What You Should Know: Psychopharmacology for Psychologists

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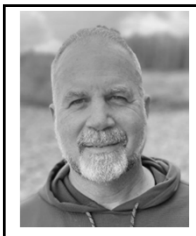

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OBJECTIVE OF THIS LECTURE

To learn about psychopharmacological principles in a way that directly impacts and influences practicing psychologists' work with patients

My goal is that you will leave today with **PRACTICAL INFORMATION** that you can immediately begin applying to your work with patients.

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WHAT WE WILL COVER TODAY

1. Who is taking antidepressants? (A: many of our patients)
2. What are Black Box warnings?
3. Review of the STAR*D Trial: what it tells us about efficacy of antidepressants
4. What are the differences between "medical" and "psychology" cultures? How knowing this will help you communicate with prescribers better.
5. Review of Pharmacology
6. Tips and Pearls (the good stuff)
7. Brief review of SSRIs, SNRIs, NDRIs, atypical antipsychotics and others
8. Disorders and Drugs that can cause anxiety and depression
9. Case examples

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WHY PSYCHOLOGISTS SHOULD UNDERSTAND PSYCHOPHARMACOLOGY

Because:

- To be an effective member of a multidisciplinary team need to know when to communicate with a presciber

Too little communication: ineffective

Too much communication: dismissed/ignored

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WHY PSYCHOLOGISTS SHOULD UNDERSTAND PSYCHOPHARMACOLOGY

Because many of our patients are taking psychotropic medications

Pratt LA, Brody DJ, Gu Q. Antidepressant use in persons aged 12 and over: United States, 2011–2014. NCHS data brief, no 76. Hyattsville, MD: National Center for Health Statistics. 2017.

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ANTIDEPRESSANT USE IN PERSONS AGED 12 AND OVER: UNITED STATES, 2011 – 2014

- AD medications are one of the three most commonly used drug classes in the US
- During 2011-2014 one in eight Americans aged 12 and older reported taking antidepressants

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ANTIDEPRESSANT USE IN PERSONS AGED 12 AND OVER: UNITED STATES, 2011–2014

- Antidepressant use increases with age
- Twice as common for females vs. males
- Non-Hispanic white people were more likely than non Hispanic black, Hispanic or Asian persons to take an AD

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ANTIDEPRESSANT USE IN PERSONS AGED 12 AND OVER: UNITED STATES, 2011–2014

- Long term use is common. ¼ of pts who took an AD in the past month had taken for 10 + years
- Antidepressant use is increasing over time; from 7.7% in 1999-2002 to 12.7% in 2011-2014

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WHY PSYCHOLOGISTS SHOULD UNDERSTAND PSYCHOPHARMACOLOGY

So psychologists can provide informed feedback to prescribers

- Speak the language and know the culture of medicine
- Psychologists know the importance of understanding culture and language

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WHY PSYCHOLOGISTS SHOULD UNDERSTAND PSYCHOPHARMACOLOGY

Because side effects may present as symptoms

- fatigue, cognitive problems, agitation, anxiety, insomnia, hyper or hypophagia, weight changes, libido/sexual functioning, nausea, headaches, tremor, bruising, sweating, slurred speech, ataxia, depression, hallucinations

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WHY PSYCHOLOGISTS SHOULD UNDERSTAND PSYCHOPHARMACOLOGY

Because many patients only have a partial response to medication and we should know what to expect:

Most common symptoms that persist after antidepressant treatment:

- Insomnia, fatigue, physical pain, concentration, lack of interest or motivation (Stahl, 2021)

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FDA BLACK BOX WARNINGS:

- In the United States, a boxed warning (sometimes "black box warning") is a type of warning that appears on the package insert for certain prescription drugs, so called because the U.S. Food and Drug Administration specifies that it is formatted with a 'box' or border around the text

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FDA BLACK BOX WARNINGS:

- A black box warning is the strictest warning put in the labeling of prescription drugs or drug products by the Food and Drug Administration (FDA) when there is reasonable evidence of an association of a serious hazard with the drug.

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FDA BLACK BOX WARNINGS:

- "There is an adverse reaction so serious in proportion to the potential benefit from the drug (e.g., a fatal, life-threatening or permanently disabling adverse reaction) that it is essential that it be considered in assessing the risks and benefits of using the drug" https://www.fda.gov/downloads/drugs/guidances/ucm075096.pdf

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FDA BLACK BOX WARNINGS:

- The FDA has required that boxed warnings be placed on all antidepressant medications warning they may result in increased risk of suicidal tendencies in children, adolescents, and young adults aged 18-24 years old.

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FDA BLACK BOX WARNINGS:

"Safety warnings about antidepressants and widespread media coverage decreased antidepressant use, and there were simultaneous increases in suicide attempts among young people. It is essential to monitor and reduce possible unintended consequences of FDA warnings and media reporting"

Conclusions from Lu et al. (2014, BMJ)

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FDA BLACK BOX WARNINGS:

- In 2005, the FDA issued a boxed warning regarding the risk of atypical antipsychotics being prescribed among elderly patients with dementia. This advisory was associated with a decrease in use of antipsychotics, especially in elderly patients with dementia.

