Ashur University
College of Medicine

Grade 2
Neuroscience

Parkinson’s Disease



Ass. Professor Internal Medicine

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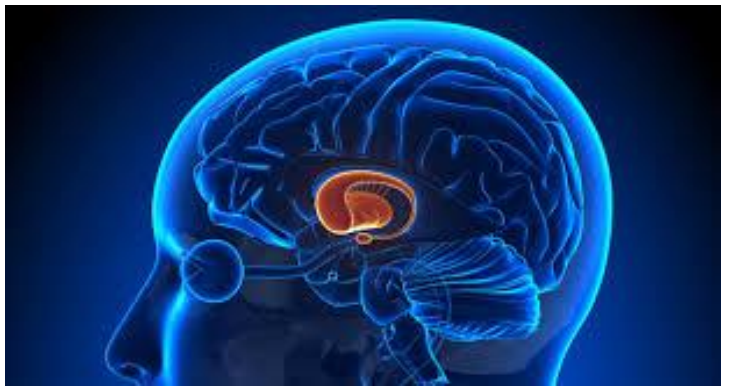
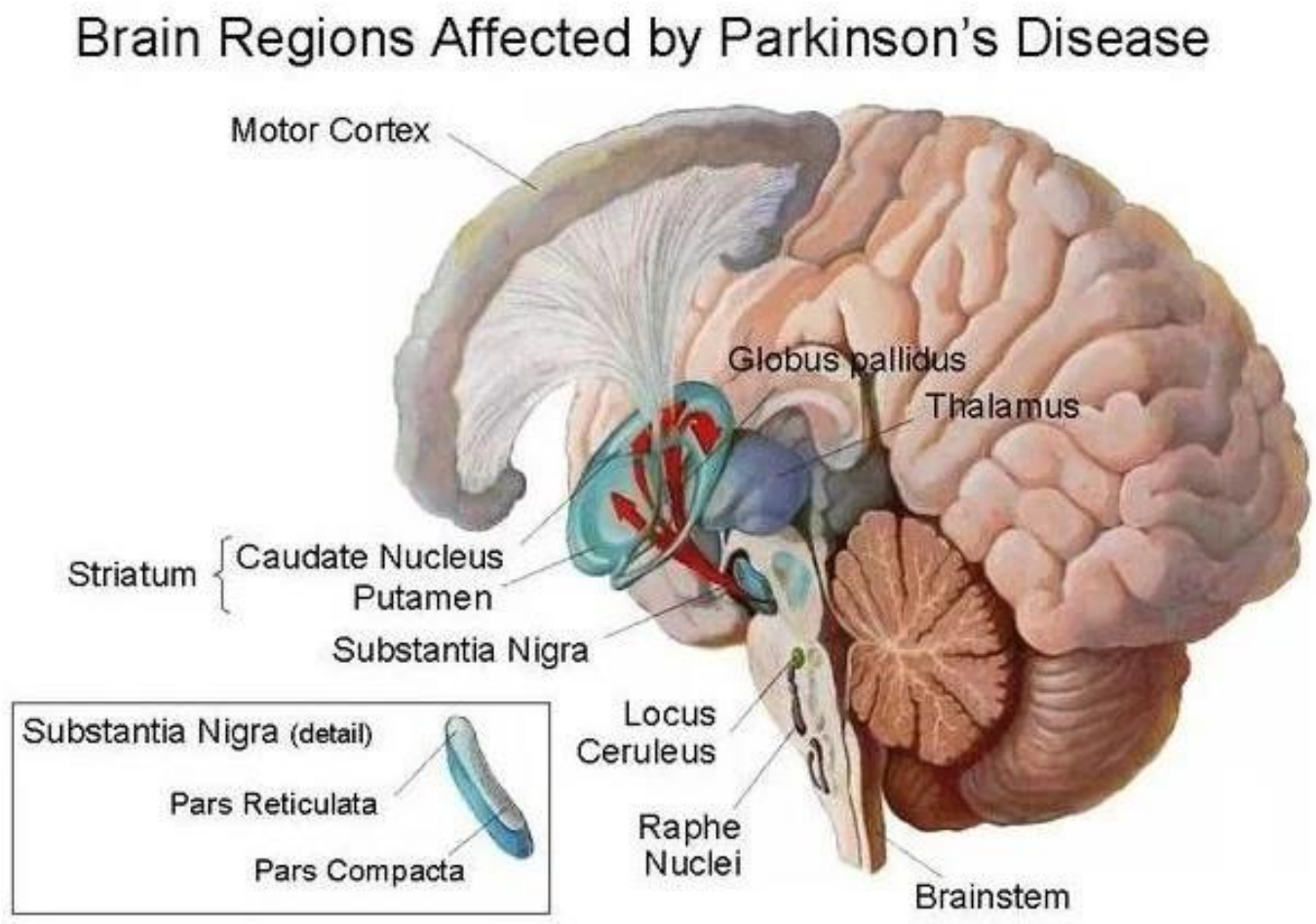
8/12/2024

