Psychopharmacology Considerations for Clinical Practice

np psych navigator

Finding the right psychotropic medication for your patients may help improve outcomes. When making treatment decisions, clinical practice guidelines and your past experience with medications can help guide your choice. However, when choosing a particular medication, it's important to consider the many factors that can influence the way different psychotropic agents can affect your patients.

Here we will discuss how pharmacology fundamentals can help inform treatment decision making and treatment monitoring. We'll start by walking through some of the key concepts as a refresher and then will discuss applications to clinical care.

PHARMACOKINETIC CONSIDERATIONS

When it comes to pharmacokinetics, or how the body affects the drug, you can remember key concepts by recalling this acronym—ADME—which stands for the 4 main physiological processes that occur in the body after drug administration (Fig. 1).[1] All of these processes affect a drug's concentration in the brain.

ADME

Absorption: the first step, when medication enters the body[1]

- Sites of absorption can include the skin, vasculature, gastrointestinal tract, and the respiratory tract.

Distribution: how medication is dispersed throughout the body[1]

- Distribution begins almost simultaneously with absorption into the systemic circulation.
- The rate of distribution is affected by speed of absorption and other characteristics, such as the patient's hydration status, regional blood flow, and the drug's ability to cross membranes to reach tissues.
- Drug concentration eventually balances out between the plasma and the tissues, but may be substantially different (higher or lower) in brain tissue depending on the patient.

Metabolism: medication breakdown[1]

- Most psychotropics are metabolized in the liver, but some are also metabolized in the brain and gastrointestinal tract.
- Oral drugs undergo "first-pass" metabolism, meaning drug concentration is greatly reduced before it reaches the systemic circulation.
- There are several factors that influence drug metabolism, including genetic variation (poor vs. rapid metabolizers), epigenetic phenomena, age, diet, comorbidities, and drug-drug interactions.

Elimination: excretion of medication from the body[1]

- Metabolic byproducts are excreted through the kidneys.

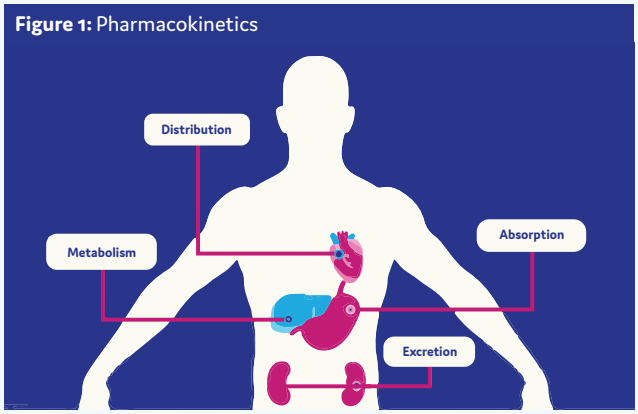
Clinical Applications

When choosing a medication, keep in mind that different routes of administration will affect absorption rate. For example, a nasal spray will be absorbed more quickly and therefore take effect more quickly than an oral pill that must first go through "first-pass" metabolism.[1] Moreover, different oral drug formulations, such as delayed-release (DR), immediate-release (IR), sustained-release (SR), and extended-release (XL) will also affect the rate and completeness of drug absorption and distribution.

Other drug characteristics, such as lipid solubility and protein binding affinity, can also slow and limit absorption and distribution.[1] Most psychotropics are highly protein-bound, which limits their bioavailability, or the amount of drug left to act on the body.

This information can be found in the drug's Prescribing Information within the Pharmacokinetics section.

Figure 1: Pharmacokinetics



Adapted from https://www.technologynetworks.com/drug-discovery/articles/what-is adme-336683

Duration of Effect

Once a medication is administered, its time course of effects can be described by 3 key concepts (Fig. 2):

Therapeutic Range[1]

- The range of drug serum or plasma concentration levels where the drug usually has its desired effects.

