

Parkinson Disease

Done by : group C3

A decorative graphic on the left side of the slide consisting of overlapping teal and light blue triangles of various sizes, creating a modern, abstract geometric pattern.

Objectives :

1. Definition & Epidemiology
2. Pathophysiology
3. Clinical features
4. Physical examination
5. Diagnosis & Prognosis
6. Management

Definition & Epidemiology

- SOHA HAJYASIN

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Definition

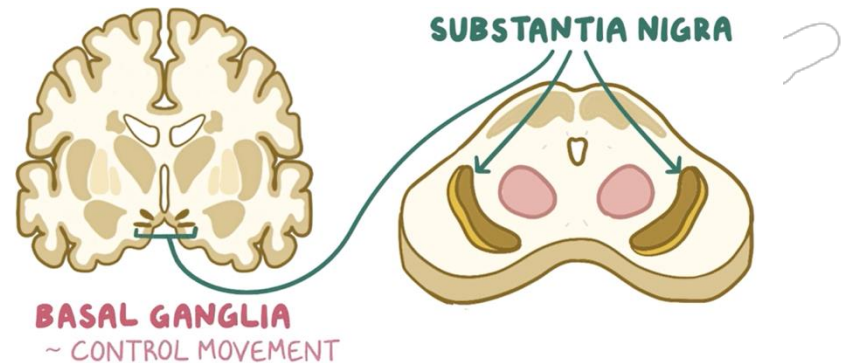
- Parkinson's disease is a degenerative condition primarily affecting extrapyramidal pathways where dopamine is the neurotransmitter . In other words, it's a **progressive degenerative disease** of the **dopaminergic neurons** in the **substantia nigra**, which can lead to altered motor movements .
- It characterized by :

Tremors

Rigidity

Akinesia

Postural instability



Definition

- **Idiopathic Parkinson disease** (PD) is the most common neurodegenerative movement disorder and is the most important form of parkinsonism
- The causes of idiopathic PD are still not fully understood. The relatively uniform worldwide prevalence suggests that a single environmental agent is not responsible. There may be multiple interacting risk factors, including genetic susceptibility.
- **Parkinsonism**: refers to a broader category of movement disorders that exhibit similar symptoms to Parkinson's disease but can arise from various causes, such as other neurological conditions, medications, or toxins. While all Parkinson's disease is a form of parkinsonism, not all parkinsonism is Parkinson's disease.

Pathophysiology

- MUATH ALTITI

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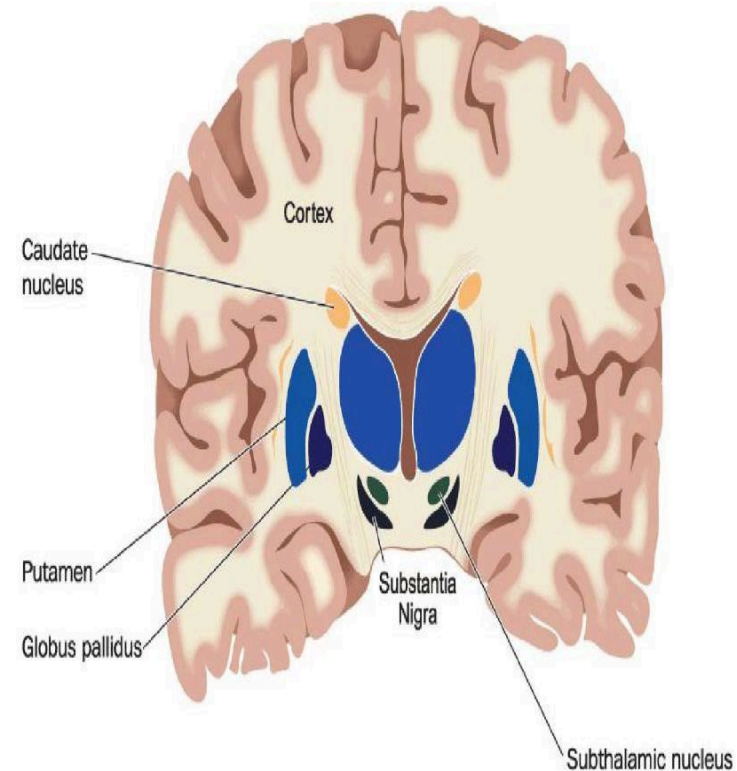
Epidemiology

- PD is most common in middle-aged and older patients, affecting approximately 1% of people over 60 years. It is typically a **sporadic** disorder
- but **hereditary** forms of PD due to mutations in genes such as PRKN, PINK1, LRRK2 and GBA may affect younger patients.