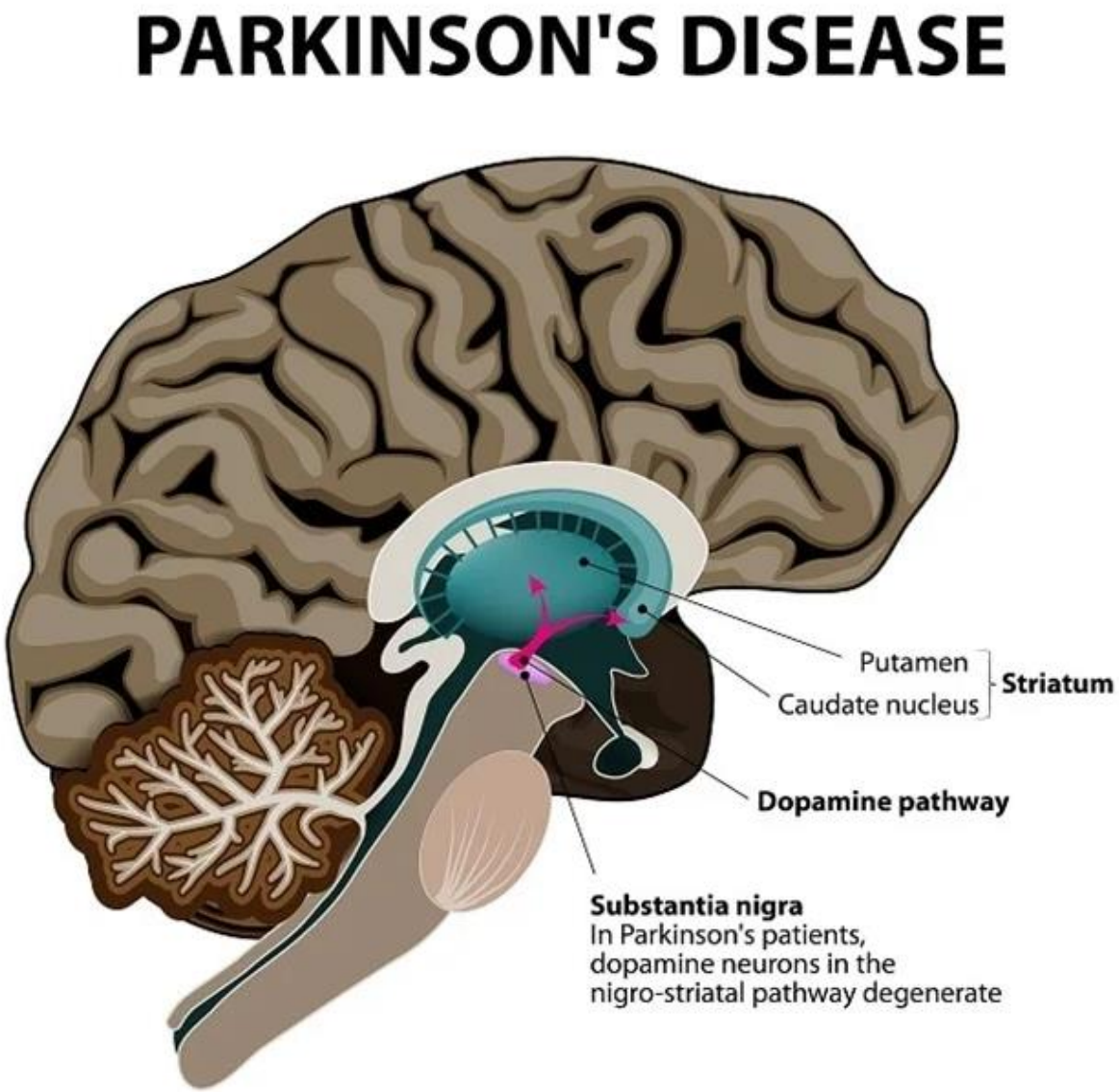


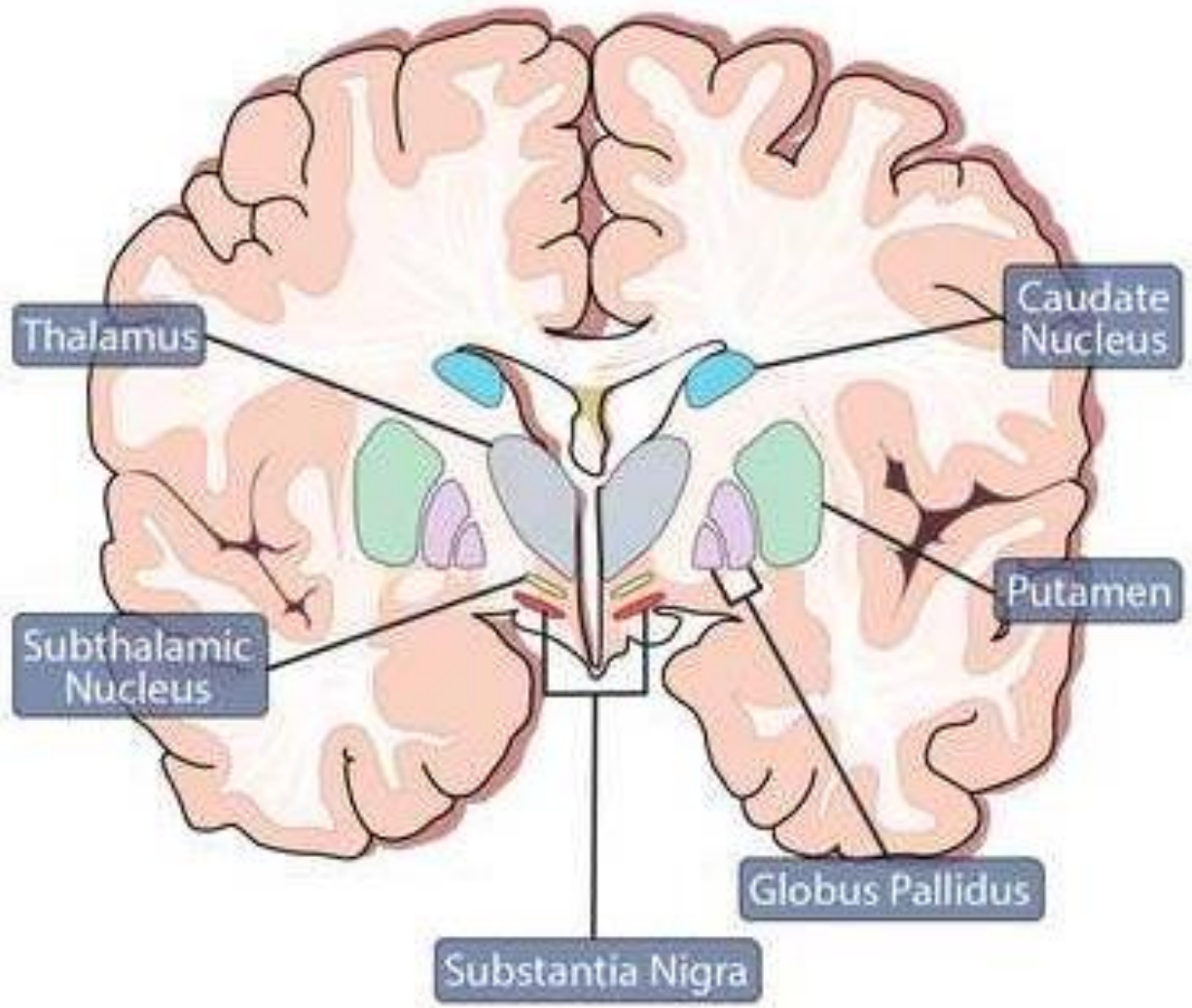
Anatomy

Parkinson's disease (PD) is a **degenerative**, progressive disorder that affects nerve cells in deep parts of the brain called the **basal ganglia** and the **substantia nigra**. Nerve cells in the substantia nigra produce the neurotransmitter **dopamine** and are responsible for relaying messages that plan and control body movement.



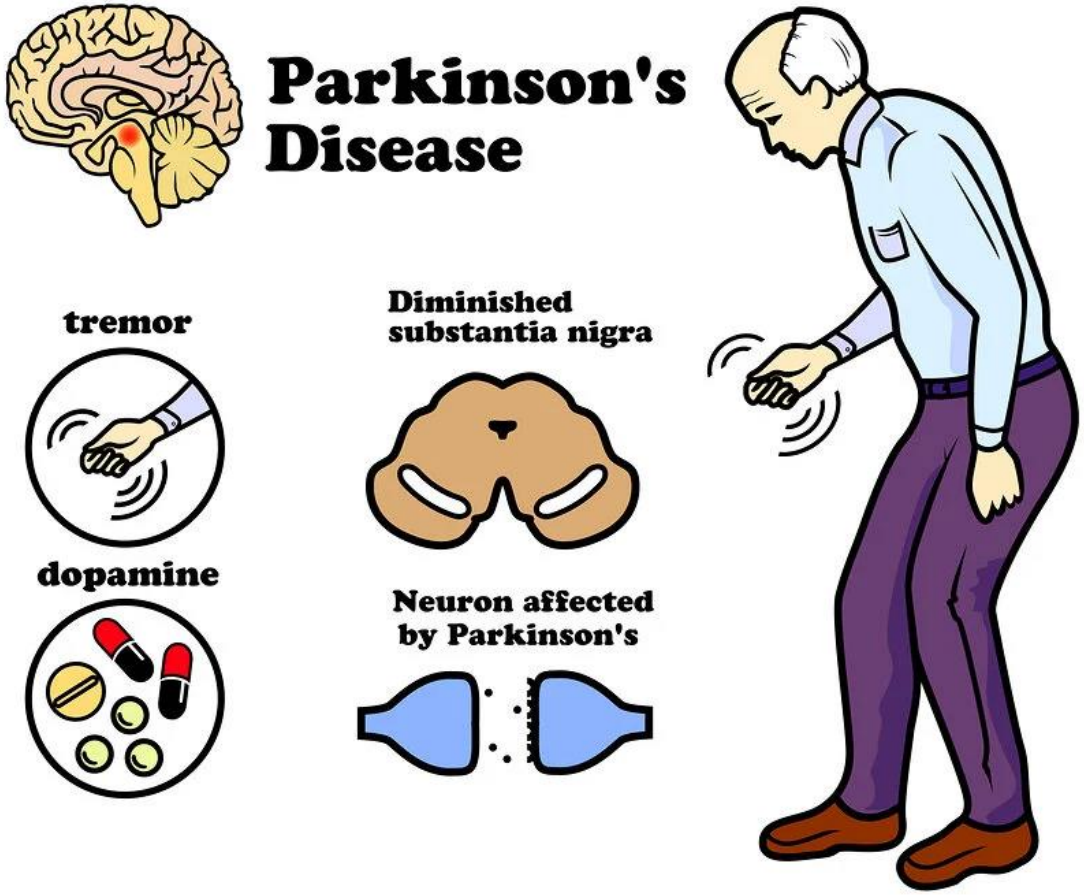
Anatomy


PARKINSON'S DISEASE
Putamen
Caudate nucleus
Striatum
Dopamine pathway
Substantia nigra
In Parkinson's patients, dopamine neurons in the nigro-striatal pathway degenerate


