Psychopharmacology: Essential Information for Mental Health Professionals

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Materials that are included in this course may include interventions and modalities that are beyond the authorized practice of mental health professionals. As a licensed professional, you are responsible for reviewing the scope of practice, including activities that are defined in law as beyond the boundaries of practice in accordance with and in compliance with your professions standards.

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Before we start

About me

ken@drkencarter.com

Questions

Scope of today's training

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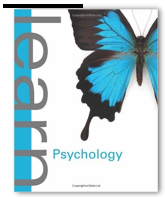
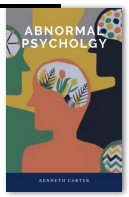
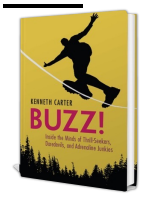
Disclosures



Learn Psychology
SAGE Publications



Abnormal Psychology
Cambridge University Press



Buzz!
Cambridge University Press

4

4

I receive no money from any pharmaceutical company

5

5

This workshop is intended solely for educational purposes. The information presented herein is to provide practical and useful information on the subject matter covered. However, the information is provided with the understanding that we are not engaged in rendering legal services. If legal advice is required, the services of a legal professional should be sought. We will not be liable for any decision or action taken on reliance on the information presented in this activity.

6

6

Disclaimer & Disclosure of Off-Label Use

- I may include discussion of unlabeled uses of agents that are not currently labeled for such use by the FDA. Please consult the product prescribing information for full disclosure of labeled uses.
- The information in this workshop is presented for educational discussion and is not meant to serve as a guideline for patient management. Any medications discussed or suggested should not be used by clinicians without evaluation of their patients' conditions and possible contraindications or dangers in use.
- Every effort has been made in to provide accurate and up-to-date information that is in accord with accepted standards and practice at the time of release. However, I make no warranties that the information contained herein is totally free from error. Clinical standards are constantly changing because of research and regulation. I disclaim all liability for direct or consequential damages resulting from the use of this material.
- Please pay careful attention to information provided by the manufacturer of any medication that you plan to use.

7

7

Psychopharmacology: Limitations of the Research and Potential Risks

- The evidence base for psychopharmacological interventions can vary and ethical considerations pertain to medication trials for certain populations
- Potentially controversial treatment practices and off-label prescribing are sometimes unavoidable for certain understudied treatments and disorders and medications with a potential for adverse consequences require increased focus on ethical issues including informed consent.

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Overview

Section 1	Section 2	Section 3	Section 4
Psychopharm Ethics	Guidelines Questions Differences	Neuroscience 101 Depression Anxiety	Bipolar ADHD Psychosis Insomnia Resources

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Psychopharmacology Ethics

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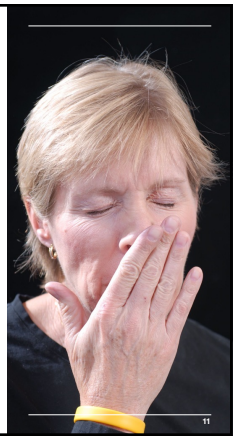
Sleepy Susan



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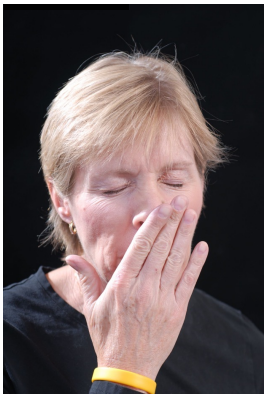

Sleepy

crying
anhedonia
problems with concentration
no appetite
initial insomnia
guilt
Diagnosis?

12

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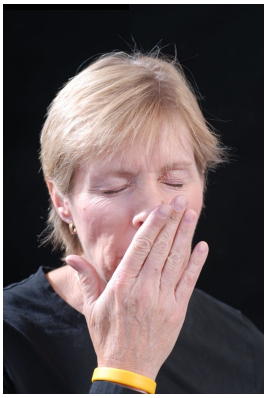

Susan is depressed

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13

went to her primary care physician

with a chief complain of insomnia

14

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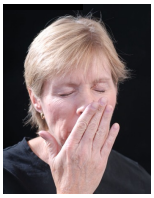

What do you do?

15

15

As a non prescriber is telling her not to take it unethical?

16

16

Is it unethical to withhold the information you have?

17

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Reasons to be knowledgable

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18

42% of current clients use psychotropic medication

19

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It is important to know the context in which clients receive their medication

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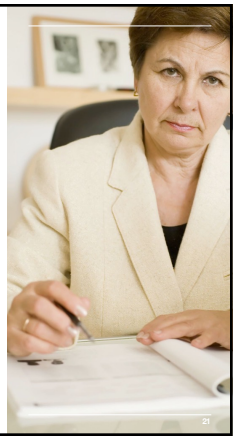
75-90%

Of antidepressants and benzodiazepines are written by non-psychiatrists. Mostly by primary care physicians

(Preston 2017)



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Psychiatrists in Canada

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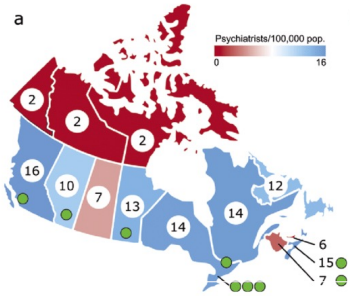

b

Ontario

LHIN	Psych./100k
Toronto Central	61
Champlain	22
South East	19
South West	16
Hamilton Niagra	12
Central West	10
Waterloo Wellington	9
Erie St. Clair	8
Mississauga Halton	8
North Simcoa Muskoka	8
North East	8
North West	7
Central East	6
Central West	4

22

Complicating such treatments is the brief time patients are typically seen by their primary care physician

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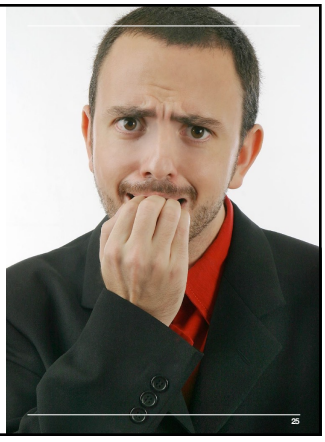
The average Primary Care visit is..

8 minutes

24

take a history
make a diagnosis
prescribe treatment
patient education
answer questions



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As clients become more empowered and "better informed"

Google

26

We hear more questions about psychotropic medications and

27

It becomes important to be knowledgeable about the professional, legal, and ethical boundaries regarding the discussion of medication-related issues with clients

28

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Because of our role in our clients' lives, it is important to be proactive in speaking with clients and prescribers

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There are several ways that non-prescribers can partner with prescribers to help increase success with medication

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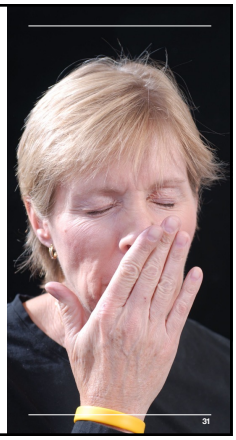
We can help clients have realistic expectations of their medications



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We observe or are told about potential side effects that may interfere with compliance

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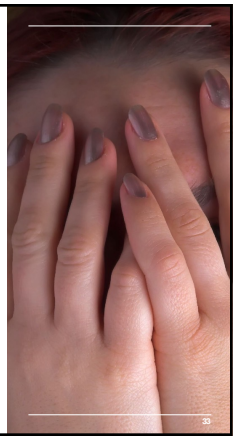
We know information clients may be too embarrassed to tell their prescribers



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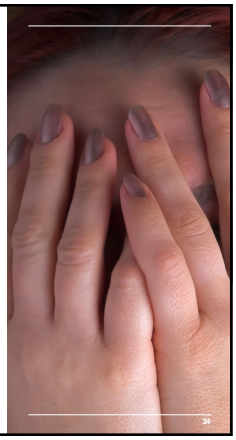
Survey from *USA Today*

Reasons people have kept health information from their doctors



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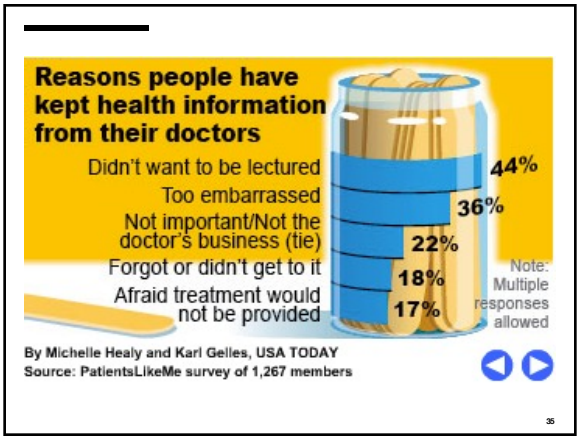

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We are aware when clients aren't taking their medications as prescribed or have stopped

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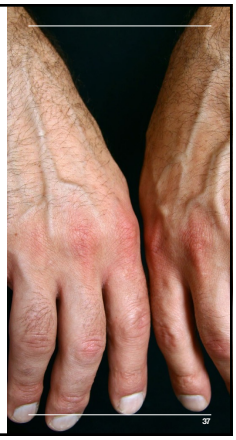
We are on the front line at witnessing the emergence of late-onset side effects



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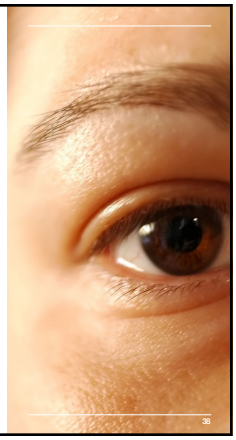
We can recognize break-through symptoms



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We can encourage clients to discuss substance use with prescribers

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We can recognize inadequate medication response which may warrant dosage adjustments or augmentation

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Practice Guidelines Regarding Involvement in Pharmacological Issues

American Psychologist 2011

Practice Guidelines Regarding Psychologists' Involvement in Pharmacological Issues

American Psychological Association

Several factors have converged that will inevitably increase psychologists' involvement in the medication management of the individuals they serve. One is the increasing use of psychotropic medications for the treatment of psychological disorders, a clinical practice which is referred to as *pharmacotherapy* in this document. A national survey of physician records suggested that the proportion of the population using antidepressants increased from 6.7% in 1990 to 15.1% in 1998, an increase of 125.4% even after adjusting for population growth (Skaer, Sclar, Robison, & Galin, 2000). According to VandenBos and Williams (2000), practicing psychologists, on average, estimated that 43% of their current patients were using psychotropic medications. Another factor is the movement for prescriptive authority within psychology. Appropriately trained psychologists are now eligible for prescriptive authority in two states (Louisiana and New Mexico) as well as in the military. With similar legislative agendas emerging in a number of other states, the number of states offering prescriptive authority to psychologists will inevitably increase further.