Dorsey et al (2010)

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WHY PSYCHOLOGISTS SHOULD UNDERSTAND PSYCHOPHARMACOLOGY

Toxicity, overdose and medication interactions

- TCAs (e.g., amitriptyline, nortriptyline, imipramine)
- BZDs rarely alone and more often with ETOH/Opioids
- Lithium toxicity
- Serotonin Syndrome: high body temperature, agitation, increased reflexes, tremor, sweating, dilated pupils, diarrhea, coma, seizures, death

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The STAR*D Trial

The Sequenced Treatment Alternatives to Relieve Depression (STAR*D, 2006)

Goal: assess efficacy of depression treatments in patients diagnosed with MDD

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THE STAR*D TRIAL

2,876 patients, ages 18 to 75, 41 clinical sites

Four levels: each tested a different medication or medication combination for 12 to 14 weeks each

Patients who did not become symptom free could move to the next level of treatment

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THE STAR*D TRIAL

Level 1:

Celexa

Level 2:

Switch to Zoloft, Wellbutrin or Effexor OR add ADD TO CELEXA Wellbutrin, Buspar or cognitive therapy

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THE STAR*D TRIAL

Level 3:

Switch to Remeron or Pamelor (nortriptyline) OR ADD TO LEVEL 2 MED Lithium or triiodothyronine (T3)

Level 4:

Taken off all medications and randomly switched to either an MAOI (Parnate) or combination of Effexor and Remeron

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THE STAR*D TRIAL

Results:

Level 1:

- about one third reached remission and about 10-15% responded

Level 2:

- In the switch group about 25% reached remission
- In the add-on group about 1/3 reached remission

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THE STAR*D TRIAL

Results:

Level 3:

- In the switch group about 12-20% reached remission
- In the Add-on group about 20% became symptom free

Level 4:

- seven to 10% of reached remission

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Results of STAR*D

- About half of participants reached remission after two treatment levels
- Over the course of all 4 levels almost 70% reached remission (of those who did not drop out; drop outs increased with each level)

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RESULTS OF STAR*D

- If a first treatment with an SSRI fails, a switch to different AD will result in 25% getting better
- If a first treatment with an SSRI fails and AD medication is ADDED about 33% will improve
- Odds of improving depression worsen with diminish with every additional strategy tried

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RESULTS OF STAR*D

CBT was equally effective comparted with medication switch and augmentation in Level 2

CBT associated with fewer side effects

Time to remission was faster with medication than CBT

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COMPARATIVE EFFICACY AND ACCEPTABILITY OF 21 ADS: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS
(CIPRIANI ET AL., 2018)

Antidepressants in the Study

Valdoxan (agomelatine)	Lexapro (escitalopram)	Paxil (paroxetine)
Elavil (amitriptyline)	Prozac (fluoxetine)	Norebox (reboxetine)
Wellbutrin (bupropion)	Luvox (fluvoxamine)	Zoloft (sertraline)
Celexa (citalopram)	Fetzima (levomilnacipran)	Desyrel (trazodone)
Anafranil (clomipramine)	Savella (milnacipran)	Effexor (venlafaxine)
Pristiq (desvenlafaxine)	Remeron (mirtazapine)	Viibryd (vilazodone)
Cymbalta (duloxetine)	Serzone (nefazadone	Trintellix (vortioxetine)

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COMPARATIVE EFFICACY AND ACCEPTABILITY OF 21 ADS: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS
(CIPRIANI ET AL., 2018)

“All ADs were more efficacious than placebo in adults with MDD”

(p 1357)

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COMPARATIVE EFFICACY AND ACCEPTABILITY OF 21 ADS: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS
(CIPRIANI ET AL., 2018)

In head to head studies **MOST EFFECTIVE** ADs:

Valdoxan (agomelatine)

Elavil (amitriptyline)

Lexapro (escitalopram)

Remeron (mirtazapine)

Paxil (paroxetine)

Effexor (venlafaxine)

Trintellix (vortioxetine)

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COMPARATIVE EFFICACY AND ACCEPTABILITY OF 21 ADS: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS
(CIPRIANI ET AL., 2018)

In head to head studies **LEAST EFFECTIVE** ADs:

Prozac (fluoxetine)	**Norebox (reboxetine)**
Luvox (fluvoxamine)	**Desyrel (trazodone)**

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COMPARATIVE EFFICACY AND ACCEPTABILITY OF 21 ADS: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS
(CIPRIANI ET AL., 2018)

In head to head studies **BEST TOLERATED** ADs:

Valdoxan (agomelatine)	**Prozac (fluoxetine)**
Celexa (citalopram)	**Zoloft (sertraline)**
Lexapro (escitalopram)	**Trintellix (vortioxetine)**

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COMPARATIVE EFFICACY AND ACCEPTABILITY OF 21 ADS: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS
(CIPRIANI ET AL., 2018)

In head to head studies **LEAST WELL-TOLERATED** ADs:

Elavil (amitriptyline)	**Norebox (reboxetine)**
Anafranil (clomipramine)	**Desyrel (trazodone)**
Cymbalta (duloxetine)	**Effexor (venlafaxine)**
Luvox (fluvoxamine)	

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COMPARATIVE EFFICACY AND ACCEPTABILITY OF 21 ADS: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS
(CIPRIANI ET AL., 2018)

Relatively **MOST EFFECTIVE AND BETTER TOLERATED**

Lexapro (escitalopram)	**Valdoxan (agomelatine)**
Remeron (mirtazapine)	**Zoloft (sertraline)**
Paxil (paroxetine)	

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OPTIONS FOR SPECIFIC SIDE EFFECTS

SIDE EFFECT OF CONCERN	CONSIDERATIONS
Sexual Dysfunction	• Consider adding buspirone (Buspar) • Consider bupropion (Wellbutrin) if no anxiety present • Avoid paroxetine (Paxil)
Weight Gain	• avoid mirtazapine (Remeron) and paroxetine (Paxil) • Bupropion associated with some weight loss
Diarrhea	• Avoid sertraline (Zoloft)
Nausea and vomiting	• Avoid venlafaxine (Effexor)
Discontinuation Syndrome	• Avoid duloxetine (Cymbalta), venlafaxine (Effexor) and paroxetine (Paxil) • Consider fluoxetine (Prozac)

