

Psychopharmacology: *The Basics and Beyond*

Part I

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Presentation Objectives

- **Increase neuroscientific knowledge about brain functioning**
- **Understand the neurobiological basis for psychiatric disorders and challenging behaviors to help reduce stigmatization**
- **Comprehend key terms and rationale associated with prescribing**
- **Understand concepts related to psychotropic metabolism**
- **Begin to differentiate between psychotropics, starting with antidepressant medications**

Test your Knowledge!

TRUE OR FALSE QUIZ

- 1. One out of three people respond to antidepressants.*
- 2. The cause of schizophrenia is generally known.*
- 3. Mood disorders are perhaps a combination of diseases.*
- 4. Medications work by disturbing the natural chemistry in the brain.*
- 5. 1 of every 5 prescriptions of anti-psychotic medications is off-label use.*

TRUE OR FALSE QUIZ

6. *50-percent of individual's chance of developing a substance abuse problem is genetic predisposition, rather than inherited traits.*
7. *In addition to alcohol, methamphetamines can be the most addictive.*
8. *To date, the eras of mental health treatment have include asylums, psychodynamic, and psychopharmacologic.*
9. *About 30% of people do not know important details about their treatment.*
10. *Americans spend more on medicines than all the people of Japan, Germany, Italy, and France, combined.*

Bonus Question:

What is the best psychotropic medication to treat an individual with I/DD?

- **Psychotropic treatment should proceed as it would for an individual without I/DD.**
- ***Although it can be challenging, particularly in the context of limited verbal abilities, optimal medication selection should always begin by establishing an accurate primary diagnosis!***
- ***Avoid a broad-brush approach and look at idiosyncratic dynamics!***

Pharmacoepidemiology

- **The first proponent of organic causes to mental illness was Hippocrates.**
- **Europeans with a health problem often go first to the pharmacy, not to their physician, as pharmacists often diagnose and prescribe remedies.**
- **In the 1950s, Donald Klein, an American psychiatrist with a background in biology, brought a new rigor to the study of whether some psychiatric problems might have a biological basis that could be treated with drugs. Thereby establishing the field of psychopharmacology.**
- **The initial psychotropics were Librium and Valium.**

Basic Terminology

**All medications are drugs,
but not all drugs are medications...**

- **Medications or medicines are taken to treat medical conditions.**
- **Drugs are taken for reasons other than treating health issues. Examples are caffeine and nicotine.**

Basic Terminology

❖ *Descriptive versus Explanatory Pathology*

- *Upset by it, rather than about it...*
Effect versus Causality

❖ *Illnesses have symptomatology with predictable courses (i.e., states)*

❖ *Disorders are a system malfunction with characteristics (i.e., traits)*

❖ *Incidence versus Prevalence*

- *For example, in the general population:
psychosis 1%; mental health disorder 5%, personality disorder 15%*

Basic Terminology

***Psychotropic, Psychoactive, and Psychopharmaceutical
are classes of drugs capable of effecting the mind***

- **“Psycho” relating to the mind or brain**
- **“Tropic” means to be attracted to or turn toward**
- **Contemporary definition is “mind-nourishing”**
- **Psychotropics describes a small group of medicines intended to treat brain illnesses or mental health disorders.**

Basic Terminology

- ***Psychoactive and psychotropic are essentially synonymous terms. They are defined as a chemical substance that crosses the blood-brain barrier, acts on the central nervous system, and affects consciousness, cognition, mood, and behavior.***
- ***The only difference between the two is the working time wherein psychoactives have greater therapeutic utility because they work in 20 to 30 minutes (e.g., anesthetics and analgesics).***
- ***All psychoactives are psychotropics (umbrella term)***
- ***Using the term psychotropic is always correct.***
- ***What are the most common psychoactive drugs?***

Basic Terminology

It's all in the name...

- Chemical Name: The description for synthesizing used by an organic chemist (e.g., 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepine-2-one)
- Street Name: Benzo, Downer, Blue
- Generic Name: diazepam (not capitalized)
- Brand Name: Valium

Basic Terminology

Psychopharmacological Error:

- **Any preventable event that may lead to inappropriate use or harm while the medication is in the control of the healthcare professional or client.**

Side Effects (Negative and Positive):

- **An undesired tilting of the body's homeostatic balance and the system's response to self-correct.**
- **Pasteur discovered that drugs have a left and right sides of their molecular structure. The left does what we want and the right causes the side effects, which are often only later apparent. *The medication name often alludes to the particular side!***
- **The basic mechanisms involved in generating the side effects are often the same as those involved in the therapeutic benefits.**

Basic Terminology

Adverse Drug Reactions (ADR):

- **A harmful occurrence (e.g., toxicity, anaphylaxis, anemia) that stems from a medicine that is given at the correct dose (either single administration or prolonged delivery).**
- **Type A reactions are predictable**
- **Type B reactions are idiosyncratic, bizarre, or novel**

Adverse Events versus Side Effects

- **Incorrectly used interchangeably; they mean separate things**
- **ADRs are never desired and require prompt interventions**
- **Most negative side effects (e.g., upset stomach) spontaneously resolve over time**
- **Some medications are utilized for their side effects (e.g., Mirtazapine used in elderly or anorexic patients due to the potential to stimulate appetite and cause weight gain)**

Basic Terminology

- **Medication Errors:** Common causes are poor interdisciplinary consultation, “medication shopping,” communication problems, provider knowledge deficits, and inadequate monitoring.
- The difference between an adverse drug reaction and a significant medical error may only be a matter of degrees (e.g., dosage)
- **Black Box Warning:** The strictest warning put on a prescription drug label by the FDA when there is reasonable evidence from research studies to indicate the potential of serious health hazards.
 - Antidepressants: Suicidality
 - Stimulants: Drug dependence
 - Atypical Antipsychotics: Mortality; Dementia

Potentially-Inappropriate Prescribing: Poorly Researched Area

Basic Terminology

- **Medication Wash: Discontinuation of all medications**
- **Drug Holiday: “Creative Non-Adherence” (i.e., Taking the weekend off)**
- **Non-Adherence: 73% is intentional, rather than accidental (e.g., reducing dosage, doubling pills, giving medications away)**
- ***While both medication washes and drug holidays allow brain receptors to reset, these practices are shunned by pharmaceutical companies.***
- ***All medications potentially stop working because the body seeks homeostasis.***
- ***Changes should always be made in isolation (i.e., one at a time)***

Basic Terminology

Off-Label Prescribing: “Clinical Innovation”

- Prescribing a medication for something not indicated by the FDA.
- Safety concerns (e.g., age, dosage, route of administration)
- Common (about 30%) but controversial

Placebo Effect versus Nocebo Effect

- Antonyms about psychological expectations to heal versus harm
- Based on the desire to please
- Thinking an inert medicine has a positive effect (placebo) or negative effect (nocebo)

How can you tell if it's placebo effect?

Active Placebo: Small doses of drug creates side effects (e.g., atropine)

Prodrug: Medication converted from pharmacologically inactive to active within the body (e.g., liver). It improves bioavailability and reduces unintended side effects, as it selects how the drug interacts.

Iatrogenic Effects: Illness caused by the treatment (e.g., opioid epidemic)

Valid Reasons to Prescribe Psychotropics:

- **Treating a clearly diagnosed psychiatric disorder**
- **For medical conditions with secondary psychiatric features**
- **When challenging behavior is resistant to environmental interventions and continues to interfere with functioning**
- **To treat discontinuation symptoms**
- **Sedation for medical procedures**

Questionable Uses of Psychotropics:

- **No re-examination of original rationale**
- **Lack of evidence for continued usage**
- **Inadequate assessment**
- **Haphazard prescribing (*the ADHD example*)**
- **For the convenience of caregivers**
- **Ignoring the function of behavior**
- **Pathologizing life events**
- **Limiting autonomy**
- **To silence complaints**
- **Exceeding therapeutic range**
- **Substituting for appropriate supports**

Basic Terminology

Polypharmacy

- **Greek words for “poly” (more than one) plus “pharmakon” (drug)**
- **Prescribing more than one drug, but there is no standard definition of a cut off point with regard to number**
- *Usually the threshold is five or more psychotropics*
- *In DDS, our threshold for psychotropics is three*

- *Technically defined as simultaneous or concurrent use of multiple drugs to treat a single condition or a single individual*

- *Alternate definitions:*
 - *More medications than necessary*
 - *Medications that are not indicated*
 - *Medications that are not effective*
 - *Duplication of medications*
 - *Polymedicine (from Oncology)*

- **The opposite is monotherapy**

Basic Terminology

Five-Types of Polypharmacology

- ❖ Same-class (intra-class)
 - ❖ Multi-class (inter-class)
 - ❖ Adjunctive (i.e., one medication to treat the secondary symptoms of another from a different class, such as Trazodone given with Wellbutrin for insomnia)
 - ❖ Augmentative (e.g., Depakote with Lamictal; Zoloft with Abilify)
 - ❖ Total (c.f., pill burden)
- *Most common are antipsychotics, followed by ADHD medications and antidepressants*

Scenarios where Polypharmacy is Acceptable:

- Treating two distinct illnesses (e.g., mood disorder and psychosis)
- Treating an adverse effect from a primary drug
- Provide symptom relief when awaiting the delayed effect of another medication
- To treat different phases of an illness
- To boost the efficacy of primary treatment
- To treat refractory illness
- To decrease the dosage of monotherapy
- Cross-titration of medications

Basic Terminology

Rates of polypharmacy

- **Polypharmacy affects approximately 40% of older adults living in their own homes**
- **About 21% of adults with intellectual disability are exposed to polypharmacy**
- **In adult outpatient settings, one-third of patients receive three or more medications**

Basic Terminology

- **Negative Effects of Polypharmacy: Individual and Systemic**
 - Diagnostic inflation
 - Increased risk of medical and drug interactions
 - Cascade of side effects
 - High cost
 - Poor quality of life due to decreased cognition and mobility
- **If an individual is taking seven or more medications, what is the risk of an interaction effect?**

99.9%

- **Can antipsychotic polypharmacy be reversed?**

In a 2011 study of 127 individuals, all stable on polypharmacy, over a 12-month period, two-thirds were successfully moved to monotherapy without significant worsening.

