Pharmacologic Treatment of Mental Health

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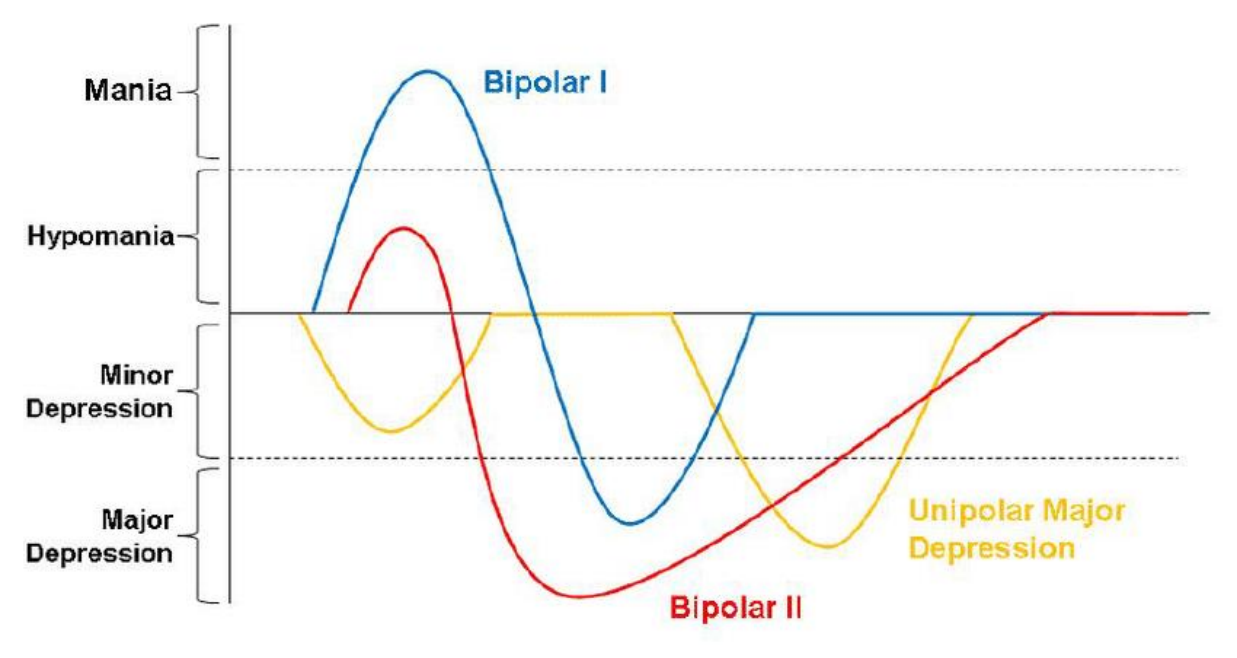
Disclosures

I have no financial interests to disclose.

Learning Objectives

1. Identify the medication classes indicated for mood, anxiety and psychotic spectrum disorders
2. Describe common side effects of psychiatric medications by class
3. Explore psychiatric prescribing in special situations, including obesity, pregnancy, heart disease, kidney disease, chronic pain, and polypharmacy

Mood Disorders



Elevated/irritable mood + increased energy + DIGFAST (3 or 4) X 4-7 days

Depressed mood + SIGECAPS (5) X 2 weeks

Major Depressive Disorder

1. SSRIs, SNRIs, + other serotonergic antidepressants
2. Tricyclic antidepressants
3. NDRIs
4. Troubleshooting

SSRIs

E.g. - fluoxetine, citalopram, escitalopram, sertraline, paroxetine, fluvoxamine

MOA = Inhibit reuptake of 5HT, causing a net increase of 5HT in the synaptic cleft