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THE CULTURE AND LANGUAGE OF MEDICINE

How the Culture of Psychology differs from Medicine

- "Axis II professionals"

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THE CULTURE AND LANGUAGE OF MEDICINE

Table 1 A Comparison of Psychological and Medical Cultures

Seperate professional cultures	
Psychologists	Family Physicians
Thorough	To the point
Covers all bases	Covers essential topics
No diagnosis until data are definitive	Makes definitive decisions on ambiguous data
Education based more on reading than apprenticeship	Education based more on apprenticeship than reading
Responsible to NOT DO something for the patient unless sure ($p < .05$)	Responsible to TO DO something for the patient even when not sure
Expected to study what they are being shown many times before acting	Expected to have to do what is demonstrated to them immediately

Hoover, M. & Andazola, J. (2012).

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THE CULTURE AND LANGUAGE OF MEDICINE

- Hoover and Andazola suggest the following ways to become familiar with medical culture:
  - Shadow a physician
  - Develop mentorships with seasoned health psychologists
  - Interview physicians about the behavioral health needs and barriers they face
  - Read books about medical culture (e.g., How Doctor's Think by Jerome Groopman)
  - Shearer's advice: observe an attending physician supervising medical residents

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THE CULTURE AND LANGUAGE OF MEDICINE

Prescribers are individuals

- You may have a favorite psychological approach for depression, they may have a favorite medication for depression

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THE CULTURE AND LANGUAGE OF MEDICINE

My suggestions on how to approach a prescriber to increase success in communication:

- Start formal (e.g. address as Doctor, Ms., Mr.)
- Know medical terms for what you are discussing (get a medical dictionary)
- Have a medication reference (e.g., Stahl's Prescriber's Guide, Epocrates)
- Make it brief
- Be SPECIFIC in your question, feedback or suggestion
- Don't practice medicine without a license

  (e.g., do not make specific medication recommendations)

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PHARMACODYNAMICS

Pharmacodynamics: what the drug does to the body (mechanism of action; MOA)

Actions of a cellular/molecular level (illustration of pre and post neuron with synaptic cleft)

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PHARMACODYNAMICS

Most common MOA is to affect neurotransmission rates

Mostly in synaptic transmission by –

Alteration in production

Interference with storage

Interaction with pre or post synaptic receptors

Interference with uptake/reuptake

Alteration or destruction of NT

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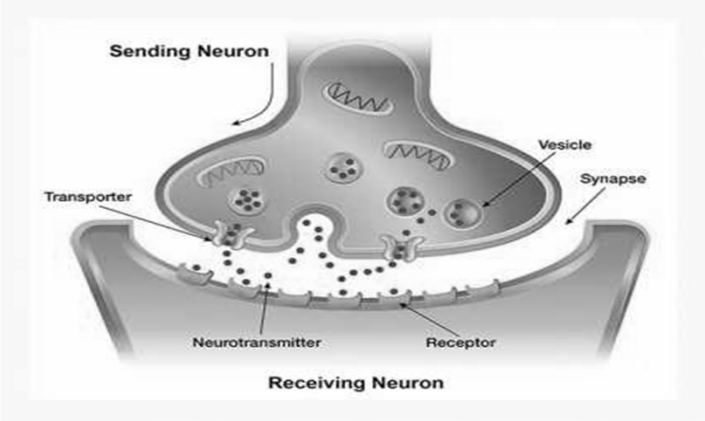
G PROTEIN-LINKED NEUROTRANSMISSION



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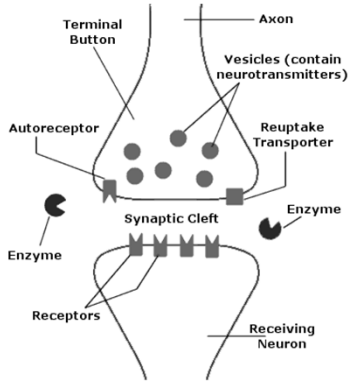
G PROTEIN-LINKED NEUROTRANSMISSION



(Source: About.com, http://bipolar.about.com/cs/neurotrans/l/aa0007_msngrs.htm)

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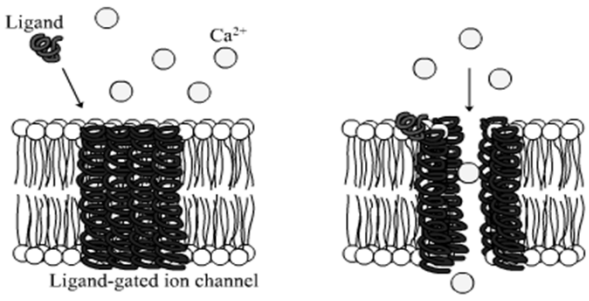
LIGAND (NT)-GATED ION CHANNEL



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PHARMACODYNAMICS

- Agonists – increase transmission
- Antagonists – inhibit or block transmission

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PHARMACODYNAMICS

- Receptors: specific neurotransmitters fit into specific receptors (like a key in a lock)
  - Autoreceptors – located on same neuron (cell body), regulates NT
  - Heteroceptors – different NT binds to adjacent receptor and inhibits release of other NT (e.g., NE inhibits 5HT)
  - Postsynaptic receptors – usually specific for a particular NT, can open adjacent gates using ligands or G protein links

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PHARMACOKINETICS

Pharmacokinetics: what the body does to the drug

- Absorption
- Distribution
- Metabolism
- Elimination

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PHARMACOKINETICS

Absorption: rate and extent to which a drug leaves the administration site and enter blood stream