Basic Terminology

Pharmacokinetics

- **How the biology of the body affects the chemistry of the medication (what the body does to the drug)**

Key Elements:

- ❖ ***Absorption***
- ❖ ***Distribution***
- ❖ ***Metabolism***
 - ***Biotransformation (alterations of a compound that occur in the body, such as enzymatic activity)***
 - ***Prodrug (turns drugs from inactive to active)***
- ❖ ***Elimination***
 - ***Liver: “watch keeper of friend versus foe”***
 - ***Kidneys: Clear it***

Basic Terminology

Pharmacodynamics

- How the chemistry of the medication affects the biology of the body (what the drug does to the body)

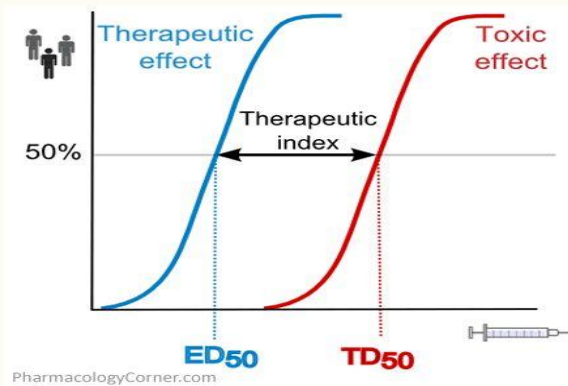
Key Elements:

- ❖ *Potency and Efficacy*
- ❖ *Dose Response Curve*
 - *Inhaling is the fastest route at 8 seconds*
- ❖ *Therapeutic Index (or window) for an effective versus a toxic or a lethal dose*
 - *Wider is safest. Cannabis is widest.*

Therapeutic Index

- The ratio of the dose that produces the desired therapeutic effect (ED_{50}) to the dose that produces a toxic effect (TD_{50}).

$$\text{Therapeutic index} = \frac{TD_{50}}{ED_{50}}$$



PharmacologyCorner.com

Basic Terminology

Biological Variance:

- **The patient-specific factors that affect the expression of the dose and the response to the medication.**

Effect = *the relationship between pharmacodynamics, pharmacokinetics, and biological variance.*

Basic Tenents

The Ten Rules

1. All drugs are prescribed because they have a mechanism of action

For example, tricyclic (TCA) antidepressants (currently SNRI) :

- **Serotonin Reuptake Inhibitor**
- **Norepinephrine Reuptake Inhibitor**
- **Alpha-1 Agonist (Sympathetic Nervous System)**
- **M-1 Antagonist (Parasympathetic Nervous System)**
- **H-1 Antagonist**
- **Na Channel Blocker**
- **5-HT(2a and 2c) Antagonist**

TCA contraindicated for diabetes, heart arrhythmia, or prostate enlargement

Basic Tenents
The Ten Rules

2. All drugs have positive and negative side effects

3. Antidepressants will not make you happy (c.f., euphorants)

4. If one pill works, then two will usually lead to side effects and even medication errors.

5. Drugs interact with each other

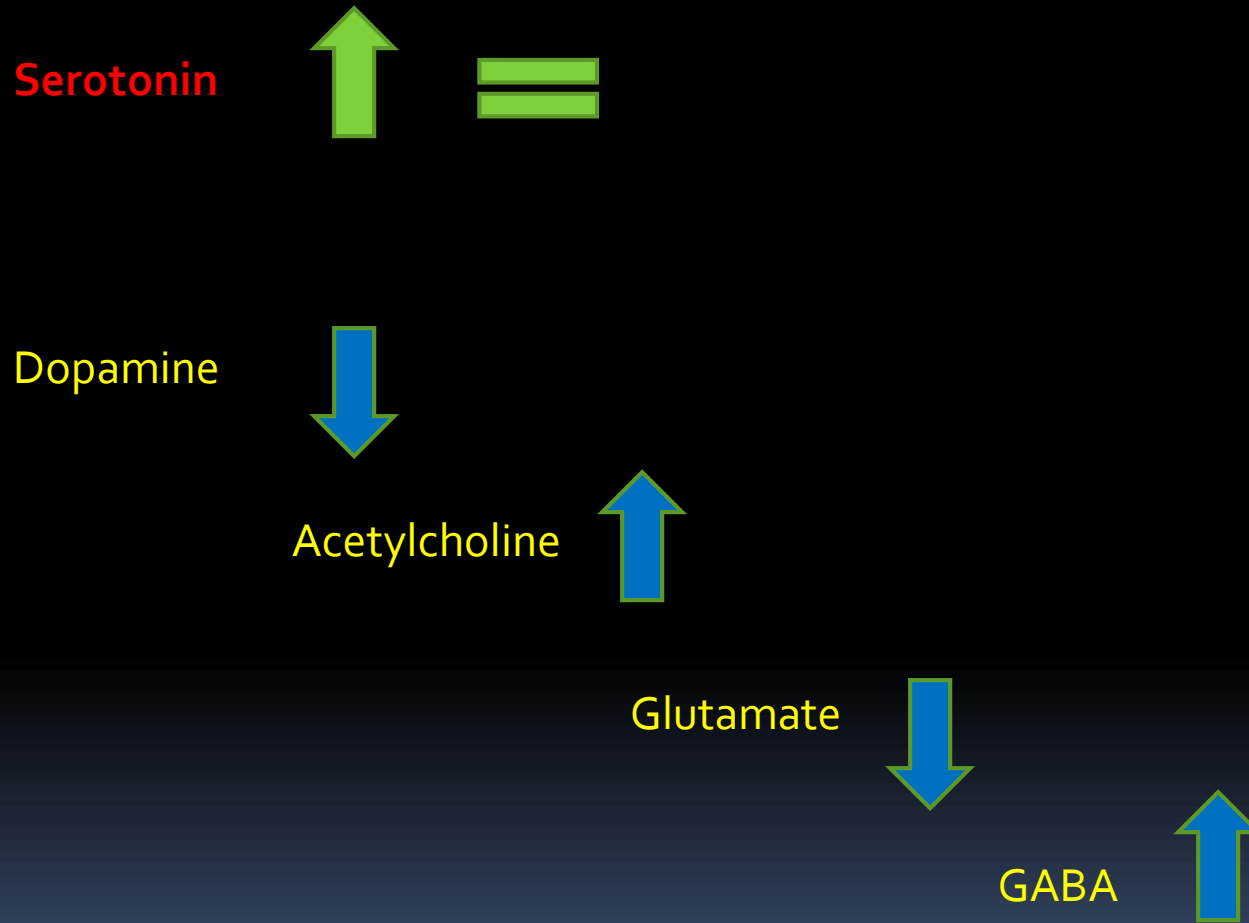
Synergistic Effect versus Contraindication

6. Medications will not resolve suffering if they are not preceded by correct diagnosis (i.e., appropriate intervention relies on accurate assessment)

Since the 1970s, across all genre including psychiatry, 40% of diagnoses are misdiagnoses or missed diagnoses.

The Ten Rules

7. Changing one neurotransmitter does more than one thing!



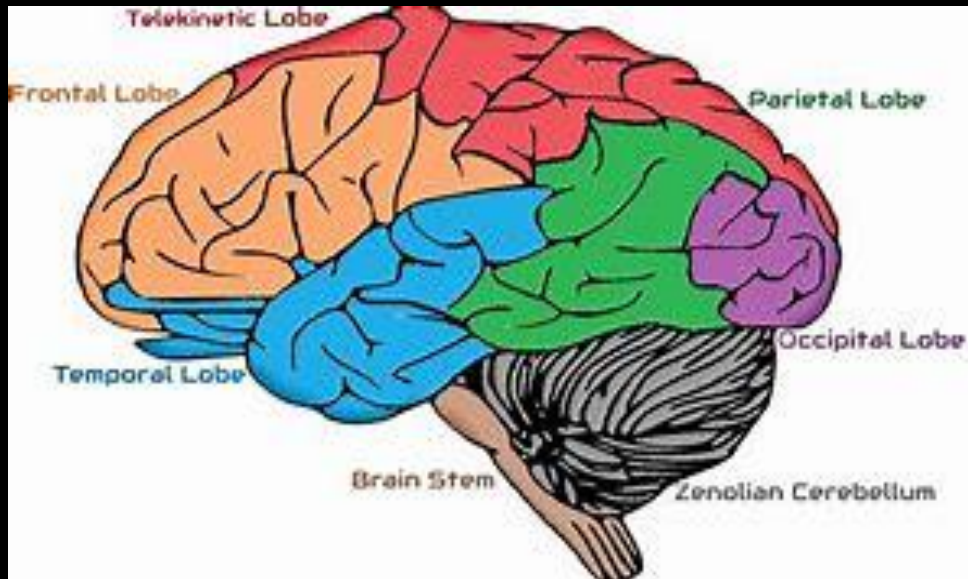
Basic Tenents

The Ten Rules

8. Withdrawal from a drug will often manifest in symptoms that are the opposite of the drug's desired intent

9. Sometimes “no diagnosis” or “no medications” are the sometimes the correct answers

10. Psychopharmacology is far more difficult than some people perceive it to be !



What is the main role of the brain?

Protection!

Front lobe (prefrontal cortex) maturation:

- Females (18 years-old)
- Males (25 years-old)
- Societal Complexity and the Age of Emancipation:
In the past it was 19 and now it's 25



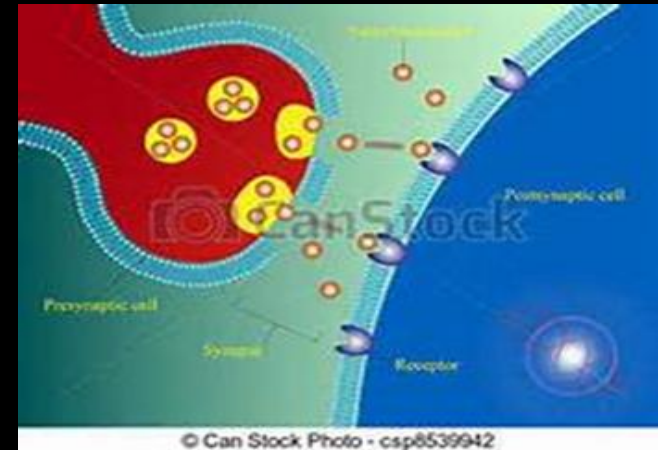
- **Neuron Organization (Types: Sensory, Motor, and Inter {throughout the body})**
 - **Soma (body)**
 - **Nucleus (genetic material)**
 - **Axon (send info)**
 - **Dendrites (receive)**
- **The brain is a collection of billions of cells (i.e., neurons) that are interconnected through networks.**
- **Neurons are “plastic” (intracellular modifiability) (e.g., new receptors and ion channels)**
- **The cells communicate primarily by sending (i.e., propagating) nerve impulses from one cell to another by chemical messengers. This process is called neurotransmission.**



- **Nerve cells tend to be linked based on the neurotransmitter they utilize in common (e.g., dopaminergic network for movement or the serotonergic network for appetite and sleep regulation).**
- **The bucket brigade analogy (intercellular)**
- ***Side effects often generate between networks. For example, an antidepressant acts primarily on the serotonergic system to change mood, but may inadvertently interact with the cholinergic system to cause dry mouth or constipation.***

Where medications work:

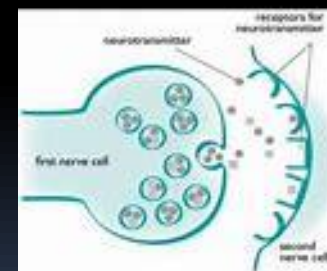
- **Receptors:** Protein molecules with binding (affinity) sites located on the cell membranes.
- “Lock and Key” analogy.
- **Bonds = ligands**



What medications do:

