

# PARKINSON'S DISEASE



**PARKINSON FOUNDATION**  
OF THE NATIONAL CAPITAL AREA





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# DISCLOSURES

- I have no disclosures.



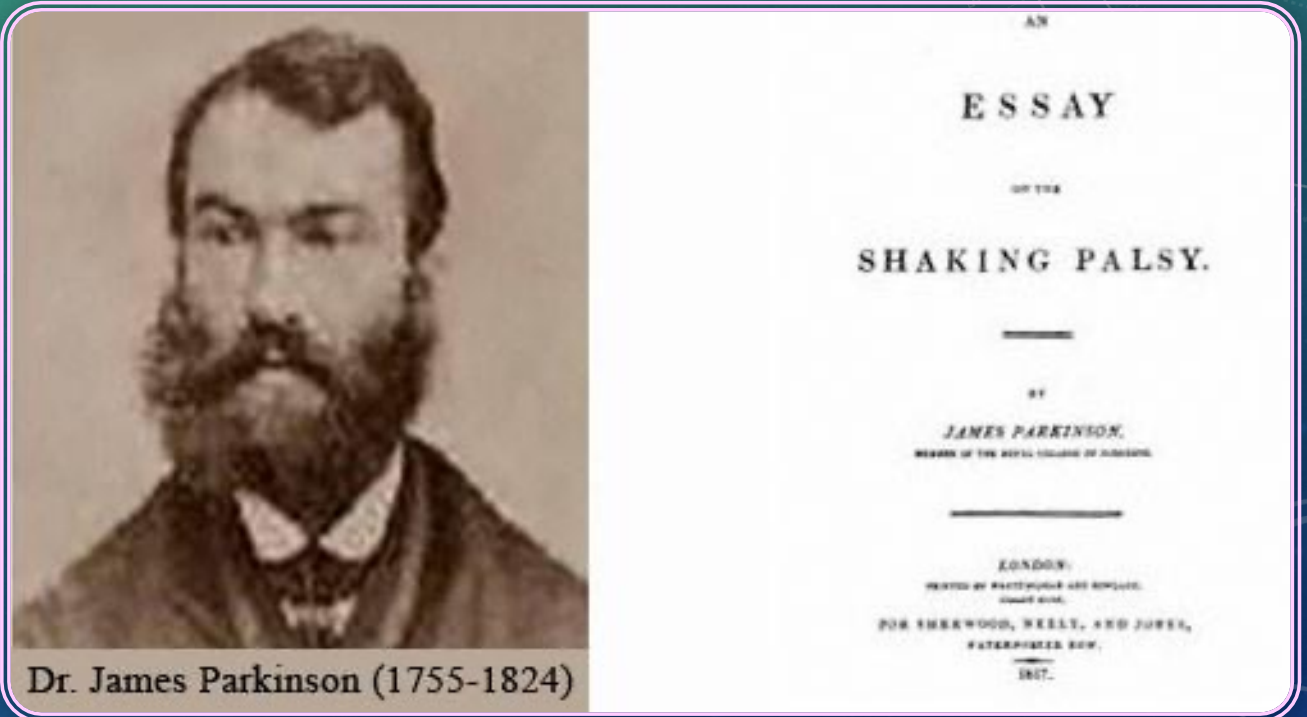
# OUTLINE

- A Brief History
- Definition
- Anatomy
- Symptoms
- Diagnosis
- Treatment of Motor Symptoms
- Treatment of Nonmotor Symptoms
- Management
- Resources



# A BRIEF HISTORY

- Parkinson's disease gets its name from an English physician, Dr. James Parkinson, who first described 6 patients with the classic features of Parkinson's disease in a paper published in 1817 called “An Essay on the Shaking Palsy.”
- The disease was originally referred to as “paralysis agitans.”
- Another neurologist, Dr. Jean-Martin Charcot, continued to study the disease and renamed it after Dr. Parkinson to honor him.