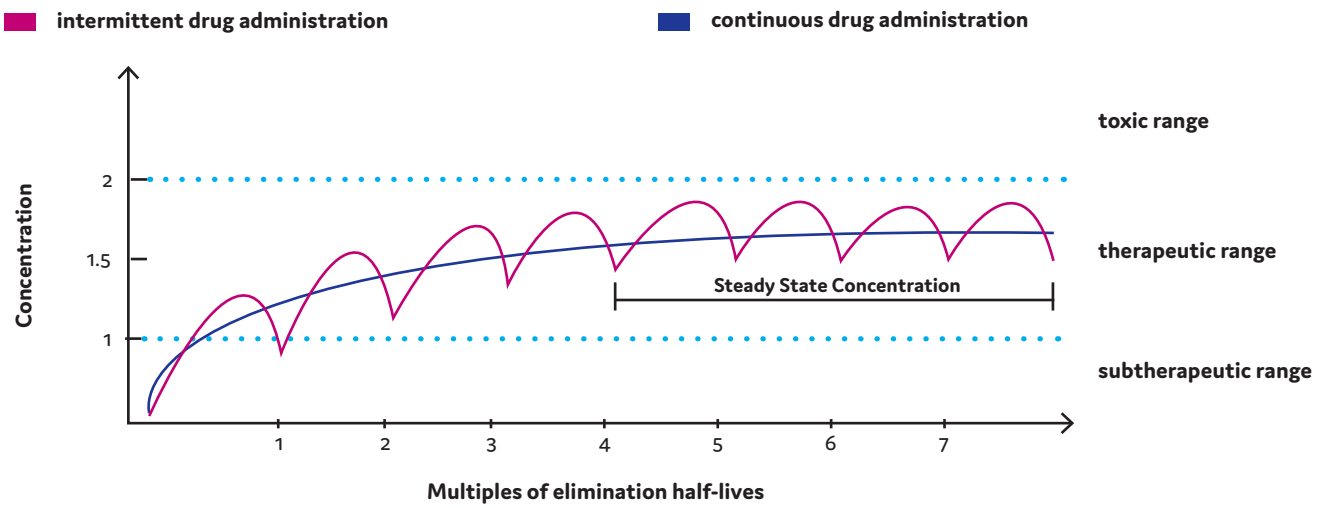
Steady State[2]

- When the amount of drug that's in the systemic circulation has peaked. (It's the same amount as what's being eliminated by the body when the drug is given continuously.)
- It's at this point that drug concentration consistently stays within the therapeutic range.

Half-Life[1]

- The time it takes for the peak plasma concentration of a drug to decrease by half.
- The half-life of a drug tells us how long it takes to reach steady state.
- For most psychotropic drugs, the time to reach steady state is 4-5 half-lives.
- So, after about 4-5 half-lives, the plasma concentration of the drug dips below the therapeutic range, and is considered to be eliminated.
- Drugs with shorter half-lives need to be tapered off more slowly to avoid discontinuation side effects.

Figure 2: Drug Duration of Effect



- Drugs with longer half-lives may be tapered off more quickly given their lower risk of discontinuation side effects. However, they may pose a higher risk of drug-drug interactions when they're discontinued and a new drug is started.

Clinical Applications

It's important to consider how drug plasma concentrations affect dosing curves. For example, if drug levels are out of therapeutic range, the medication could be less effective or even toxic.[1] Medication half-lives also affect the rate of elimination, which affects the time course of drug effects.[1] The goal of symptom management with medications is to ensure that the drug prescribed remains within therapeutic range.

This information can be found in the drug's Prescribing Information within the Pharmacokinetics section.

PHARMACODYNAMIC CONSIDERATIONS

How the drug affects the body is referred to as pharmacodynamics.[1] Each medication class has a different mechanism of action, which describes how they work in the body.

Mechanism of Action

Psychotropic medications take effect by interacting with:[2]

- Ion channels
- Intracellular G-protein coupled receptors (GPCRs)
- Inner membrane enzymes
- Intranuclear receptors

The resulting effects from these interactions are determined by the nature of the drug (Fig. 3):

Agonists[2]

- Drugs that bind to receptors and mimic their natural actions, thereby increasing activity levels.
- Partial agonists bind to a receptor and increase its activity but not to a full extent; therefore, the effects are not as strong as a full agonist.
- Inverse agonists bind to the same receptor as agonists but induce the opposite pharmacological response.

Antagonists[2]

- Drugs that block receptors, thereby decreasing activity levels.
- Antagonists can also be competitive, noncompetitive, or nonreceptor mediated in nature; partial antagonists will block a receptor but not to a full extent.

Clinical Applications

Understanding a drug's mechanism of action can help you determine rate of onset. Drugs that work on ion channels can produce effects within milliseconds, whereas others produce slower responses.[2] It's also important to note if, for example, the drug is a partial agonist rather than a full agonist.

This information can be found in the drug's Prescribing Information within the Mechanism of Action and Pharmacodynamics sections.