- **Agonist (enhance)**
- **Partial Agonists (diminish)**
- **Antagonists (block)**
- **Inverse Agonists (same site as agonist but different effect)**

Psychotropic Medications



Either:

1. Modify reuptake into the neuron (nerve cell)
2. Activate receptors
3. Inhibit receptors
4. Inhibit enzyme activity

Understanding Neurotransmitter Major Functions

While 100 are identified, only 20 are understood

- GABA: **Cognition and Inhibition**
- Serotonin (5HT): **Mood**
- Norepinephrine (NE): **Motivation and Vigilance**
- Dopamine (DA): **Reward and “Little” Movements**
- Acetylcholine (ACh): **Memory and “Big Movements”**
- Histamine (H): **Sedation**
- Glutamate: **Excitation (the “master switch” for all brain neurons)**

Understanding Neurotransmitters

Serotonin (5HT) *5-hydroxytryptamine*

- **Concentrations: 2% Brain, 8% Blood, and 90% GI (Enteric and Peripheral NS)**
- **Regulation of mood, appetite, sleep, pain, and suicidal ideation**
- **Mediates both excitatory and inhibitory activity**

Understanding Neurotransmitters

Norepinephrine (NE)

- **Noradrenaline**
- **Adrenergic system: “Fight, Fright, or Flight”**
- **Responsible for motivation, fatigue and executive functions (e.g., concentration, problem solving, planning)**

Understanding Neurotransmitters

Dopamine (DA)

- **Reward and Risk**
- **Fine motor movements**
- **Makes work seem effortless**
- **Peaks at age 16**
- **“Dopamine hijack”**
- **Different pathways**

Understanding Neurotransmitters

Acetylcholine (Ach)

- **Memory**
- **Cognitive functions**
- **Movement**
- **Needs to balance with dopamine**

Understanding Neurotransmitters

Glutamate “Gas Pedal” (Sympathetic NS)

- **Excitatory**
- **Memory**
- **Plasticity**
- **Can reach neurotoxicity**
- **Sympathomimetics**

GABA “Brake Pedal” (Parasympathetic NS)

- **Inhibitory (sedatives, hypnotics)**
- **Anticonvulsants**
- **Anxiolytics (anti-anxiety)**
- **Parasympatholytics**

Balance each other out

Half-Life:

- Estimated time for half of the original dose to be metabolized and eliminated from the bloodstream (plasma concentration)
- For example, the half-life of a NSAID is about two hours. If you take Ibuprofen 400 mg at 12:00, then half of the dose (i.e., 200 mg) will have been eliminated by 2:00. By 4:00, 100 mg will have been eliminated.
- Those with a short half-life become effective more quickly, but are harder to withdraw from and can lead to dependency over a period of time (e.g., Paxil is highly prone to serotonin discontinuation syndrome because its half-life is 15 hours)
- Generally it is considered that it takes 5.5-to-6 half-lives for a drug to no longer have a clinical effect or to clear the body.

Steady-State:

- **The dose that stays at therapeutic level**
- **The goal of any medication (e.g., antidepressant) is to achieve a point where the amount that goes into the body is equal to the amount that is eliminated.**
- **It takes about four times the half-life for the concentration of a drug to reach a steady-state in the body.**

The Implications of the P450 Enzymes for Psychopharmacology

Drug-Metabolizing Enzymatic Genes

- **Pharmacogenomics (i.e., drug-gene testing) study how genes affect the body's response to medication**
- **Tests search for genetic variations (e.g., related to ethnicity) to determine whether a medication could be an effective treatment or whether side effects are likely to occur from a specific medication.**
- **Thus far, about 12 genes measured for about 50 drugs**
- **Hope versus Hype**

Function: Narrowing the Operational Parameters of the Prescribing

The Implications of the P450 Enzymes for Psychopharmacology

Examples:

- **3A4 breaks down most medications**
- **2D6 breaks down most psychotropics. Specifically, this enzyme primarily metabolizes fluoxetine, paroxetine, venlafaxine, desipramine, and nortriptyline**
- **2C19 primarily metabolizes citalopram, escitalopram, clomipramine, and amitriptyline**

Genetic Enzyme Testing



GeneSight Psychotropic Results



Patient, Sample

DOB: 7/22/1984

Reference: 1456CIP
Clinician: Sample Clinician

Order Number: 9299
Report Date: 1/24/2014

Antidepressants

USE AS DIRECTED

bupropion (Wellbutrin®)
desvenlafaxine (Pristiq®)
levomilnacipran (Fetzima®)
vilazodone (Vibryd®)
vortioxetine (Brintellix®)

USE WITH CAUTION

citalopram (Celexa®) [2,4]
clomipramine (Anafranil®) [3]
desipramine (Norpramin®) [1]
doxepin (Sinequan®) [3]
duloxetine (Cymbalta®) [1]
escitalopram (Lexapro®) [2,4]
fluoxetine (Prozac®) [3,4]
fluvoxamine (Luvox®) [1,4]
mirtazapine (Remeron®) [1]
nortriptyline (Pamelor®) [1]
sertraline (Zoloft®) [2,4]
trazodone (Desyrel®) [3]
venlafaxine (Effexor®) [3]

USE WITH INCREASED CAUTION AND WITH MORE FREQUENT MONITORING

amitriptyline (Elavil®) [1,6]
imipramine (Tofranil®) [1,6]
paroxetine (Paxil®) [1,4,6]
selegiline (Emsam®) [2]

Antipsychotics

USE AS DIRECTED

asenapine (Saphris®)
clozapine (Clozaril®)
fluphenazine (Prolixin®)
haloperidol (Haldol®)
lurasidone (Latuda®)
olanzapine (Zyprexa®)
piperidone (Invega®)
quetiapine (Seroquel®)
thiothixene (Navane®)
ziprasidone (Geodon®)

USE WITH CAUTION

aripiprazole (Abilify®) [1]
chlorpromazine (Thorazine®) [1]
iloperidone (Fanapt®) [1]
perphenazine (Trilafon®) [3]
risperidone (Risperdal®) [1]
thioridazine (Mellaril®) [3,8]

USE WITH INCREASED CAUTION AND WITH MORE FREQUENT MONITORING

Report will be different for each person

- [1]: Serum level may be too high, lower doses may be required.
[2]: Serum level may be too low, higher doses may be required.
[3]: Difficult to predict dose adjustments due to conflicting variations in metabolism.

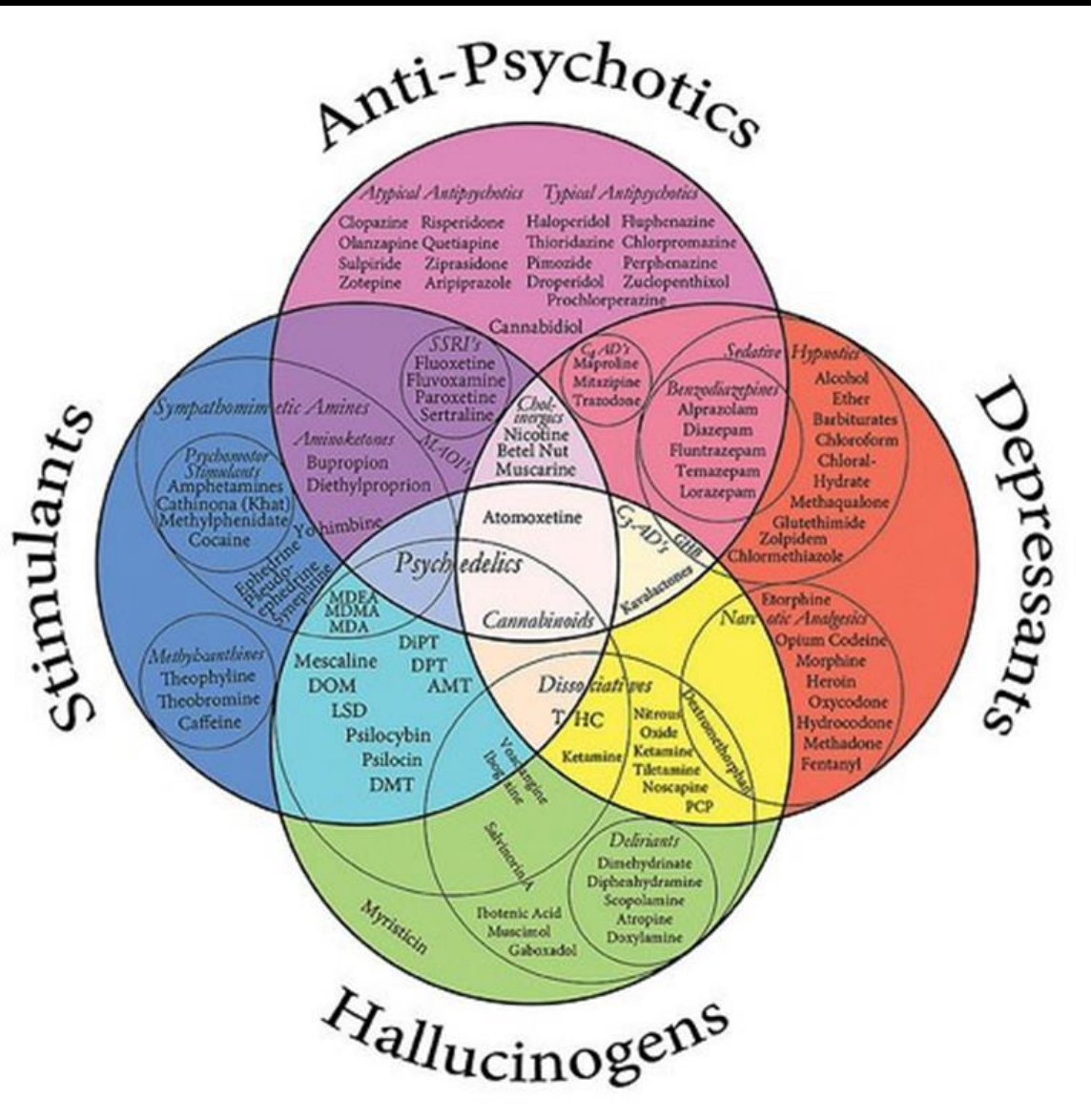
- [4]: Genotype may impact drug mechanism of action and result in reduced efficacy.
[6]: Use of this drug may increase risk of side effects.
[8]: FDA label identifies a potential gene-drug interaction for this medication.

All psychotropic medications require clinical monitoring.

