



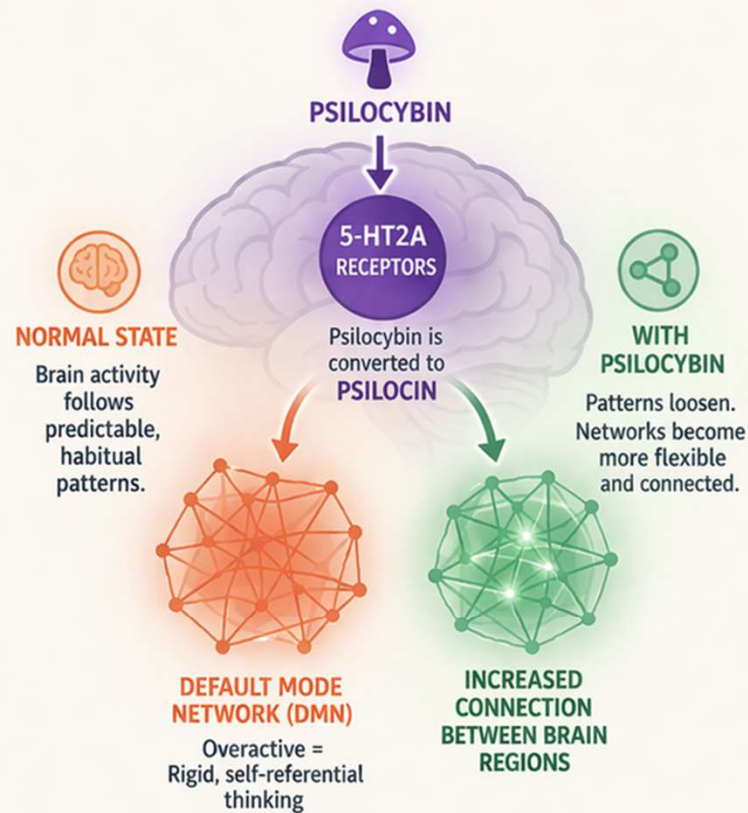
5 DEGREES NORTH HEALING FOUNDATION

PHARMACOKINETICS & PHARMACODYNAMICS CONSIDERATIONS

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How Psilocybin Works in the Brain

Simple, High-Level Mechanism



WHAT IT DOES:

-  Activates serotonin 5-HT2A receptors
-  Temporarily quiets the Default Mode Network (the brain's "habit" or autopilot system)
-  Increases communication between brain regions



WHAT YOU EXPERIENCE:

-  Altered perception
-  New perspectives & insights
-  Greater mental flexibility



BRAIN PLASTICITY:

The brain's ability to:

-  Adapt
-  Learn
-  Reorganize

Psilocybin may create a window where this natural ability is enhanced.



KEY TAKEAWAY:

Psilocybin temporarily shifts the brain out of rigid patterns and into a more **open, connected, and adaptable state**.

DRUG-DRUG INTERACTIONS

- **Drug-Drug Interactions (DD)** are when two separate substances act differently when taken together. These can happen because of pharmacodynamics *and* pharmacokinetics:
- **Pharmacodynamic drug-drug interactions** can happen when drugs with similar mechanisms of action overlap
 - These interactions aren't necessarily one substance's effect's compiling on another. They can be synergistic, where the two substances work more strongly together. They can be additive, where one substance enhances the effect of the other. They can also be diminutive, where one substance inhibits the action of the other.
- **Pharmacokinetic drug-drug interactions** happen when the metabolism or transport of a substance is changed. For instance, CYP liver enzymes can inhibit or increase blood concentrations of substances. These enzymes can be inhibited or induced by certain substances.
- **Drug-Disease Interactions** are when a drug exacerbates disease conditions, or when a disease interferes with a drug's action

DRUG-DRUG INTERACTIONS

- There are several ways that psilocybin and psilocin and medications can interact with each other, or with a pathophysiological diseases. Current literature has pointed out that few drugs have been shown to have pharmacodynamic influences on psychedelics, but individual patients with underlying disease process can affect their safety during their administration phase.
- For instance, blood thinners likely would not affect the metabolism of psilocybin or psilocin, but an individual patient will likely be on a blood thinner with a history of cardiovascular disease, or a with history of clotting or arrhythmia.
- While medications may not preclude patients from getting psychedelic therapy, their health history still can. Obtaining an individual patient's Medical History can be a significant factor for determining eligibility for psychedelic therapy.
- What we do know is that drug-drug interactions with psychedelics can have consequences on the safety and efficacy of psychedelic therapy.