In response to a series of articles describing the professional challenges faced by psychologists as they become prescribers (e.g., Antonuccio, Danton, & McClanahan, 2003; Buelow & Chafetz, 1996; DeLeon, Robinson Kurpius, & Sexton, 2001; McGrath et al., 2004), it was recognized in discussions among members of American Psychological Association (APA) Division 55, the American Society for the Advancement of Pharmacotherapy, that the implications of the APA (2002b) "Ethical Principles of Psychologists and Code of Conduct" (the Ethics Code) specifically concerning psychologists' involvement in pharmacotherapy merited clarification. Beth Rom-Rymer, president of the division in 2004, convened the Division 55 Task Force on Practice Guidelines to explore the issue. Four of seven task force members were psychologists with prescriptive authority in the civilian or military sector, while three supervised postdoctoral programs in clinical psychopharmacology for psychologists. The task force also included representation from Division 18 (Psychologists in Public Service).

Members of the task force reviewed relevant literature and participated in formulating the content of the guidelines. The literature review began with a document titled *Policies of Other Organizations and Background Materials: Pharmaceutical Marketing, Gifts, and Financial Support* (APA, 2002c), which provided primary sources addressing the relationship between prescribing professionals and the pharmaceutical industry. This document was updated with more recent publications on the topic. Medicine, nursing, pharmacy, and the pharmaceutical industry have all generated guidelines relevant to the practice of pharmacology, and these were reviewed as well. Finally, the task force considered specific implications of APA's (2002b) Ethics Code for psychologists' involvement in the practice of pharmacotherapy.

The guidelines presented in this document are intended to provide a resource to psychologists interested in the issue of what represents optimal practice in relation to pharmacotherapy. They are not intended to apply to those psychologists who choose not to become directly or indirectly involved in medication management regardless of their level of competency. As background to these guidelines, it may be noted that psychologists' involvement in pharmacotherapy can be conceptualized as a continuum, though prior APA documents (e.g., Smyer et al., 1993) have identified three particularly salient steps along that continuum. The first occurs when the psychologist serves as the prescriber. As indicated above, psychologists currently can only prescribe in the U.S. military and in two states, though the latter authority also allows psychologists to prescribe in the Public or Indian Health Services. The population of psychologists with prescriptive authority is therefore small but is one

These guidelines were developed by the American Psychological Association (APA) Division 55 (American Society for the Advancement of Pharmacotherapy) Task Force on Practice Guidelines. The task force was chaired by Robert E. McGrath. Task force members included Stanley Berman, Elaine LeVine, Elaine Mantell, Beth Rom-Rymer, Morgan Sammons, and James Quillin. Additional input on the guidelines was provided by Robert Ax, representing Division 18 (Psychologists in Public Service). None of the individuals involved in the development of this document has any personal investment in pharmaceutical products of any kind, nor did the developers receive any financial support for its creation.

The task force anticipates that these guidelines may deserve reconsideration in a relatively brief time frame, given anticipated changes in psychologists' role in pharmacotherapy as well as changes in the perceptions and use of psychotropic medications. In particular, it is the belief of the members of the task force that future efforts should include consideration of whether some elements of the enclosed guidelines merit elevation to the level of practice standards. Accordingly, this document is scheduled to expire as APA policy in August 2014, five years after the date of its approval and adoption by the APA Council of Representatives. After this date, users are encouraged to contact the APA Practice Directorate to confirm whether this document remains in effect.

Correspondence concerning this article should be addressed to the Practice Directorate, American Psychological Association, 750 First Street, NE, Washington, DC 20002-4242.

American Psychologist 1

DOI: 10.1037/a0025890

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Evaluate your own feelings and attitudes about the role of medication in treatment.

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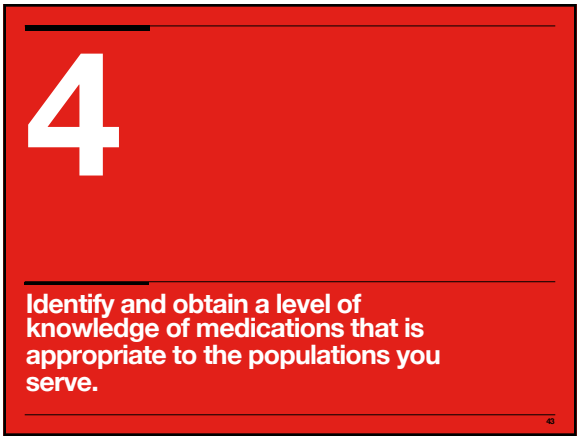
4
Identify and obtain a level of knowledge of medications that is appropriate to the populations you serve.
43

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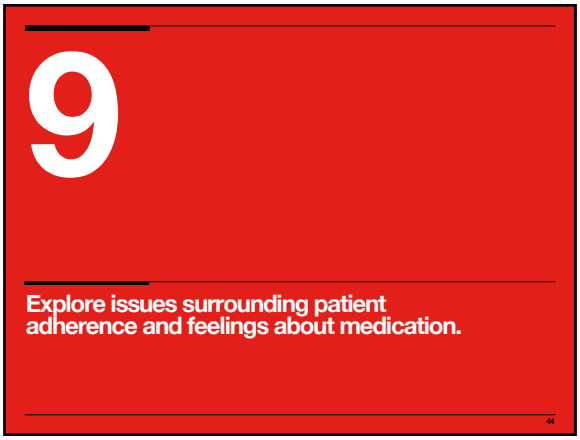
9
Explore issues surrounding patient adherence and feelings about medication.
44

44


10
Develop a relationship that will allow clients to feel comfortable exploring issues surrounding medication use.
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17

Maintain appropriate relationships with prescribers.

46

46

Expanded Informed Consent Process

- describe agent
- problems it will address
- estimate of the duration
- time to therapeutic effect
- cost of treatment
- possible drug interactions
- risks associated with sudden discontinuation
- explanation of any examinations or labs
- references for patient education
- describing ongoing non-prescriber partnerships
- inviting questions and concerns

47

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Ask Questions

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What are some common questions that you are asked about medicines?

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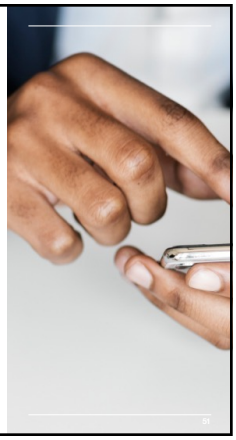
Particular issues that necessitate consultation with a prescriber

...or to empower the client to discuss the issue with the prescriber



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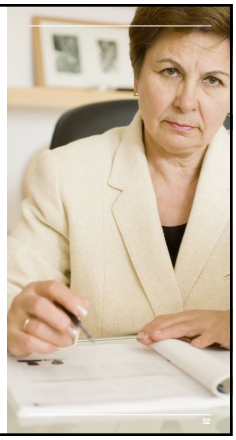
Prescriber recommends stopping a medication when the client is benefiting

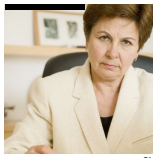


52

Client is being under-treated

53

Treatment recommended is not successful and not standard



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A medication that is cautioned for a suicidal client


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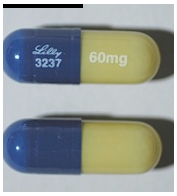
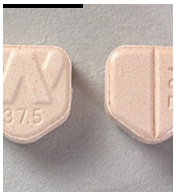
SNRI are more lethal in overdose than SSRIs



Venlafaxine (Effexor)



Desvenlafaxine (Pristiq)

Duloxetine (Cymbalta)

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56

but how?

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Complementary colleague vs one down approach

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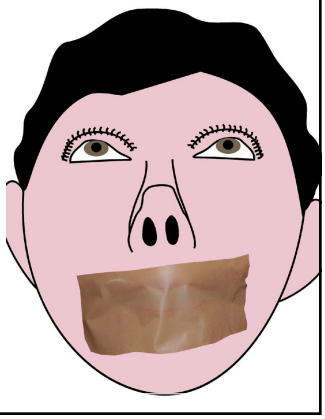
Advise against any of the following



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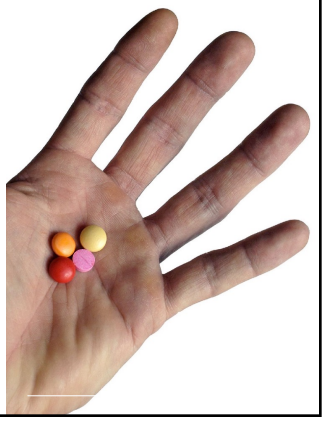
Not okay to administer or dispense drugs

samples
OTC



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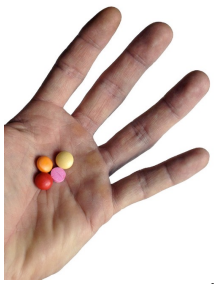
Not okay to tell clients to stop taking medication

Unless they are having an adverse effect that requires immediate discontinuation



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Not okay to advise clients to change medication dose or switch to another medication

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Questions?

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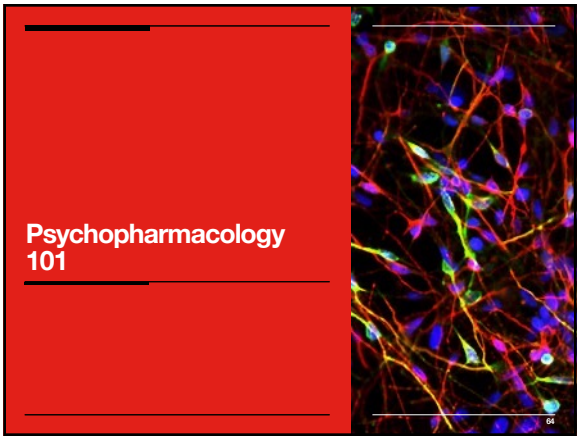
Psychopharmacology 101
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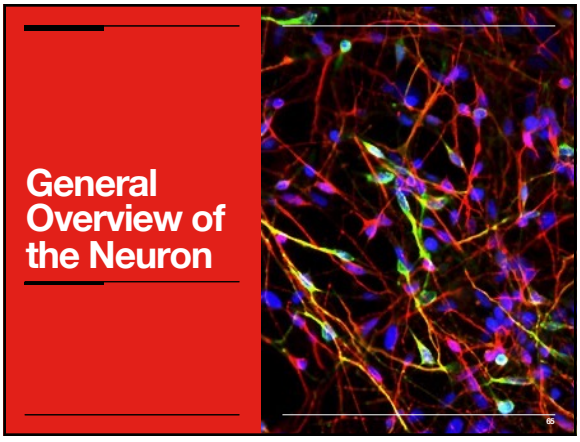
General Overview of the Neuron
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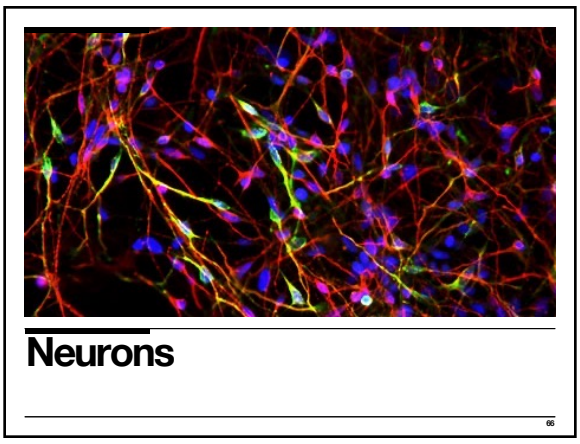
Neurons
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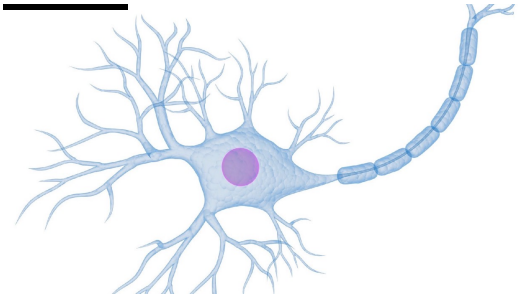