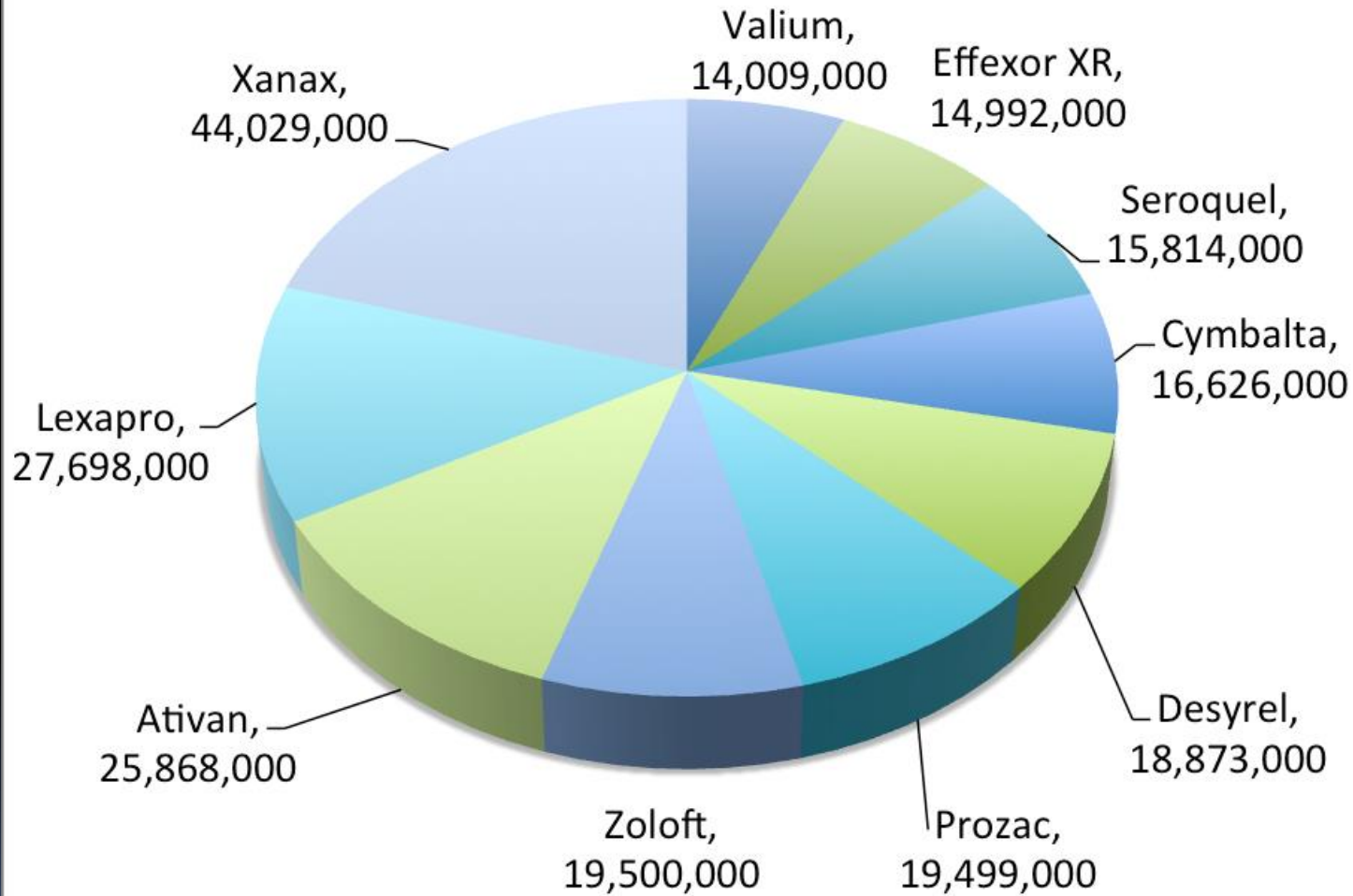
Drugs are reported in alphabetical order. This report is not intended to imply that the drugs listed are approved for the same indications or that they are comparable in safety or efficacy. The brand name is shown for illustrative purposes only; other brand names may be available. The prescribing physician should review the prescribing information for the drug(s) being considered and make treatment decisions based on the patient's individual needs and the characteristics of the drug prescribed.

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10 most prescribed psychiatric drugs in the U.S.



Treatment of Depression

- **Symptoms are out of proportion for the circumstances and persistent**
- **Rule-out medical causes:**
 - **Sleep disorders**
 - **Gastrointestinal (e.g., leaky gut, poor diet, vitamin D or B12 deficiency)**
 - **Hypothyroidism (20% of depressive cases)**
 - **Urinary Tract Infection**
 - **Low testosterone**
 - **Mild cognitive disorder**
- **Consider depressive equivalents (e.g., irritability, aggression, conflicts, somaticizing, brooding)**
- **Mild-to-moderate depression: psychotherapy is indicated**
- **Moderate-to-severe depression: combination of psychotherapy and medication**

Treatment of Depression

Hypotheses Across Time...

- Catecholamine hypothesis (1965), particularly related to norepinephrine. ***No evidence to support the neurotransmitter deficiency or chemical imbalance theory.***
- Cortisol hypothesis: Stress response
- Down-regulation hypothesis: Auto-receptors
- Neurotropic hypothesis: New discoveries
 - Existing neurons are able to repair through homeostatic equilibrium (drugs “insult” the brain which tries to protect and compensate)
 - Neurogenesis

Treatment of Depression

Tricyclic Antidepressants

- **Three ring molecular structure**
- **Mechanism of action (if released today) is SNRI**
- **Narrow therapeutic index: lethality**
- **Often prescribed for their side effects (e.g., imipramine [enuresis] and amitriptyline [sedation, pain management])**

Treatment of Depression

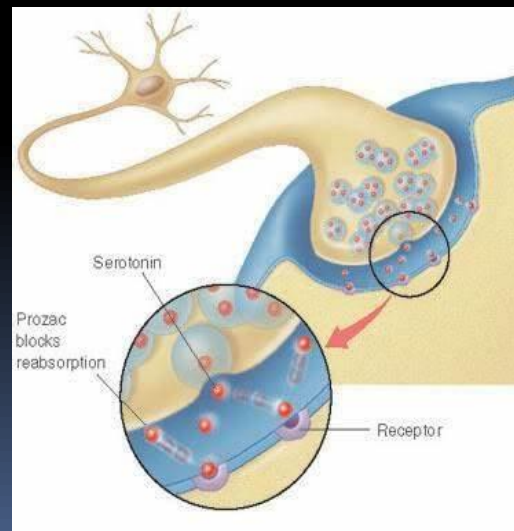
Monoamine Oxidase Inhibitors

- **First discovered as an anti-tuberculosis drug**
- **Blocks breakdown of neurotransmitters**
- **More effective than tricyclics for atypical depression**
- **Nardil is the gold standard; now Emsam as a transdermal patch**
- **Common adverse drug reactions: dietary restrictions (food with tyramine), anticholinergic effects, and hypotension**

Treatment of Depression

Selective Serotonin Reuptake Inhibitors

- They are intended to have little effect on NE, DA, GABA, glutamate, and Ach; hence the term “selective”
- Typical point of maximum benefit is 35 weeks



Treatment of Depression

Selective Serotonin Reuptake Inhibitors

Fluoxetine (Prozac)

- The “grandfather “ (1986)
- Indicated for major depression, OCD, PMDD, bulimia, and panic disorder
- Positive for childhood depression
- 7 day half-life (no withdrawal syndrome)
- Weekly doses as Serafem
- Marketed as Symbyax (combined with Olanzapine) for bipolarity and treatment resistant depression

Fluvoxamine (Luvox)

- FDA approved for OCD and social anxiety disorder
- Up to 4 weeks to generate good effect
- 17 hour half-life

Treatment of Depression

Selective Serotonin Reuptake Inhibitors

Sertraline (Zoloft)

- FDA approved for MDD, PMDD, panic disorder, PTSD, OCD and Social Anxiety
- Mild antipsychotic properties
- Most potent SSRI, but also most dangerous
- Safe for pregnancy

Citalopram (Celexa)

- FDA approved for depression
- 36 hour half-life with few side effects
- Doses not greater than 40 mg
- Safe for elderly; unsafe for pregnancy
- Antihistamine effect (sedating)
- Left and right sides of molecular structure

Escitalopram (Lexapro)

- Indicated for major depression and generalized anxiety
- Best tolerated antidepressant and most effective at lower doses
- About 30 hour half-life
- Only the left side of the molecular structure (cleanest)

Treatment of Depression

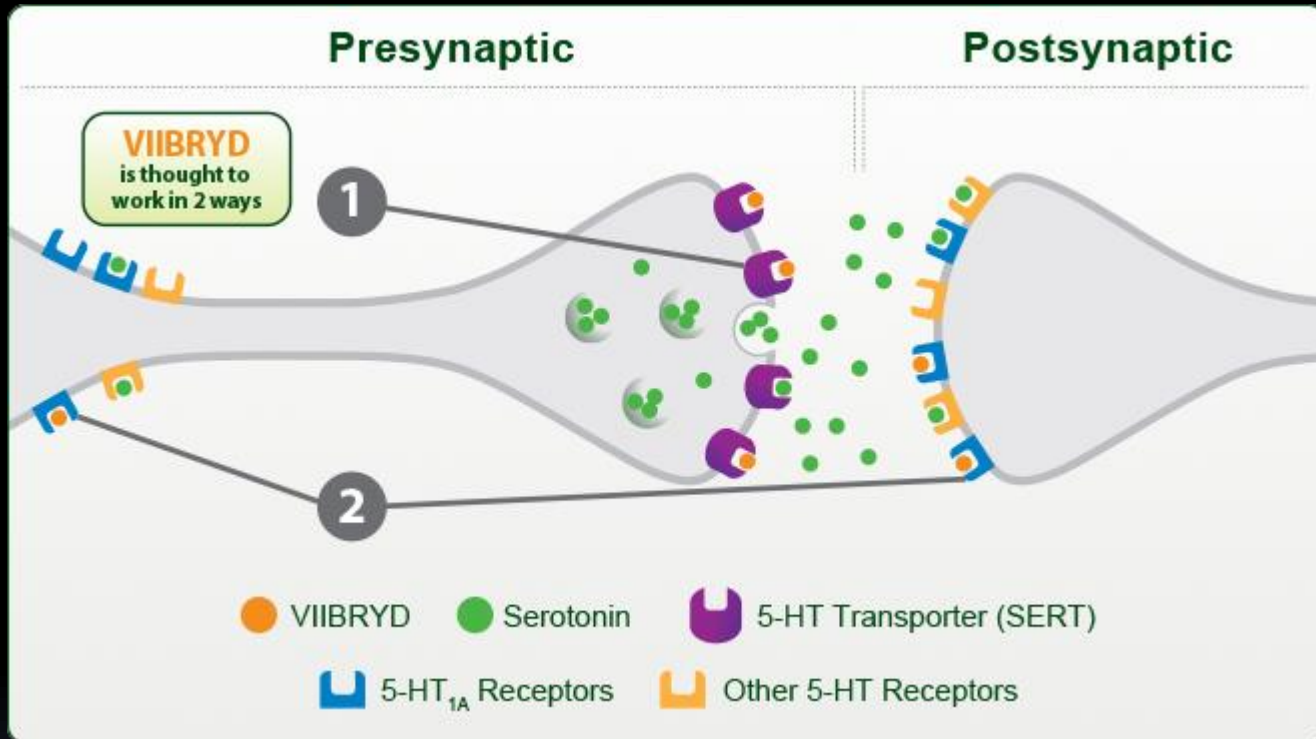
Serotonin Modulators and Stimulators

Vilazodone (Viibryd)

