clozapine issues
Mood Stabilizers or Medications for Bipolar Disorder
Medications for Mood Stability

- Lithium
- Valproic Acid (Depakote)
- Carbamazepine (Tegretol)
- Atypical Antipsychotics
- Lamotrigline (Lamictal)
Lithium

• Mechanism of Action
  – Unclear

• Therapeutic for both mania and depression
  – As well as maintenance

• Reduces risk for suicide
Lithium- Therapeutic Issues

- Requires monitoring of therapeutic levels
- Thyroid monitoring
  - Can cause hypothyroidism or goiter
- Renal Function
  - Can have long term effects on renal function
- Teratogenic
  - First trimester exposure linked to birth defects
Lithium Side Effects

• Dehydration
  – Acts in the kidney to reduce antidiuretic hormone and will therefore cause the kidneys to diurese
• Weight gain
• Tremor
• Acne
Mechanism of Lithium

Somehow effects second messenger proteins and G proteins. They inhibit the breakdown of inositol phosphate which in a nutshell, quiets the neuron down. There is a theory that bipolar neurons fire too quickly, lithium acts to quiet them.

With all that being said, it is only a theory and it is not proven that this is the therapeutic effect in bipolar.
Mechanism of Action of Mood Stabilizers

- **Figure 1. Intracellular signaling cascades involved in long term stabilization of mood by lithium (Li) and valproic acid (VPA).**
  
  Activation of receptors coupled to PI hydrolysis results in the breakdown of phosphoinositide 4,5-biphosphate (PIP$_2$) into two second messengers: IP$_3$ and diacylglycerol (DAG), which is an endogenous activator of PKC. Lithium is an uncompetitive inhibitor of inositol monophosphatases, whereas both lithium and VPA, upon chronic administration, decrease myo-inositol uptake. These perturbations by mood stabilizers likely contribute to the reduction in PKC activity and the reduced levels of PKC-, PKC- and myristoylated alanine-rich C kinase substrate (MARCKS), a major PKC substrate in the CNS, that occur after chronic exposure to lithium or VPA. One pathway gaining attention in the adult mammalian brain is the Wnt signaling pathway. Binding of the Wnt signal to the Wnt receptor (WntR) activates an intermediary protein, 'disheveled', which regulates GSK-3. GSK-3 regulates cytoskeletal proteins, and also has an important role in determining cell survival and cell death. Lithium (and possibly VPA) directly inhibit GSK-3, which may underlie, at least in part, the increases in -catenin that occur after chronic treatment with these agents. The ERK MAP kinase cascade regulates several important transcription factors, most notably CREB and activator protein-1 (Ap-1). Recent studies have demonstrated that both lithium and VPA activate the ERK MAP kinase cascade, which may contribute to the long term changes in synaptic plasticity and morphology that follow chronic treatment. Together, the regulation of these signaling pathways brings about an enhancement of synaptic connectivity potentially necessary for long-term stabilization of mood.
Valproate (Depakote)

- Established efficacy in bipolar mania and maintenance
- Not very useful for depressive episodes
- Mechanism of action unclear
Valproate (Depakote) Therapeutic Issues

• Blood level monitoring
• Hepatic inflammation
• Low platelets
• Teratogenic
Valproate (Depakote) Therapeutic Issues

- Weight gain
- Gastrointestinal upset
- Sedation
- Tremor
- Alopecia
Carbamazepine (Tegretol)

• Another anticonvulsant
• Effective for mania and maintenance, not depression
• Side effects include vertigo, ataxia, leukopenia, cardiac conduction slowing
• It induces the breakdown of many other medications and therefore lowers their levels
Atypical Antipsychotics

- FDA approved for use in acute manic episodes
- Unclear use for bipolar maintenance
- Same side effects profile as with psychotic disorders
- Drug companies are exploring their use in bipolar depression
Atypical Antipsychotics with Indication in Bipolar Disorder

- Olanzapine (Zy prexa) mania and maintenance
- Risperidone (Risperdal) mania and maintenance
- Ziprasidone (Geodon) mania and maintenance
- Quetiapine (Seroquel) mania, depression and maintenance
- Asenapine (Saphris) mania and maintenance
- Aripiprazole (Abilify) acute mania
- Paliperidone (Invega) schizoaffective disorder
Lamotrigine (Lamictal)

- Approved for bipolar depression and maintenance
- Not approved for mania
- Requires slow titration
- Interaction with other medications esp. valproate
Side Effects of Lamotrigine

- Stevens Johnson rash
- Weight neutral
- Dizziness
- Sedation
- GI upset
Used in Bipolar but Not Proven Useful