PHARMACOKINETIC CHANGES IN THE ELDERLY

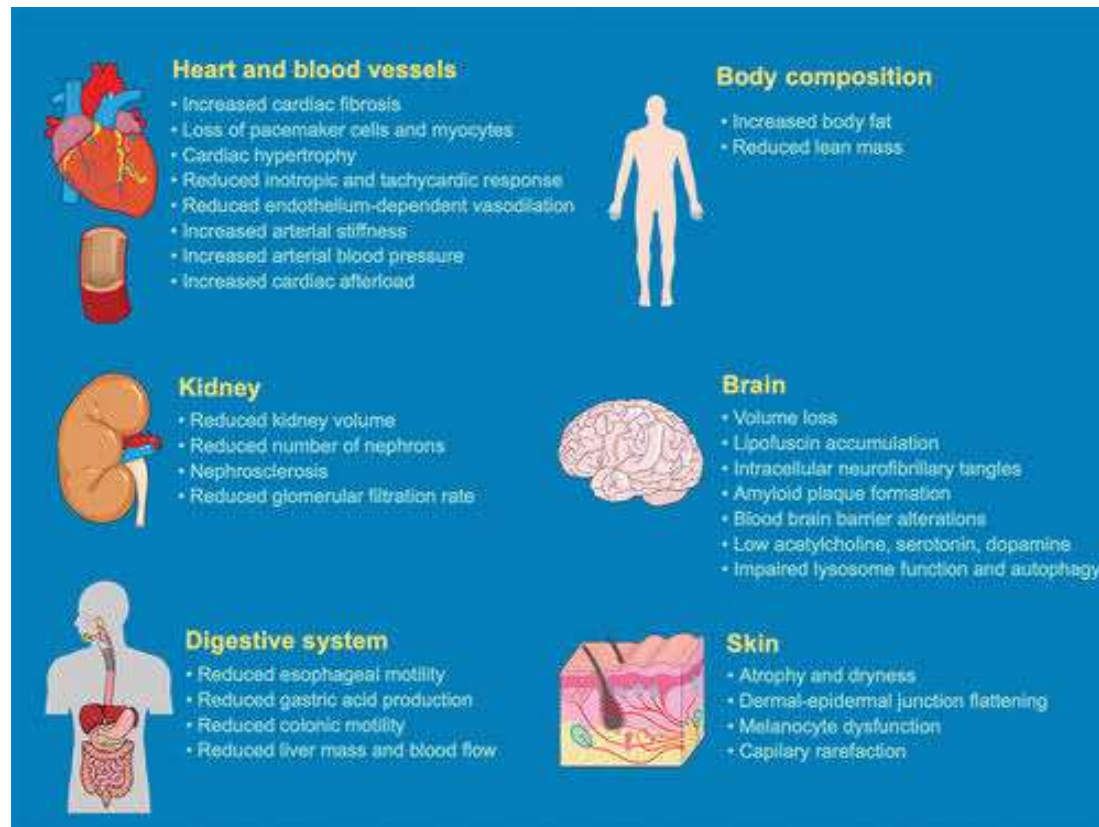
- **Pharmacokinetic (PK) Definition**: How the human body process a substance. It helps to quantify Psilocybin and Psilocin effective dosing to achieve therapeutic effects while minimizing toxicity.
- Aging affects the **Pharmacokinetics** in the body by altering your **absorption**, **distribution**, **metabolism**, and **excretion**. These Pharmacokinetic changes will lead to a slower elimination, and an increased sensitivity of substances.