Parts of the neuron

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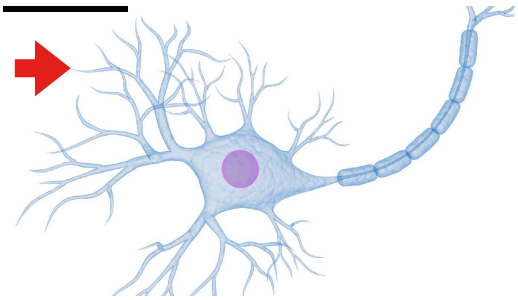

Dendrites

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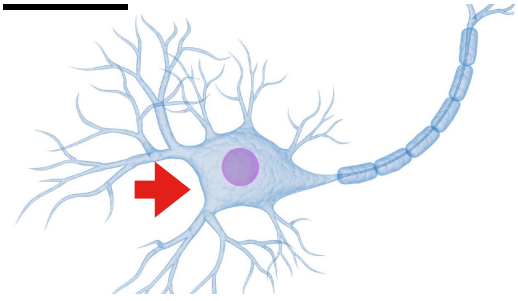

Soma

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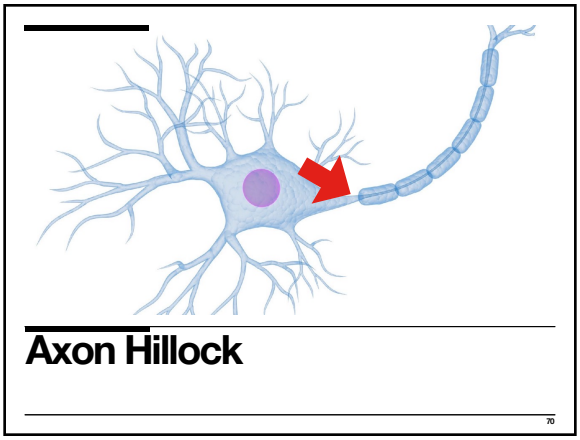

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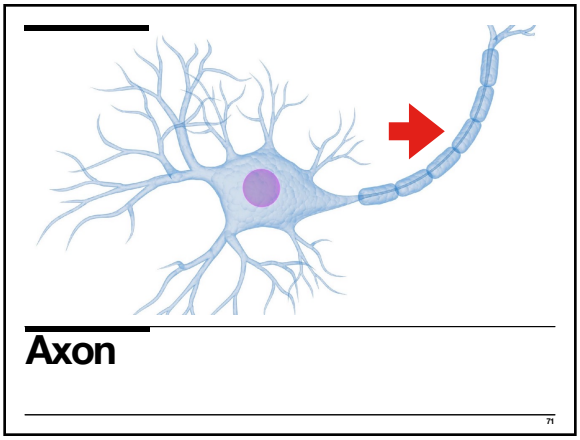

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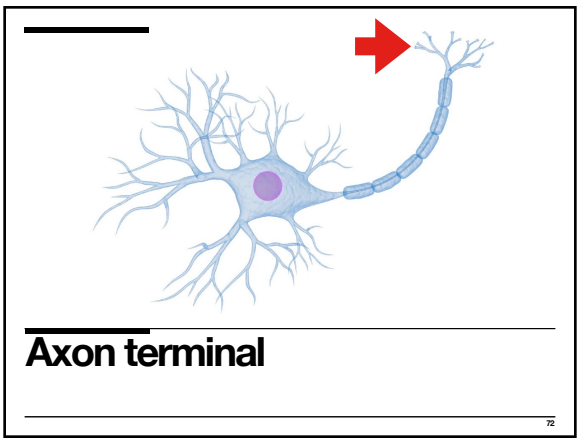

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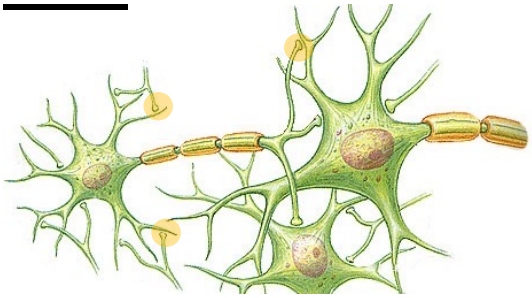

Synapses

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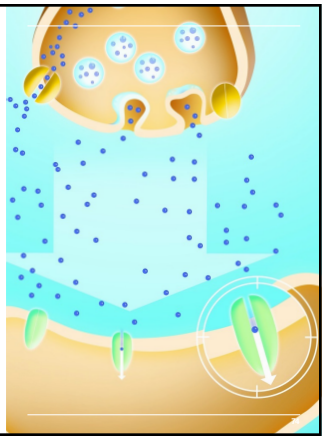
The Synapse

- An area that is comprised of 3 structures
  - The axon terminal
  - Synaptic Gap
  - Dendrite of next Neuron



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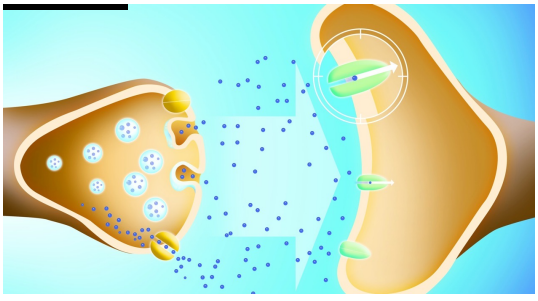

Synapse

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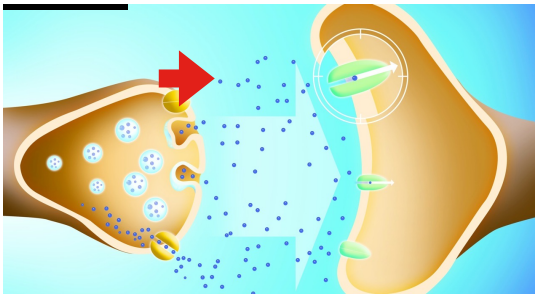

Neurotransmitter

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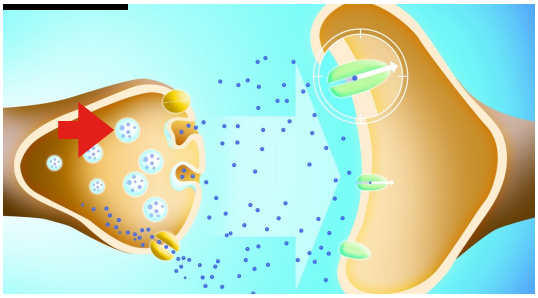

Synaptic Vesicle

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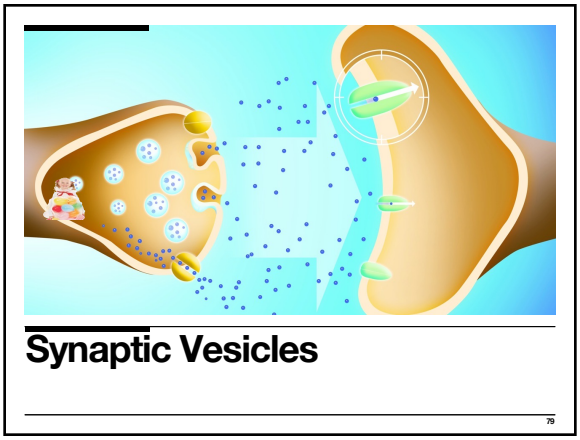
Synaptic Vesicles
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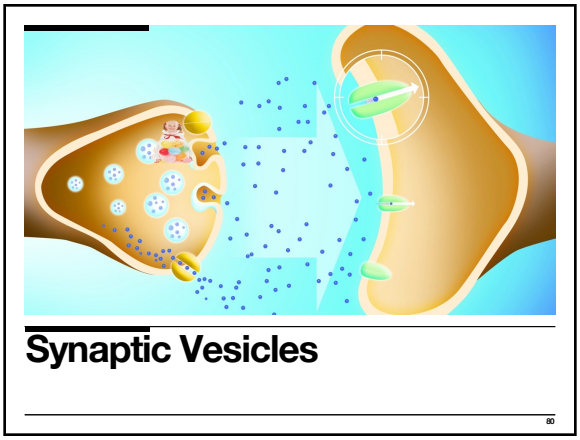
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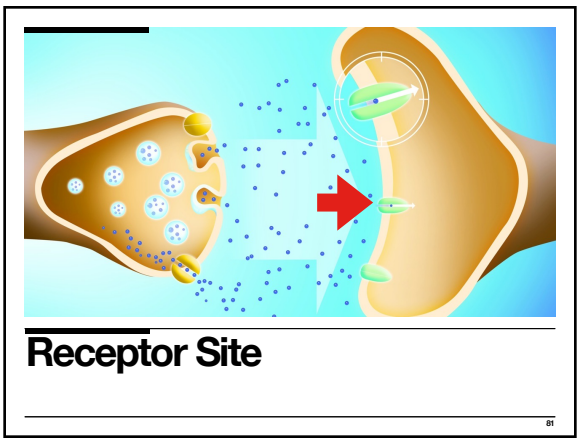
Receptor Site
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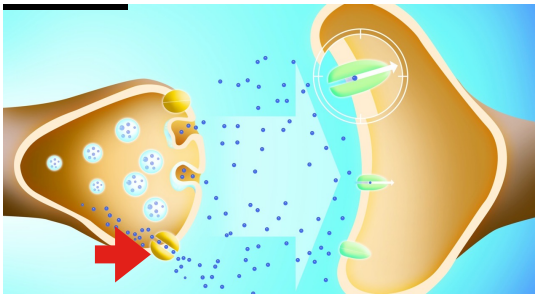

Transporter

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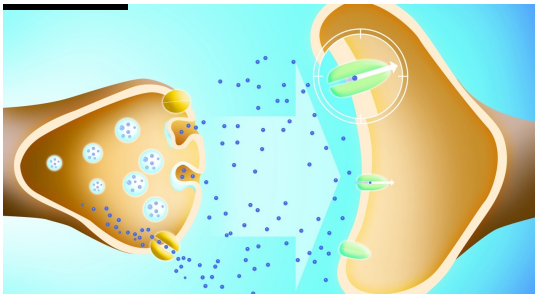

Monoamine oxidase

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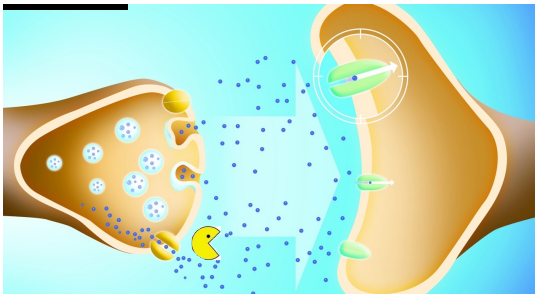

Monoamine oxidase

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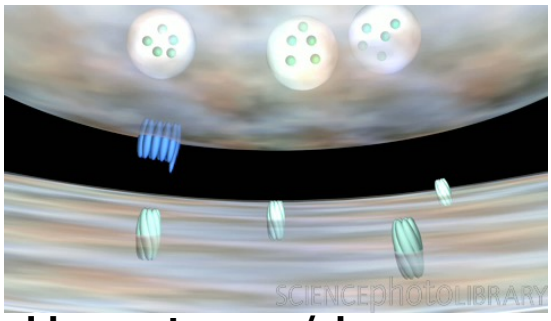

drkencarter.com/pipe

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mouse party!