- Gabapentin (Neurontin)
- Oxcarbazepine (Trileptal)
- Tiagabine (Gabitril)
- Topiramate (Topamax)
Medications for Sleep
Medications for Sleep

• Benzodiazepines
• Zolpidem (Ambien) works like a benzo
• Zaleplon (Sonata) Works like a benzo
• Eszopiclone (Lunesta) works like a benzo
• Ramelteon (Rozerem) melatonin receptor agonist
• Trazodone antidepressant that is sedating
• Benadryl antihistamine that is sedating
• Seroquel atypical that is sedating
Medications for ADHD
Medications for ADHD

- Psychostimulants
- Non-stimulants
Medications for ADHD

• Stimulants
  – Methylphenidate (Ritalin, Ritalin SR, Ritalin LA, Concerta, Metadate CD, Daytrana patch)
  – Dexmethylphenidate (Focalin)
  – Amphetamine/Dextroamphetamine (Adderall, Dexedrine)
  – Lisdexamphetamine (Vyvanse)
Mechanism of amphetamine
Psychostimulants

• Almost 80% effective for treatment of symptoms
• Mechanism of action is to increase dopamine by inhibiting the dopamine reuptake transporter in the anterior cingular gyrus and prefrontal cortex
Stimulants and addiction

• Individuals with ADHD have increased incidence of substance use disorders overall but treating ADHD actually decreases the rate of abuse.

• Extended release stimulants have low risk for abuse potential
Side Effects of ADHD Medications

Psychostimulants

• Appetite suppression
• Jitteriness
• Headache
• Gastrintestinal upset
• Elevation in heart rate, palpitations
• Insomnia
Nonstimulants

• Non-Stimulant Treatments
  – Atomoxetine (Strattera)
  – Bupropion (Wellbutrin)
  – Guanfacine (Intuniv)
  – Clonidine (Catapres, Tenex)
  – Modafinil (Provigil)
Side Effects of Nonstimulants

- Insomnia
- Activation
- Sedation (Tenex, Catapres, Intuniv)
Miscellaneous Medications

• Modafinil (Provigil)
  – A wakefulness promoting agent
  – Used off label for alertness in medication side effects

• Topiramate (Topamax)
  – Some studies show usefulness to reduce binging in bulimia or binge eating disorder
When to refer for medication evaluation

• Marked interference in functioning
• Suicidality
• Vegetative symptoms in depression (anhedonia, insomnia, loss of appetite)
• Symptoms fail to improve with therapy
• Symptoms are jeopardizing marriage or occupation
Symptoms that I would automatically refer for medication

- Psychotic symptoms
- OCD symptoms
- Manic symptoms
- Symptoms patient is self medicating with drugs or alcohol
When to contact the prescriber

• Suicidal Ideation
• Exacerbation of symptoms
• Patient is noncompliant or will not follow up with prescriber
• Patient is embarrassed to discuss side effects (especially sexual side effects)
• Medication may be causing symptoms (mania)
• Medication may be interfering with treatment
How Medication can Interfere with Therapy

- An antidepressant causes mania
- An antidepressant causes affective blunting
- Anxiety is gone and there is no motivation to work in therapy
- A stimulant causes anxiety
- Patient uses benzodiazepine too readily and refuses to tolerate any anxiety
How to discuss realistic medication expectations

• Medication is not a panacea
• Medication frequently has side effects
• Medication has minimal effect on reactive symptoms
• If patients only want to be on medication temporarily, then they need to work on improved coping skills
• Medication does not change your environment
Medication Expectations

- Stimulants work almost immediately
- Antipsychotics and mood stabilizers should exert therapeutic effects in a few days
- Benzodiazepines work almost immediately
- Antidepressants take 2 to 6 weeks to work
Questions

• Why are medications viewed as something an individual has to take for the rest of their lives instead of stabilizing them enough to do the work they need to do in therapy?
Stop Medication??

- OCD, Bipolar disorder and psychotic disorders use medication as their primary treatment-long term
- If you have more than two depressive episodes, current recommendations are to be on maintenance medication
- Temporary medication use is useful for anxiety and depression (especially adjustment reactions)
• “If it ain’t broken, don’t fix it”
  – Some people don’t want to come off medication
  – They have minimal side effects and no ambivalence about staying on them
• Preferably need a low stress period of time to taper
• Taper should take a while to reduce chance to relapse
• Many people do well coming off medication—try it!
O.K. This is the end of the line.
Next stop... Crazy

Crazy Train, No Diagnosis Needed