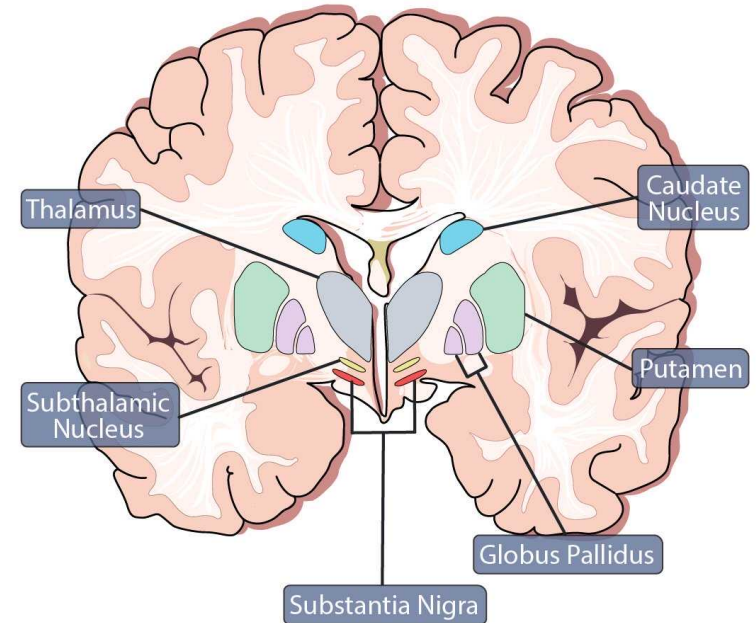
# PARKINSON'S DISEASE - DEFINITION

- A chronic and progressive disorder caused by degenerative loss of dopaminergic neurons in the brain and characterized clinically by asymmetric parkinsonism and a clear and dramatic benefit from dopaminergic therapy.

What does THAT mean!?



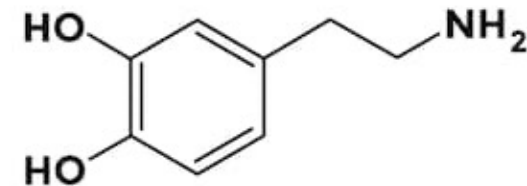
# PARKINSON'S DISEASE ANATOMY



# WHAT IS DOPAMINE?

- Dopamine is a hormone and a neurotransmitter.
- It is a chemical used to pass along signals in the brain and the rest of the nervous system.
- It plays a role in motivation/reward, pleasure, and movement, though it has other functions as well.

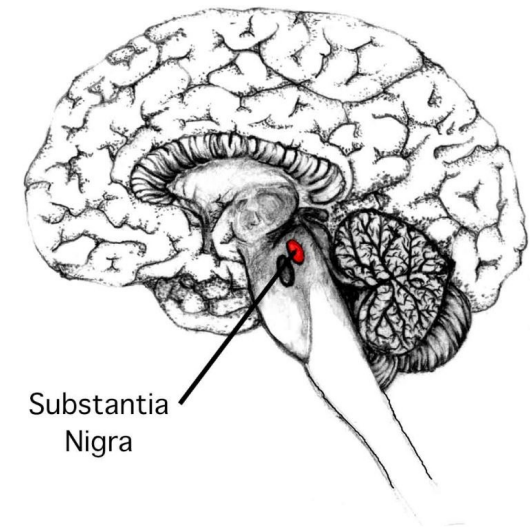
## DOPAMINE





# WHERE IS DOPAMINE?

- Dopamine can be found all over our body.
- The substantia nigra is an area in the brain that makes A LOT of dopamine.
- The substantia nigra is made up of neurons, or brain cells, that create dopamine.