Thalamus
Caudate Nucleus
Subthalamic Nucleus
Putamen
Globus Pallidus
Substantia Nigra

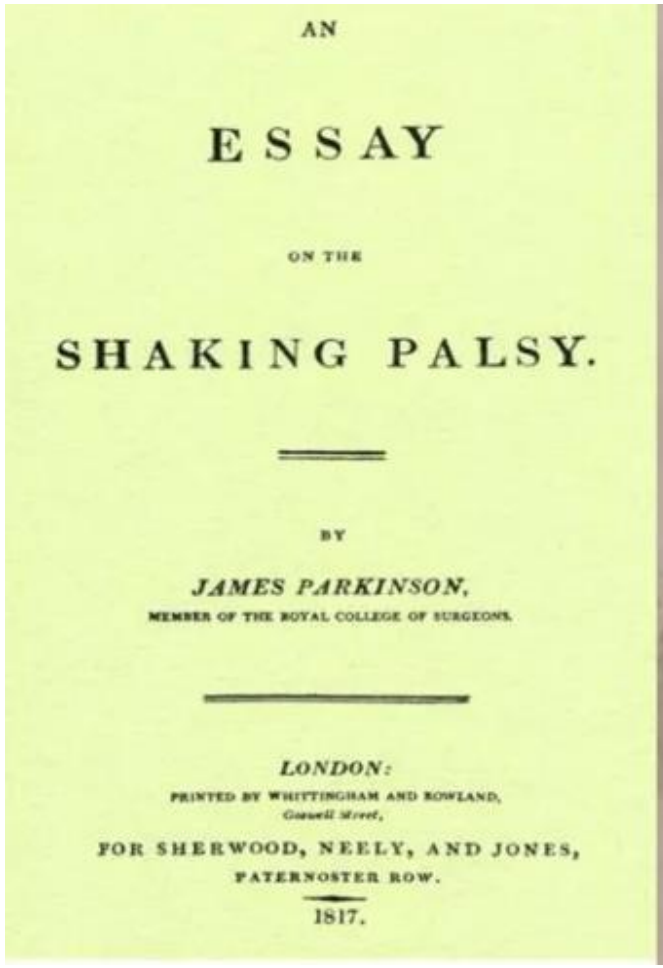
Definition

- Parkinson’s disease is a chronic progressive neurological condition, resulting from the **degeneration of dopamine producing neurons** in the **substantia nigra pars compacta**, which is located within the **basal ganglia**, deep in the lower region of the brain, on either side of the brain stem.



History & Naming

- Parkinson's disease was first described by **Dr. James Parkinson** in a little book entitled **An Essay on the Shaking Palsy**, published in 1817 .
- For the next century, the condition was known popularly as the shaking palsy and in the medical community by its Latin equivalent, **paralysis agitans** .


AN

ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON,

MEMBER OF THE ROYAL COLLEGE OF SURGEONS.

LONDON:

PRINTED BY WHITTINGHAM AND ROWLAND,

Goswell Street,

FOR SHERWOOD, NEELY, AND JONES,

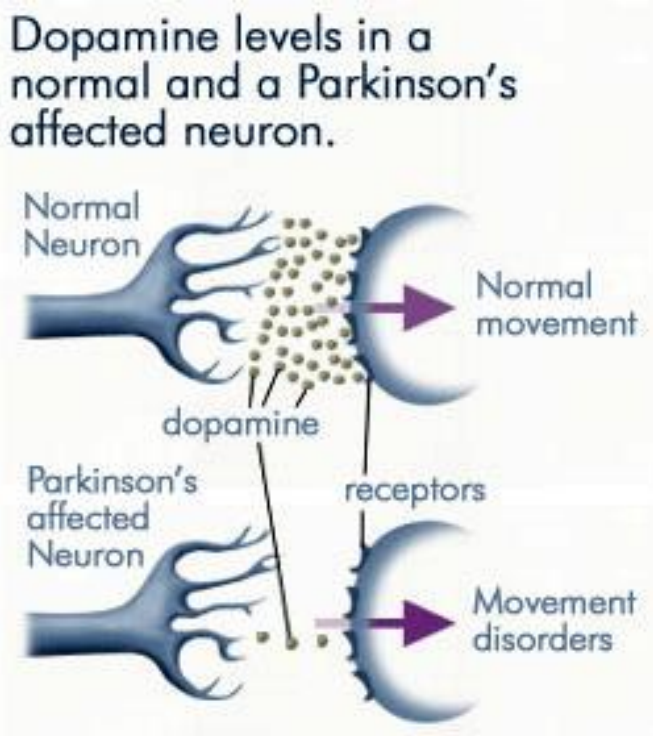
PATERNOSTER ROW.

1817.



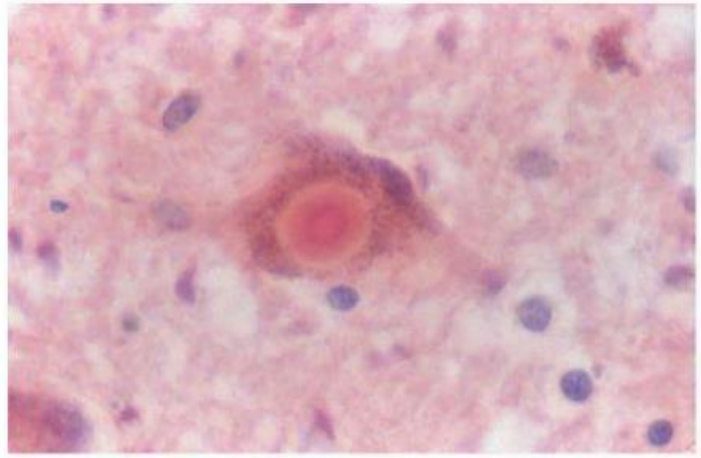
Pathophysiology

- Although mutations in several genes have been identified in a few cases, in most patients the cause remains unknown. The discovery that **methyl-phenyl-tetrahydropyridine (MPTP)** caused severe parkinsonism in young drug users suggested that PD might be due to an environmental toxin but none has been convincingly identied. **The pathological hallmarks of PD are depletion of the pigmented dopaminergic neurons in the substantia nigra** and the presence of **α-synuclein** and other protein inclusions in nigral cells **(Lewy bodies).**



- It is thought that environmental or genetic factors alter the α-synuclein protein, rendering it toxic and leading to Lewy body formation within the nigral cells. **Lewy bodies →→**

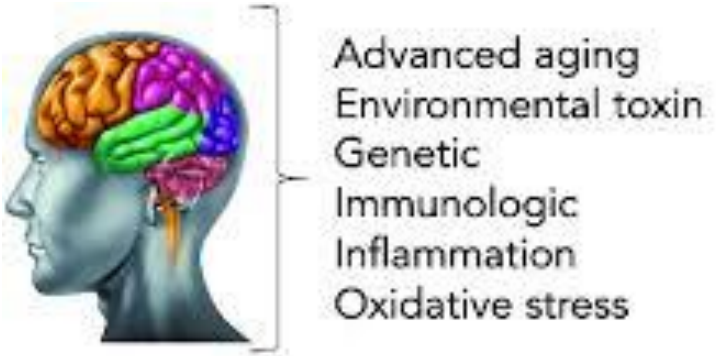
  Lewy bodies also found in the basal ganglia, brainstem and cortex, and increase with disease progression.