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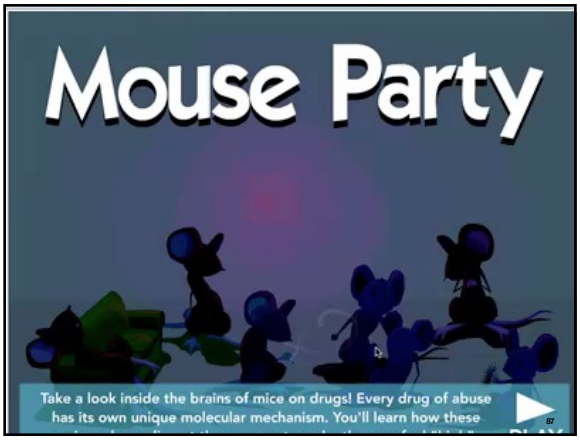

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Depressive Disorders

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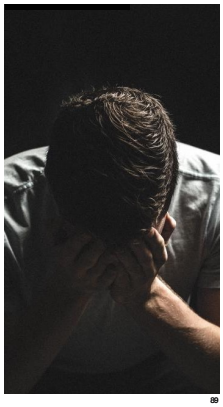
Impact of Depression

- WHO estimates that over 340 million people worldwide suffer from an episode of major depression each year
- Leading cause of disability worldwide
- In the United States, depression affects 19 million people (9.5%)
- It is estimated that 15% of people with major depression will have a suicide attempt



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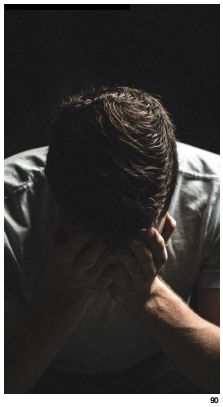
Impact of Depression

- 50% of people with major depression will have one or more recurrences
- 90% of people with major depression who have had 2 previous episodes will have a 3rd
- Relapse rate is 65% within the first year if untreated



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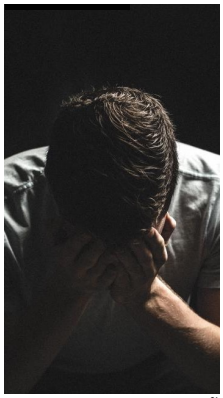
Diagnosing Depression

S-problems with sleep
P-psychomotor agitation/retardation
A-changes in appetite
C-lack of concentration
E -lack of energy
D-depressed mood
I - lack of interest
G-guilt
S - suicidal behaviors or thoughts of death



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Disruptive Mood Dysregulation Disorder

- Persistent irritability and frequent episodes of inability to control behavior
- Intended to reduce the over diagnosis and over treatment of bipolar disorder in children
- Diagnosed between 6-18
- 2%-5% prevalence

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Monoamine hypothesis of depression

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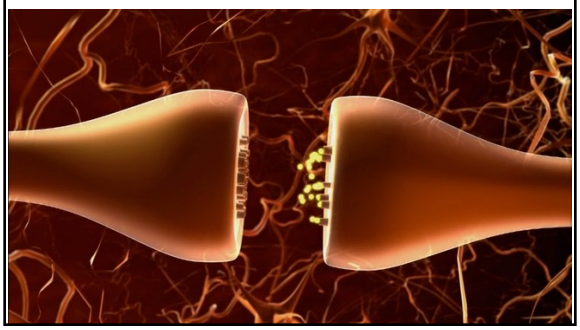
Neurobiology of depression



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Monoamine hypothesis of depression

- Suggests that symptoms of depression are caused by malfunctions in a family of neurotransmitters called monoamines
  - Serotonin (5-HT)
  - Norepinephrine
  - Dopamine

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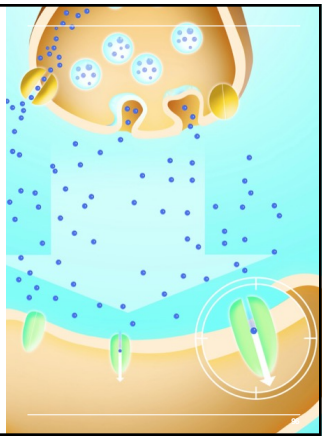
Malfunction can occur in many ways

- Decreased release in the synapse
- Excessive reuptake
- Overactive MAO
- Receptor abnormality



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Categories of antidepressants

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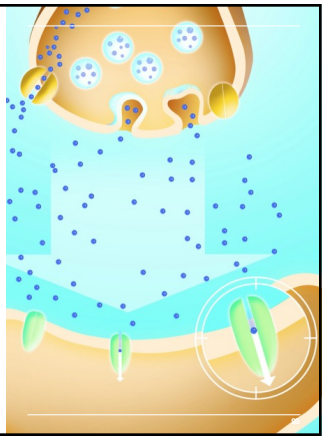
Antidepressants

Many antidepressants try to keep one (or more) of the monoamines in the gap longer



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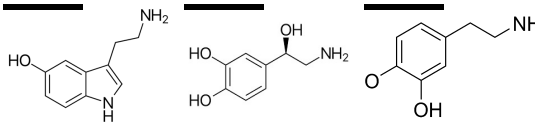
Monoamines

Serotonin **Norepinephrine** **Dopamine**



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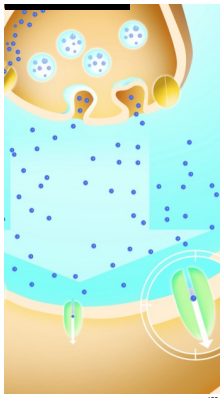
Categories of Antidepressants

- MAOI
- Serotonin (mostly)
- Serotonin and norepinephrine
- Norepinephrine (mostly)
- Dopamine (mostly)



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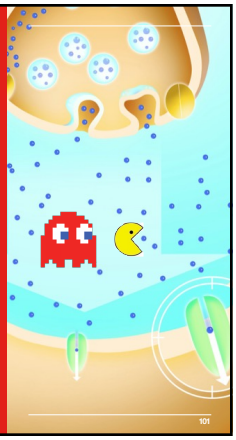
Monoamine Oxidase Inhibitors

Disrupt monoamine oxidase from getting rid of the monoamines



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Hypertensive Crisis

•Potentially fatal reaction characterized by

- High blood pressure
- Headache
- Palpitation
- Neck stiffness or soreness
- Nausea
- Vomiting
- Sweating
- Dilated pupils
- Photophobia

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Foods to avoid

- Alcohol
- Matured or aged cheese
- Fermented or dry sausages like pepperoni or salami
- Improperly stored meat, fish, or poultry
- Fava or broad bean pods
- Soy sauce
- Most over the counter cold medicines

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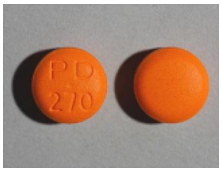
Phenelzine (Nardil)

MOA: blocks monoamine oxidase (MAO) from breaking down norepinephrine, serotonin, and dopamine

Side effects: Dizziness, sedation, headache, sleep disturbances, fatigue, weakness, tremor, movement problems, blurred vision, increased sweating

Advantages: Treatment resistant or atypical depression

Disadvantages: Like all MAOIs, there are food restrictions



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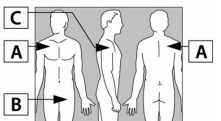
Selegiline (Emsam)

- **MOA**: MAOI (patch)
- **Advantages**: At low doses, no food restrictions; with a high dose high dose patch (80mg) you might need 25-30 pieces of pizza for a hypertensive crisis
- **Disadvantages**: Treatment compliance can be an issue



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Tricyclics

Work mostly on serotonin and norepinephrine

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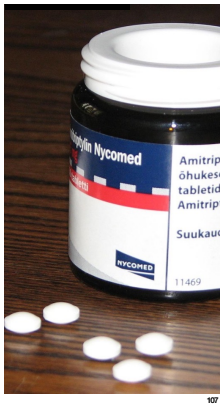
Amitriptyline (Evavil)

- One of the most favored TCSs
- Sometimes used to treat chronic pain and insomnia
- Sedation is common
- Tolerance to sedative effects may develop over time
- **Advantages**: helpful for patients with chronic pain
- **Disadvantages**: weight gain



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Clomipramine (Anafranil)

- First pass metabolism: SSRI
- Second pass: desmethyl-clomipramine which is a NRI
- Fatal interaction with MAOI (hypertensive crisis)
- Fatal interaction with SSRI (serotonin syndrome)

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Anticholinergic Side Effects

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Anticholinergic side effects

- Due to their effect on acetylcholine, medications that aim to target specific symptoms of an illness or disorder often end up causing other unwanted side effects. For some, these effects are only temporary and diminish as a person adjusts to the medication

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Common Anticholinergic Side Effects

- Blurred vision
- Difficulty urinating
- Dry mouth
- Constipation
- Decreased sweating
- Dizziness

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111

Common anticholinergic side effects

- Blurred vision (can't see)
- Difficulty urinating (can't pee)
- Dry mouth (can't spit)
- Constipation (can't defecate)
- Decreased sweating
- Dizziness

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Antidepressants with Anticholinergic Effects

- **Amitriptyline (Elavil)**
- **Desipramine (Norpramin)**
- **Imipramine (Tofranil)**
- **Nortriptyline (Pamelor)**
- Paroxetine (Paxil)

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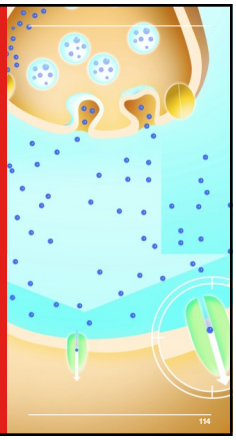
SSRIs

Block the areas that would normally recycle serotonin



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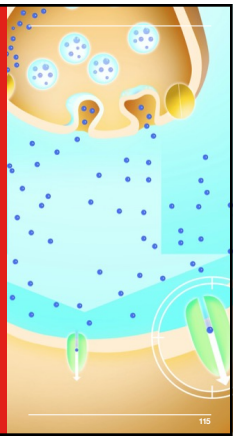
SSRIs

This results in a buildup of serotonin in the synaptic cleft, which results in increased binding with serotonin receptors.