- Indicated for major depression (2011)
- Why the double “l” in the spelling?
- **Multimodal or two mechanisms of action**
- Serotonin reuptake inhibitor and 5-HT_{1A} receptor partial agonist
- An antidepressant and anxiolytic in one pill
- Fewer sexual side effects and weight gain liability

Vortioxetine (Trintellix) formerly Brintellix

- “Me-Too Drug”
- FDA approved for major depression with a new mechanism of action
- Agonist of 5-HT_{1A} and antagonist of 5-HT₃ and 5-HT₇
- Causes nausea
- Expensive at \$200 monthly (versus generic SSRI at \$20)



Presynaptic: Sends Impulses
Postsynaptic: Receives Impulses

Treatment of Depression

Common SSRI Adverse Drug Reactions:

- Insomnia
- Sexual dysfunction
- Restlessness
- Gastrointestinal symptoms
- Suicidal (disinhibiting effect)
- Apathy or amotivation (affects DA)

Serotonin Withdrawal/Discontinuation Syndrome

- **Autonomic Nervous System Dysfunction**
 - Dizziness
 - Anxiety
 - Muscle aches or spasms
 - Fever
 - Tachycardia
 - Nausea
- *To be expected with Paxil and Luvox!*
- *Watch for polypharmacy effects (e.g., Need “wash-out” period switching MAOI to SSRI; Caution using with other 5-HT agonists, such as St. John’s Wort, TCAs, Decongestants)*

Serotonin and Norepinephrine Reuptake Inhibitors

The Dual Agents

Venlafaxine (Effexor)

- Indicated for MDD, generalized anxiety, social phobia and panic disorder
- Half-life up to 13 hours
- Initiation and withdrawal issues
- Contraindicated with hypertension and cardiac history

Desvenlafaxine (Pristiq)

- Metabolite of Venlafaxine
- Fewer side effects

Duloxetine (Cymbalta)

- Depression plus treats fibromyalgia, neuropathic and musculoskeletal pain
- Originally a bladder stabilizer
- 12 hour half-life (offers 30% pain reduction but many discontinue due to side effects)

Levomilnacipran (Fetzima and Savella)

- Depression with fibromyalgia
- Strong NE Inhibitor

Atypical Antidepressants

Mirtazapine (Remeron)

- Tetracyclic antidepressants (TeCA)
- Noradrenaline and Serotonin Antagonist
- Sedation and weight gain (“Big Benadryl”)

Bupropion (Wellbutrin)

- NE and DA reuptake Inhibitor
- Activating and stimulating effects
- Nicotine cessation
- Few side effects as it's not serotonin based

Desyrel (Trazodone)

- Developed in 1982
- Serotonin antagonist reuptake inhibitor (SARI)
- Sedating Antidepressants (treats depression and insomnia)

Other Treatments

- Transcranial Magnetic Stimulation
- Electroconvulsive Therapy
- Cardiovascular Exercise
- St. John's Wort

Treatment of Depression

Spravato (Esketamine)

- Treatment for major depression
- Plant-based spray
- PCP analog
- Possible psychotomimetic effect

Star*D Study:

- **The largest real-world study of treatment-resistant depression sponsored by NIMH and published in 2006**
- **Sequenced Treatment Alternatives to Relieve Depression**
- **47% response rate to SSRI, but the odds of beating the depression diminish as additional treatment strategies are needed**
- **Boosting agents (e.g., Lithium)**

Psychopharmacology: *The Basics and Beyond*

Part II

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Services***

Presentation Objectives

- Differentiate between psychiatric medications, such as mood stabilizers, anxiolytics, antipsychotics, and somnolents
- Recognize side effects associated with the psychotropic medications
- Learn ways to assess medication usage and seek psychiatric consultation
- Better understand prescribing with special populations
- Identify future trends in psychotropics

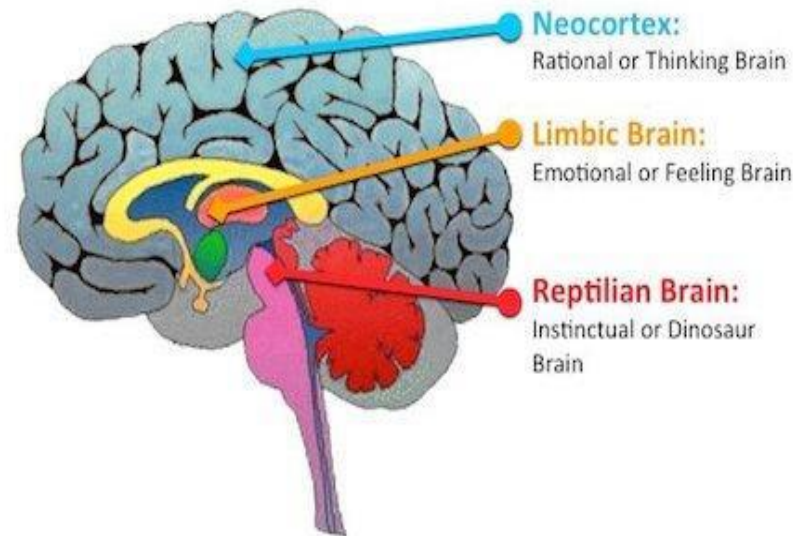
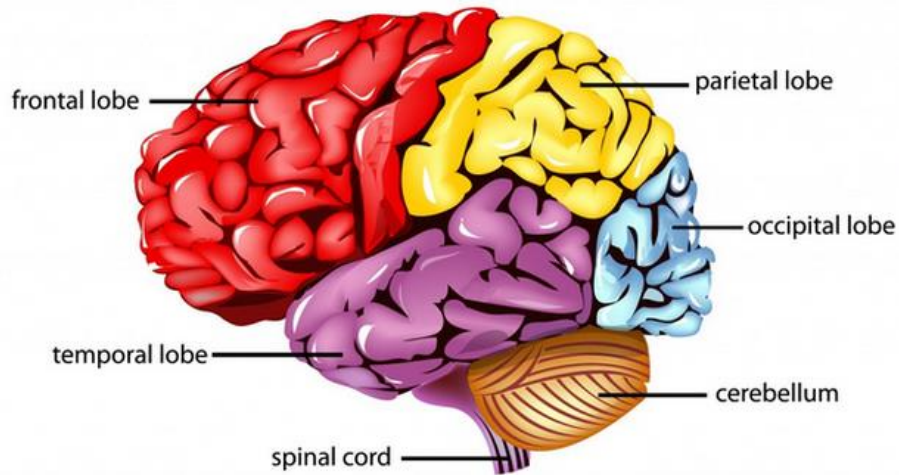
Anxiety-Based Disorders

- ***Anxiety is the most ubiquitous symptom***
- ***Autonomic Nervous System: Sympathetic vs. Parasympathetic***
- ***Diagnoses include the following:***
 - ❖ ***Generalized Anxiety***
 - ❖ ***Panic Disorder***
 - ❖ ***Social Phobia***
 - ❖ ***PTSD***
 - ❖ ***OCD***

The anxiety and trauma-response systems in the brain are overlapping

Integration of Brain Regions

Parts of the Human Brain



Limbic System

- Amygdala that detects threat (fight, flight, and freeze reactions)
- Hippocampus for memory storage
- Hypothalamus relays sensory information and activates the autonomic nervous and endocrine systems

Frontal Cortex

Responsible for planning, emotional control, thinking flexibly, self-monitoring, and decision-making.

CROSS SECTION OF THE HUMAN BRAIN

Corpus callosum

A large band of nerve fibres through which information flows back and forth between the left and right hemispheres of the brain

Thalamus

The relay station for most information going into the brain

Hypothalamus

Regulates sex hormones, blood pressure and body temperature

Pituitary Gland

The master gland of the body - produces its own hormones and also influences the hormonal production of the other glands in the body

Amygdala

Regulates the heartbeat and other visceral functions and process the emotion fear

Hippocampus

Helps establish long-term memory regions of the cerebral cortex

Basal ganglia

A control system for movement and cognitive functions

Cingulate gyrus

Cooperation, cognitive flexibility, and ability to see options

Cerebellum

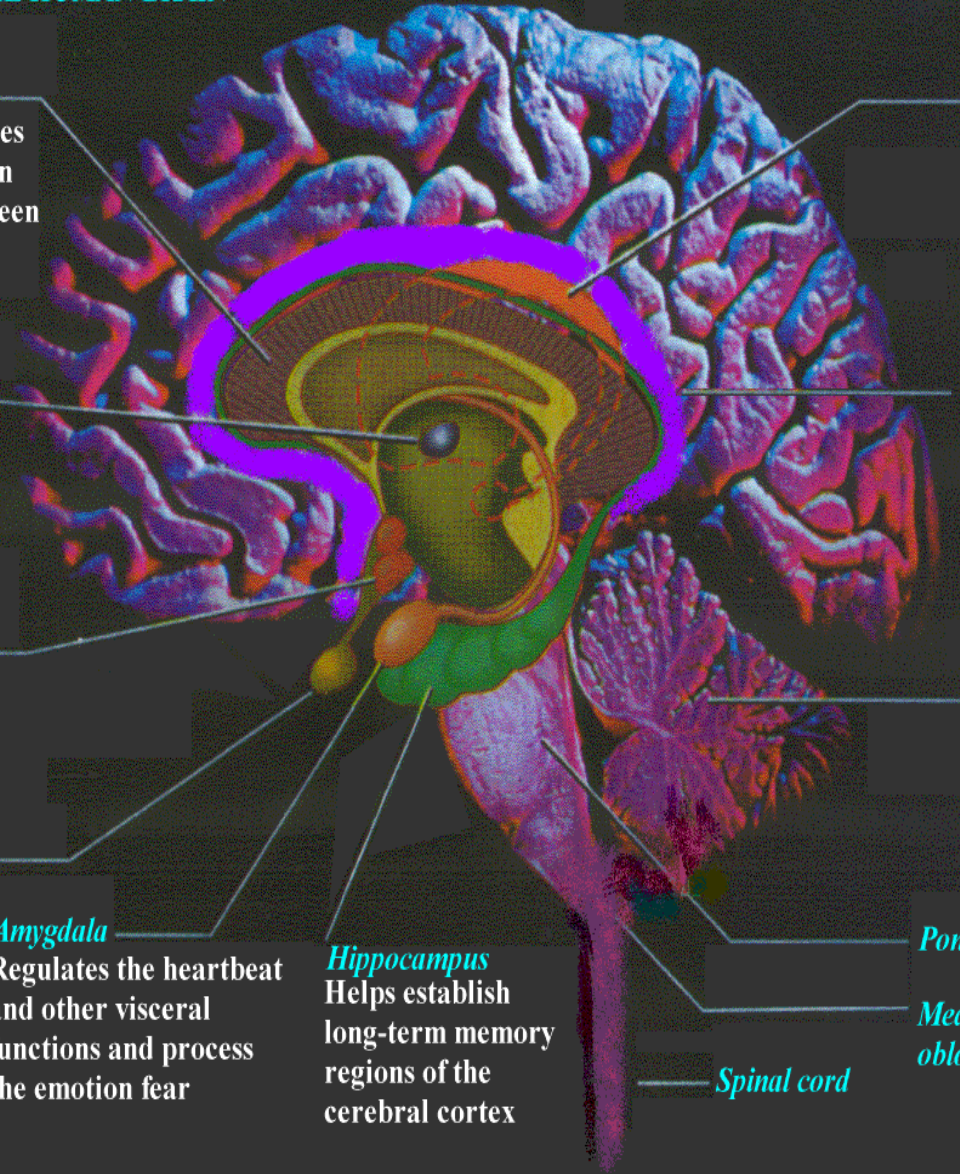
Essential for coordination of movement

Pons

Medulla oblongata

Control of breathing, circulation, heartbeat and digestion

Spinal cord



Two Pathways to Anxiety:

Bottom-Up: A swift triggering of emotions that links senses and/or perceptions with the “igniting” of the amygdala, which then activates the sympathetic nervous system. You react in milliseconds even before your cortex can think!

