Antipsychotic Agents Summary

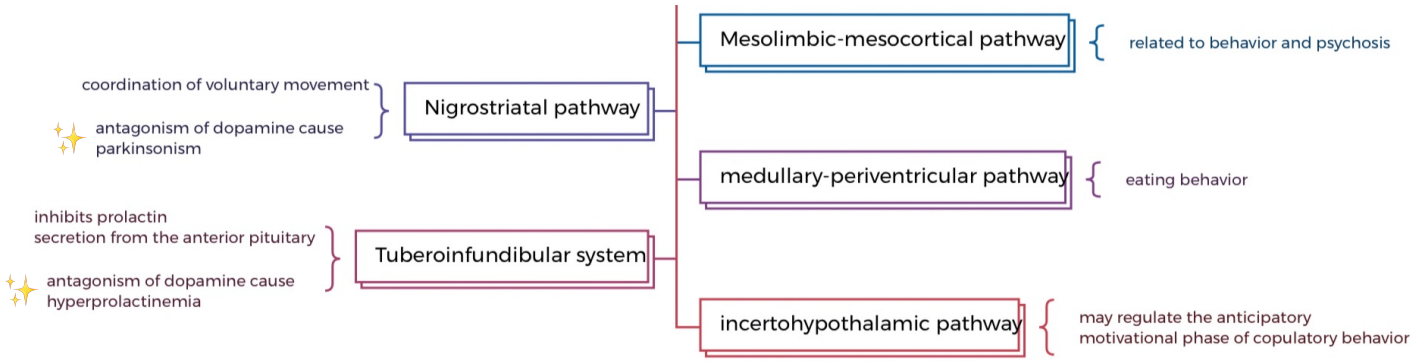
Things marked with ✨ are highly important

Nature of Psychosis & Schizophrenia

- Marked thinking and perceptual disturbance

1. delusions
2. hallucinations
3. grossly disorganized thinking in a clear sensorium

Dopaminergic systems in the brain



Mechanism of Action

1. Serotonin Hypothesis

- **block 5-HT2A** ➡️ modulate the release of dopamine and other neurotransmitters
- **Stimulation of 5-HT2C** ➡️ inhibition of cortical and limbic dopamine release

2. Dopamine Hypothesis

block postsynaptic D2 receptors in in the **mesolimbic** and **mesocortical** systems

3. Glutamate Hypothesis

- Agonists of NMDA receptor

-Antagonists of NMDA receptor [phencyclidine and ketamine] exacerbate psychosis in patients with schizophrenia