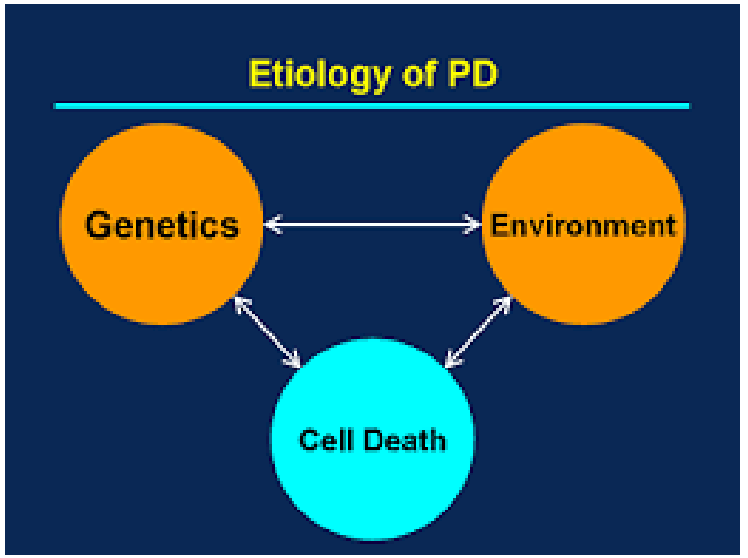
- **The loss of dopaminergic neurotransmission is responsible for many of the clinical features**.

Etiology

- **Parkinson's disease** is an idiopathic disorder. Although, there are some genetic and environmental factors which have been related to the disease.
- **Genetic factors**: It is estimated that up to 5% of cases may have a genetic cause. The remaining 95% are considered "idiopathic".
- **Environmental factors**: Several toxins, including the chemical **MPTP** (**1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine**) have been shown to cause Parkinson-like symptoms. There may also be a link between the use of herbicides and pesticides and the development of Parkinson's disease.

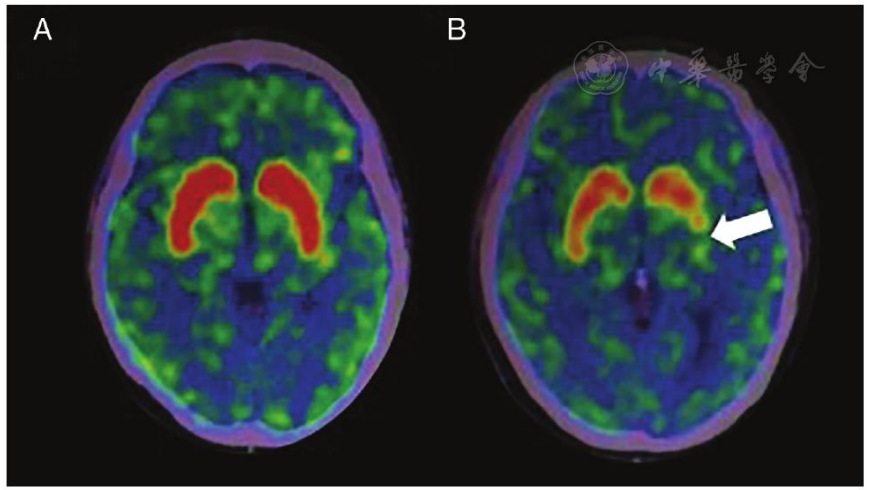


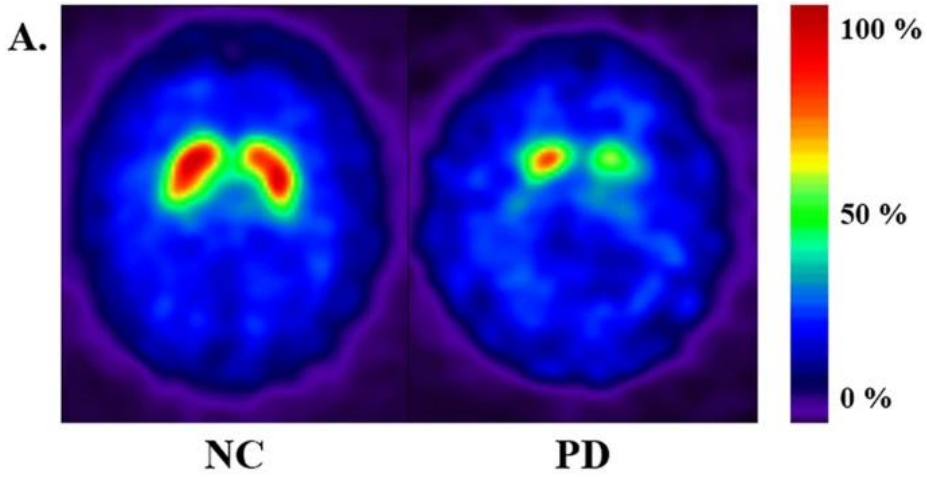


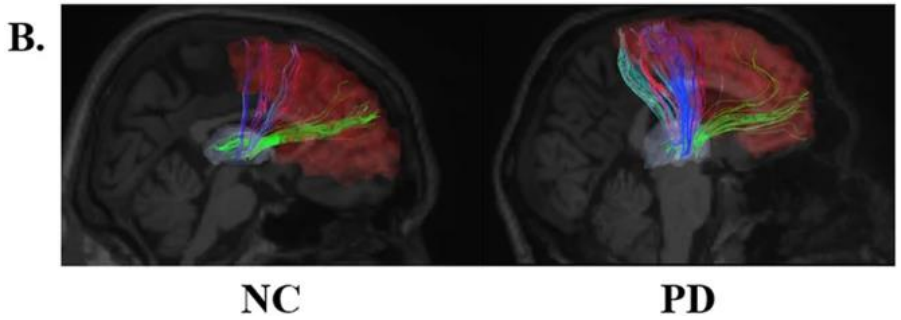


Diagnosis

- **Diagnosis is based almost exclusively on the history of the person's illness and the physician's clinical examination.** There are no really adequate nor specific blood or radiologic tests in common usage to make an absolute diagnosis of PD.
- While **Single Proton Emission CT (SPECT)** scanning may assist in making the diagnosis, this is only available in some centers. It is more likely to be used to exclude other conditions that may have similar symptoms.







NC : Normal Control

PD: Parkinson's Disease

Signs & Symptoms

Can be divided to the following :

1- Primary symptoms : rest tremor, rigidity, bradykinesia, gait disturbance and postural instability.

2- Secondary symptoms : Speech (palilalia), dysphagia, Drooling, Seborrheic dermatitis, Ankle Swelling, Visual problems, Weight loss, Constipation, Urinary disturbances, Sexual Dysfunction (↓ libido), Dizziness, Aches, pains, dystonia & Sweating.

3- Symptoms Related to Mentation, Behavior, or Mood : Depression, Anxiety, Panic attacks, sleep disturbances, Dementia, Memory loss, Confusion, Hallucinations and Psychosis.