First line for MDD, GAD, PTSD, Panic disorder, OCD, PMDD

GI distress

Headaches

Sexual dysfunction

escitalopram
paroxetine
sertraline
citalopram
fluoxetine

SNRIs

E.g. - venlafaxine, duloxetine, desvenlafaxine

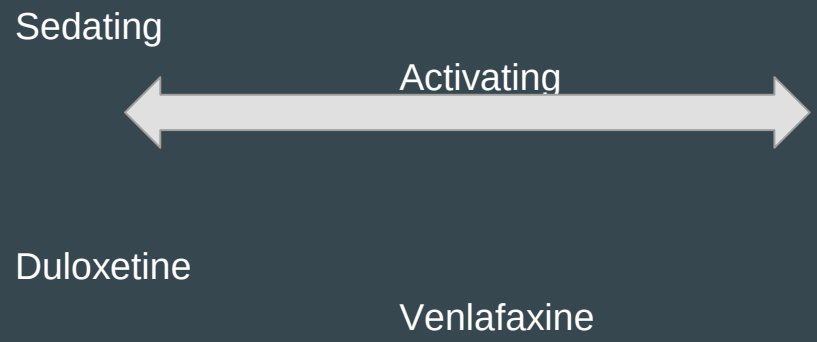
MOA = block reuptake of both 5HT and norepinephrine

Similar indications as SSRIs

GI distress

Headaches

Sexual dysfunction



Other Serotonergic Antidepressants

mirtazapine

MOA = alpha 2 antagonism plus specific 5HT receptor antagonism, plus antihistamine effects

MDD, Panic, PTSD, GAD

Sedation

Increased Appetite

vilazodone

MOA = SSRI plus partial agonism of a 5HT receptor

MDD, OCD

Same as SSRIs

vortioxetine

MOA = blocks 5HT reuptake, interacts with multiple 5HT receptors in various ways

MDD, GAD

Same as SSRIs

*these seem to have fewer sexual side effects than SSRI/SNRIs in general

Tricyclic Antidepressants

E.g. - amitriptyline, nortriptyline, clomipramine, desipramine, nefazodone, and others

MOA = blocks norepinephrine and 5HT reuptake, with downstream dopaminergic effects; also some antihistaminergic and anticholinergic activity

Indicated for MDD, Panic, OCD, GAD, insomnia, neuropathic pain

Sedation

Sexual dysfunction

Blurred vision

Weight gain

Dry mouth

Constipation

Orthostatic hypotension

Lowers seizure threshold

QTc prolongation

Dangerous drug-drug interactions

NDRI

E.g. - bupropion

MOA = blocks NE and dopamine reuptake; no effect on 5HT

Indicated for MDD, ADHD and nicotine dependence

***No benefit for anxiety disorders and may actually worsen anxiety**

Lowers seizure threshold

Insomnia

Dry mouth

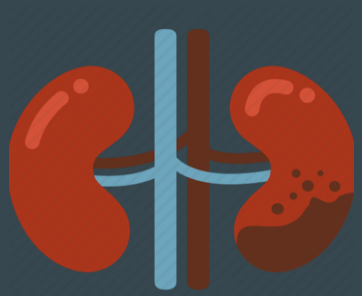
Decreased appetite/weight

Troubleshooting

1. It works!
   - Great! Continue x 1 year before attempting to taper off.
   - Patients with recurrent episodes may need lifelong treatment
2. It partially works...
   a. Augment with: buspirone, bupropion, or a SGA like aripiprazole
   b. OR Switch (usually cross taper)
3. It doesn't work at all.
   - Confirm your diagnosis. If correct, then switch to:
   a. Different SSRI
   b. Different class
4. It works! But there are side effects..
   - Great! Most side effects wane after a few weeks of treatment
   - If sexual dysfunction, try adding bupropion or buspirone
   - Consider a switch if above options not helpful

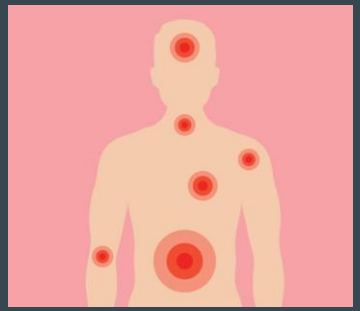
TCAs, mirtazapine, escitalopram, paroxetine, duloxetine
fluoxetine, sertraline, venlafaxine, vortioxetine, vilazodone
bupropion

Avoid TCAs and citalopram doses >40mg/day
SNRIs and NDRI (can increase BP)
SSRIs, especially sertraline



Most will need doses decreased

SIADH can occur with SSRIs, but rare



Consider TCAs and SNRIs!