- Parenteral (IV Intravascular, IM Intramuscular, SC subcutaneous)
- Oral
- Rectal
- Transdermal
- Topical
- Sublingual
- Inhalation
- Intranasal

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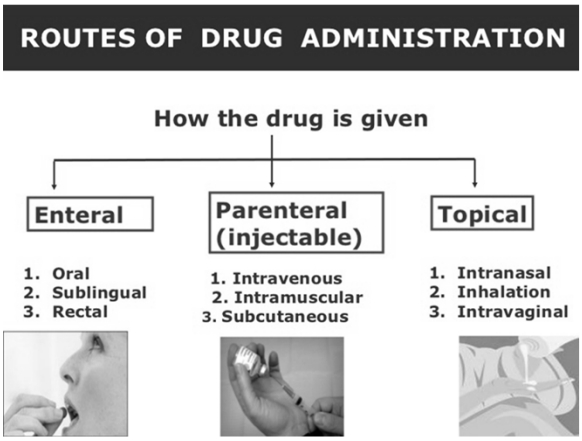

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PHARMACOKINETICS

Bioavailability:

- the fraction of administered drug that reaches the systemic circulation

Factors that influence Bioavailability:

- First Pass Hepatic Metabolism
- Solubility of a Drug
- Chemical Instability
- Drug formulation

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PHARMACOKINETICS

First Pass Hepatic Metabolism:

- When a drug is absorbed across the GI tract it enters portal circulation before entering systemic circulation. Portal vein sends blood from GI tract to liver

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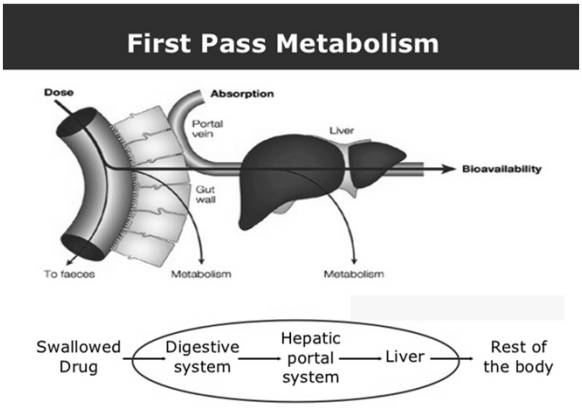
PHARMACOKINETICS



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PHARMACOKINETICS

Factors that affect absorption:

- Solubility of a Drug: very hydrophilic and very hydrophobic drugs are poorly absorbed. To be absorbed easily the drug must be mostly hydrophobic but have some solubility in water
- Chemical Instability: some drugs are unstable in the pH environment of the stomach. Others (e.g., insulin) are destroyed in the GI tract by enzymes
- The way the drug is formulated: chemistry of drug may influence bioavailability

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PHARMACOKINETICS

Distribution: process by which drug reversibly leaves blood stream and enters the extracellular fluid and/or the cells of the tissues

- BBB – Blood Brain Barrier – tight junctions between cells do allow some substances into the brain

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PHARMACOKINETICS

Metabolism: process that involves a chemical alteration of a drug in the body

- Drugs can be "biotransformed" into more excretable forms
- Liver is the principal organ of drug metabolism

Other

GI track

Lungs

Skin

Kidneys

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PHARMACOKINETICS

METABOLISM

Liver protects the body from toxic substances (see first pass metabolism)

Orally administered drugs delivered to liver from GI track where they are transformed

The compounds that transform the drug are called enzymes (proteins)

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PHARMACOKINETICS

METABOLISM

CYP 450 System: Cytochrome P450 System
(family of enzymes)

- **This is where many DRUG INTERACTIONS occur**

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PHARMACOKINETICS

METABOLISM

CYP450 Inducers and Inhibitors:

- Some drugs induce specific CYP450
- Some drugs inhibit specific CYP450

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PHARMACOKINETICS

METABOLISM

When a CYP450 enzyme is induced more of the isozyme is made, therefore, it metabolizes a substrate drug more quickly and less of the drug is distributed and more is eliminated (can cause drug levels to be too low)

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PHARMACOKINETICS

METABOLISM

When a CYP450 enzyme is inhibited less of the isozyme is made, therefore, it metabolizes a substrate drug more slowly and more of the drug is distributed and less is eliminated (can cause drug levels to be too high)

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PHARMACOKINETICS

METABOLISM

For example, grapefruit juice is a common INHIBITOR of P450 3A4

What happens if you drink grapefruit juice with a drug (e.g., Remeron) that is metabolized by an enzyme that is INHIBITED by grapefruit juice?

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PHARMACOKINETICS

METABOLISM

Answer: less enzyme is available to breakdown the drug and more drug enters the system (think side effects)

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PHARMACOKINETICS

ELIMINATION

Elimination: process by which drug is removed from body

- Urine
- Bile
- Intestine (stool)
- Lung
- Milk in nursing mothers
- Dialysis for kidney failure (removes small molecules such as drugs)

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PHARMACOKINETICS

ELIMINATION – Half Life

Drug Elimination Half Life – time it takes to reduce the initial peak level in blood stream by 50%

Drug is effectively eliminated after 4-5 half lives

Steady State – of blood level concentrations achieved in about 6 elimination half lives

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PSYCHOPHARMACOLOGY: TIPS AND PEARLS

- SSRI's and other psychotropics are often not prescribed at high enough doses for long enough periods of time.