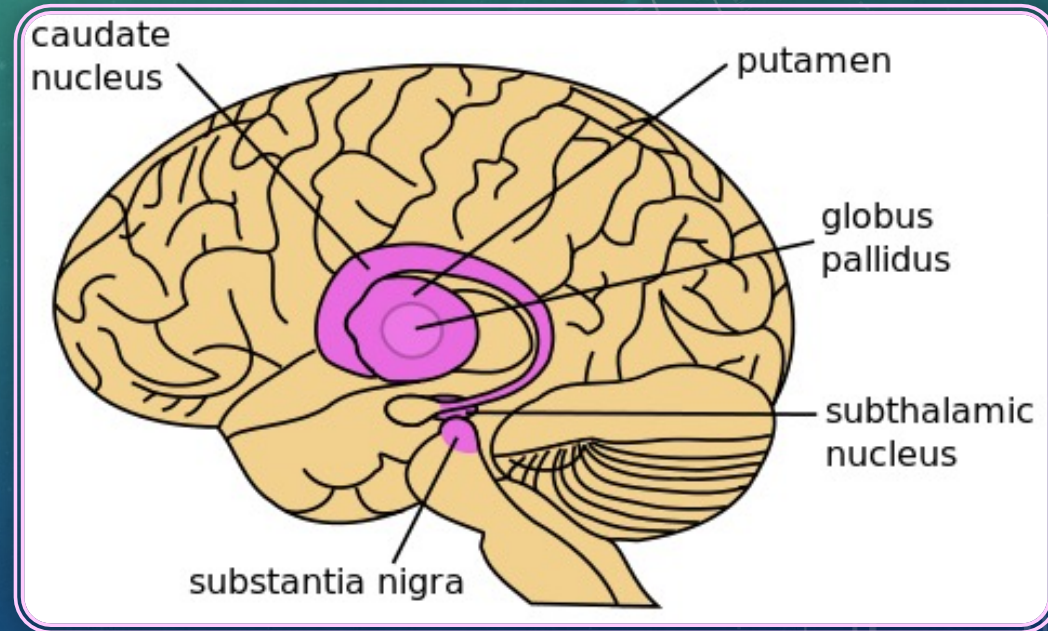


Substantia  
Nigra



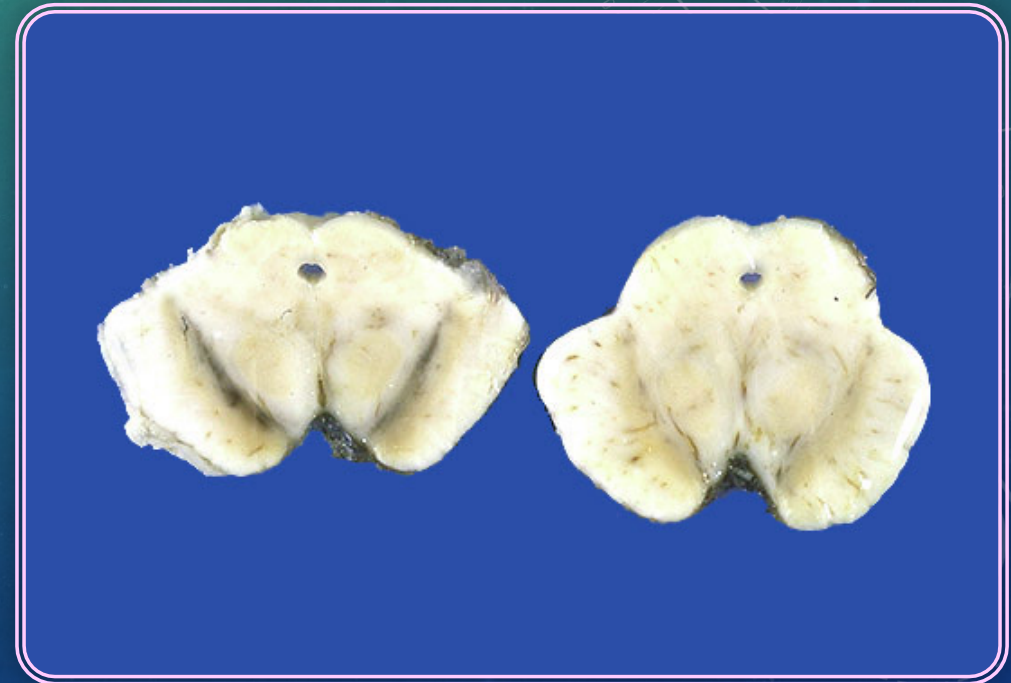
# HOW IS DOPAMINE USED?

- Dopamine leaves the substantia nigra and can be used to send signals to the rest of the basal ganglia.
- The basal ganglia are different areas of the brain that contain groups of neurons which help people to have normal movements.
- Once dopamine has served its purpose, it is broken up and recycled.

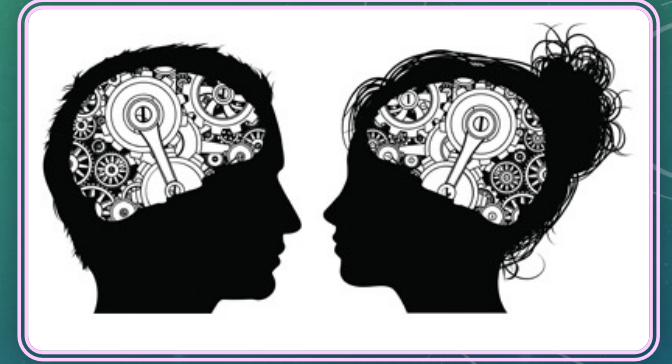


# WHAT HAPPENS IN PARKINSON'S DISEASE?

- People with Parkinson's Disease start to develop an abnormal protein called  $\alpha$ -synuclein (alpha-synuclein).
- This protein can accumulate all over the body, including in the substantia nigra.
- The  $\alpha$ -synuclein injures the neurons that make dopamine in the substantia nigra which causes the neurons to die and disappear.
- When people start making less dopamine, they begin to experience the symptoms of Parkinson's disease.