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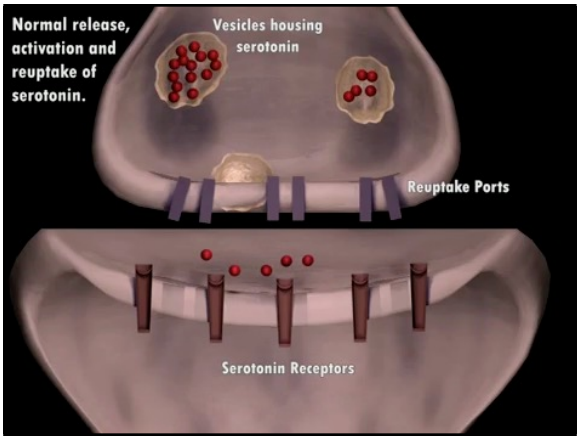

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	Prozac	Zoloft	Lexapro	Celexa	Paxil
Sedation	1	1	3	3	5
Activation	5	4	3	3	1
Weight Gain	2	2	3	3	5
Sexual Dysfunction	3	2	3	3	5

117

Stephen M. Stahl (2013) Stahl's Essential Psychopharmacology (4th ed). New York: Cambridge University Press.

117

Genetic Testing

118

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Fluoxetine (Prozac)

- Activating antidepressant
- Very long half-life
- **Side effects:** gastrointestinal symptoms, sexual dysfunction, insomnia, headache, dizziness
- **Advantages:** comes in weekly format, helpful for patients with low energy

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Sertraline (Zoloft)

- Activating
- More prone to gastrointestinal side effects than other SSRIs
- May be a first-line choice for atypical depression (e.g., hypersomnia, hyperphagia, low energy, mood reactivity)

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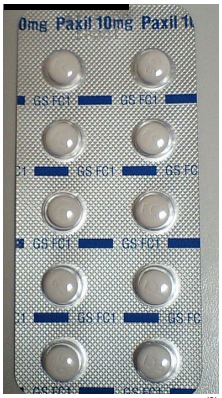
Paroxetine (Paxil)

- May be contraindicated in pregnancy
- More prone to discontinuation symptoms



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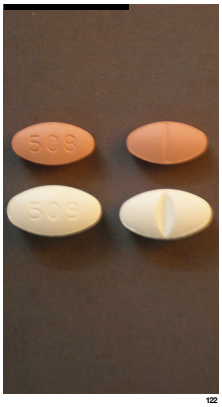
Citalopram (Celexa)

- Minimal sedation and weight gain



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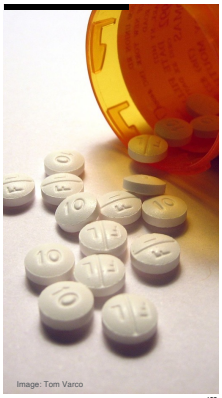
Escitalopram (Lexapro)

- Minimal sedation and weight gain



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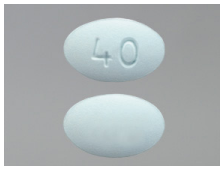
Vilazodone (Viibryd)

- No sexual dysfunction
- Gastrointestinal difficulty
- The most commonly observed adverse reactions in patients treated with Viibryd in placebo-controlled studies were: diarrhea (28% vs. 9%), nausea (23% vs. 5%), insomnia (6% vs. 2%), and vomiting (5% vs. 1%).



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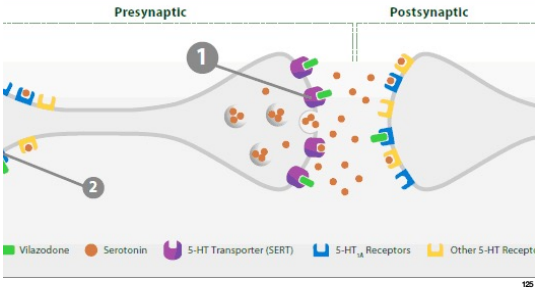
Vilazodone



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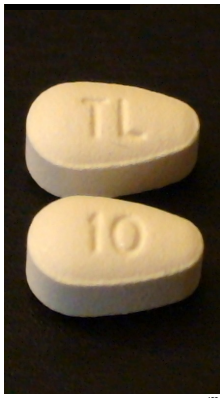
Vortioxetine (Trintellix)

- May also affect dopamine
- Possible benefit of improved cognition



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Genetic Testing

- Genetic variations and response to different medications
- DNA testing can detect slow, normal, or fast metabolizer for specific drug
- Negative and positive consequences of additive therapeutic effects

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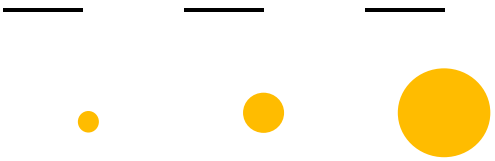
Genetic Testing



Slow metabolizer | Typical Metabolizer | Ultra Rapid Metabolizer

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Significance of Genetic Testing in the Determination of Drug Dosage for an Antidepressant

	Normal metabolizer	Slow metabolizer	Fast metabolizer
Genetic variation	Your genes produce a typical amount of enzyme.	Your genes produce too little enzyme.	Your genes produce too much enzyme.
Effects on you	The antidepressant helps your depression and causes few side effects.	The antidepressant builds up in your body, causing intolerable side effects.	The antidepressant is eliminated too quickly, providing little or no improvement in depression.
Treatment options	Follow the recommended dosage.	Switch antidepressants or reduce your dosage.	Switch antidepressants or increase your dosage.

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SNRI

Venlafaxine (Effexor)
Desvenlafaxine (Pristiq)
Duloxetine (Cymbalta)
Levomilnacipran (Fetzima)

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Venlafaxine (Effexor)

- **MOA**: **Increases** release of several different neurotransmitters (serotonin, norepinephrine, dopamine, glutamate, acetylcholine, and histamine) and **reduces** the release of GABA
- **Side effects**: May cause hypertension, GI upset,
- **Advantages**: Less sexual dysfunction than SSRIs, helps cognitive symptoms,
- **Disadvantages**: can cause cardiac problems in overdose

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Desvenlafaxine (Pristiq)

- Metabolite of venlafaxine
- May have fewer GI side effects than venlafaxine
- Contraindicated in pregnancy

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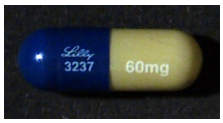
Duloxetine (Cymbalta)



- Can also treat neuropathic pain
- Balanced for effects on serotonin and norepinephrine

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Levomilnacipran (Fetzima)

- **MOA**: SNRI; much more balanced reuptake inhibitors of serotonin and norepinephrine
- **Side effects**: GI, sweating, sexual dysfunction
- **Advantages**: may be more helpful for somatic symptoms, fatigue, and pain
- **Disadvantages**:cost; may increase hypertension in people with high blood pressure

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serotonin: norepinephrine ratios of SNRIs

- venlafaxine = 30:1
- duloxetine = 10:1
- desvenlafaxine = 14:1
- milnacipran = 1.6:1
- levomilnacipran = 1:2

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NRI

Atomoxetine (Strattera)

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Atomoxetine (Strattera)

- Good for cognitive symptoms
- Minimal sexual symptoms

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Other

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Bupropion (Wellbutrin)

- Energizing
- Few sexual side effects
- Less weight gain
- May increase anxiety and insomnia

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Esketamine Nasal Spray for Treatment Resistant Depression

- Increases the amount of glutamate in the synapse
- Helps neurons communicate with each other along new pathways
- Can cause high blood pressure, nausea, perceptual disturbances during use

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Anxiety

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DSM-5 Disorders with Anxiety Components

Anxiety Disorders	Trauma and Stress Related Disorders	OCD and Related Disorders
Specific Phobia	Posttraumatic Stress Disorder	Obsessive Compulsive Disorder
Social Phobia	Acute Stress Disorder	Body Dysmorphic disorder
Agoraphobia		Hoarding Disorder
Panic Disorder		Excoriation Disorder
Panic Attack Specifier		Hair Pulling Disorder
Generalized Anxiety Disorder		

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Deconstructionist Approach

- Rather than looking at anxiety disorders in their respective categories, some psychopharmacologists use a deconstructionist approach
- Examine the biological links to the symptoms and use that information to choose medicines to treat symptoms
- Anxiety disorders may be deconstructed into just two different kinds of symptoms

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Neurobiology of Anxiety

Fear	Worry
Panic	Anxious misery
Phobia	Apprehensive expectation
	Obsessions

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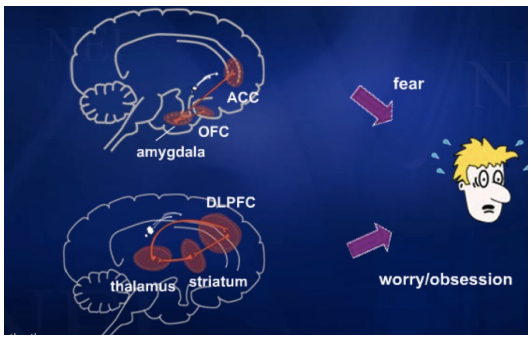

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Treatment Effects: Fear

- There are GABA neurons in the cortex and amygdala
- GABA is an inhibitory neurotransmitter
- Anything that will "turn on" GABA should calm things down
- Inputs from serotonin will also smooth out activity in the fear loop as well

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Anything that increases **GABA** or increases **serotonin** should smooth out activity in the fear loop

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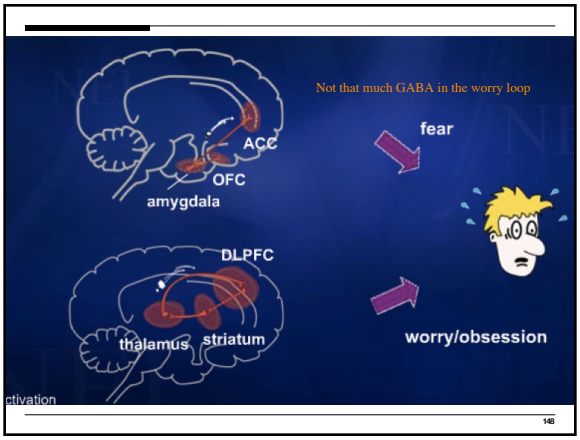