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PSYCHOPHARMACOLOGY: TIPS AND PEARLS

- SSRIs may cause sexual side effects (e.g., decreased libido, anorgasmia, delayed ejaculation) in over 50% of patients. (Ferguson, 2001; SSRI AD Medications: Adverse Effects and Tolerability)
- How SSRIs cause sexual side effects: complicated, may involve nitric oxide, may be attributable to stimulation of postsynaptic 5HT2 receptors in the spinal cord (agonism at 5HT2A can block dopamine release)

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PSYCHOPHARMACOLOGY: TIPS AND PEARLS

Therapeutic effects of SSRI's may be delayed 2 to 4 weeks.

Initial SSRI side effects often resolve after first week or few days.

"Poop out:" some initial responders may relapse. Consider increasing dose, switching agents or adding adjunct.

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PSYCHOPHARMACOLOGY: TIPS AND PEARLS

When depression or anxiety resolved with SSRI/SNRI continue treatment for one year to decrease risk of relapse

Anxiety vs depression may require higher doses

Initiation of SSRI may agitate (increase anxiety) in some anxious pts. In very anxious pts you may wish to start at a lower dose

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PSYCHOPHARMACOLOGY: TIPS AND PEARLS

In undiagnosed or latent bipolar SSRI's or other antidepressant treatments may trigger a hypomanic or manic episode

SSRI's should not be combined with MAOI's due to possible fatal serotonin syndrome (need a two week washout period).

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PSYCHOPHARMACOLOGY: TIPS AND PEARLS

Increasing serotonin can cause a decrease in dopamine (e.g. in basal ganglia and nucleus acumbens) release which might contribute to:

- Emotional flattening
- Cognitive slowing
- Apathy
- Akathisia
- Dystonic movements
- (try adding bupropion to address these SE's)

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PSYCHOPHARMACOLOGY: TIPS AND PEARLS

Bupropion is not considered an anxiolytic, it should not generally be used as monotherapy for an anxiety disorder

If pt experiences SSRI as sedating have them take it in the evening (qhs). If activating, take in the morning (qam)

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PSYCHOPHARMACOLOGY: TIPS AND PEARLS

Continue SSRI treatment for one year following remission of symptoms for FIRST episode of depression. For SECOND and later episodes treatment may be indefinite for depression.

Partial Response in SSRIs: typical persisting symptoms include insomnia, fatigue, physical pain, concentration, lack of interest or motivation

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PSYCHOPHARMACOLOGY: TIPS AND PEARLS

Some antidepressants have a high risk for a "discontinuation syndrome"

For example: Effexor (venlafaxine), Cymbalta (duloxetine), and Paxil (paroxetine)

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ANTIDEPRESSANT (AD) MEDICATION CLASS ABREVIATIONS

- SSRI – Selective Serotonin Reuptake Inhibitors (e.g., citalapram)
- NDRI – Norepinephrine Dopamine Reuptake Inhibitors (e.g., buproprion)
- SNRI - Selective Serotonin-Norepinepherine Reuptake Inhibitors (e.g., venlafaxine)
- SARI – Serotonin 2 Antagonist/Serotonin Reuptake Inhibitors (e.g., trazadone, nefazadone)
- NaSSA – Noradrenergic/Specific Serotonin Antidepressant (e.g., mitrazapine)
- Tricyclic – (e.g., amitryptaline, nortryptaline, imipramine, desipramine, clomipramine)

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ANTIDEPRESSANT (AD) MEDICATION CLASS ABREVIATIONS

- SPARI: serotonin partial agonist reuptake inhibitor (e.g., vilazidone)
- Multimodal antidepressant (.e.g, vortioxetine) (influences release of 5HT, NE, glutamate, acetylcholine and histamine)
- NMDA Receptor Agonist + NDRI (e.g., Auvelity; dextromethorphan + bupropion)

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SSRI'S

- **Celexa (citalopram)**
- **Zoloft (sertraline)**
- **Lexapro (escitalopram)**
- **Prozac (fluoxetine)**
- **Paxil (paroxetine)**
- **Luvox (fluvoxamine)**

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SSRI advantages
over tricylics (TCAs):
less sedating and
less lethal in OD

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Therapeutic Effect: 7 to 28 days for all antidepressants

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SOME COMMON INDICATIONS FOR SSRI'S

- MDD (all except fluvoxamine)
- Bulimia Nervosa (fluoxetine and sertraline)
- Panic (paroxetine, sertraline, fluoxetine)
- Social Anxiety (paroxetine, sertraline)
- PTSD (paroxetine, sertraline)
- PMDD (fluoxetine, paroxetine, sertraline)
- GAD (paroxetine, escitalopram)
- OCD (paroxetine, fluoxetine, sertraline, fluovoxamine)

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As a group, the SSRIs possess the following adverse effects:

- nausea
- sexual dysfunction, including decreased libido, orgasm difficulties, abnormal ejaculation
- diarrhea
- headache
- nervousness
- insomnia

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SSRI SIDE EFFECTS, CONTINTUED

- agitation
- sweating
- dry mouth
- tachycardia
- anorexia
- increased appetite
- weight gain
- anxiety
- insomnia
- drowsiness

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SOME PROS AND CONS OF SSRI'S

Prozac (fluoxetine)

- may be activating or cause activation
- good for pts with fatigue/low energy
- can increase anxiety or agitation initially so dose low to start with
- avoid in agitated insomniacs
- possible sexual side effects
- may take longer for onset of therapeutic effect

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SOME PROS AND CONS OF SSRI'S

Paxil (paroxetine):

- Good for anxiety and mixed anxiety/depression
- May be somewhat more sedating
- Good for insomnia, bad for hypersomnia
- May not be first choice for pts with low energy/fatigue
- More withdrawal effects than other SSRI's when discontinued (akathisia, restlessness, GI sx, dizziness, tingling, nausea, stomach cramps)
- May cause affective flattening
- possible sexual side effects