4- Symptoms Related to Treatment : End-of-dose failure, on-off phenomenon & Dyskinesias

Parkinsonism comprises four cardinal motor features

- **Bradykinesia** : (slow and small movements). Reduced blink, face expression, and gesturing. Soft voice. Difficulty getting out of chair, shuffling steps, reduced arm swing, freezing
- **Tremor** : (usually resting) “pill rolling”, often involves thumb
- **Rigidity** (different from spasticity)
- **Postural changes** :Imbalance, falls; stooped flexed posture

Parkinson's disease

(TRAP)



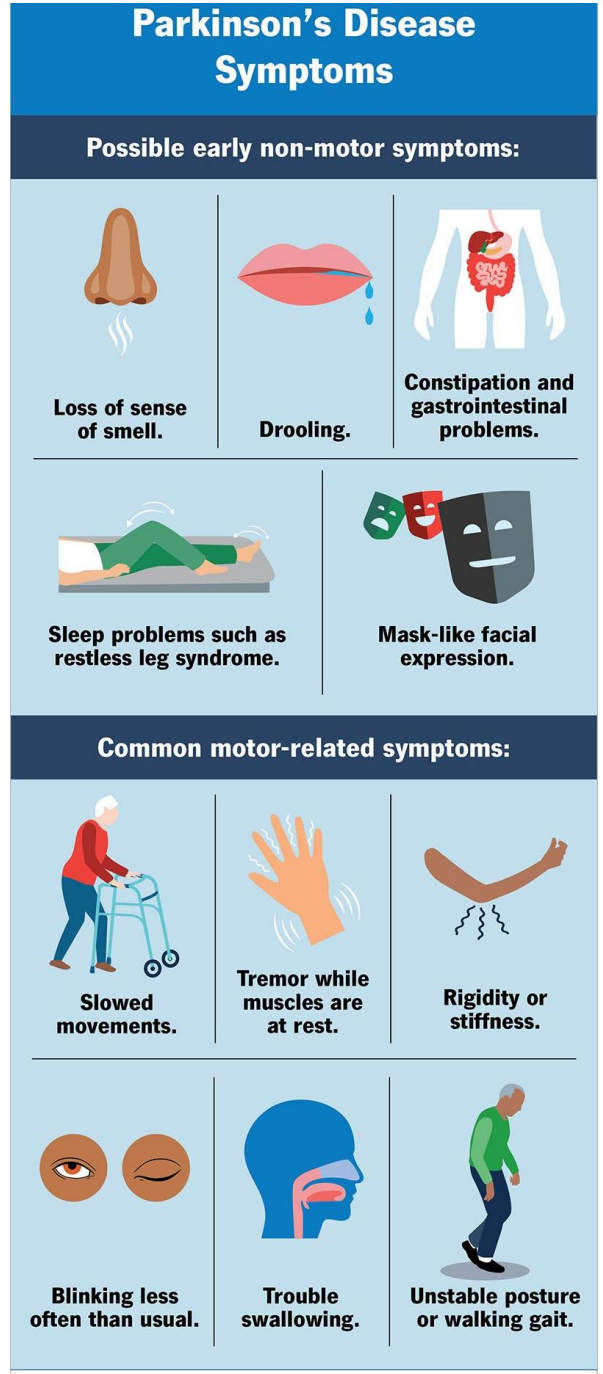
✓ **T** remors (pill rolling)

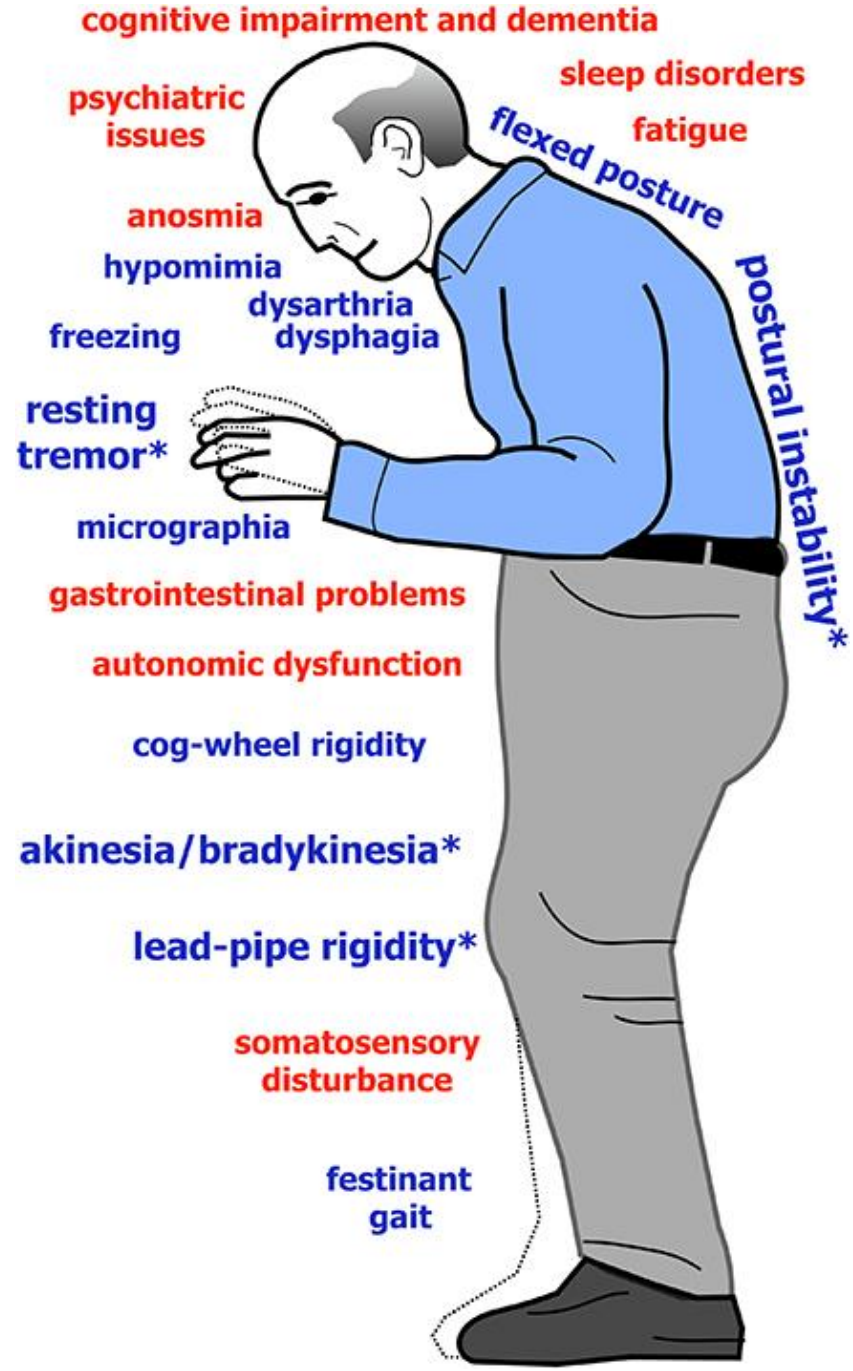
✓ **R** igidity(cogwheel)