PHARMACOKINETIC CHANGES IN THE ELDERLY

Aging causes progressive declines in organ function:

- **Liver**- Reduced CYP450 enzymes (slower metabolism)
- **Brain** – Reduced Volume & Cognition
- **Renal** – Reduced Number of Kidney Nephrons – Reduced Filtration ability and function
- **Cardiovascular System** – Reduced Cardiac Output and increased Stiffening of Arteries (atherogenesis)
- **Musculoskeletal** – Loss of Muscle Mass and Strength, Reduced B
- **Respiratory** – Reduced Lung Capacity, and impaired gas exchange
- **Digestive** – Reduced Liver Function, and Reduced GI Motility and Increase in Constipation
- https://www.merckmanuals.com/home/older-people-s-health-issues/the-aging-body/changes-in-the-body-with-aging#Eyes_v8967857
- <https://www.ncbi.nlm.nih.gov/books/NBK556106/>

PHARMACOKINETIC CHANGES IN THE ELDERLY



PHARMACOKINETIC CHANGES IN THE ELDERLY

What Does this Mean and How Will it Affect my Patient(s):

- Examples: Diazepam and Clonazepam have an active metabolite and is metabolized by CYP450 enzymes. CYP450 enzymes activity is reduced due to aging. This translates to a long half-life in elderly patients. Making the patient have an increased risk of falls and drowsiness.
- Example: Psilocybin and Psilocin have an active metabolite and is metabolized by CYP450 enzymes. CYP450 enzymes activity is reduced due to aging. This translates to a long half-life in elderly patients. Making the patient have an increased risk of hallucinations and an increased length of session.

A individuals patient's age will play a important role in how they will metabolize, and respond to psilocybin. This response will impact both the physiological and psychological aspects of their experience. Understanding age-related differences will enable the facilitator the ability to tailor dosing strategies.

PRATICAL APPLICATIONS FOR FACILITATORS

Facilitators should access the client's overall medical history during the preparation phase to help anticipate the potential metabolic differences. Adjust the initial doses from patients with known liver or GI Conditions:

Liver Health – Patients with liver impairments (Hepatitis, Cirrhosis, & Fatty Liver Disease) will metabolize psilocybin at a slower rate.

Suggestions:

1. Start with lower doses to avoid prolonged or intensified effects.
2. Monitor the patient closely for delayed reactions during and after the administration session.

Medications - Patients taking medications metabolized by the liver (antidepressants, anticonvulsants, others) may experience drug-drug interactions that will affect the metabolism of psilocybin.

PRATICAL APPLICATIONS FOR FACILITATORS

- **Gastrointestinal Health** – Discuss the history of gastrointestinal conditions and diseases, dietary habits, and stress levels that can affect the metabolism of psilocybin.
- **Weight & Body Composition** – Body weight and composition are important considerations in determining the patient's psilocybin dosage. While these factors can influence the metabolism and distribution with the body, they are not standalone determinants.
 - Example: **If a patient has a Higher Body Mass (HBM) vs a Lower Body Mass (LBM)** – HBM patient's often require larger doses of psilocybin to achieve the same level of effects as LBM. LBM patient's will experience a stronger or have more intense effects from the same given dosage. Example: A Men vs Women taking the same dose.
 - Example: **If a patient has a Lean Body Mass** – Patients with higher muscle mass percentages metabolize psilocybin at a quicker rate. A higher overall metabolic rate will lead to a quicker onset of action and a short duration of effects. Example: Athletes vs a Coach Potato
 - Example: **Hydration** – Adequate hydration is crucial for optimal metabolism and distribution of psilocybin. A dehydrated patient will experience a delayed onset and can have heightened effects.

PRATICAL APPLICATIONS FOR FACILITATORS

Example: **GLP1 Medications**

- If a patient is taking GLP-1 Medications, the patient will experience a delayed onset of action from the psilocybin dose due to the delayed gastric absorption caused by the GLP-1 medication. This slowing of gastric absorption can delay the onset by 2 to 6 hours depending on the patient previous GLP-1 dose, and the patient's individual pharmacokinetics and pharmacodynamics.
- Combinations of Psilocybin and Psilocin and GLP-1 medications can cause an increases in the occurances of Nausea and Vomiting. Both of these agents cause the nausea and vomiting individual, and when combined can caused an increased effects.