Anatomy of basal ganglia :

- **Striatum:** Comprised of the caudate nucleus and putamen, it plays a critical role in movement and reward.
- **Globus Pallidus:** Involved in the regulation of voluntary movement, it has two segments: internal (GPi) and external (GPe).
- **Substantia Nigra:** Produces dopamine and is crucial for motor control; its degeneration is associated with Parkinson's disease.
- **Subthalamic Nucleus:** Involved in the regulation of motor functions and the modulation of movement.



Direct and indirect pathways in Basal ganglia :

- The **basal ganglia** play a crucial role in regulating voluntary movement through two major pathways: the **direct** and **indirect** pathways. These pathways have opposing effects on movement control and are modulated by dopamine, primarily released from the **substantia nigra**. The balance between these two pathways determines how the basal ganglia influence the motor cortex and movement.

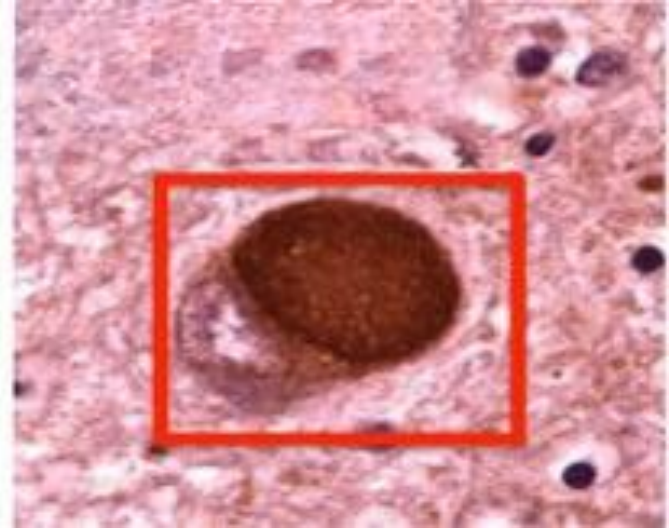
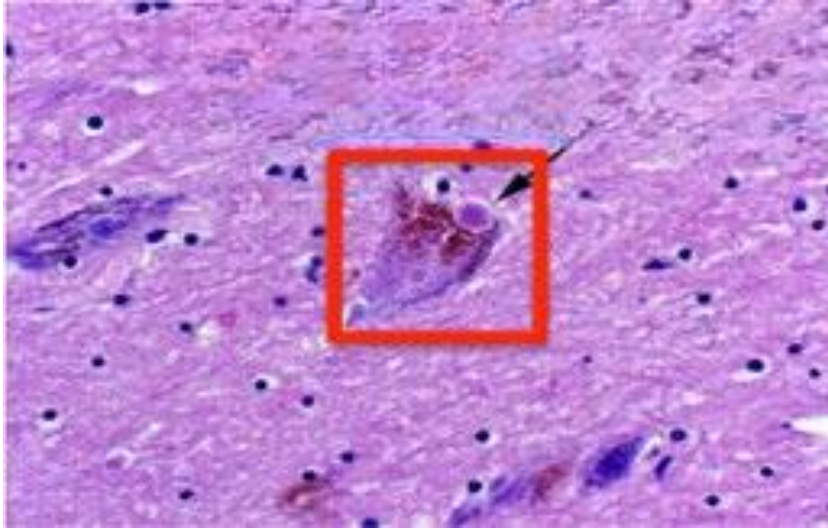
1. Direct Pathway (Facilitates Movement)

- **Purpose:** The direct pathway **promotes movement** by reducing the inhibitory signals to the thalamus, which in turn activates the motor cortex.
- **Role of Dopamine:** Dopamine, acting on **D1 receptors** in the striatum, **enhances the activity** of the direct pathway. This further promotes movement by increasing inhibition of the GPi and SNr, leading to greater activation of the motor cortex.
- **Simplified Pathway:**
- **Cortex (excitatory)** → Striatum (inhibitory) → GPi/SNr (inhibitory) → Thalamus (excitatory) → Cortex (movement facilitated).

pathology of Parkinson's disease (PD)