✓ **A** kinesia/ bradykinesia

✓ **P** ostural disability

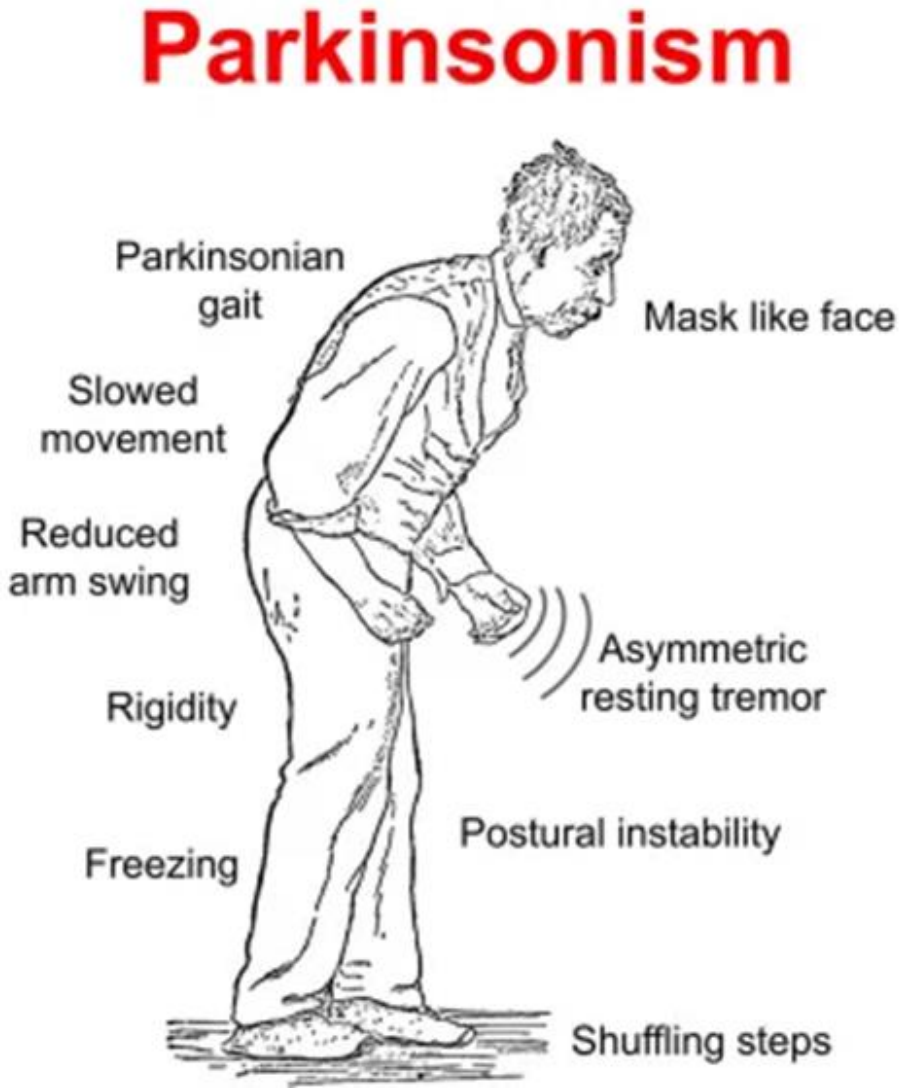
Signs & Symptoms cont…





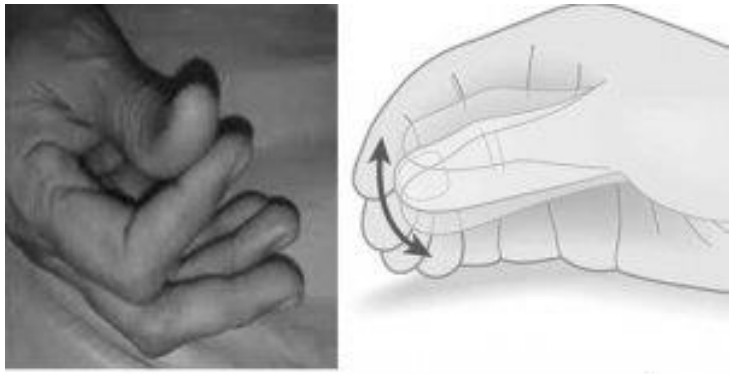
Other symptoms that may or may not occur:

- Freezing or being stuck in place
- Shuffling gait or dragging of one foot
- Stooped posture
- Small, cramped handwriting
- Sleep problems, insomnia
- Apathy, depression
- Lowered voice volume or tremor when speaking
- Difficulty swallowing
- Constipation
- Cognitive impairment



Rest Tremor

- It is the **characteristic feature of PD**.
- It is slow, rhythmic and usually begins unilaterally then, only later, spreads to involve the other side.
- It is a low-frequency **pill-rolling tremor**
- Onset of parkinsonian tremor is generally after age 60.
- **The tremor usually reduces or disappears upon performing a purposeful movement (as compared to intention tremor of cerebellar diseases that appears with active movement)**



Typical Pill rolling tremor of Parkinson

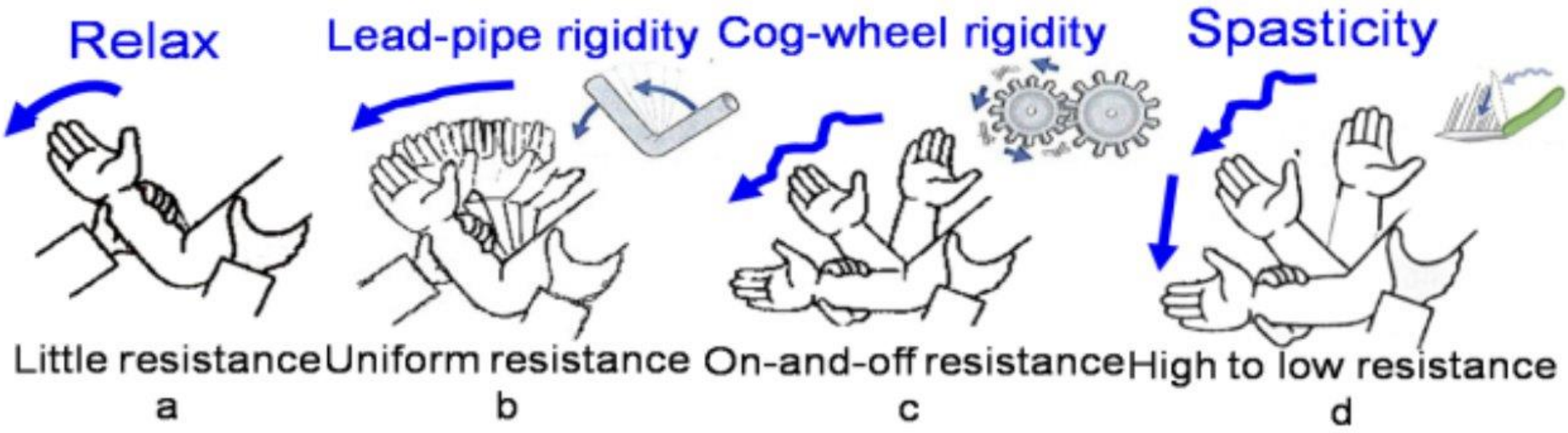


Rigidity

- **It is the increase in muscle tone** at rest and throughout the whole range of movement.
- Two types are identified :

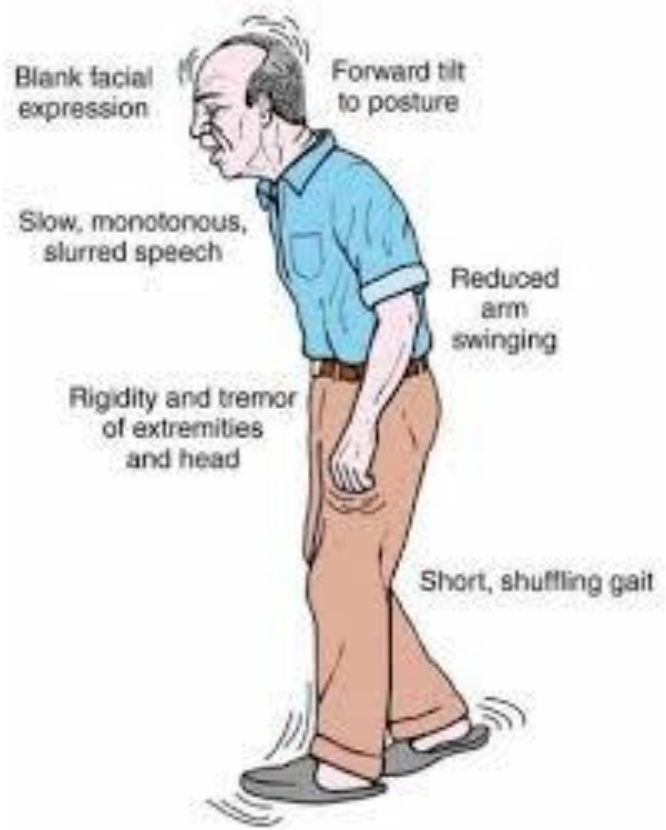
leadpipe rigidity and Cogwheel rigidity.

- **leadpipe rigidity**: an increase in muscle tone causes a sustained resistance to passive movement throughout the whole range of motion, with no fluctuations.
- **Cogwheel rigidity**: a combination of leadpipe rigidity and tremor which presents as a jerky resistance to passive movement.