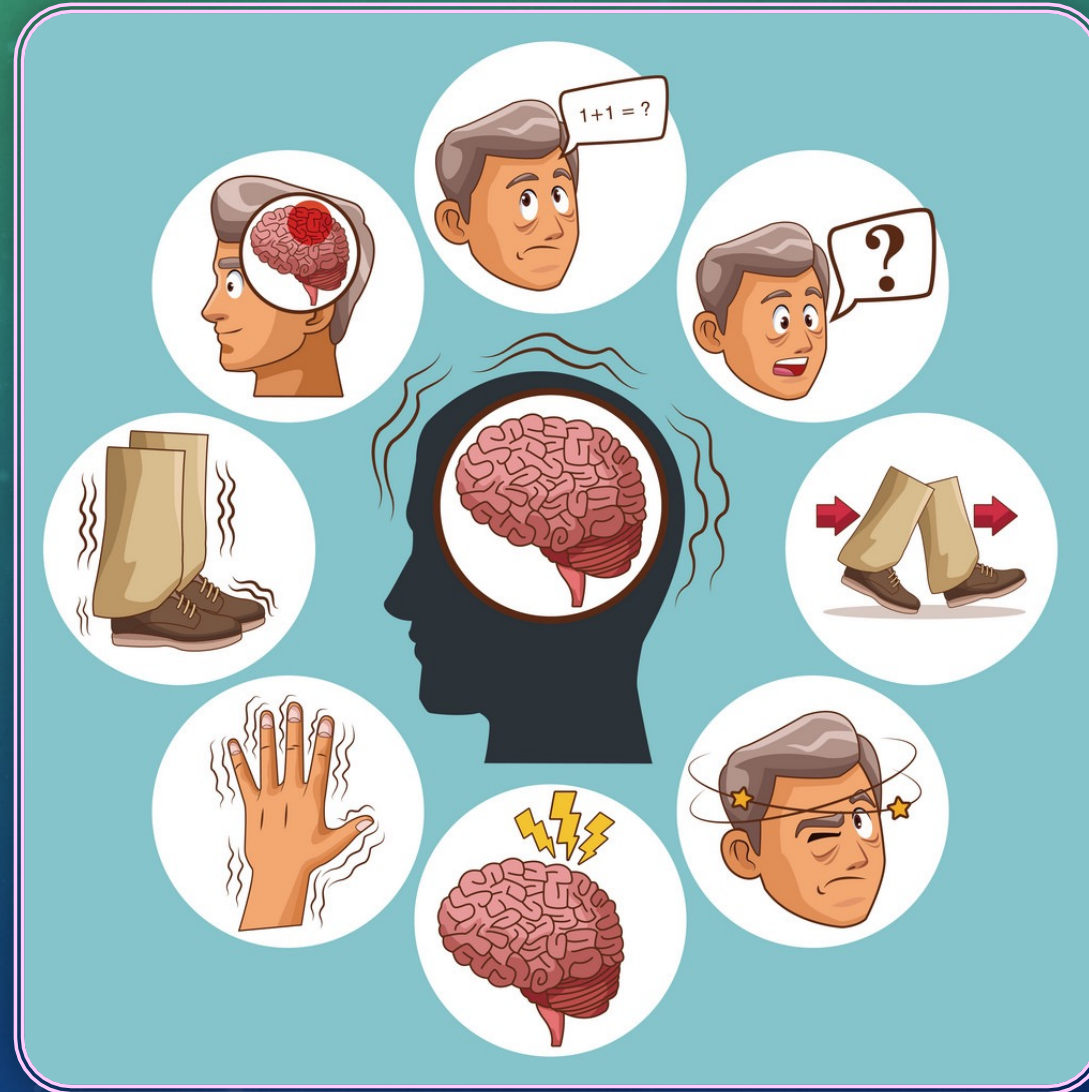
# WHO GETS PARKINSON'S DISEASE?



- Parkinson's Disease affects millions of people worldwide.
- It affects about 1% of people older than 60 years of age in the United States.
- The median number of new cases of Parkinson's disease, per year, in people over 65 years of age who live in high-income countries is 160 per 100,000.
- The number of new cases below age 50 is low.
- The lifetime risk of Parkinson's disease in men is 2% and 1.3% in women aged 40 and older.
- Men have a higher chance of having Parkinson's disease than women.