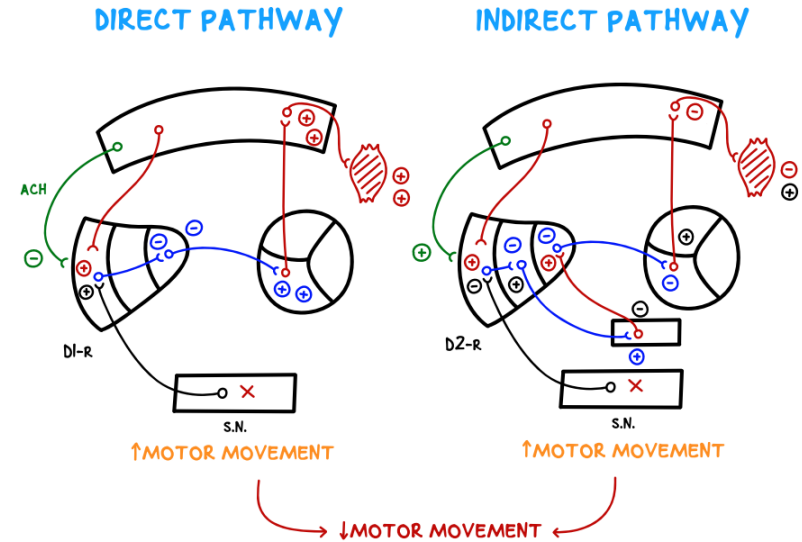
- progressive degeneration of specific brain regions, particularly those involved in the regulation of movement. The most significant pathological hallmark is the loss of **dopaminergic neurons** in the **substantia nigra pars compacta**, which leads to a reduction in dopamine levels. Additionally, the accumulation of **Lewy bodies** and the protein **alpha-synuclein** is a critical feature in Parkinson's disease.
- **Lewy bodies** are abnormal clumps of proteins found in the neurons of people with Parkinson's disease. They are a major pathological hallmark.
- The primary component of Lewy bodies is the protein **alpha-synuclein**, which accumulates abnormally and forms aggregates inside neurons.
- **Lewy bodies** are found not only in the substantia nigra but also in other regions of the brain, which may explain some of the **non-motor symptoms** of Parkinson's disease, such as **cognitive decline, sleep disturbances, and autonomic dysfunction**.

Lewy Bodies in the substantia nigra region in brains of Parkinson's patients



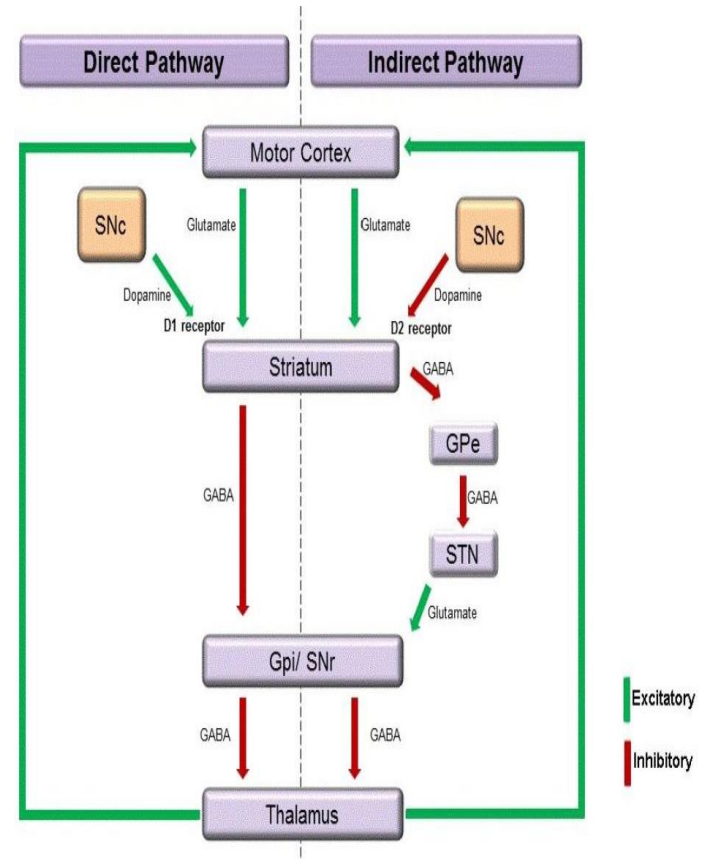
Parkinson's Disease and the Basal Ganglia Pathways:

- **Direct Pathway:** Reduced dopamine results in decreased stimulation of the direct pathway (via D1 receptors), causing **less facilitation of movement**.
- **Indirect Pathway:** Reduced dopamine leads to overactivity of the indirect pathway (due to reduced inhibition via D2 receptors), resulting in **increased inhibition of movement**.
- This imbalance between the two pathways leads to the hallmark motor symptoms of Parkinson's disease, such as **bradykinesia** (slowness of movement), **rigidity**, and **tremor**.



2. Indirect Pathway (Inhibits Movement)

- **Purpose:** The indirect pathway **inhibits movement** by increasing the inhibitory signals to the thalamus, which reduces its excitatory input to the motor cortex, thus suppressing movement.
- **Role of Dopamine:** Dopamine, acting on **D2 receptors** in the striatum, **inhibits the activity** of the indirect pathway. By inhibiting this pathway, dopamine reduces the suppression of movement, allowing more freedom of motion
- **Simplified Pathway:**
- **Cortex (excitatory)** → Striatum (inhibitory) → GPe (inhibitory) → STN (excitatory) → GPi/SNr (inhibitory) → Thalamus (inhibited) → Cortex (movement suppressed).