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Serotonin will help with worry
GABA is LESS successful in shutting down worry

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Anxiety can be either **acute** or **persistent** (chronic)

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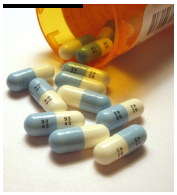
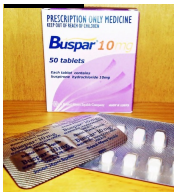
Medications for Anxiety Disorders



SSRI
Fluoxetine
Sertraline
Paroxetine

Benzodiazepines
Alprazolam
Clonazepam
Lorazepam



Buspirone

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SSRIs for Anxiety

- Should work for fear and for worry
- With the same adverse effects as when they are used as an antidepressant
- But remember, they take a few weeks to start working
- Often need to be given at higher doses to be effective
- Some clients have an increase in anxiety for the first week or so on an SSRI

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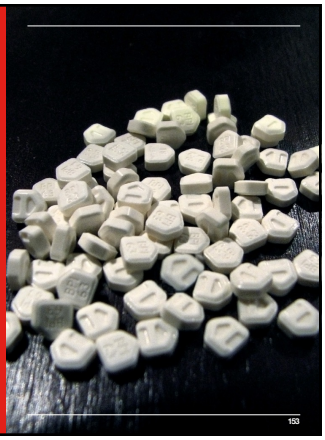
Benzodiazepines

Diazepam (Valium)
Chlordiazepoxide (Librium)
Clonazepam (Klonopin)
Lorazepam (Atavan)
Alprazolam (Xanax)



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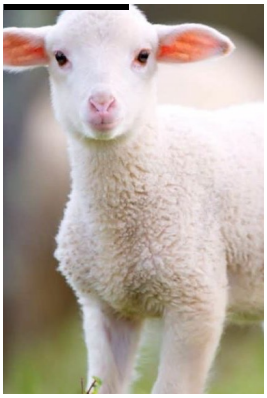

Benzodiazepines

Action is on GABA

Increase in GABA will increase inhibition, which quiets down abnormally activated circuits

Works quickly

Will not work as effectively for worry as it might for fear

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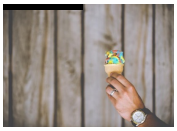

Short	Intermediate	Long
•Midazolam (Versed)	•Lorazepam (Ativan)	•Chlordiazepoxide (Librium)
•Triazolam (Halcion)	•Estazolam (ProSom)	•Clorazepate (Tranxene)
•Alprazolam (Xanax, Niravam)	•Clonazepam (Klonopin)	•Diazepam (Valium)
•Oxazepam (Serax)		•Flurazepam (Dalmane)
•Temazepam (Restoril)		•Halazepam (Paxipam)

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Side effects

- BZDs work on GABA to increase inhibition
- Sedation and hypnosis
- Cognitive and psychomotor inhibition
- Physical dependence

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Side effects

- Sedation, drowsiness, ataxia, lethargy, mental confusion, motor and cognitive impairments, disorientation, slurred speech, amnesia,
- Physical and psychological dependence, especially in those with substance abuse disorders
- Interactions with alcohol and other sedatives

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Diazepam (Valium)

- Binds to benzodiazepine receptors at the GABA-A ligand-gated chloride channel complex to enhance the inhibitory effects of GABA
- Rapid onset of action
- Long-acting benzo (half-life 30-60 hours)
- May lead to abuse
- One of the most commonly prescribed benzodiazepine
- Useful to treat alcohol withdrawal
- One of the few benzos available in an oral liquid formulation

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Chlordiazepoxide (Librium)

- Rapid onset of action
- Can also treat alcohol withdrawal

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Clonazepam (Klonopin)

- One of the most popular benzodiazepines for anxiety
- Easier to taper than some other benzodiazepines because of its long half-life
- May have less abuse potential than some benzodiazepines

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Lorazepam (Ativan)

- Short and inactive metabolites
- **MOA**: Binds to benzodiazepine receptors at GABA-A
- **Advantages**: available in liquid and injectable formulation, rapid onset
- **Disadvantages**: may lead to abuse, possibly more sedation than other benzos

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Alprazolam (Xanax)

- Binds to GABA receptors to enhance the effects of GABA
- Less sedating than other benzodiazepines
- Half-life about 12 hours

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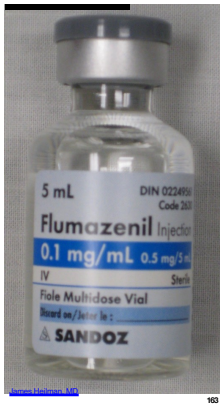
Flumazenil (Anexate)

- Reduces the sedative effects of benzodiazepines
- Blocks benzodiazepine receptors preventing benzodiazepines from binding there
- Onset in 1-2 minutes
- Can sometimes wear off before the benzo wears off



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Other anti-anxiety agents

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Buspirone (Buspar)

- Works on serotonin
- Takes about 2-4 weeks to work (can take up to 8 weeks)
- Gradual onset
- Dizziness, headache, nervous, sedation, nausea, and restlessness are the most common side effects
- Lack of dependence or withdrawal symptoms

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Hydroxyzine (Vistaril)

- **MOA**: Blocks histamine receptors
- **Side effects**: Dry mouth, sedation, tremor
- **Advantages**: No abuse, dependency, or withdrawal
- **Disadvantages**: Can be sedating; not as effective as benzodiazepeines

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Prazosin (Minipress)

- Indicated for nightmares

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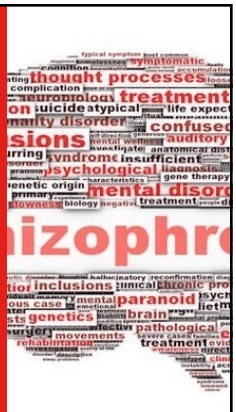
Psychosis



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Psychosis

Positive

Delusions
Hallucinations
Thought disorder

Negative

Anhedonia
Affective Blunting
Alogia
Avolition

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Key Dopamine Pathways involved in Psychosis

mesolimbic pathway	mesocortical pathway to DLPFC	mesocortical pathway to VMPFC	nigrostriatal pathway	tubero-infundibular pathway
High	Low	Low	Normal	Normal
Positive symptoms	cognitive and negative symptoms	affective and negative symptoms		

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Choosing an Antipsychotic

- Nature of psychiatric condition
- Target signs and symptoms
- Past history of drug response
- Patient preference, history of adherence
- Need for special monitoring
- Consider risk of obesity, diabetes

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Receptor	Treatment Effects	Adverse Effects
Alpha 1		Sedation, Postural hypotension, Sexual dysfunction, Weight gain
5-HT 1a	Decreased depression, anxiety, EPS Increased cognition	
5-HT 2a	Relief of negative symptoms	
5-HT 2a / DA2	Causes dopamine to decrease with leads to reduced EPS	
5-HT 2c	Increase in cognition Decrease in depression	Weight gain
5-HT 2c	Increased cognition Decreased depression	Weight gain
5-HT 2d	Decreased depression Decreased anxiety	
D2	Relief of negative simptoms	Increases EPS
D3	Decreased depression Increase in cognition	
H1	Sedation	Sedation Weight gain
M1		Memory impairment GI symptoms
SRI	Decreased depression and anxiety	

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Tardive Dyskinesia (TD)

- Involuntary hyperkinetic movements, often of the face and tongue but also of the trunk and limbs; can be disabling

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Haloperidol (Haldol)

- Introduced in 1967 as the first alternative to phenothiazines
- **MOA**: Conventional antipsychotic; blocks D2 receptors
- **Side effects**: akathisia, extrapyramidal symptoms, parkinsonism
- **Advantages**: weight gain is rare; available as 4 week injection; low cost
- **Disadvantages**: extrapyramidal symptoms

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Clozapine (Clozaril)

- Reduces symptoms in ~ 30% of those who do not improve with standard drugs.
- It lower incidence of parkinsonian side effects or tardive dyskinesia, meaning patients who also could not tolerate other drugs because of these side effects can be helped by clozapine.

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Clozapine (Clozaril) Side Effects

- Greatest concern with clozapine is risk of developing severe, life-threatening agranulocytosis
- Sedation (40% of patients)
- May affect compliance
- Weight gain (80% of patients); 20 pounds or more is not unusual

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Bipolar

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Diagnostic Criteria

- Bipolar I: At least one episode of mania
- Bipolar II: Major depressive and hypomanic episodes
- Cyclothymia

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A Double-blind placebo-controlled trials with adequate samples
B Double-blind comparator studies with adequate samples
C Open trials with adequate samples
D Uncontrolled observation or controlled study with ambiguous result
E No published evidence
F Available evidence negative

	Acute mania/ Mixed	Mood stabilizer prophylaxis	Acute bipolar depression
Lithium	A+	A+	A
Valproic acid	A+	A−	D
Carbamazepine	A	B−	D
Lamotrigine	F	A+	A
Gabapentin	F	E	D
Topiramate	D	E	D
Aripiprazole	A	E	E
Haloperidol	A	E	E
Olanzapine	A+	E	A
Risperidone	A	E	D
Quetiapine	A	E	E
Ziprasidone	A	E	E
Omega-3	E	D	E

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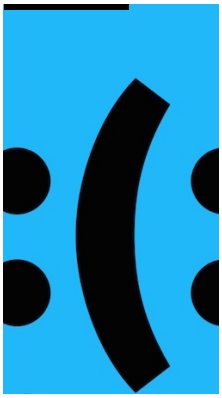

Pharmacotherapy for Bipolar Disorder

Lithium	Anticonvulsants
Atypical antipsychoticsics	Antidepressants

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Lithium

- Demonstrated efficacy for acute mania, acute depressive episodes, and maintenance treatment for relapse prevention
- Effective in 60–80% of acute episodes.
- About 1/3 relapse

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Lithium

- Compliance with therapy is very poor
- Side effects become intolerable
- Miss the "highs" and the mood swings

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Side Effects

- Occurrence and intensity of side effects and toxic reactions are usually related to plasma drug concentrations and involve the nervous system, gastrointestinal (GI) tract, kidneys, thyroid, cardiovascular system, and skin.
- Tremor
- Cognitive impairment
- Nausea, weight gain
- Increased urination

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Toxicity

- Early signs
  - Ataxia, lack of coordination
- Mild (1.5–2.0 mEq/L)
  - Listlessness, nausea, slurring, diarrhea, coarse tremor
- Moderate (2.0–2.5 mEq/L)
  - Coarse tremor, confusion, delirium, pronounced ataxia
- Severe (2.5–3.0 mEq/L)
  - Alteration in consciousness, hyperextension of extremities, seizures, coma, death