Paroxetine
Bupropion, vilazodone, vortioxetine, mirtazapine
All other SSRIs, especially sertraline

Avoid use of TCAs with other antihistaminergic or anticholinergic agents
CYP450 system affected by SSRIs and TCAs
*Serotonin syndrome

Bipolar disorders

1. Lithium
2. Antiepileptic mood stabilizers
3. Antipsychotics
4. Troubleshooting

Lithium

*Long time gold standard of treatment

MOA = unknown!

Indicated for bipolar disorders and treatment-resistant depression

*Once daily dosing protects the kidney
*Baseline blood work including kidney and thyroid functioning
*therapeutic [trough] level 0.6-1.0

Antiepileptic Mood Stabilizers

E.g. - valproic acid, carbamazepine, oxcarbazepine, lamotrigine, topiramate

(NOT typically used → levetiracetam, phenytoin, gabapentin)

MOA = variable, heterogeneous group

*most require monitoring bloodwork (liver function, kidney function, blood counts, and sodium levels)

Hepatotoxicity **SIADH** **Some dangerous drug interactions**

Hyponatremia **Alopecia**

Stevens-Johnson syndrome

Highly teratogenic **Pancreatitis** **Bone marrow suppression**

Troubleshooting

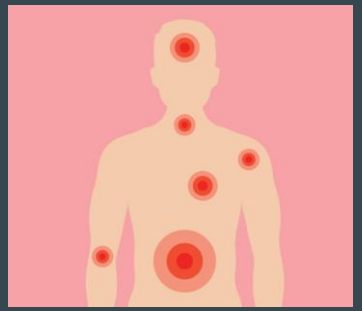
1. My patient is in active mania/hypomania
    a. Consider hospitalization
    b. Consider lithium, valproic acid, SGAs, carbamazepine
2. My patient is in a MDE
    a. If SI, hospitalize.
    b. Consider lamotrigine, quetiapine, and lurasidone
    c. Probably avoid antidepressants
3. My patient is in maintenance
    a. Great! Continue stabilizing regimen.
    b. Consider whether augmenting agent is needed (ie- oxcarbazepine, topiramate, gabapentin, antipsychotic, etc).

Carbamazepine, valproic acid, lithium, most SGAs
Lurasidone, aripiprazole
Lamotrigine, topiramate, ziprasidone

Lithium, topiramate
lamotrigine
Valproic acid

Many APs, especially ziprasidone, prolong QTc

Lithium associated with arrhythmias



Consider gabapentin if neuropathic

Consider valproic acid or topiramate if migrainous

Avoid antiepileptics

Lamotrigine, lithium

SGAs and high potency FGAs

Valproic acid *increases* levels of lamotrigine twofold
Lithium level increased by diuretics, ACE-I's and NSAIDs
Many CYP450 interactions with antiepileptics