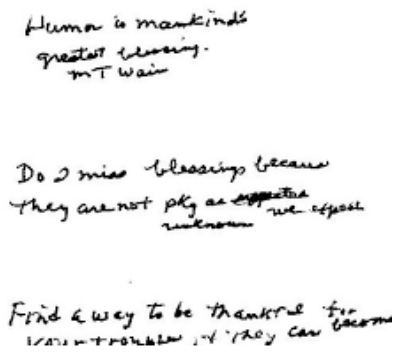
Bradykinesia

- **It is the 'slow movement'** that characterizes all forms of PD.
- It manifests in a variety of ways, including the **mask-like expression** (hypomimia), slowness in arising or initiating movement, and decrease in fine motor coordination.
- **Difficulty with turning over in bed** is a mark of bradykinesia, as are problems with **handwriting becoming slow and small (micrographia)**











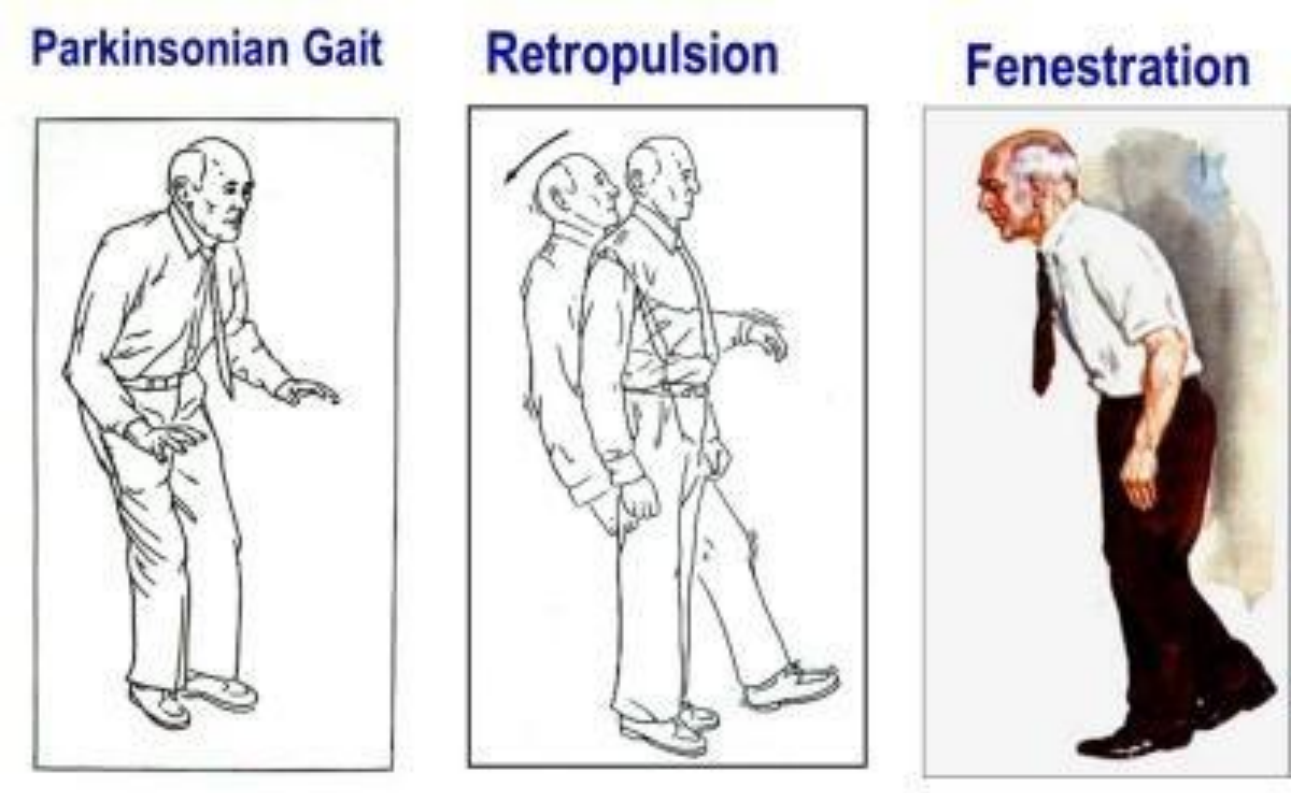
Gait Disturbances

- **Decrease in the natural swing is seen first**.
- Later, slow, small steps and **shuffling (festination)** occur.
- Patients may begin to propel themselves forward as they accelerate with rapid, short steps **(propulsion).**
- In advanced PD, there may be **episodes of freezing** in which the feet appear to be glued to the floor



Postural Instability

- Patients occasionally complain of **"dizziness"** when they mean that their balance or equilibrium is off.
- Usually occur late in the course of typical PD.
- Patients are complaining of falling and tend to go backwards as well **(retropulsion).**
- The **use of balance aids** (canes) becomes necessary, and patients may eventually require a wheelchair



Secondary symptoms

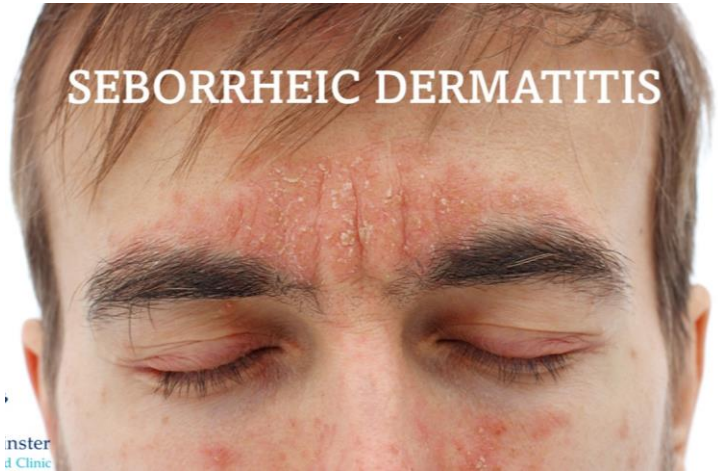
Speech : may talk in a monotone, like a computer.

Swallowing: Problems with swallowing ,dysphagia.

Drooling : (sialorrhea) that saliva pools in the back of the throat.

Seborrheic dermatitis : particularly on the forehead and scalp.

Visual Problems: may have difficulty reading (especially small print)



Secondary symptoms cont…

Weight Loss : decreased appetite , swallowing difficulties.

Gastrointestinal disturbances : constipation

Urinary problems: Urinary frequency , Urinary urgency.

Aches, pains, and dystonia : particularly in the feet and legs.

Blepharospasm: eye are unable to be opened normally.



Dyskinesias

- Dyskinesias : Abnormal involuntary movements
- Dyskinesias may be choreic or dystonic in nature.
- Chorea (from the Greek word for “dance”) .



Symptoms Related to Mentation, Behavior, or Mood

- **Depression :**

Occurs in as many as 50% of PD patients.

- **Panic attacks:**

The initial symptom may be frank panic attacks, with palpitations, hyperventilation, sweating and pallor.

- **Sleep disturbances :**

Inability to fall asleep (primary insomnia) is less common in PD than the inability to stay asleep (secondary insomnia).

- **Dementia :**

Problems with thinking, word finding, judgment, and other features of cognitive function (dementia) may occur in up to 40- 50% of PD patients.