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Anticonvulsant Drugs

- Originally developed as anticonvulsants
- Used in bipolar disorder; to treat relapse to substance abuse; as detoxification agent for alcohol withdrawal
- Stephens Johnson Syndrome

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Carbamazepine (Tegretol)

- Anticonvulsant effects may occur because it reduces neuronal excitation by blocking sodium channels and thus. ability of sodium to initiate action potentials
- Side effects: GI upset, sedation, ataxia, visual disturbances, skin reactions, cognitive impairments
- Reduces frequency of episodes; may be better for mixed mania and rapid cycling episodes
- Drug interactions

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Oxcarbazepine (Trileptal)

- Analogue of carbamazepine
- Does not induce hepatic enzymes
- Fewer drug-drug interactions compared to carbamazepine
- Side effects: tiredness, headache, dizziness and ataxia, some allergic reactions, teratogenic effects likely
- Has been shown to be superior to placebo in the treatment of acute mania

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Valproic Acid (Depakene, Divalproex, Depakene, Depacon, Depakote)

- Stabilizes GABA-B receptors in hippocampus
- Used to treat acute mania, mixed states, and rapid cycling bipolar disorder
- 70% response rate in lithium-resistant patients
- Side effects: GI, sedation, lethargy, tremor, hair loss, liver enzyme changes, some weight gain
- Reduced cognitive function
- Can inhibit metabolism of other drugs (e.g., can "double" the blood level of lamotrigine)

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Lamotrigine (Lamictal)

- Effective in acute bipolar depression and rapid cycling bipolar II disorder, and in prevention of recurrent depressive disorders
- Poorly effective in treating acute mania
- Side effects: dizziness, tremor, somnolence, headache, nausea, and rash. Most serious side effect is rash, which may be severe enough to require hospitalization and prove fatal
- Valproate doubles and carbamazepine halves the half-life of lamotrigine
- FDA-approved for long-term maintenance treatment of bipolar I in adults

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Gabapentin (Neurontin)

- GABA-Q analogue-but little action on GABA receptor
- Inhibits glutamate release from cortex and hippocampus
- Pharmacokinetics: excreted unchanged; few interactions; half-life = 5 to 7 hours
- Not effective as monotherapy for bipolar disorder; may benefit neuropathic pain and some types of anxiety disorder

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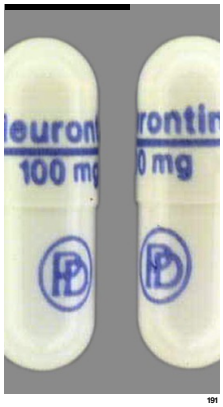
Gabapentin (Neurontin)

- Not effective as monotherapy in bipolar
- Side effects: dizziness, dry mouth, sedation, nausea, flatulence, reduced libido
- Seems to improve depression and anxiety



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Atypical Antipsychotics for Bipolar Disorders

- Traditional Antipsychotics
  - Haloperidol, risperidone and olanzapine: most effective when dropout rates considered
  - Clozapine: more antimanic than antidepressant
  - Risperidone: more antidepressant than antimanic

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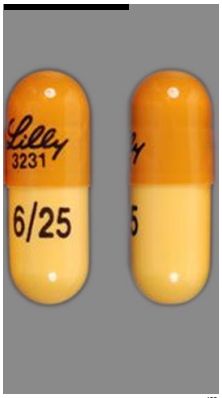
Olanzapine-Fluoxetine (Symbyax)

- Same risks (i.e., drug interactions) as those associated with each drug alone.
- Warning re: MAOIs (serotonergic syndrome – 5 weeks)
- Warning re: Thioridazine (conduction disturbances)
- Same side effects as those associated with each drug alone
- Orthostatic hypotension
- Sedation



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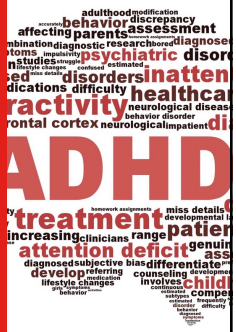
Attention Deficit Hyperactivity Disorder



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Weak norepinephrine (NE) and dopamine (DA) signals in prefrontal cortex are associated with ADHD

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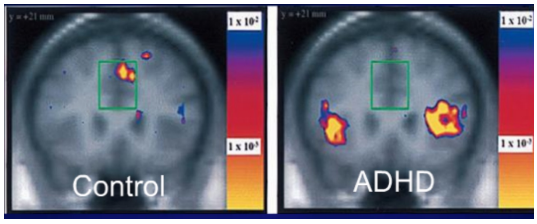
ADHD: Impaired activation in attentional networks



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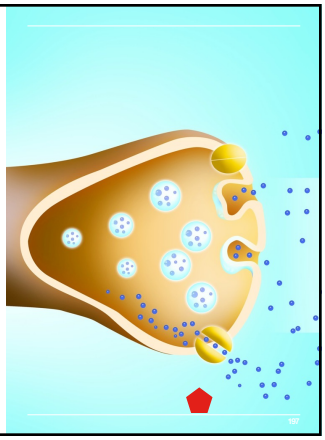
Methylphenidate

Dose-dependently blocks DAT (dopamine transporter) in striatum



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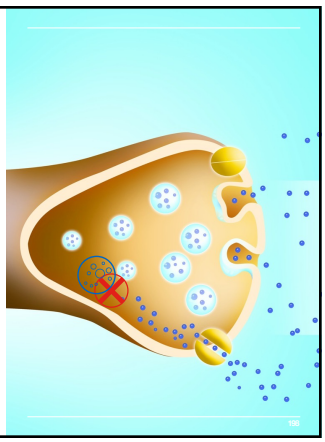
Amphetamines

Blocks vesicular monoamine transporters (VMATs) in cortex, releasing dopamine



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Methylphenidate and Amphetamines

- Methylphenidate: dose-dependently blocks DAT (dopamine transporter) in striatum
- Amphetamine: blocks vesicular monoamine transporters (VMATs) in cortex, releasing dopamine
- Both: increase spontaneously released dopamine responsive to environmental stimuli
  - Increases signal-to-noise ratio
  - Increases saliency of stimuli

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Drug Delivery Systems

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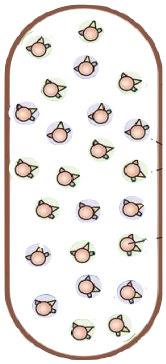
Immediate Release

All goes in



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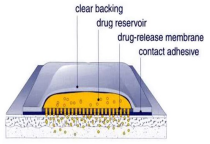
Administration through the skin

- Transdermal patches provide continuous, controlled release
- Allows for slow, continuous absorption over hours or days, minimizing side effects
- Examples
  - Selegiline (depression)
  - Methyphenidate (AD/HD in children)



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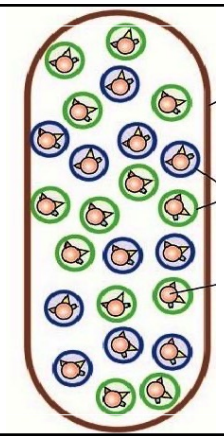
Beads

Slow release system



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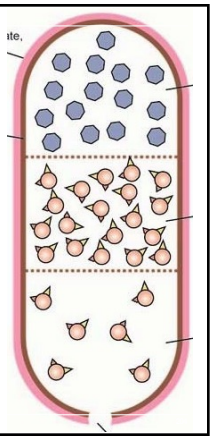
OROS

Osmotic controlled-released oral deliver system (OROS) Concerta



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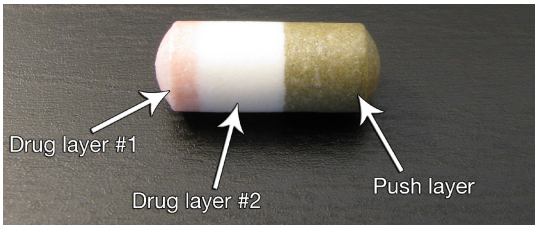
OROS

Osmotic controlled-release oral delivery system (OROS)



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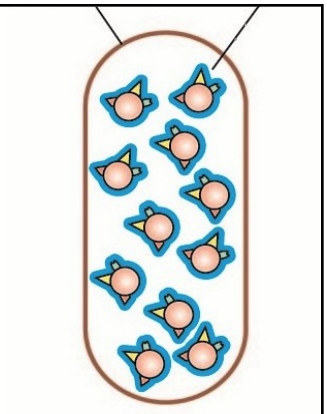
Prodrug

A prodrug is a compound that is not pharmacologically active. It needs to be metabolized by the body to be active.



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Intramuscular

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Insomnia

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Sleep and Insomnia Basic Concepts

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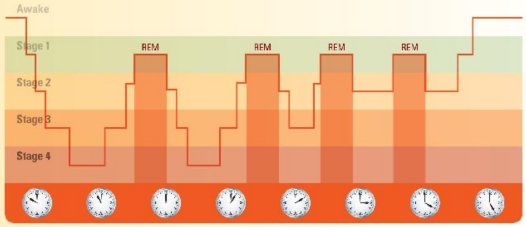
Visual Overview Sleep Cycles



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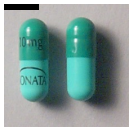
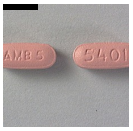
Lunesta
eszopiclone



Sonata
zaleplon



Ambien
zolpidem

Belsomra
suvorexant

Sleep Medicines

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Benzodiazepine Receptor Agonist (BZRA) Hypnotics

- BZRA: Any drug that activates benzodiazepine receptors
- Structurally not classified as benzodiazepines
- Prescribed as hypnotic drugs intended for treatment of insomnia; can create amnestic-like behaviors

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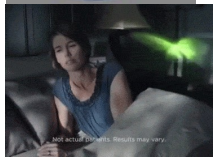
Eszopiclone (Lunesta)

- Binds to a site near the benzodiazepine area of the GABA receptor
- Half life: 6 hours



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Eszopiclone (Lunesta)

- day-time drowsiness, dizziness, "hangover" feeling
- problems with concentration
- anxiety, depression, nervous feeling
- headache
- nausea, stomach pain, loss of appetite, constipation
- dry mouth
- unusual or unpleasant taste in your mouth
- mild skin rash

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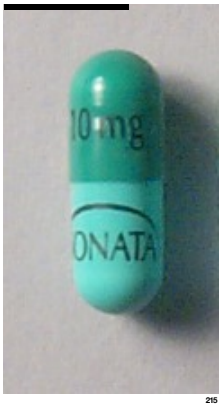
Zaleplon (Sonata)

- Binds to a site near the benzodiazepine area of the GABA receptor
- Half life 1 hour



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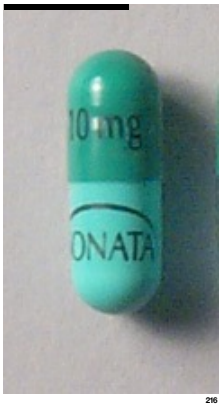
Zaleplon (Sonata)