Psychotic Disorders

1. First generation antipsychotics
2. Second generation antipsychotics
3. Long-acting injectable APs

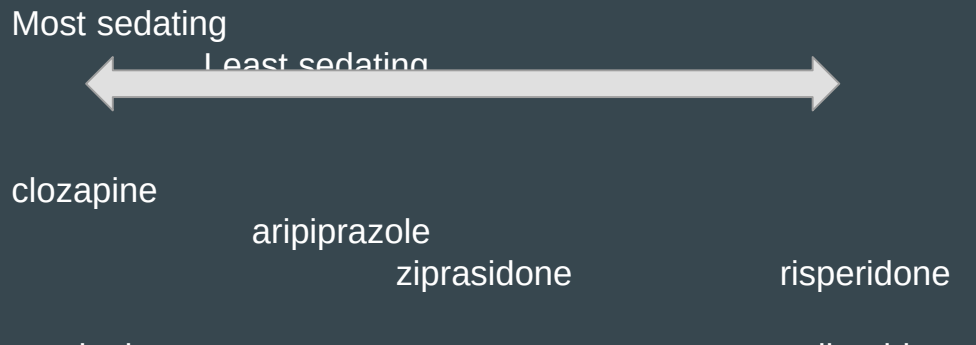
Second generation antipsychotics

E.g. - risperidone, quetiapine, lurasidone, aripiprazole, olanzapine, ziprasidone, paliperidone, clozapine

MOA = varying degrees of 5HT and dopamine antagonism; some with serotonin partial agonism

Indicated for: bipolar disorders, psychotic disorders; some indicated for augmentation of antidepressants; some indicated for agitation related to delirium
Often used off-label for insomnia, anxiety, and/or agitation

Weight gain	**Dry mouth**
Insulin resistance	**Hyperprolactinemia**
EPS/TD	**Orthostatic hypotension**



First generation antipsychotics

E.g. - haloperidol, chlorpromazine, perphenazine, loxapine, thiothixene, trifluoperazine

MOA = primarily dopamine antagonism

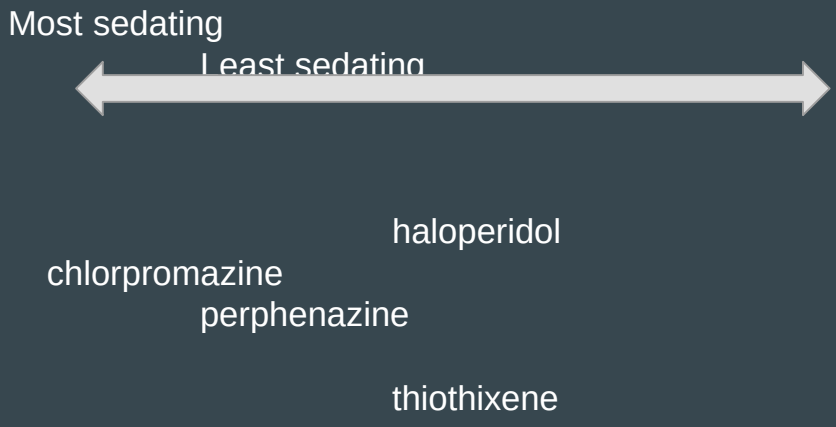
Extrapyramidal symptoms (Parkinsonian movements)

Tardive dyskinesia (involuntary mouth/tongue/face movements)

Dystonic reaction (acute involuntary muscle contraction)

Prolactinemia

QTc prolongation



Long-acting injectable APs

Given Q2 weeks, Q4 weeks, or Q3 months depending on formulation

*Good efficacy, better treatment adherence

*Unlikely to be managed outside a psychiatric treatment setting

Similar to oral antipsychotics

Troubleshooting

1. It doesn't work.
    a. Evaluate adherence
    b. Check for comorbid substance use
    c. Keep trying!
2. It works! But so much weight gain..
    a. Consider adding metformin or topiramate for weight loss
    b. Carefully weigh switching to more weight-neutral agent
3. It works! But they keep coming off of it..
    - This is the reason LAI APs exist!
4. It works! But akathisia/EPS..
    a. Possible to lower the dose?
    b. Consider adding beta-blocker, benztropine, benadryl, or low dose benzodiazepine
5. Antipsychotics scare me a little..
    - It's OK to refer to psychiatry!