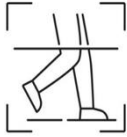
Clinical Features

- HAMZA JEBRIL

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Clinical features: motor Signs & symptoms



Gait



Tremor



Rigidity



Bradykinesia





Gait

- Festinant gait (**shuffle**) : steps are small and shuffling
- Loss of normal arm swing
- Unable to maintain normal stance in response to pressure from behind ,they may fall forward propulsion or from in front falling backward retropulsion
- Freezing : pt unable to initiate walking or unable to turn,they will stop in their place unable to move themselves
- Patients typically adopt a flexed, or stooped, posture, sometimes unkindly described as apeline.



Tremor

- Involuntary repetitive rhythmic movement.
- Approximately 80% of patients with PD have a resting tremor (present at rest and exacerbated by anxiety or stress)
- Primarily affects the hands involving the thumb and forefinger is classic (described as pill rolling)
- Improves on action



Rigidity

increase in muscle tone, which is equal in both flexion and extension of a body part

- ➡ **Lead pipe rigidity:** muscular rigidity that produces steady resistance to passive movement of the limbs.
- ➡ **Cogwheel rigidity:** Resistance starts and stops (jerky movements) as the limb is moved through its range of motion.



Bradykinesia

- is often the most disabling feature of PD and involves both axial and appendicular muscles.
- Patients with Parkinson's disease may complain that they have “ slowed down” Physically.
- Difficulties along the whole course of the movement process, from planning to initiation to execution, leading to difficulty with everyday tasks, e.g. dressing, eating, bathing.
- quiet and monotonous speech and swallowing difficulty.
- It effects all muscles including facial muscles so patients will experience loss of facial expressions (symmetrical hypomimia) which we call masked faces.
- Akinesia is most commonly associated with advanced Parkinson disease due to the degeneration of dopaminergic neurons.

Non motor Signs & symptoms

Personality changes:

- Depression
- Apathetic
- Anxiety
- Panic
- Hallucinations

Autonomic dysfunction:

- Orthostatic hypotension
- Constipation

Sleeping disorders:

- Insomnia
- (REM) sleep behavior disorder is characterized by violent enacting of dreams, due to the failure to induce muscle atonia

Impairment of cognitive function:

- Dementia (advanced stages)

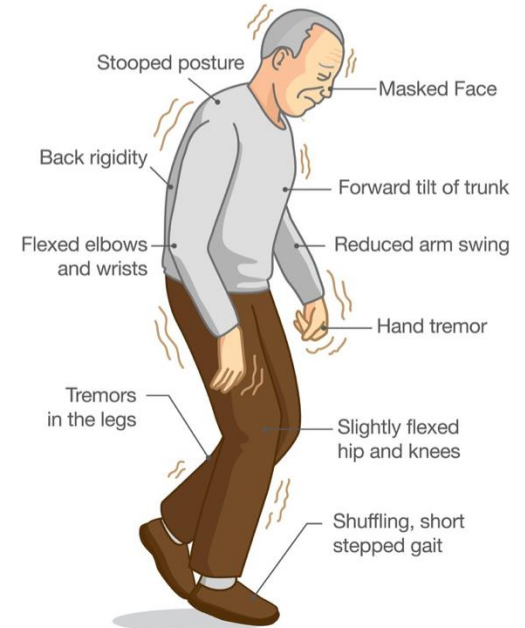
Physical Examination

- MOHAMMAD ALSHALABY

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General inspection

- Perform a brief **general inspection** of the patient, looking for clinical signs suggestive of Parkinson's disease:
 - Reduced spontaneous movements and hand gestures
 - Less frequent blinking
 - Hypomimia: a lack of facial expression.
 - Tremor: typically asymmetrical and present at rest, often described as '**pill-rolling**' in character.
 - Hypophonia: soft, indistinct speech.
 - Abnormal posture: typically stooped in appearance.
- It is important to remember that the inspection starts as soon as the patient walks in to the room.



Bradykinesia

It can be assessed by asking the patient to perform **rapid alternating movements** (as fast as possible). You just need to assess one or two of the following:

Finger tapping: Ask the patient to oppose their thumb and other fingers repeatedly, as fast as they can.

Hand grip: Ask the patient to make a fist and open their hand wide repeatedly, as fast as they can.

Pronation/supination: Ask the patient to pronate and supinate their hand repeatedly, as fast as they can.

Toe tap: Ask the patient to keep their heel on the ground and tap their toes against the floor whilst seated as fast as they can.



Whilst observing the patient perform of the above movements observe for the progressive reduction in speed and amplitude, asymmetry and slowness in the initiation of movement.

Rigidity

Passive Manipulation of Limbs: If the disease is in its early stage or the symptoms are well controlled with medications, we may not be able to see rigidity. We will need to use some activation maneuvers – ask the patient to actively tap their thigh with their contralateral arm whilst you perform the movement.