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SOME PROS AND CONS OF SSRI'S

Zoloft (sertraline):

- May be better for atypical depression (e.g., increased appetite and hypersomnia)
- May be activating, especially initially, so may exacerbate insomnia
- More GI effects (diarrhea) than other SSRI's
- May cause affective flattening
- Good for anxiety and depression
- possible sexual side effects
- should be taken with food

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SOME PROS AND CONS OF SSRI'S

Celexa (citalopram):

- Pts may tolerate better than other SSRI's, fewer side effects
- However, Lexapro may be better tolerated than Celexa
- Can be sedating in some pts
- Good for anxiety and depression, panic attacks, insomnia and hypersomnia
- May have less sexual dysfunction
- May be better tolerated in elderly
- May cause affective flattening
- possible sexual side effects
- New FDA Guidelines (max 20 mg qd over 60, under 60 max is 40 mg qd)

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SOME PROS AND CONS OF SSRI'S

Lexapro (escitalopram)

- Active metabolite of Celexa (S enantiomer of citalopram)
- May be best tolerated SSRI
- May cause less sexual dysfunction than other SSRI's
- May cause affective flattening
- May have faster onset than Celexa
- Good for anxiety and depression, panic attacks, insomnia and hypersomnia

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SSRI's can reduce platelet aggregation (protective cardiovascular effect); can be problematic if pt is on blood thinner (anticoagulant e.g., Coumadin, heparin, Lovenox)

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SSRI INDUCED ANORGASMIA, ED, LOSS OF DESIRE

SSRI sexual side effects can be problematic for patients.

Some options:Treat with Wellbutrin, Viagra, switch medications, or skip dose for 24 hours.

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STOPPING SSRI'S

Most patients can tolerate dose decrease (taper) of 50% for three days, then another 50% decrease for three days, then stop (what about SNRIs, paroxetine and TCAs?)

Prozac is an exception: it does NOT require a taper

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NDRI – NORADRENERGIC DOPAMINERGIC REUPTAKE INHIBITOR

Wellbutrin (bupropion)

- FDA approved to treat: Depression, nicotine addiction, SADS
- Off-label to treat: SSRI induced sexual dysfunction, ADHD
- Increases energy and motivation
- Seizure risk over 450 mg daily
- INCREASES REM (vivid dreams, nightmares)
- Fine tremor
- May exacerbate tics, Tourette's

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SNRI - SELECTIVE SEROTONIN-NOREPINEPHERINE REUPTAKE INHIBITORS

- **Effexor (venlafaxine)**
  - **Depression, GAD, social phobia, panic,** PTSD, PMDD
- **Cymbalta (duloxetine)**
  - **MDD, Diabetic Periph Neuropathic pain, fibromyalgia, GAD, chronic musculoskeletal pain,** stress incont, neuropathic pain, other anxiety
- **Pristiq (desvenlafaxine)**
  - **MDD,** fibromyalgia, GAD, social phobia, panic, PTSD, PMDD
- **Savella (milnacipran):**
  - **Fibromyalgia,** MDD, neuropathic pain
- **Fetzima (levomilnacipran):**
  - **MDD,**fibromyalgia, neuropathic pain

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SNRI'S CONTINUED

- Use Effexor to treat: depression, generalized anxiety disorder, social anxiety, neuropathic pain (e.g., diabetic neuropathy, fibromyalgia)
  - Modest hypertension (HTN) for Effexor, use with caution in HTN pts
- Use Cymbalta to treat: depression, neuropathic pain

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SARI – SEROTONIN 2 ANTAGONIST/SEROTONIN REUPTAKE INHIBITORS

Serzone (nefazodone)

Desyrel (trazadone)

Antogonism at 5HT2A stimulates dopamine release which acts as an antidepressant

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SARI – SEROTONIN 2 ANTAGONIST/SEROTONIN REUPTAKE INHIBITORS

Trazodone

- Use Trazadone to treat: depression, anxiety, insomnia
- Trazadone may INCREASE QT interval (risk of cardiac problems, especially in OD)
- Low dose Trazadone is often used as a sleep agent (antihistamine and blockade of alpha adrenergic 1 receptors)
- Sedative effects after a few hours

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NASSA – NORADRENERGIC/SPECIFIC SEROTONIN ANTIDEPRESSANT

Remeron (mirtazapine)

- For treatment of depression and anxiety
- May help with SSRI induced sexual dysfunction
- Improves sleep onset/duration due to H1 blockade (antihistamine)
- Mild anxiolytic at low doses
- Comes in SolTabs (oral disintigrating tabs)

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NASSA – NORADRENERGIC/SPECIFIC SEROTONIN ANTIDEPRESSANT

Remeron (mirtazapine)

- May be ideal for underweight depressed and/or anxious patients with insomnia
- Paradoxical dose to sedation ratio
- Weight gain
- Fatigue/Sedation common
- Sexual dysfunction may occur (30%)
- May cause agranulocytosis or neutropenia
- Monitor WBC if signs of infection; low WBC = discontinue

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SPARI SEROTONIN PARTIAL AGONIST AND SEROTONIN TRANSPORT INHIBITOR

Viibryd (vilazidone)

- FDA indication: MDD
- Acts as a 5HT1A partial agonist and serotonin reuptake inhibitor (SSRI + buspirone)
- 5HT1A partial agonist effects more potent than buspirone's actions
- Relative lack of sexual dysfunction and weight gain
- Consider for pts with comorbid anxiety

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MULTIMODAL ANTIDEPRESSANT

Vortioxetine – Trintellix

(influences release of 5HT, NE, glutamate, acetylcholine and histamine)

- FDA approved for major depression
- Likely helpful for anxiety as well
- Usual dose: 10 to 20 mg qd (range 5 to 20 mg qd)
- May have less sexual side effects, good for cognitive sx of dep, low weight gain

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ATYPICAL ANTIPSYCHOTICS

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WHAT MAKES AN ATYPICAL "ATYPICAL"?