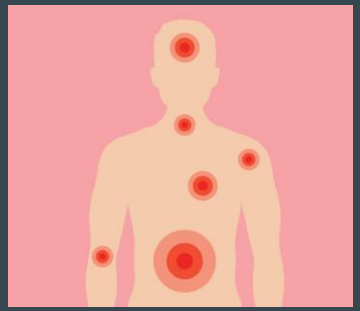
Most SGAs, chlorpromazine
Lurasidone, aripiprazole, haloperidol
Ziprasidone, loxapine, thiothixene, trifluoperazine

Risperidone, FGAs

Quetiapine

Many APs, especially ziprasidone, prolong QTc and/or cause orthostatic hypotension

Aripiprazole, lurasidone



None particularly indicated for use in chronic pain

Low-potency FGAs (ie - chlorpromazine)
High-potency FGAs (ie - haldol)
SGAs

APs have black box warning for increased mortality in dementia

*Neuroleptic malignant syndrome

Anxiety Disorders

Generalized anxiety disorder

Panic disorder

Obsessive-compulsive disorder

Post traumatic stress disorder

Anxiety Disorders

1. Antidepressants
2. Benzodiazepines
3. Antihypertensives
4. Other agents

Antidepressants

E.g. - SSRIs, SNRIs, TCAs, other serotonergic antidepressants

*bupropion NOT indicated for anxiety disorders

*SSRIs are first line

*If using a more activating antidepressant, do a *gentler titration*

*OCD may require higher doses

Benzodiazepines

E.g. - alprazolam, lorazepam, clonazepam, diazepam, etc.

MOA = bind to GABA-a receptor (similar to alcohol)

*Can be added to SSRIs for short term relief before SSRI takes effect

***Relatively contraindicated in PTSD, the elderly, and if comorbid OSA or substance abuse**

Sedation	**Disinhibition**
Rebound anxiety	**Memory problems**
Deliriogenic	**Increased risk of falls**

Tolerance, dependence, and abuse potential

Antihypertensives

E.g. - prazosin, propranolol, clonidine

MOA = reduce adrenergic tone, causing reduction of physical symptoms of anxiety

*Not typically helpful in OCD
***Usually adjunct medications**
*Prazosin for PTSD related nightmares

Hypotension	**Sexual dysfunction**
Dizziness (BB)	**bronchospasm**
Bradycardia	

Other agents

Buspirone

MOA = partial agonist at some 5HT receptors

Indicated for anxiety and as adjunct for depression

*typically no sexual side effects

Sedation

Hydroxyzine

MOA = antihistamine

Mild **PRN** anxiolytic

Dry mouth

Sedation

Ineffectiveness?

Gabapentin

MOA = multiple GABA-ergic actions, causing general CNS depression; antiepileptic

Off-label for anxiety and some weak mood stabilization action

Abuse potential

Withdrawal possible

Sedation

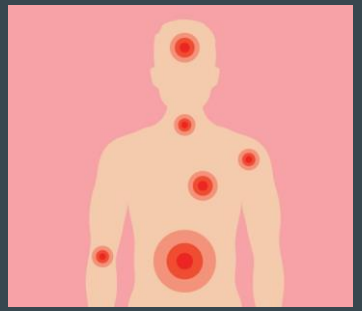
Troubleshooting

1. My patient needs to feel better NOW, and antidepressants take too long.
    a. Augment with psychotherapy
    b. Consider brief course of a PRN medication, like hydroxyzine or benzodiazepines
2. My patient has side effects to everything.
    - Fairly common in highly anxious patients
    - Consider mild agents like buspirone or hydroxyzine
    - Do very slow and gentle titrations with extra reassurance
3. It worked! But now it doesn't work..
    a. Is it a benzodiazepine heavy regimen (ie - is physiological tolerance present)?
    b. Add an antidepressant and/or therapy

Antidepressants - variable
Gabapentin, hydroxyzine
Buspirone, benzodiazepines, antihypertensives

Gabapentin, prazosin, clonidine, benzodiazepines
Propranolol, hydroxyzine

Antihypertensives (unless effect is accounted for)
Benzodiazepines can affect heart rate
Hydroxyzine



Consider gabapentin if neuropathic

Consider propranolol if migrainous

Gabapentin
Benzodiazepines
Hydroxyzine
Antihypertensives
buspirone

Benzodiazepines and hydroxyzine are deliriogenic
Beta blockers worsen asthma
Buspar may increase concentrations of haloperidol and diazepam

Questions?