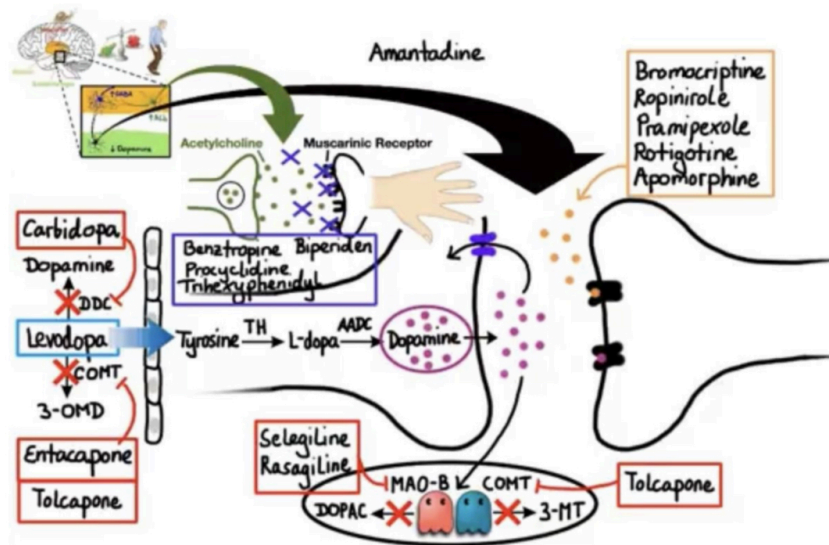


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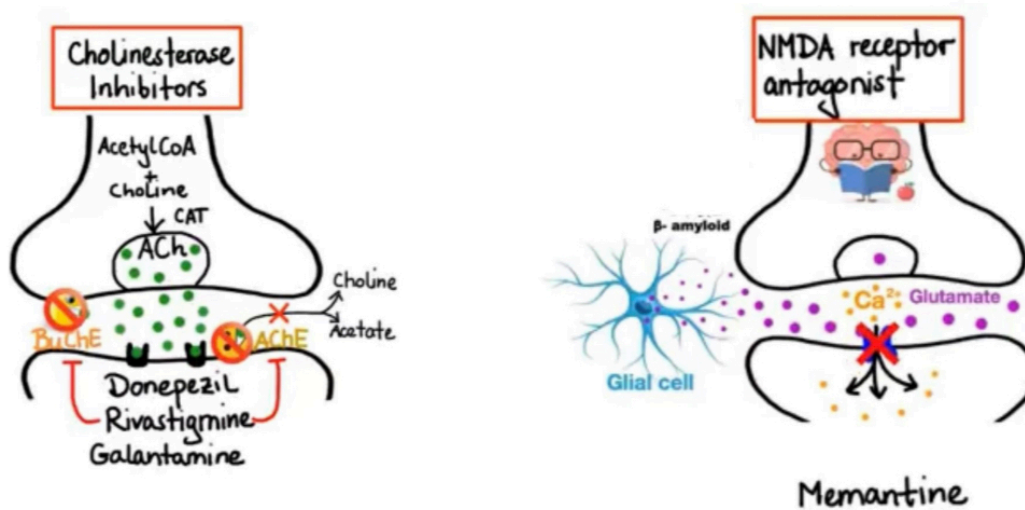
First lecture :

Parkinsonism Drugs/ Antiparkinsonism agents :



- **levodopa** : metabolic precursor of dopamine, restores dopaminergic neurotransmission in the corpus striatum by enhancing the synthesis of dopamine in the surviving neurons of the substantia nigra.
- **Carbidopa** : dopa decarboxylase inhibitor that does not cross the blood- brain barrier, diminishes the metabolism of levodopa in the gastrointestinal tract and peripheral tissues; thus it increases the availability of levodopa to the CNS.
- **Tolcapone & entacapone**: COMT inhibitor -> leads to decreased plasma concentrations of 3-O-methyldopa
- **Selegiline & rasagiline** : MAO-B inhibitors
- **Bromocriptine, Apomorphine, pramipexole, ropinirole, rotigotine** : Dopamine-receptor agonists