Top-Down: Negative cognitive interpretations of stimuli (e.g., catastrophizing, pessimism, perfectionism, guilt) trigger the amygdala and then the autonomic nervous system.

- **Ways to create anxiety:**
 - **Frontal lobe anticipates**
 - **Right hemisphere produces images**
 - **Left hemisphere worries and ruminates**

Presentation Exercise: Activating the Amygdala

Anxiety-Based Disorders

- **One amygdala on each side of the brain, but they work as a unit.**
- **The amygdala has hundreds of cellular circuits dedicated to different purposes and timetables (e.g., aggression, fear, attachment, etc.). It “pairs” information for “relevance.”**
- **Amygdala has many connections to monitor and influence the cortex; it controls the reaction (i.e., fight, flight, freeze, etc.) where some are preprogrammed and others are “trained.”**
- **The amygdala is irrational (it errs toward caution) and learns from experience through neuroplasticity (“exposure versus avoidance”)**
- **Aerobic exercise and REM sleep reset the amygdala (e.g., completing the circuit).**

Why do first responders react different to threat or athletes differently to stress?

They train in safe environments to quiet the amygdala...

Anxiety-Based Disorders

Anxiolytics or Antianxiety Medications

- ✓ **Benzodiazepines**
 - ✓ **Antidepressants (SSRI or SNRI)**
 - ✓ **Beta Blockers**
 - ☐ **Buspar**
 - ☐ **Monoamine Oxidase Inhibitors (MAOIs)**
 - ☐ **Anticonvulsants**
 - ☐ **Atypical Antipsychotics**
-
- ✓ *...Plus Psychotherapeutic Approaches (we can quiet the amygdala with medications, but not necessarily the negative thinking)*
 - ✓ *Individuals with anxiety and depression who engage in forms of self-mutilation (e.g., hair pulling, nail biting) are most vulnerable to endorphin and dopamine “rush”*

Benzodiazepines (Mild Tranquilizers)

A benzo is a benzo...it's all about half-life and potency

Ativan

Xanax

Klonopin

Valium



- Inhibit GABA by opening chloride channels
- Produce widespread sedation in the body
- Reduce anxiety by inhibiting the neural process
- Temporary solution that doesn't rewire the brain

Pros

- Rapid psychoactive effects (fast relief)
- Only intended for time-limited use (2-4 weeks)

Cons

- Highly addictive (tolerance and dependence)
- Risk for fatal overdose from respiratory suppression, especially with alcohol
- Prone to paradoxical reactions: Disinhibition and Impulsivity
- Side effects include emotional blunting and memory problems
- Depression and even seizures with abrupt withdrawal
- Poor sleep agents because they decrease REM

Rebound Effect: Benzodiazepines and the Amygdala

Anxiety-Based Disorders

Beta Blockers:

- **Inderal (Propranolol)**
- **Lopressor (Metoprolol)**
- **Terormin (Atenolol)**

- **These drugs reduce palpitations, sweating, and tremors**

- **Often are prescribed for individuals with social phobia, panic, and essential anxiety**

- **Works from keeping epinephrine related neurotransmitters (e.g., adrenaline) from binding to receptors**

- **They keep the body from responding with fight or flight (reduce the sympathetic response)**

- **They interfere with the effectiveness of exposure-based psychotherapy**

Bipolar Disorder

- **Bipolar I, II, and III subtypes (e.g., mania, hypomania, cyclothymia, mixed episodes, and rapid cycling)**
- **Watch for irritability, increased energy, and awareness of effects of destructiveness as risk factors for suicide, especially during inpatient admissions and post-discharge from hospitalizations (i.e., the six-day warning signs; the amazing reversal; ideators vs. completers)**

Differential Diagnosis between Bipolar Disorder and Borderline Personality Disorder

- ***Comorbidity only 18%***
- ***Mood Swing Triggers: Bipolar Internal and Borderline External***
- ***Depression: Bipolar disabling and borderline still impulsive***
- ***Thinking: Only borderline is dichotomous***
- ***Affect: Bipolar lacks intensity***
- ***Care-seeking: Higher with borderline diagnosis***
- ***Conflicts: Bipolar ignores realities, whereas borderlines split***
- ***Mood states: Bipolar enduring and borderline few hours/days***

Treatments for Bipolar Disorder

- **Mood Stabilizers (term comes from pharmaceutical companies) and neuromodulators**
- **Primary side effect is cognitive dulling (e.g., anticonvulsants can lower IQ testing by one standard deviation in children)**
- **Mechanism of Action: Increase GABA or Decrease Glutamate**
- **Traditional Medications:**
 - **Lithium (suicide and self-harm preventative)**
 - **Depakote**
 - **Tegretol**
 - **Lamictal (Stephens-Johnson Syndrome)**
 - **Topamax**
 - **Neurontin**

Psychotic Disorders

- **Etiology: Dopamine hypothesis to Schizophrenia (1963)**

First Generation (1960s):

- **Neuroleptics and Phenothiazines**
- **Typical Antipsychotics (Positive Symptoms)**
 - **MOA: D2 Antagonist**
 - **Thorazine and Haldol**
 - **Prolixin Decanoate (Injectable)**
 - **Deinstitutionalization Movement**

Psychotic Disorders

Second Generation (1990s): Atypical Antipsychotics

- **Treat Positive and Negative Symptoms**
- **MOA: Serotonin-Dopamine Antagonist**
- **Primary risks include movement disorders, metabolic syndrome, and cardiac arrhythmia**

Mechanisms of Action of Antipsychotic Drugs

- **Major action is to block receptors for dopamine**
- **Typical antipsychotics are potent antagonists for dopamine receptors D2, D3, and D4**
- **As a result, they are powerful in treating target symptoms but also producing extrapyramidal side effects.**
- **Newer atypicals like Clozaril are relatively weak blockers of D2, which lowers the incidence of EPS.**
- **Atypicals also inhibit reuptake of serotonin that helps to treat the depressive features of schizophrenia.**

Common Atypical Antipsychotics

- Zyprexa (Olanzapine)
- Risperdal (Risperidone)
- Geodon (Ziprasidone)
- Seroquel (Quetiapine)
- Saphris (Asenapine)
- Clozaril (Clozapine)
- Latuda (Lurasidone)

Third Generation Antipsychotics (with adjunctive mood treatment)

- Abilify (Aripiprazole)
- Rexulti (Brexpiprazole)
- Vraylar (Cariprazine)

Approximately 20% of antipsychotics are prescribed in primary care settings

Risks with Antipsychotic Medications

- **Black box warnings for dementia-related psychosis and suicide risk**
- **Dystonia (involuntary muscle movements)**
- **Akathisia (mental and physical restlessness)**
- **Extra-Pyramidal/Extra-Parkinsonian Side Effects (neurons in the brain for movement are affected causing rigidity, tremors, and swallowing problems)**
- **Tardive Dyskinesia**
 - **Usually abnormal movements of the mouth and face; may also include rocking of the trunk and irregular breathing**
 - **Lower dose, change medications, or administer anticholinergic medication**
 - **The body always tries to balance acetylcholine and dopamine**
 - **Tongue is most sensitive to acetylcholine issues**
 - **Abnormal Involuntary Movement Scale (AIMS) used to detect and track the severity of tardive dyskinesia**
 - **Treated with Cogentin (Benzatropine) and Ingrezza (Valbenazine)**

Risks with Antipsychotic Medications

- **Cardiac arrhythmia (i.e., polarization changes cause elongation of the Q-T interval or the approximate time for the heart ventricles to start contracting to finish relaxing)**
- **Metabolic Syndrome (Cluster of cardiovascular and diabetic risks especially with Zyprexa and Clozaril) such as glucose intolerance and poor lipid metabolism**
- **Weight Gain Liability**
- **Neuroleptic Malignant Syndrome: Dopamine blockade can cause potentially lethal effects. Fatal in 11% of cases. Higher risk with typical antipsychotics. Creatine phosphokinase (CPK) blood marker.**

Posttraumatic Stress Disorder

- **Pre-existing vulnerability**
- **Becoming symptomatic versus resiliency development**
- **Zoloft and Paxil**
- **CBD**
- **Eye Movement Desentization and Reprocessing (EMDR) Therapy**

Attention-Deficit/Hyperactivity Disorder

- **Previously Attention Deficit Disorder**
- **Evidence before the age of 12**
- **Three Types: Inattentive, Hyperactive, and Combined**
- **Most common in children (up to 18%)**
- **Risk Factors: low birth weight, malnutrition, fetal alcohol exposure, lead poisoning, acetaminophen use during pregnancy**
- **Heritability factor**
- **Hypoactivation of prefrontal cortex and parietal network**
- **Disruption in synaptic pruning**

Attention-Deficit/Hyperactivity Disorder

- **Psychostimulants: Paradoxical mechanism of action on sympathetic nervous system toward “freeze”**
- **Increasing Dopamine raises risk of cardiac event**
- **Methylphenidate: Ritalin, Concerta, Quillivant , and Focalin**
- **Amphetamine: Dexedrine, Adderall, Aptensio, Adzenys, Mydayis, and Evekeo**
- **Methamphetamine: Desoxyn; highly addictive**
- **Vyvanse: Drug of choice for Adult ADHD (lisdexamfetamine the prodrug of dextroamphetamine)**

Attention-Deficit/Hyperactivity Disorder

- **Strattera: NE and DA reuptake inhibitor; up to 8 weeks before results**
- **Antihypertensives: Blocks sympathetic nervous system to decrease energy; dosed at night**
 - **Guanfacine: Tenex and Intuniv**
 - **Clonidine (Catapres and Kapvay)**
- **Nutritional approach: Vayarin and Accentrate**
- **“Academic Doping” of stimulants**

Anti-Dementia Medications

1. Acetylcholinesterase inhibitors are prescribed for mild-to-moderate symptoms. They are intended to preserve functioning or delay worsening. These include Aricept, Cognex, and Exelon.
2. Other medications that regulate glutamate can be prescribed to treat moderate-to-severe symptoms. For example, Namenda.