The risk of Extrapyramidal Symptoms (EPS) is related to D2 receptor occupancy (think Tardive Dyskinesia)

Conventional APs may block up to 90% of D2 receptors while atypical APs may block 70 to 80% which is below the threshold for causing EPS in most patients

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WHAT MAKES AN ATYPICAL “ATYPICAL”?

- **#1: Adding 5HT2A Antagonist makes antipsychotics atypical**
- **5HT2A Antagonism STIMULATES dopamine release**

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WHAT MAKES AN ATYPICAL “ATYPICAL”?

- **#2: Rapid dissociation of D2 makes antipsychotics atypical**
- Theoretically, this allows long enough binding of D2 antagonists to exert antipsychotic action, but not so long that it causes EPS

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WHAT MAKES AN ATYPICAL "ATYPICAL"?

- **#3: D2 Partial Agonism makes antipsychotics atypical**

- bind to D2 in a way that is neither too strong nor too weak

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WHAT MAKES AN ATYPICAL "ATYPICAL"?

- **#4: 5HT1A partial agonism make antipsychotics atypical**
- 5HT1A partial agonism will cause some increased dopamine release
  - **Also called a Serotonin Partial Agonist (SPA)**

Of Note: Buspar is a 5HT1A partial agonist

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Side Effects and Risks of Atypicals

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SIDE EFFECTS AND RISKS OF ATYPICALS

Extrapyramidal Symptoms EPS:

- Parkinsonism
- akathisia
- acute dystonia

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SIDE EFFECTS AND RISKS OF ATYPICALS

Parkinsonism:

- rigidity
- akinesia/bradykinesia
- resting tremor

Recall this can be caused by blocking D2 in the Nigrastriatal Dopamine Pathway

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SIDE EFFECTS AND RISKS OF ATYPICALS

Akathisia:

- “cruel restlessness”
- inability to remain seated
- with motor restlessness and a feeling of muscular quivering
- sometimes a side effect of antipsychotic medication

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SIDE EFFECTS AND RISKS OF ATYPICALS

Dystonia:

- abnormal muscle contraction
- produces involuntary twisting movements and abnormal posturing of the neck, trunk, face and extremities

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SIDE EFFECTS AND RISKS OF ATYPICALS

- Tardive Dyskinesia TD: involuntary rhythmic movements of jaw, lips, tongue and extremities (can alleviate with BZ or GABA agonist)
- Risk of TD about 5% per year of use of conventional APs (5 years 25%, 10 years 50%)

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SIDE EFFECTS AND RISKS OF ATYPICALS

Neuroleptic Malignant Syndrome (NMS)

- Sx: fever, rigidity, autonomic instability, clouding of consciousness, death
- Tx: withhold neuroleptics, hydrate, consider dantrolene (muscle relaxant)
- neuroleptic: any class of drugs used to treat psychosis, particularly schizophrenia

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SIDE EFFECTS AND RISKS OF ATYPICALS

- **Metabolic Syndrome:**
- Large waistline: 35 inches or greater for women, 40 inches or more for men (apple shape).
- triglyceride level > 150 mg/dL
- HDL cholesterol < 50 mg/dL for women and < 40 mg/dL for men
- blood pressure > 130/85
- fasting blood sugar > 100 mg/dL (110 to 125 is prediabetes, > 126 is diabetes)

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SIDE EFFECTS AND RISKS OF ATYPICALS

- But note that the risk of developing tardive dyskinesia on conventional APs is **much** higher than the risk of developing cardiometabolic risks on atypical APs.

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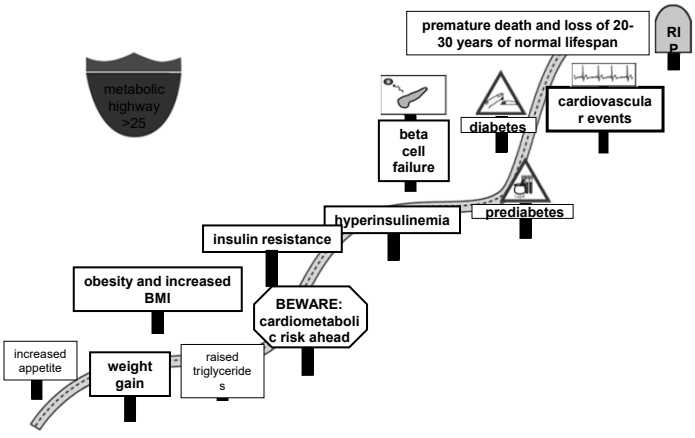
The Metabolic Highway



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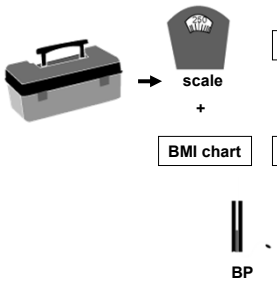
Psychopharmacologist's Metabolic Monitoring Toolkit



FLOW CHART John Doe			
	baseline	visit 1	visit 2
wt/BMI			
fasting glu			
fasting TGs			
BP			

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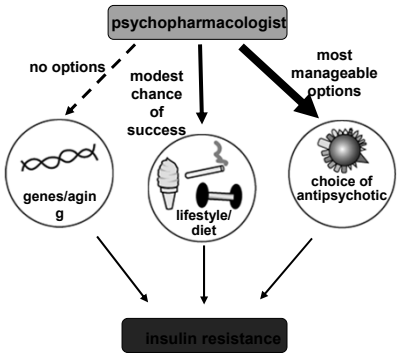
Insulin Resistance: What Can a Psychopharmacologist Do?