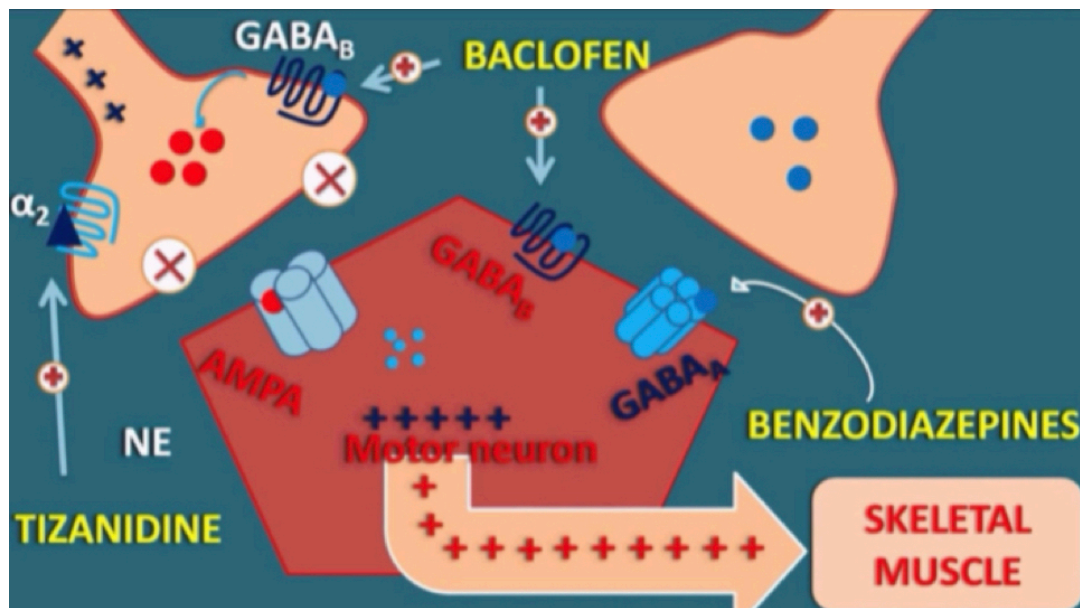
Drugs for treating Alzheimer's disease :



- **Donepezil, Rivastigmine, Galantamine** : cholinesterase inhibitors, inhibit the enzyme acetylcholinesterase from breaking down the neurotransmitter acetylcholine into choline and acetate
- **Memantine** : NMDA receptor antagonist

Second lecture :

Spasmolytic drugs :



Diazepam

- Benzodiazepine
- Facilitates GABA-mediated presynaptic inhibition

Baclofen

- GABA agonist causing membrane hyperpolarization
- Increased K⁺ conductance
- Decreases the release of excitatory neurotransmitters including substance P

Tizanidine

- Imidazoline related to clonidine
- With significant α_2 agonist activity
- Reinforces both presynaptic and post-synaptic inhibition in the spinal cord

Dantrolene

- Acts on the sarcoplasmic reticulum of the skeletal muscle by reducing the release of activator Ca²⁺
- Used to treat and prevent **Malignant hyperthermia**
- Malignant hyperthermia is Massive release of Ca²⁺ , Uncontrolled contraction and stimulation of metabolism in the skeletal muscle , General anesthesia protocols with succinylcholine and tubocurarine

Third lecture :

Stimulants and Related Drugs drugs :

CNS Stimulants :

- Drugs that stimulate a specific area of the brain or spinal cord
- Neurons contain receptors for excitatory neurotransmitters, including dopamine (dopaminergic drugs), norepinephrine (adrenergic drugs), and serotonin (serotonergic drugs)
- Sympathomimetic drugs

Classification

Classified according to :

- 1) **Chemical structural similarities** : amphetamines, serotonin agonists, sympathomimetics, and xanthines
- 2) **Site of therapeutic action in the central nervous system (CNS)**
- 3) **Major therapeutic uses** : anti-attention deficit disorder, antinarcotic, anorexiant, antimigraine, and analeptic drugs

Indirect-Acting Sympathomimetics

Indirect-acting sympathomimetics can have one of two different mechanisms :

- 1) May enter the sympathetic nerve ending and **displace stored catecholamine transmitter**, Such drugs have been called **amphetamine-like or "displacers"**.
- 2) May **inhibit the reuptake of released NE** by interfering with the action of the NE transporter e.g. Cocaine.