Pharmacokinetics

- Most antipsychotics are readily but incompletely absorbed

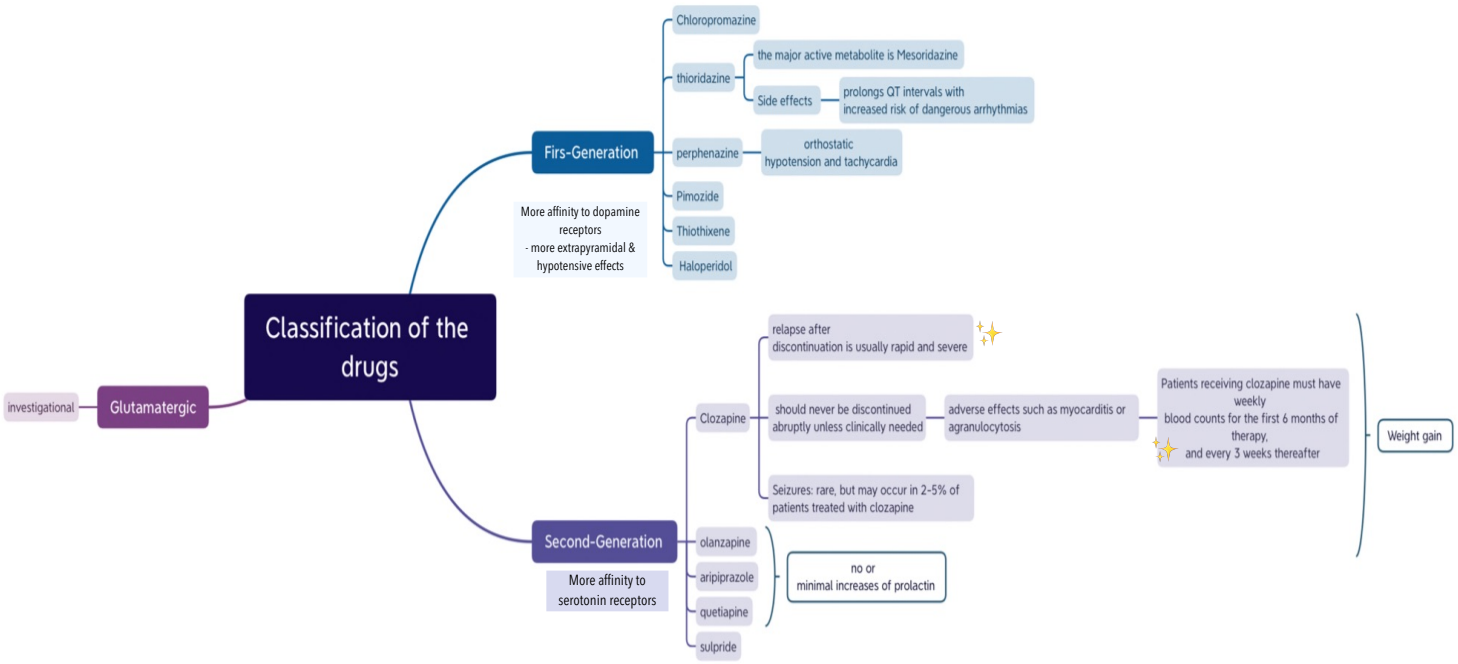
-They tend to have **large volumes** of distribution

-Most are **highly lipid** soluble, and highly **protein**-bound (92-99%)✨

-They have a much **longer duration** of action than that anticipated from their half-lives✨

-Full relapse may not occur **until 6 weeks** or more after discontinuation of many antipsychotics ✨

-Cytochrome P450 enzymes (**CYP2D6, CYP1A2, and CYP3A4**) are the major isoforms involved



Therapeutic uses of Antipsychotic Agents

A. Psychiatric indications:

1. Schizophrenia.
2. Bipolar affective disorder

B. Nonpsychiatric indications:

1. **Antiemetics** – prochlorperazine and benzquinamide
2. **Relief of pruritus** — H1-blockers . promethazine

Pharmacological effects

1. Psychological effects

- unpleasant subjective effects in nonpsychotic individuals
- Psychotic individuals show improvement in performance
- lower seizure threshold

First generation drugs	Second generation drug
elevations of prolactin ✨	cause no or minimal increases of prolactin metabolic syndrome ✨

Side effects

1. **Tardive dyskinesia** [the most important adverse effect] ✨
2. Behavioral effects

- **Toxic confusional state** may occur with very high doses of drugs with antimuscarinic actions
- **Pseudodepression -** might be due to drug-induced akinesia

3. **Metabolic and endocrine effects**

- Weight gain - common with clozapine and olanzapine ✨
- Hyperglycemia
-Hyperlipidemia
- Hyperprolactinemia

4. **Extrapyramidal reactions** [more with first generation drugs] ✨

-Parkinson's syndrome
- Akathisia
-Acute dystonic reactions

Treatment of :

Parkinson's syndrome - antimuscarinic drugs or with amantadine

🚫Levodopa should never be used in these patients ✨

Akathisia and dystonic reactions -
antimuscarinic drugs or with amantadine, but it is preferable to use a sedative antihistamine with anticholinergic action (diphenhydramine)

Tardive dyskinesia - ✨

1. stop the drug or reduce the dose
2. eliminate all drugs with central anticholinergic actions
3 Patients treated with old antipsychotics should be switched to quetiapine or clozapine.
4. If these steps fail, add diazepam

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