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MONITORING AND LABS

Four parameters to measure:

- Weight (BMI)
- Fasting triglycerides
- Fasting glucose
- Blood pressure

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SOME COMMON TRICYCLIC USES:

- Anafranil (clomipramine): Obsessive Compulsive Disorder
- Tofranil (imipramine): enuresis, panic
- Elavil, Pamelor (amitriptyline, nortriptyline): insomnia, headache prophylaxis, neuropathic pain
- Desyrel (Trazadone): insomnia

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TREATING NIGHTMARES IN PTSD:

Prazosin (Minipress):

an antihypertensive (alpha 1 adrenergic blocker) that may reduce nightmares in people who have experienced trauma.

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COMMON DISORDERS THAT MAY CAUSE DEPRESSION:

- AIDS
- Alzheimer's
- Anemia
- Sleep Apnea
- Asthma
- Chronic Fatigue Syndrome

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COMMON DISORDERS THAT MAY CAUSE DEPRESSION:

- Chronic infection
- Chronic Pain
- Congestive Heart Failure
- Diabetes

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COMMON DISORDERS THAT MAY CAUSE DEPRESSION:

- Hyperthyroidism
- Hypothyroidism
- Hepatitis
- Cancer
- Menopause
- Multiple Sclerosis

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COMMON DISORDERS THAT MAY CAUSE DEPRESSION:

- Parkinson's Disease
- Post Partum hormonal changes
- Premenstrual Syndrome
- Rheumatoid Arthritis
- Systemic Lupus Erythematosis

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COMMON DRUGS THAT MAY CAUSE DEPRESSION:

- Antihypertensives (e.g., beta blockers)
- Steroids
- Antianxiety drugs (e.g, diazepam)
- Birth control pills
- Alcohol

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COMMON DISORDERS THAT MAY CAUSE ANXIETY:

- Adrenal Tumor (pheochromocytoma)
- Alcoholism
- Angina Pectoris
- Cardiac arrhythmia
- Delirium
- Hypoglycemia
- Hyperthyroidism

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DRUGS THAT MAY CAUSE ANXIETY:

- Appetite suppressants
- Asthma medications
- caffeine
- CNS Depressants (withdrawal)
- Cocaine
- Nasal decongestants
- Steroids
- Stimulants

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CASE SCENARIOS

Case 1:

A 23 yo married female with a history of depression and social anxiety was prescribed fluoxetine 20 mg once daily starting three months ago. She isn't reporting any SE's, but she is not reporting any therapeutic effects either. What are your thoughts?

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Case 1:

Consider increasing the dose

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Case 2:

A 32 yo single male reports onset of anxiety symptoms two years ago. He was started on bupropion SR 100 mg twice daily approximately 8 months ago. He says he does feel better in general, but still has significant anxiety, especially at night when he is trying to fall asleep. He is not interested in pursuing psychotherapy at this time. What might be a reasonable next step?

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Case 2:

Bupropion is not an anxiolytic. Consider switching to an SSRI or SNRI or adding one of these to bupropion. Encourage therapy.

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Case 3:

A female patient's PCM has been increasing her Zoloft for the past month and she is currently at 100 mg qd. She came to you with a previous diagnosis of depression and ADHD. At her next appointment with you she says she now has a terrific amount of energy, has been accomplishing a great deal of tasks, has quit her old job and started a new one, and has met the love of her life. She has only been requiring about 3 or 4 hours of sleep a night and this is helping her get a lot more done around the house. What concerns might you have?

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Case 3:

Talk to her prescriber as the SSRI may have unmasked previously unidentified bipolar disorder.

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Case 4:

A 24 yo female is reporting full remission of depression symptoms after 6 months of treatment of paroxetine 40 mg daily. She has been experiencing depressive episodes about twice a year since she was age 16. This is the first time she has experienced a treatment that has been this effective. However, she hates relying on medication and asks when she can stop taking the medication. She says she feels fine and would like to d/c the medication as soon as possible. What is are your thoughts?

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Case 4:

- For first episode pt should stay on medication for one year following full remission.
- For second and following episodes may need to stay on medication indefinitely

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Case 5:

A 30 yo married male with no children has been treated by his PCM in Florida with fluoxetine 40 mg qd for mixed anxiety and depression. He has recently moved here and you are his new therapist. He says his depression and anxiety symptoms have all but disappeared and he has "never felt better." However, he is having marital problems because, although he has interest in sex, he is unable to maintain an erection. His wife has accused him of cheating on her and they have started marital therapy. This has never been a problem before starting the fluoxetine, but he is afraid to stop because he doesn't want the mood and anxiety problems to return. What are your thoughts?

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Case 5:

- Consider adding bupropion
- Consider using vardenifil, tadalafil, sildenafil
- Drug holiday (skip dose 24 h prior to sexual activity (not effective for fluoxetine)

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Case 6:

You hare seeing aa 28 yo married female who is 8 months pregnant. She has had three children previously and each time has developed severe post partum depression with homicidal ideation toward her infant. She has never tried to harm her children, but is worried she will have these thoughts again. She has asked her PCM to prophylactically start her on an SSRI. She has heard good things about Paxil. What are your thoughts?

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Case 6:

Paxil is the only SSRI contraindicated in pregnancy due to known risks to the fetus

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QUESTIONS AND COMMENTS?

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