Management of Parkinson's Disease

Can be divided into :



Medical:

Levodopa, Sinemet, MAO Inhibitors (Selegiline & Rasagiline),

Dopamine Agonists (Pramipexole &Ropinirole), Anticholinergics

(trihexyphenidyl, benztropine, and biperiden), Amantadine,

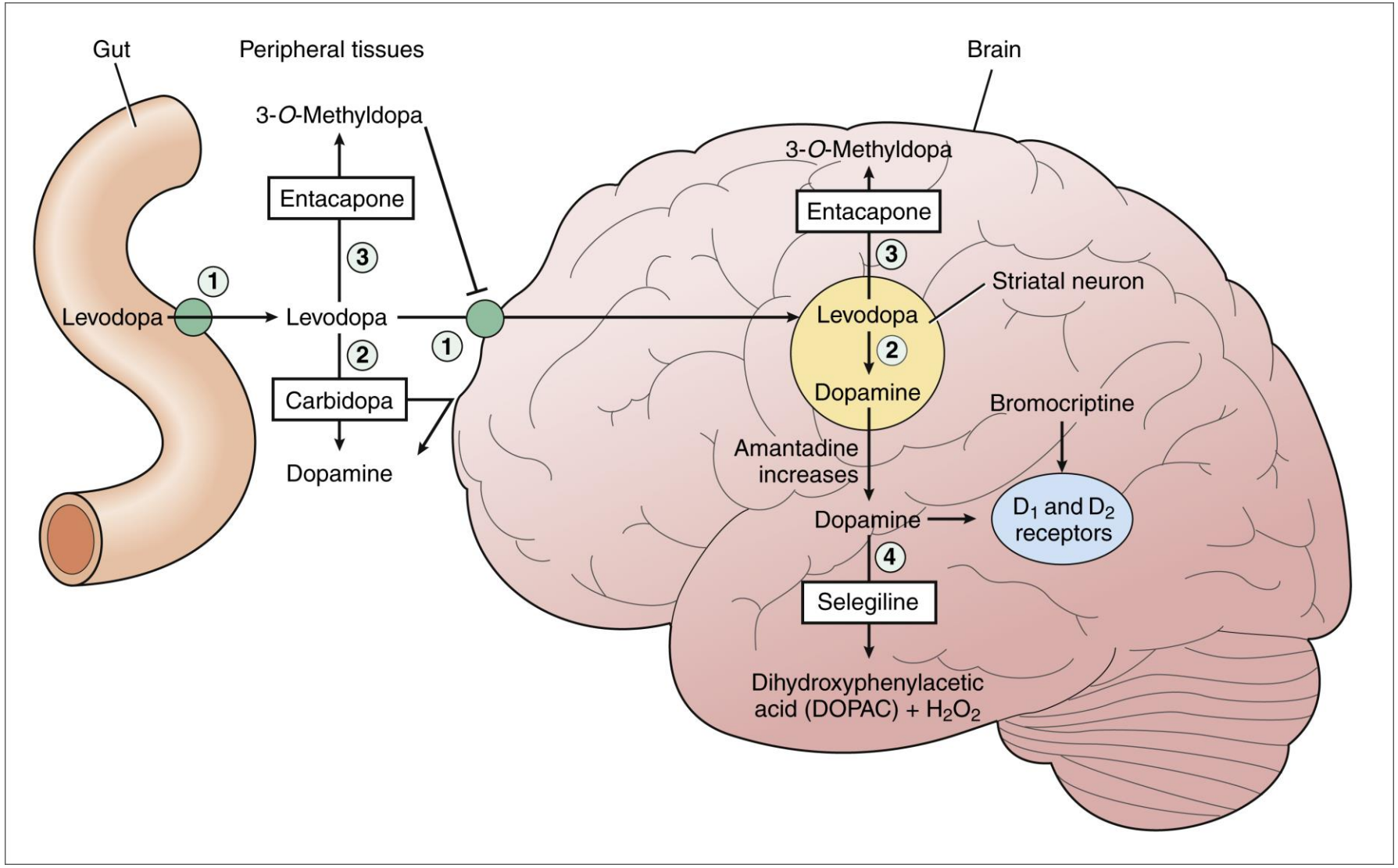
B blockers (propranolol), & COMT inhibitors (Tolcapone & Entacapone).

Surgical:

Thalamatomy, Pallidotomy, and Subthalamic stimulation

Medical:

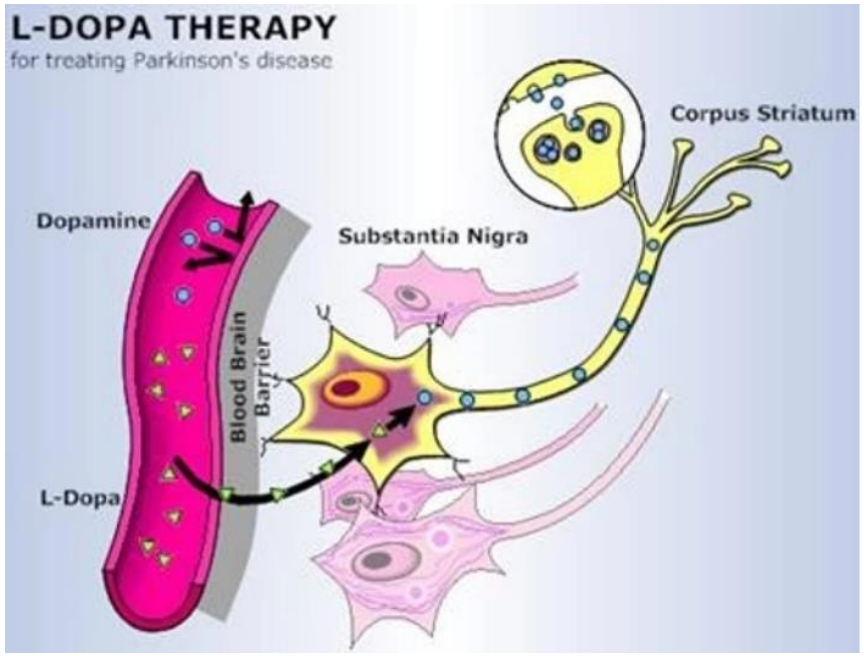
- 1 = pump that transports large neutral amino acids;
- 2 = l-aromatic amino acid decarboxylase (LAAD);
- 3 = catechol-*O*-methyltransferase (COMT);
- 4 = monoamine oxidase type B (MAO-B).



Levodopa

- **The most important and most effective drug.**
- As it crosses the blood brain barrier (BBB), it is **converted to dopamine** that restores the amount of dopamine in the substantia nigra and striatum to near normal levels.
- **Side effect** : **Nausea is the most common** side effect. Nausea is caused by the conversion of levodopa to dopamine in the intestine and blood before levodopa reaches the brain, and by direct stimulation by levodopa of the vomiting center in the brain.





Levodopa/carbidopa (Sinemet ®)

- Because of the nausea many patients experience when taking levodopa alone, it is invariably taken in **combination with carbidopa (trade name: Sinemet®).**
- **SINEMET tablets** are available in a 1:4 ratio of carbidopa to levodopa (SINEMET 25-100)and other dosages.





Monoamine Oxidase Inhibitors (Selegiline & Rasagiline)

- They interfere with one of the enzymes that break down dopamine (monoamine oxidase, or MAO-B), they can enhance and prolong the effect of dopamine.
- Dosage:
- Selegiline : 5 mg BD /day P.O.
- Rasagiline : 1 mg/day P.O



- **Dopamine Agonists:**

Pramipexole and Ropinirole. These are synthetic compounds that mimic the action of dopamine at the dopamine receptor in the striatum.

- **Anticholinergics :**

Trihexyphenidyl (Artane®) , Benztropine, and Biperiden .

Acetylcholine interacts with dopamine receptors in the striatum . Blocking acetylcholine serves to reduce the inequality that results from the loss of dopamine .

Amantadine (Symmetrel ®)

Has both antiviral and antiparkinsonian activities.



- **B-blockers :**
- Propranalol (Inderal ®).
- Although the most characteristic tremor associated with PD is a resting tremor, **many patients have tremors** that worsen with posture or action. **For these tremors Propranalol is prescribed.**
- **COMT inhibitors :**
- Tolcapone (Tasmar®) and Entacapone (Comtan®)
- **are Catechol-Omethyltransferase (COMT) inhibitor**. COMT inhibitors help more levodopa reach the brain, where it is converted into dopamine.



©

Surgical Management

- All the major surgical procedures performed to relieve symptoms of PD are done stereotactically (i.e. by the use of stereotactic frame)
- **Thalamatomy :**
- Thalamic stimulation affects the Ventralis Intermedius Nuclues (Vim nucleus) .To abolish tremor.
- **Pallidotomy :**
- Destroys a group of cells in the internal globus pallidus Gpi. relieving dyskinesias and tremor.
- **Subthalamic Stimulation:**
- current preferred procedure.






Thank
You