Gait

Sitting to standing: Ask the patient to stand from their seated position with their arms across their chest to screen for postural instability. Make sure to stand close to the patient so that you are able to intervene if they lose their balance.

Observe gait: ask the patient to walk whilst you observe their gait paying attention to Initiation, Step length, Arm swing, impaired balance on turning, ...etc.

Pull test: in this test the examiner stands behind the patients and by pulling on their shoulder tries to make them fall backwards. If the patients are able to correct their center of gravity in just one or two steps, the test is negative for a balance abnormalities. The test is instead considered positive if the patients catch their balance in more than two steps or if they do not stabilize at all and tend to fall to the ground.

Tremor

- **Resting tremor:** a small tremor in the index finger and thumb is common, causing the typical '**pill-rolling**' **appearance**. The best position to uncover a resting tremor is with the patient sitting on the chair with both hands lying relaxed on the thighs.
- **Postural tremor:** it occurs during the maintenance of a position against gravity. It can be assessed by asking the patient to raise their arms in front of their body and spread their fingers.
- **Kinetic tremor:** it occurs during hand movement. Assessed by performing a **finger-nose test**.

Diagnosis & Prognosis

- HAYTHAM ALQUDAH

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Diagnosis

- The diagnosis of Parkinson's disease is based on the presence of the **triad of clinical features** (i.e., bradykinesia and either resting tremor, rigidity, or both)

Asymmetry of signs at onset is important



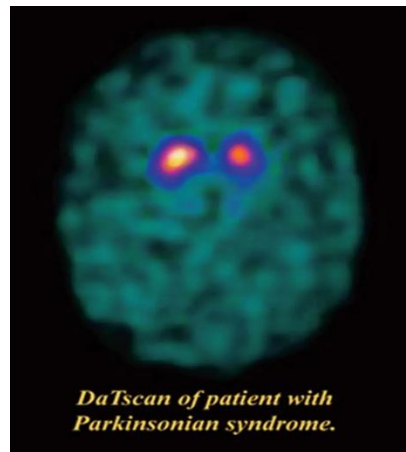
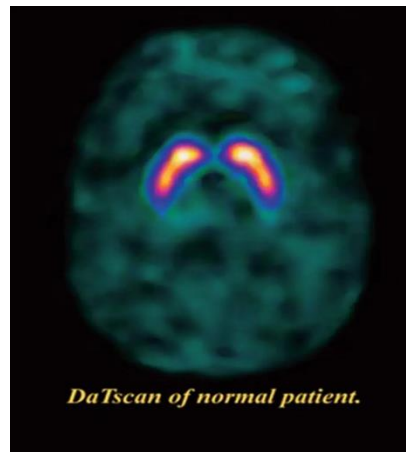
Parkinson is a clinical diagnosis.

Diagnostic tests

- MRI
- **DaTscan**: assess the integrity of dopaminergic neurons in **striatum**.

N.B.: Imaging is **not** routinely required for diagnosis ,changes are not specific for PD.

- **Levodopa challenge test** :
The result is positive if administration of levodopa relieves symptoms.
- A definitive diagnosis requires postmortem confirmation of lewy bodies.



Parkinson's disease Vs Parkinsonism

i.e., Idiopathic Parkinson

- PD is a form of parkinsonism which might be caused by other diseases but usually with atypical features e.g., vertical gaze palsy.
- Also called Parkinson-plus syndromes

TABLE 16-1. Parkinsonian Syndromes

Parkinsonian Syndrome	Distinguishing Clinical Features
Progressive supranuclear palsy	Supranuclear ophthalmoplegia, with greatest limitation of downward gaze; axial rigidity; early falls due to rigidity, impaired postural reflexes, neck hyperextension, and inability to look down
Corticobasal ganglionic degeneration	Limb apraxia; cortical sensory impairment; alien-limb phenomenon; asymmetric rigidity; dementia
Diffuse Lewy body disease	Early dementia; prominent visual hallucinations; cognitive fluctuations; extreme sensitivity to extrapyramidal side effects of antidopaminergic neuroleptic drugs
Vascular parkinsonism	“Lower-half” parkinsonism in which rigidity in the legs is greater than in the arms, resulting in slow, shuffling gait
Multiple system atrophy	Early and prominent features of autonomic dysfunction (MSA-A); cerebellar dysfunction (MSA-C); parkinsonism refractory to levodopa (MSA-P); high-pitched, quivering dysarthria

Prognosis

- **Parkinson's disease is progressive** and typically divided into three stages:

1. Early Stage:

- Symptoms are **well controlled** with treatment.
- Patients maintain a high level of function.

2. Mid Stage:

- Development of **motor fluctuations** and **dyskinesias** (involuntary movements).
- Symptoms become more variable with on-off periods.