DRUG-DRUG INTERACTIONS

- There are several ways that psilocybin and psilocin and medications can interact with each other, or with a pathophysiological diseases.
- **Example:** For Blood thinners likely would not affect the metabolism of psilocybin or psilocin, but an individual patient will likely be on a blood thinner with a history of cardiovascular disease, or a with history of clotting or arrhythmia.

EXAMPLES OF DRUG INTERACTIONS

- **Example #1:** Fluoxetine (Prozac) a SSRI which tends to take a longer time to be completely eliminated from the body. For fluoxetine (Prozac) users may need the 6 weeks of antidepressant-free time before a full effect is restored.
- **Example #2:** Bupropion (Wellbutrin) a DNRI acts by inhibiting the reuptake of both NE and Dopamine. Bupropion and Psilocybin have different MOA's and do not directly compete at the receptors, therefore it is highly unlikely that you will experience a drug interaction.
- **Example #3:** Duloxetine (Cymbalta) a SNRI tends to take at least 2 weeks prior.

EXAMPLES OF DRUG INTERACTIONS

- **Example #4:** Mirtazapine (Remeron) blocks at the 5HT_{2A} receptor, thus is predicted to cause a Blunting effect. Discontinue 2 weeks prior.
- **Example #5:** Trazodone (Desyrel) blocks 5HT_{2A} receptors at low doses, and blocks serotonin reuptake pump with high doses. Discontinue at least 5 days prior.

Other Types Drug Interactions

Some substances that can interact poorly with mushrooms:



Stimulants

- Increase energy & anxiety



Opioids

- Slow reaction times, sedation



Alcohol

- Impairs judgment & coordination



Marijuana

- Enhances hallucinations



SEROTONIN SYNDROME (RARE RISK...USUALLY ENCOUNTERED WITH POLYPHARMACY)

- A rare condition caused by **excess serotonin activity**, usually from **multiple medications combined**
- Most often associated with:
 - **MAOIs**
 - **High-dose SSRIs/SNRIs with other serotonergic drugs**
- **Psilocybin alone → extremely low risk**
- **What to watch for (rare):**
 - Agitation or confusion
 - Sweating, rapid heart rate
 - Tremor or muscle twitching
- **Bottom Line:**
 - In **healthy individuals not on interacting medications**, this is **very unlikely**

HPPD (HALLUCINOGEN PERSISTING PERCEPTION DISORDER) VERY VERY RARE

- A rare condition where **visual effects persist after a psychedelic experience**
- **Examples:**
 - Visual trails
 - Light sensitivity
 - Mild visual distortions
- **What we know:**
 - Occurs in a **very small percentage of users**
- **More likely with:**
 - **High or repeated dosing**
 - **Polysubstance use**
 - **Underlying mental health conditions**
- **Bottom Line:**
 - In **healthy individuals, with preparation and controlled use**, this is **uncommon and typically mild**

MANAGEMENT OF SEROTONIN SYNDROME

Five principles are central to the management of Serotonin Syndrome:

- Discontinuation of all serotonergic agents
- Supportive care aimed at normalization of vital signs
- Sedation with benzodiazepines
- Administration of Serotonin Antagonists – Cyproheptadine is a histamine-1 receptor antagonist with nonspecific 5-HT_{1A} and 5-HT_{2A} antagonistic properties. It also has weak anticholinergic activity.
- Assessment of the need to resume use of causative serotonergic agents after resolution of symptoms

PSILOCYBIN AND PSILOCIN IN PARKINSON'S DISEASE

Early results from recent studies are showing Psilocybin and Psilocin, when combined with psychotherapy, is well-tolerated, and the potential benefits for treating both the Motor and Non-motor symptoms of Parkinson's Disease.

Positive Results:

- Improvements in mood
- Improvements in cognition
- Improvements in motor function
- reduces neuroinflammation, thus promoting neuroplasticity

Negative Results:

- Severe anxiety by individual patients during sessions
- Increased risk of hallucinations

- <https://www.ucsf.edu/news/2025/04/429906/how-magic-mushrooms-could-help-parkinsons-disease-patients>
- <https://www.nature.com/articles/s41386-025-02097-0>
- <https://clinicaltrials.gov/study/NCT06455293>

TIME FOR Q&A SESSION

**WHAT QUESTIONS DO
YOU HAVE?**

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