Amphetamine-Like drugs

Amphetamine

- A racemic mixture that is important because of its use and misuse as a **CNS stimulant** .
- Readily enters the CNS, where it has marked stimulant effects on **mood and alertness and a depressant effect on appetite**.
- Its D-isomer is more potent than the L-isomer. Amphetamine's actions are mediated through the release of NE and dopamine.

Methamphetamine (N- methylamphetamine)

- Very similar to amphetamine with an even higher ratio of central to peripheral actions.

Methylphenidate

- Its major pharmacologic effects and abuse potential are similar to those of amphetamine.
- Methylphenidate may be effective in some children with **attention deficit hyperactivity disorder**.

Catecholamine Reuptake Inhibitors :

- Many antidepressants, particularly tricyclic antidepressants inhibit **NE & serotonin reuptake** leading to orthostatic tachycardia as a side effect.

Atomoxetine

- A selective inhibitor of the NE reuptake transporter used in the **treatment of attention deficit disorders**

Sibutramine

- A serotonin and NE reuptake inhibitor and was used as **appetite suppressant for long-term treatment of obesity.**

Modafinil

- A **psychostimulant.**
- Inhibits both NE & DA transporters
- Increases interstitial concentrations of NE, DA , serotonin and glutamate
- Decreases GABA levels
- It is used primarily to improve wakefulness in **narcolepsy**
- It is often associated with mild increases in BP & HR
- Modafinil may also be useful in ADHD
- A new amphetamine substitute, with fewer side effects than amphetamine is used in this condition.
- Use : improvement of wakefulness in patients with excessive daytime sleepiness associated with narcolepsy and with shift work sleep disorder
- Less abuse potential than amphetamines and methylphenidate
- Schedule IV drug
- Armodafinil : similar to modafinil

Tyramine

- Found in ↑ conc. in some fermented foods such as **cheese.**
- Metabolized by MAO in GIT & the liver so it is inactive orally.
- If administered parenterally, it has an **indirect sympathomimetic action caused by the release of stored catecholamines**
- In patients treated with MAO inhibitors , tyramine may cause **marked increases in blood pressure (Cheese reaction)**

Cocaine

- A local anesthetic with a sympathomimetic action that results from inhibition of NE reuptake .
- Readily enters CNS causing an **amphetamine-like psychological effect** that is shorter lasting and more intense than amphetamine.
- Its major action in the CNS is to inhibit dopamine reuptake into neurons in the pleasure centers.
- it can be smoked, snorted into the nose, or injected.
- **It is a heavily abused drug**
- Coca Cola name refers to kola nuts, a source of caffeine, and coca leaves a source of cocaine, In 1903 cocaine was removed from coca cola drink.

Attention Deficit Hyperactivity Disorder (ADHD)

- Most common psychiatric disorder in children, affecting 4% to 10% of school-age children
- Boys are affected from two to nine times more often than girls.
- Primary symptoms of ADHD are inappropriate ability to maintain attention span or the presence of hyperactivity and impulsivity.
- Drug therapy for both childhood and adult ADHD is the same.

Narcolepsy

- Incurable neurologic condition in which patients unexpectedly fall asleep in the middle of normal daily activities. These "sleep attacks" are reported to cause car accidents or near-misses in 70% or more of patients.
- Cataplexy : sudden acute skeletal muscle weakness. Associated symptom in at least 70% of narcolepsy cases. It involves sudden acute skeletal muscle weakness.