Medication Interactions

Psychotropic medications often affect the monoamine neurotransmitter systems. Some medication classes include:[3]

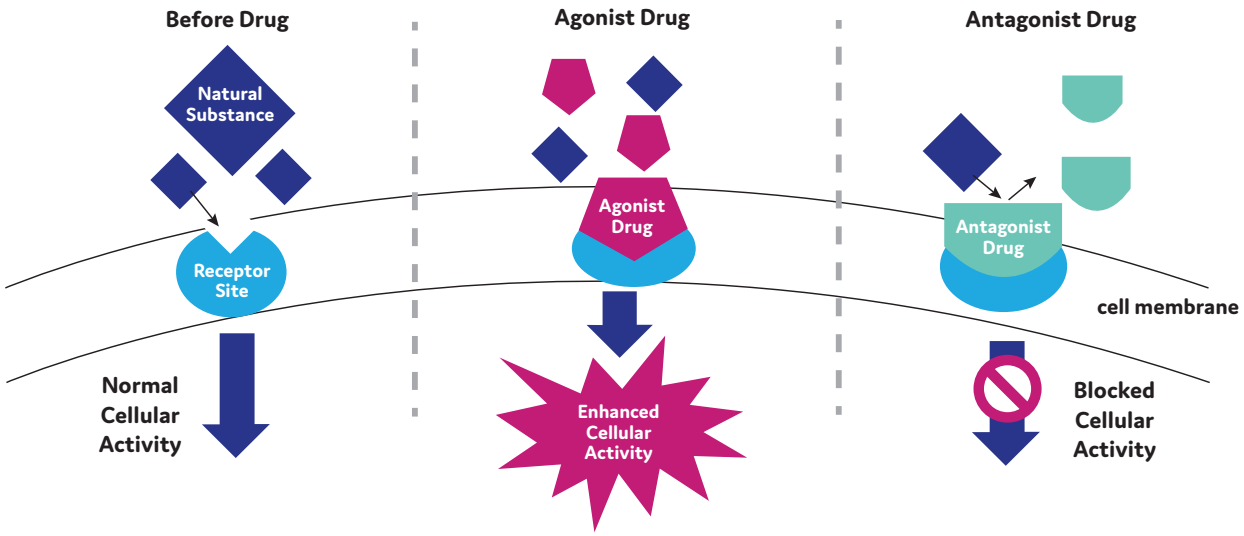
- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin and norepinephrine reuptake inhibitors (SNRIs)
- Monoamine oxidase inhibitors (MAOIs)

While there are differences in the way that each class is broken down, often they are metabolized by different isozymes of the CYP 450 pathway.[3] However, many other nonpsychotropic drugs, foods, and supplements are also broken down by this common pathway, thus causing:

Drug-Drug Interactions[4,5]

- The effects of psychotropic medications can be affected by medications taken for other conditions (e.g., oral contraceptives can interact with tricyclic antidepressants) and vice versa.
- Some commonly prescribed classes of medications that can interact with psychotropic drugs include antidepressants, anxiolytics, non-benzodiazepine hypnotics, opioids, statins,

Figure 3: Pharmacodynamics—Agonists and Antagonists



Adapted from https://en.wikipedia.org/wiki/Agonist-antagonist

calcium channel blockers, and beta-blockers.

- Drug-drug interactions may result in decreased or increased actions of the drugs and/or adverse effects.

Drug-Supplement Interactions[6]

- Common supplements like St. John's Wort affect this pathway.

Drug-Food Interactions[7]

- Common aged foods like cheese affect this pathway.
- For example, when combined with foods high in tyramine, like cheese, MAOIs can result in dangerously high levels of tyramine that can cause a hypertensive crisis.

Clinical Applications

It's very important to avoid drug-drug interactions. Concomitant medication use can increase or decrease the effects of psychotropic medications and negatively impact outcomes.[3] Be sure to get a full list of all medications and supplements your patients are taking prior to prescribing, and ask for any medication updates at their follow-up visits.

This information can be found in the drug's Prescribing Information in the Drug Interactions and Pharmacodynamics sections.

Making Informed Treatment Decisions

We've highlighted key points throughout, tying back key psychopharmacology fundamentals to clinical practice. Here we'll review a few important reminders:

- Identify factors specific to individuals that can affect the rate and extent of medication absorption, distribution, metabolism, and elimination.
  - Be sure to review your patient's entire medical history, including other medications they take, before prescribing; remember to ask about these at follow-up visits.
- Learn each drug's metabolic pathway to avoid side effects and drug-drug interactions.
  - Let your patients know about common side effects they may expect when they start treatment.
- Review the Prescribing Information of drugs you are considering prescribing.
  - In addition to the sections we've referenced, also take a look at Warnings and Precautions and Use in Specific Populations.

If you are ever unsure about a certain medication, remember to check the Prescribing Information so you can be properly prepared to set your patients up for success.

References

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