3. Late Stage:

- Emergence of **treatment-resistant symptoms** such as **dementia** and frequent **falls**.
- Patients may experience severe mobility issues and increased risk of complications.

• **Without treatment:**

Severe immobility and life-threatening complications such as **bronchopneumonia**, **sepsis**, or **pulmonary embolism** may develop within 7–10 years.

Management

- HEBA YOUSEF

- RANEEM AMRO

06

Parkinson Management



Drug therapy

Therapy is aimed at restoring dopamine in the basal ganglia and antagonizing the excitatory effect of cholinergic neurons, thus reestablishing the correct dopamine/ acetylcholine balance.



Deep brain stimulation

Deep brain stimulation of the subthalamic nucleus (STN) and globus pallidus internus may be helpful for patients with advanced disease.



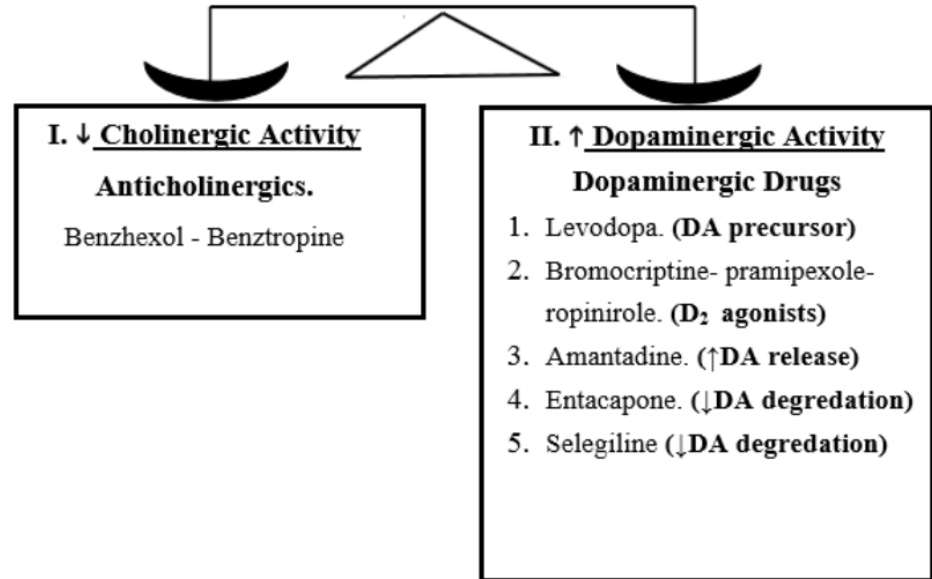
Surgical treatment

Stereotactic thalamotomy (a surgical lesion to the thalamus) is infrequently used with improved drug therapy, though it has a role in patients with severe tremor unresponsive to medication.

Drug therapy

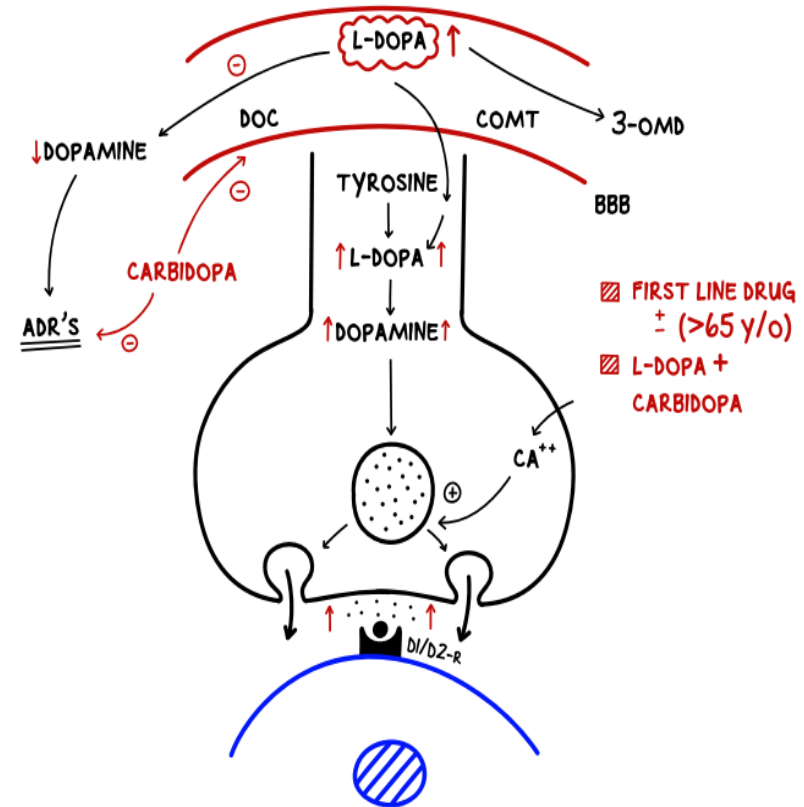
- The most effective medical treatment for PD is replacement of deficient endogenous dopamine with levodopa.
- (Indeed, if this does not help, one should consider the possibility of illnesses other than idiopathic PD.)