Unfortunately, dementia is typically not detected and diagnosed until the middle-to-late stages, especially for individuals with I/DD.

Wakefulness Promoting:

- Provigil and Nuvigil
- Hypothetical mechanism of action: dopamine reuptake inhibitor

Sleep Aids

One-third of adults in US report insomnia

Benzodiazepine-Based:

- **Most commonly used treatment of insomnia**
- **Safer than older sleep medications such as the barbiturates**
- **Should only be used on short term basis since psychophysiological dependence can occur.**
- **Can produce a "hangover" effect the following day.**
- **Concerns about REM suppression leading to poor restorative sleep**
- **Examples include Halcion (Triazolam), Restoril (Temazepam), and Klonopin (Clonazepam)**

Sleep Aids

Non-Benzodiazepine Sedative-Hypnotic Drugs (Benzodiazepine Receptor Agonists)

- **Better safety profiles and less adverse effects**
- **Ambien (Zolpidem)**
 - **Helps fall and stay asleep**
 - **Half-life is two hours**
- **Sonata (Zaleplon)**
 - **Fast-acting**
 - **Half-life is one hour**
- **Lunesta (Eszopiclone)**
 - **FDA-approved in 2004 as a longer-lasting sleep agent**
 - **Six hour half-life**

Rozerem (Ramelteon): melatonin receptor agonist

Cannabis (THC)

- **Limited research**
- **70 unique compounds (“it hits everything”) with multiple MOA**
- **Endocannabinoid System (ECS) involved in an array of processes from reproduction to memory**
- **Increases need for cognitive effort (memory, processing speed) especially for those under 17 years-old**
- **CBD (cannabidiol is the medicinal part; marijuana’s “first cousin”)**
 - **About 40% of the plant’s extract (THC below 0.5)**
 - **No interference with psychological or psychomotor activity**
 - **Treats multiple issues (e.g., seizures, neuropathic pain)**
- **Epidiolex**
 - **Investigational drug**
 - **Liquid formulation of highly purified CBD**
 - **Remarkable effects for epilepsy**
 - **Approved for seizures related to Dravet and Lennox-Gestaut syndromes**

Opiates and Opioids

- **Analgesic: Relieve pain without unconsciousness**
- **Historical events: World War I, Hospice movement, Perdue Pharma, and “Pseudo-addiction”**
- **Epidemic: Opioid Triad (coma, pupil constriction, and depressed respiration)**
- **Diversion by healthcare professionals (1914 Harrison Act)**
- **Opiate Receptors: Naturally occurring Endorphins, Enkephalins, and Dynorphins**
- **Addiction (Tolerance, Withdrawal, and Compulsion)**
- **Chronic Use: Decreases in testosterone, estrogen, melatonin, and adenosine**

- **Natural Narcotics: Morphine and Codeine**
- **Semisynthetic Narcotics: Heroin, Dilaudid, Oxycontin, Percocet**
- **Totally Synthetic Narcotics: Demerol, Fentanyl, Methadone**

- **Partial Agonists:**
 - **Butrans (patch) and Belbuca (film)**
 - **Potentially lower abuse potential due to ceiling effect**
- **Antagonists: Narcan (Naloxone)**
- **Mixed Agonist-Antagonist: Suboxone (Buprenorphine and Naloxone)**

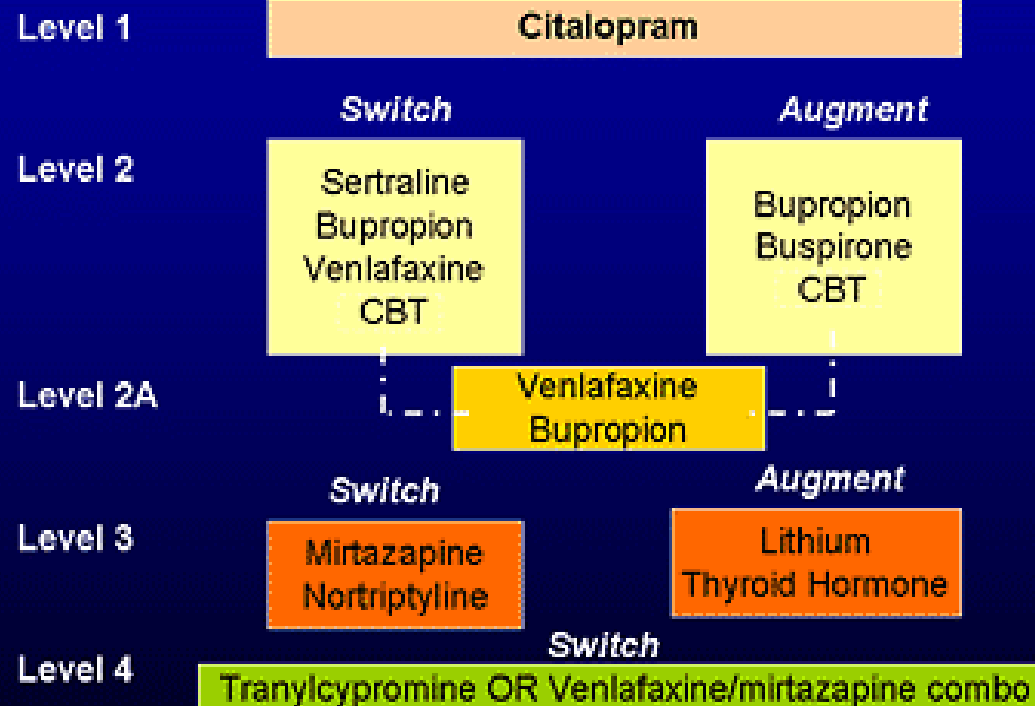


When are Psychotropics Appropriate?

- Failure of non-psychotropic based interventions, rather than an inadequacy or unavailability of services
- Risk of harm to self or others
- High intensity and frequency of challenging behaviors
- Presence of a accurately diagnosed psychiatric disorder
- To stabilize an individual in order to implement non-medication-based interventions
- Favorable past response to psychotropics
- Individual/Guardian preference as part of their person-centered plan (risk-to-benefit profile as part of informed consent)

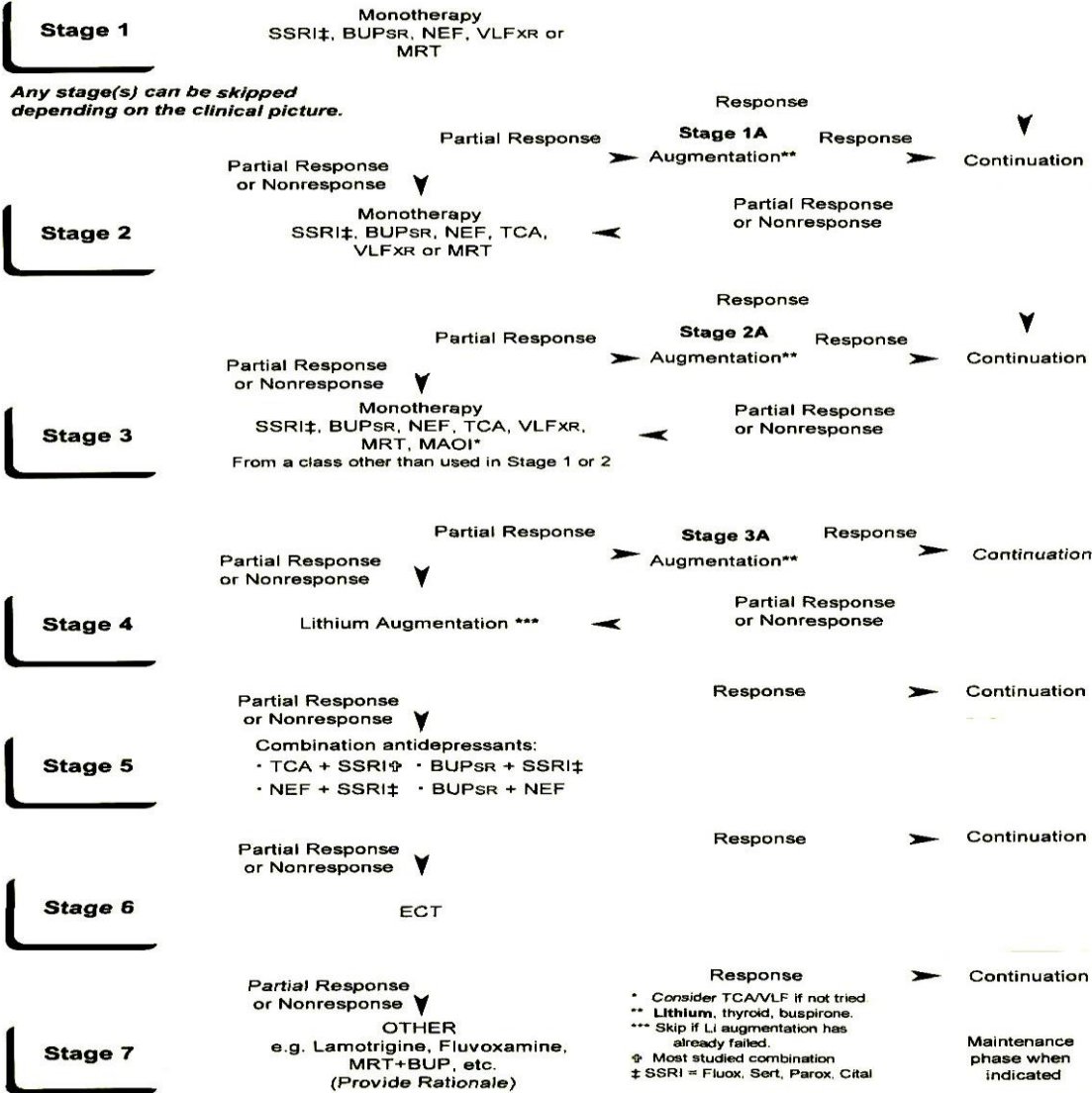
** Start low and go slow...lowest possible dose and minimum duration*

STAR-D† Algorithm for Depression



†Sequenced treatment alternatives to relieve depression, target enrollment N=4000
 Rush AJ et al. *Control Clin Trials*. 2004;25:119-142.

The Texas Medication Algorithm Project (TMAP) Nonpsychotic MDD



Psychotropic Medications and Special Populations

- **Developmental Disabilities**
- **Elderly**

Developmental Disabilities

- There was an expectation that psychotropic prescribing for those with I/DD would eventually decrease just like institutionalization, but it never fully materialized.
- In the area of I/DD, currently only two psychotropic medications are FDA-Approved. That is, Risperdal and Abilify to treat “irritability” (i.e., aggression, tantrums, SIB) in children and adolescents with autism spectrum disorder.

Developmental Disabilities

Why is there so much polypharmacy with IDD?