- day-time drowsiness
- problems with concentration
- numbness or tingling
- anxiety, depression, nervous feeling
- problems with vision
- headache
- nausea, stomach pain, loss of appetite, constipation
- dry mouth
- increased menstrual pain (cramps)
- back pain, joint or muscle pain
- mild skin rash



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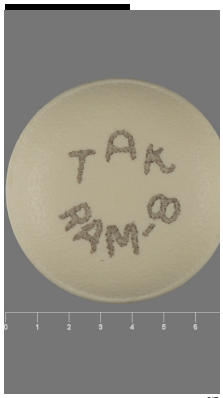
Ramelteon (Roserem)

- selective melatonin receptor agonist
- Melatonin is regulated by pineal gland on a 24-hour cycle, with levels increasing towards bedtime.
- Nonaddictive
- Very modest effect in controlled trials
- Sleep onset only 10–15 minutes earlier than placebo
- Little affect on total sleep time



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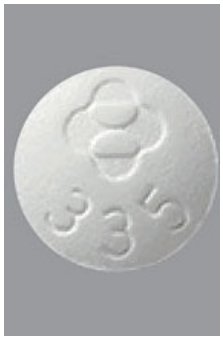
Suvorexant (Belsomra)

- **MOA:** Works on the wakefulness system
- **Side effects:** headache, dizziness, abnormal dreams, dry mouth
- **Advantages:** might work when other medicines haven't
- **Disadvantages:** Cost



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What you should know about psychopharmacology during COVID-19

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Some things to consider

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1

Addressing medication adherence

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Sleep patterns

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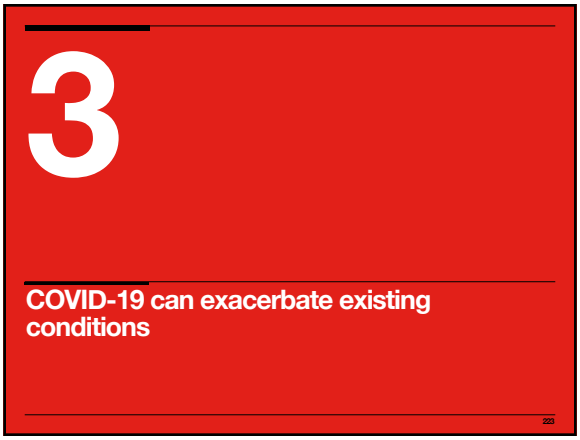
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COVID-19 can exacerbate existing conditions
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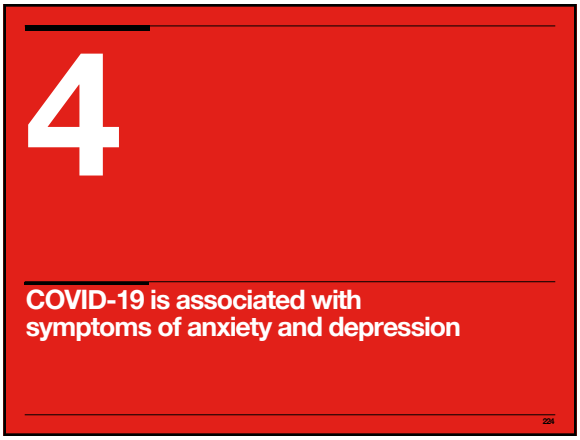
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COVID-19 is associated with symptoms of anxiety and depression
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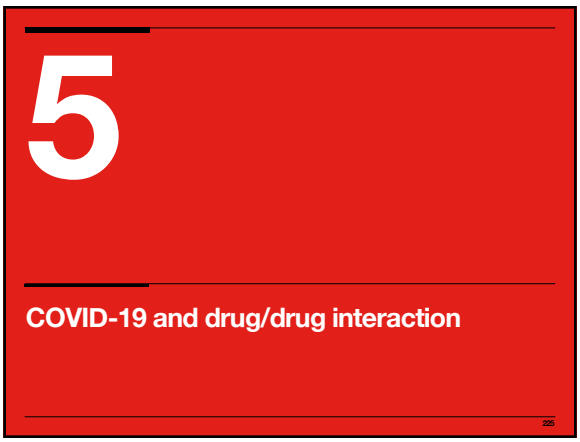
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COVID-19 and drug/drug interaction
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COVID-19 and medications

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COVID treatments and drug/drug interactions

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Mental health medications might interact with COVID-19 treatments

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Review current treatments and dose

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We are always learning more

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Resources

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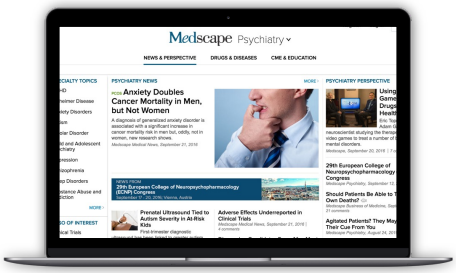

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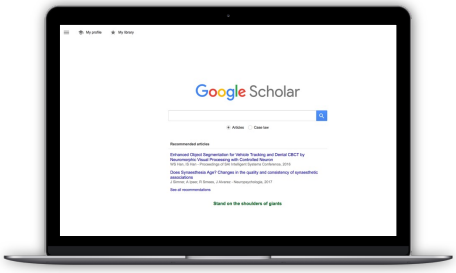

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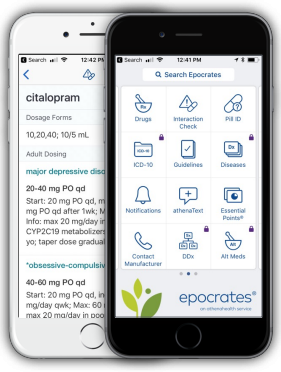

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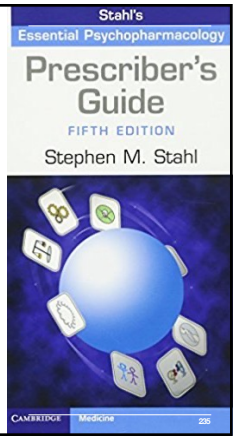
Stephen M. Stahl



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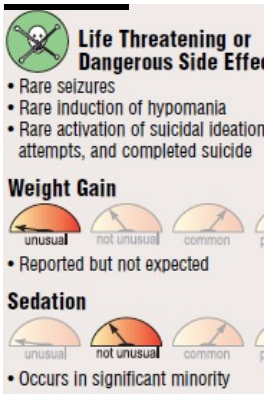

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How the drug works

How long until it works

If it doesn't work

Notable side effects

Dangerous side effects

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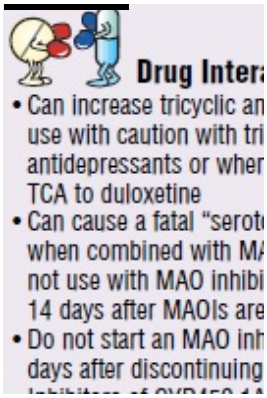

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Drug interactions

When NOT to use

Information on special populations

Advantages

Disadvantages

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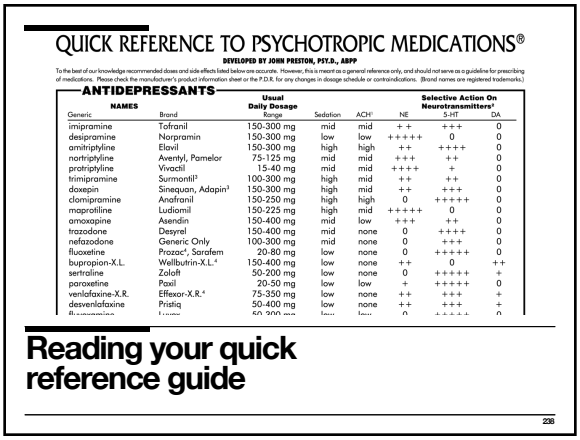
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ANTIDEPRESSANTS
NAMES
Generic
Brand
Usual Daily Dosage
Range
Sedation
ACH[1]
NE
Selective Action On Neurotransmitters[2]
5-HT
DA
imipramine Tofranil 150-300 mg mid mid + + +++ 0
desipramine Norpramin 150-300 mg low low +++++ 0 0
amitriptyline Elavil 150-300 mg high high ++ ++++ 0
nortriptyline Aventyl, Pamelor 75-125 mg mid mid +++ ++ 0
protriptyline Vivactil 15-40 mg mid mid ++++ + 0
trimipramine Surmontil[3] 100-300 mg high mid ++ ++ 0
doxepin Sinequan, Adapin[3] 150-300 mg high mid ++ +++ 0
clomipramine Anafranil 150-250 mg high high 0 +++++ 0
maprotiline Ludiomil 150-225 mg high mid +++++ 0 0
amoxapine Asendin 150-400 mg mid low +++ ++ 0
trazodone Desyrel 150-400 mg mid none 0 ++++ 0
nefazodone Generic Only 100-300 mg mid none 0 +++ 0
fluoxetine Prozac[4], Sarafem 20-80 mg low none 0 +++++ 0
bupropion-X.L. Wellbutrin-X.L.[4] 150-400 mg low none ++ 0 ++
sertraline Zoloft 50-200 mg low none 0 +++++ +
paroxetine Paxil 20-50 mg low low + +++++ 0
venlafaxine-X.R. Effexor-X.R.[4] 75-350 mg low none ++ +++ +
desvenlafaxine Pristiq 50-400 mg low none ++ +++ +
Reading your quick reference guide
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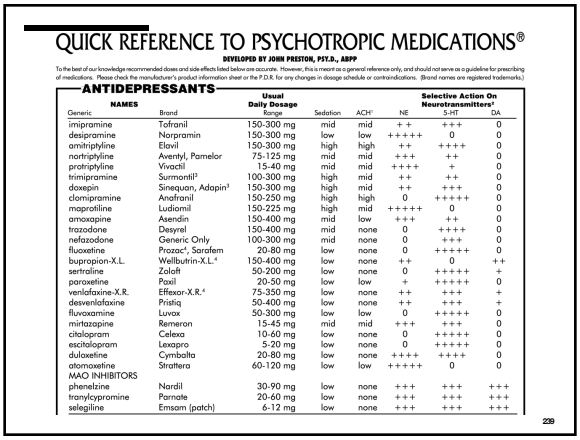
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fluvoxamine Luvox 50-300 mg low low 0 +++++ 0
mirtazapine Remeron 15-45 mg mid mid +++ +++ 0
citalopram Celexa 10-60 mg low none 0 +++++ 0
escitalopram Lexapro 5-20 mg low none 0 +++++ 0
duloxetine Cymbalta 20-80 mg low none ++++ ++++ 0
atomoxetine Strattera 60-120 mg low low +++++ 0 0
MAO INHIBITORS
phenelzine Nardil 30-90 mg low none +++ +++ +++
tranylcypromine Parnate 20-60 mg low none +++ +++ +++
selegiline Emsam (patch) 6-12 mg low none +++ +++ +++
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final questions
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