Antiparkinsonian Drugs aim to restore DA/Ach balance



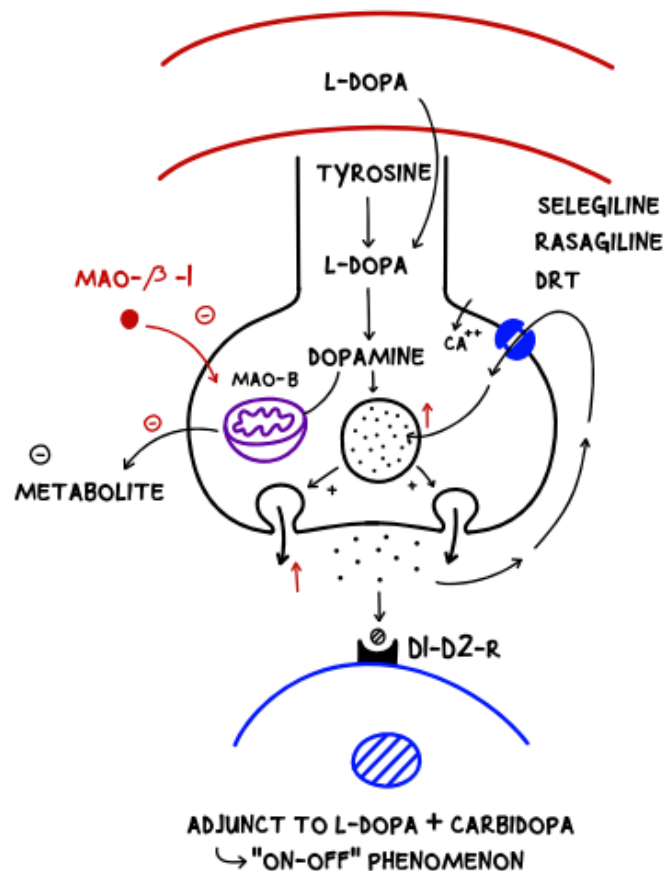
1. L-dopa and carbidopa

- Levodopa is combined with carbidopa, an inhibitor of peripheral dopamine decarboxylase, which allows the levodopa to cross the blood-brain barrier and reach its target, while also reducing peripheral dopaminergic side effects including nausea, vomiting, and hypotension
- Initially, levodopa is quite effective for most patients with PD, but over time it loses its effectiveness, and disabling dyskinesias develop.



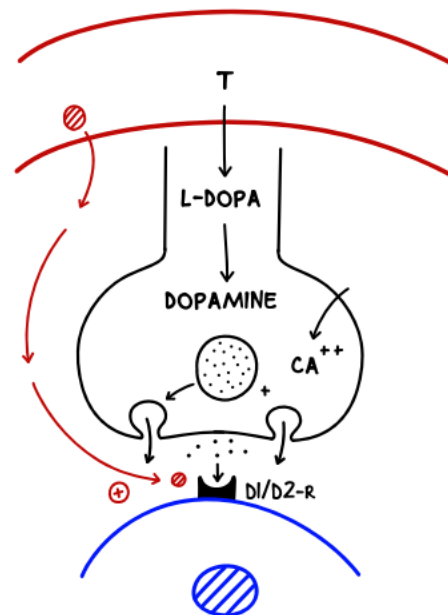
2. MAO Inhibitors

- The monoamine oxidase B inhibitors **rasagiline** and **selegiline** may provide slight benefit to patients with PD and are often used in early stages of the disease as monotherapy or as a supplement to levodopa.



3. Dopamine agonists

- **pramipexole** and **ropinirole** are also options for the treatment of mild or early PD. These medications may improve symptoms and reduce levodopa requirement, thereby minimizing the long-term probability of dopamine-related dyskinesias.
- **Rotigotine** is a dopamine agonist available in patch form and is designed to prevent excessive fluctuation in drug levels.



ERGOT
↳ BROMOCRIPTINE

NON-ERGOTS
↳ PRAMIPEXOLE
↳ ROPINIROLE

⊗ FIRST LINE
(<65 y/o)

4. Other medications

- **Anticholinergics** including benztropine and trihexyphenidyl are used to treat tremor but generally have little effect on other PD symptoms
- **Amantadine** is helpful in the management of dyskinesias and dystonia associated with PD.
- The **COMT inhibitor** entacapone inhibits levodopa metabolism, thereby extending the duration of levodopa action in patients who experience "wearing off."