Diagnostics:

- Albeit difficult to diagnose, multiple studies reflect that those with I/DD have a higher prevalence of mental illness when compared to the general population and that they can suffer from the entire range of psychiatric diagnoses.
- The diagnostic prevalence rate of psychotic disorders in the I/DD population is 3-5%. However, 30-50% of psychotropics prescribed to those with I/DD are antipsychotics.
- **Psychiatric misdiagnosis: One issue is providers “working backwards” by using the response to prescribed medications as the guide to arrive at a working diagnosis.**
- **“Inherited” prescribing combined with poor advocacy**
- **Developmental disabilities is a marginal area of training in psychiatry and psychology**
- **Staff and caregiver attitudes about destabilizing or worsening**

Developmental Disabilities

Concerns about Psychotropic use for those with I/DD

- Higher than recommended doses
- Excessive reliance on medications
- Unknown long-term effects
- Lack of compelling evidence to support effectiveness
- Use of medications without informed consent
- Difficulty determining and communicating adverse effects

Unknowns...

- Individuals with I/DD are a heterogeneous group with complex and fragile neurological profiles, which makes them more vulnerable to adverse effects (e.g., metabolism and tolerability issues).
- Growing neurological evidence (e.g., fMRI) suggests that those with developmental disabilities (i.e., ID and ASD) experience problems with synaptic pruning and dendrite malformation. Medications may help to “fertilize” synaptic connections.

Developmental Disabilities

Mistaken Belief in the Power of Psychotropics to Manage Challenging Behaviors

- Although often used beyond their FDA indications, psychotropic medications are regularly used to manage behaviors of concern among those with I/DD.
- In general, approximately 20-45% of those with I/DD receive psychotropic medications, many of whom to treat problem behaviors in the absence of a psychiatric diagnosis.
- Medication trials should be:
 - Targeted at specific symptoms (e.g., irritability)
 - Monitored for effectiveness using data collection
 - Regularly evaluated for risk versus benefit of continuation

Developmental Disabilities

- **Symptomatic treatment versus understanding the etiology! (e.g., headache)**
- **We need to thoroughly investigate medical conditions, environmental contributions, emotional issues and psychiatric disorders that influence a behavior of concern before giving consideration to a trial of medication.**
- **Mental health issues might not be recognized and are attributed to the I/DD (i.e., diagnostic overshadowing bias).**
- **Adults with I/DD have higher rates of sensory impairments, cardiovascular disease, and gastrointestinal problems—all of which can influence prescribing and metabolism.**

***DDS Program Review Committee
Changes in 2018***

- 1. Individuals below the statewide average (currently 2.87) complete a psychiatric medication data entry form.***
- 2. Individuals above the average (i.e., 3 or more) with no additions of new medications or aversives, submit a PRC packet for paper review.***
- 3. Additions of new medications and/or new aversives require a full (in-person) PRC presentation.***

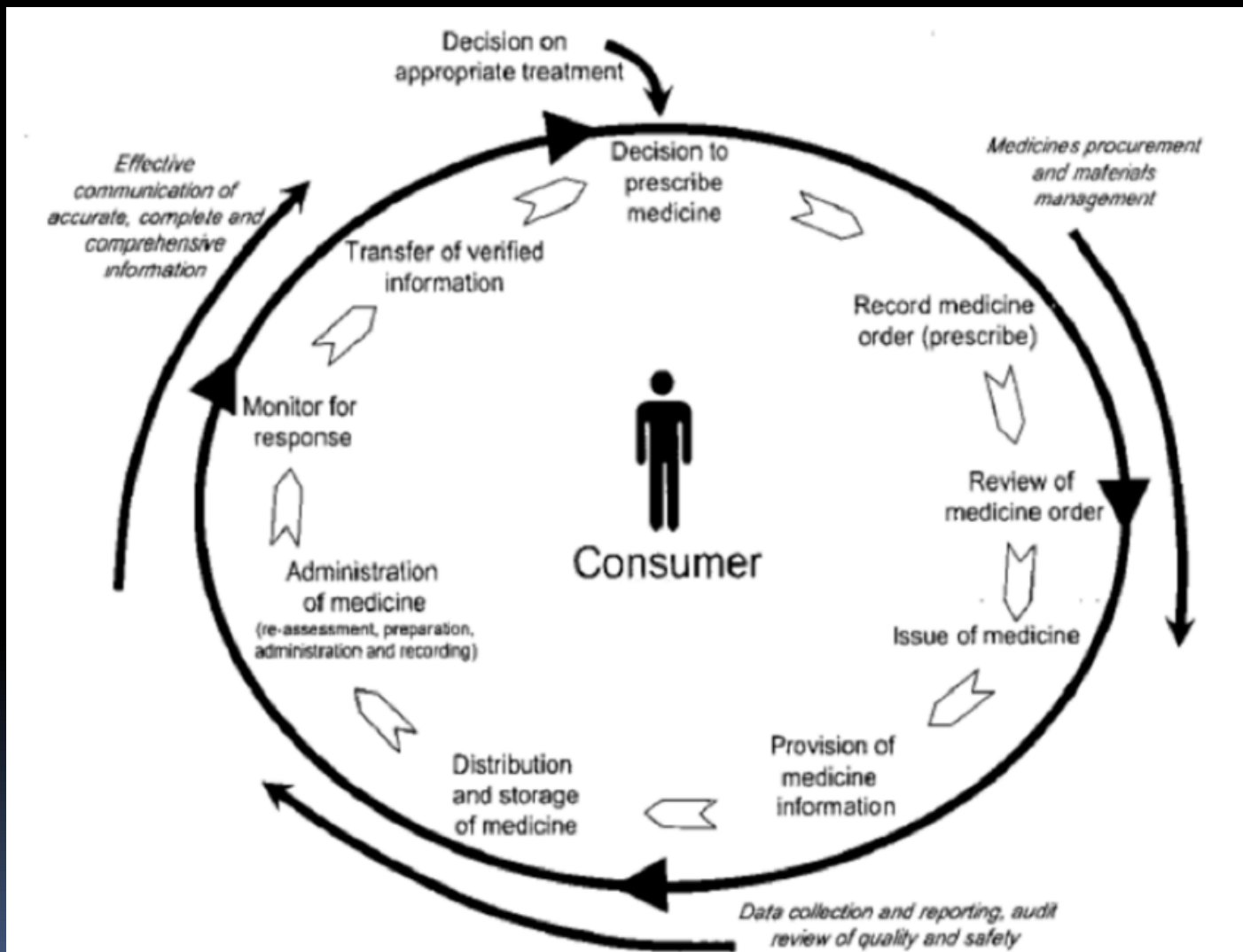
A number of challenges exist in determining the average number of psychotropic medications per individual-served due to the following:

- Newer psychotropics might not be in our database**
- Medications could falsely be entered as non-psychotropic**
- Anti-seizure medications used for mood might be listed as non-psychotropic.**

Elderly

- **Poorly researched group. Avoided due to confounds from medical illnesses.**
- **Beers Criteria (for Potentially Inappropriate Medication Use in Older Adults)**
- **Every year past 30, we lose up to 0.76% of liver and kidney functioning, so lower doses of medications may be most appropriate for this population.**
- **High-Risk Psychopharmacology**
 - **Tricyclic antidepressants**
 - **Benzodiazepines**
 - **Antipsychotics**
 - **Anticholinergics**
- **Disease Creep: the promotion of medications for conditions that pose no serious threat.**

Psychiatric Consultations



Helpful Tips for Psychiatric Consultations

- **Identify the specific symptoms and behaviors to target (e.g., insomnia and low motivation)**
- **Saying anxiety or depression is too generic**
- **Limiting to 3 or 4 symptoms helps reduce polypharmacy**
- **Focus on symptoms rather than sources of psychosocial and emotional distress (e.g., loneliness and sadness)**
- **Reducing intensity of symptoms (e.g., making affect manageable) might warrant consideration of PRN instead of a standing order**

Areas for Medication Evaluation

Risk

- Developmental factors
- Education and language
- Gender and sex
- Culture and Ethnicity
- Weight (gained or lost)
- Allergies
- Addictions
- Health Status and Medical Conditions (e.g., diabetes, seizures)
- Past drug interactions

Risk-to-benefit analysis: Why expose someone to risk of adverse side effects if we are not getting a symptom reduction?

Areas for Medication Evaluation

Knowledge and Monitoring

- Informed consent versus assent
- Educate which medications do what
- Diagnosis and Treatment Plan?
- Dosages and Appearance of Drugs?
- Side Effects?
- What to do if a dose is missed?
- What OTC medications are taken?
- At minimum, select one valued outcome that can be operationally defined, measured, and observed as a clear indication of improvement.
- Baseline versus interventional data collection (e.g., blood pressure)

Areas for Medication Evaluation

Communication

- Why are you taking these medications?
- Do they work? Validate concerns about medications.
- Any recent medication changes?
- Are you comfortable discussing medications with your provider?

Adherence

- Have you stopped taking medications on your own?
- Are you afraid of your medications?
- Do you know the potential risks to your medications?
- Do you do things to make the medications last longer?
- Are the medications that you are taking cause problems?

Areas for Medication Evaluation

- **If a combination of medications is effective, then try to reduce or remove the first medication (i.e., return to monotherapy as soon as possible)**
- **Studies suggest that a reduction in polypharmacy improves quality of life**
- **Psychotropic medications should be used to treat specific psychiatric disorders, rather than symptoms, and be just one part of treatment along with behavioral and psychosocial supports.**

Keys to Informed Consent *Prior to Initiation*

- **Medications are not dispensed without thorough evaluation**
- **Discussion of the specific condition to be treated**
- **Alternatives to medications are considered**
- **Risks and benefits associated with each medication are identified**
- **Least restrictive interventions primary**
- **Proper administration is ensured**
- **Monitoring safeguards**
- **Withdrawal strategies**
- **Drug tapering plan**

It's never inappropriate to inquire as to why a person is receiving overlapping medication treatments because the risk of negative side effects increases with the addition of each new drug.

De-Prescribing Protocols: *Concept from Geriatric Medicine*

- **Ascertain all the drugs the person is currently taking and the reasons for each one**
- **Consider the current and future benefit compared to harm potential**
- **Prioritize drugs for discontinuation starting with those that have least benefit, lowest adverse withdrawal reactions, and lowest disease rebound effect**
- **Monitor closely for improvement or adverse effects**

Future Directions in Prescribing

- **The era of molecular neurobiology (e.g., receptor specificity)**
- **The role of inflammation (e.g., corticotropic-releasing antagonists)**
- **Neurogenic Theory of Depression Treatment (i.e., *Neurogenesis: medications stimulate changes in the brain, especially neural integration*)**
- **Poor profitability for affective spectrum medications**
- **Focus on early stages of diseases**
- **Elective or Enhancement Psychopharmacology**

It is an art of no little importance to administer medicines properly, but it is an art of much greater and more difficult acquisition to know when to suspend or altogether omit them.”

-Philippe Pinel 1809