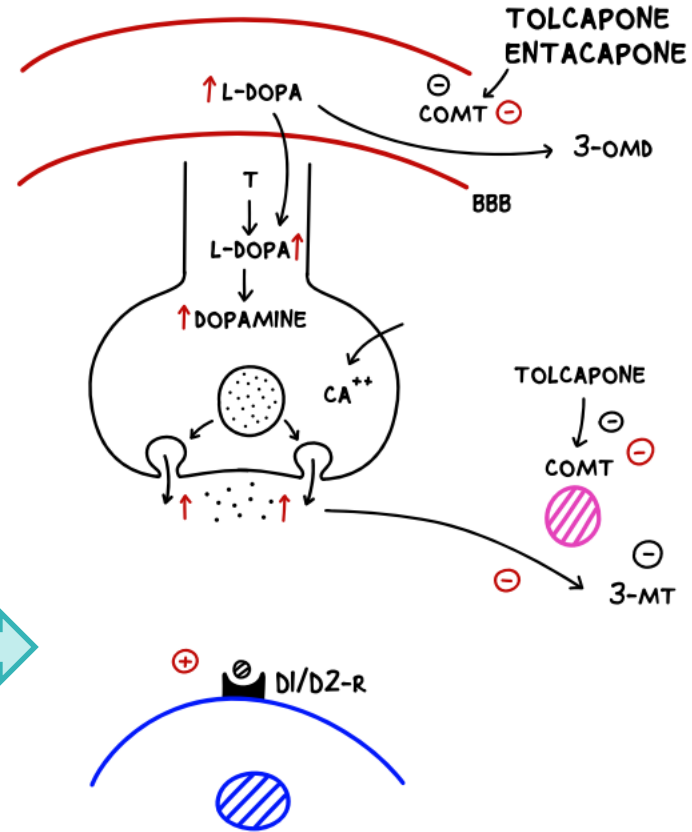


TABLE 16-3. Pharmacologic Treatment of Parkinson Disease

Drug	Mechanism of Action	Dosing	Side Effects
Levodopa/carbidopa	Dopamine precursor/dopa decarboxylase inhibitor	Start with a half of a 25/100 tablet bid; increase dose as needed; typically dosed 3–5 times a day	Anorexia, nausea, psychosis, hallucinations, orthostatic hypotension, dyskinesia
Trihexyphenidyl	Anticholinergic	Start with 1 mg bid–tid; increase to 4 mg tid as needed	Dry mouth, constipation, urinary retention, confusion, hallucinations, narrow-angle glaucoma
Benztropine	Anticholinergic	Start with 0.5–1 mg at bedtime; increase to 2 mg qid as needed	As above
Amantadine	NMDA antagonist	100 mg bid	Hallucinations, leg edema, livedo reticularis
Pramipexole	Dopamine agonist	Start with 0.125 mg tid; titrate gradually to 1.5 mg tid as needed	Lightheadedness, sleep attacks, pathologic gambling, and other impulse control disorders
Ropinirole	Dopamine agonist	Start with 0.25 mg tid; titrate gradually to 1 mg tid as needed	As above
Rotigotine patch	Dopamine agonist	2 mg qd; titrate to 6 mg qd	As above, patch site reactions
Entacapone	COMT inhibitor	200 mg with each L-dopa dose	Nausea, diaphoresis, lightheadedness
Rasagiline	MAO-B inhibitor	1 mg qd	Dizziness, flulike syndrome
Selegiline	MAO-B inhibitor	5 mg bid	Confusion, orthostatic hypotension, nausea
COMT, catechol O-methyl transferase; MAO-B, monoamine oxidase B; NMDA, N-methyl d-aspartate.			

TABLE 16-2. Therapeutic Strategies in Parkinson Disease

Scenario/Problem	Therapeutic Approach
Initial treatment	Levodopa, dopamine agonist, or MAO inhibitor
Poor or no response to initial treatment	Increase levodopa dose and consider alternative diagnoses
Tremor-predominant disease	Anticholinergic or amantadine
Overnight or early morning bradykinesia	Consider overnight controlled-release preparation of levodopa
Levodopa-induced hallucinations	Discontinue concurrent therapy with anticholinergics, amantadine, selegiline, or dopamine agonists Decrease dose of levodopa Low-dose atypical antipsychotic (with quetiapine, clozapine, or pimavanserin)
“Wearing off”	More frequent dosing Extended release formulation of levodopa Add COMT inhibitor
Dyskinesia	Reduce dose of levodopa Add or increase dose of dopamine agonist Change dopamine agonist Add amantadine Consider deep brain stimulation
COMT, catechol O-methyl transferase; MAO, monoamine oxidase.	

References :

- Blueprints Neurology 5th Edition
- AMBOSS
- Lecture Notes: Neurology





Thank You !

Do you have any Questions ?