# PARKINSON'S DISEASE SYMPTOMS



MOTOR  
SYMPTOMS  
(PARKINSONISM)

Bradykinesia

Rigidity

Tremor

Postural and  
Gait  
Impairments



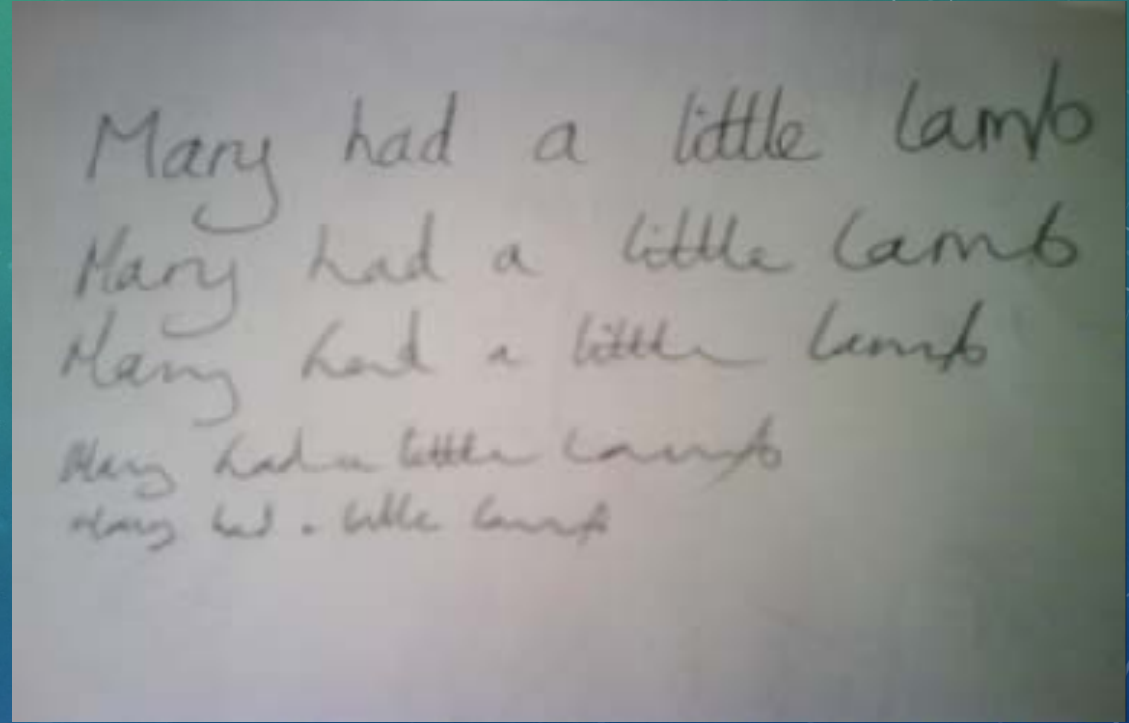
# CARDINAL SIGNS AND SYMPTOMS: BRADYKINESIA

- Bradykinesia means slowness of movement.
- Patient's **MUST** have bradykinesia and one other cardinal symptom to make the diagnosis of Parkinson's Disease.
- Bradykinesia can present as the following:
  - **Hypomimia** is a reduction in facial expression (masked face).
  - **Hypophonia** is soft speech.
  - **Micrographia** is small handwriting.





Hypomimia – “Masked Face”



Micrographia





# CARDINAL SIGNS AND SYMPTOMS: RIGIDITY

- Rigidity is resistance of muscles to passive movement around a joint.
- It can commonly present as a reduced range of motion and shoulder pain or difficulty turning over in bed at night.
- It can feel like a stiffness or inability to move well.
- Some people first speak with their primary care provider or an orthopedist before seeing a neurologist.



# CARDINAL SIGNS AND SYMPTOMS: RESTING TREMOR

- Tremor is an involuntary, rhythmic, and oscillatory movement of a body part.
- The tremor typically occurs at rest, such as when the person's body parts are resting comfortably and not being held up or performing an action.
- The tremor is usually slow and affects one side of the body but can affect both sides of the body over time.
- Tremor is present in 70% of patients with Parkinson's Disease.
- While a tremor at rest is the most common type of tremor seen, tremor can be present with activity. It can also affect the jaw, neck, voice, and head.



# CARDINAL SIGNS AND SYMPTOMS: POSTURAL/GAIT INSTABILITY

- The way a person walks, maintains their posture, and keeps and recovers their balance can become impaired in Parkinson's disease.
- This can be present as a normal finding in the elderly.
- Walking changes include:
  - Taking shorter steps or shuffling.
  - Swinging the arms less.
  - Having difficulty turning and changing directions.
  - "Freezing" or having the sensation of one or both feet stuck or glued to the floor.
- Problems with balance can ultimately lead to falls, though this usually happens late in the disease course.



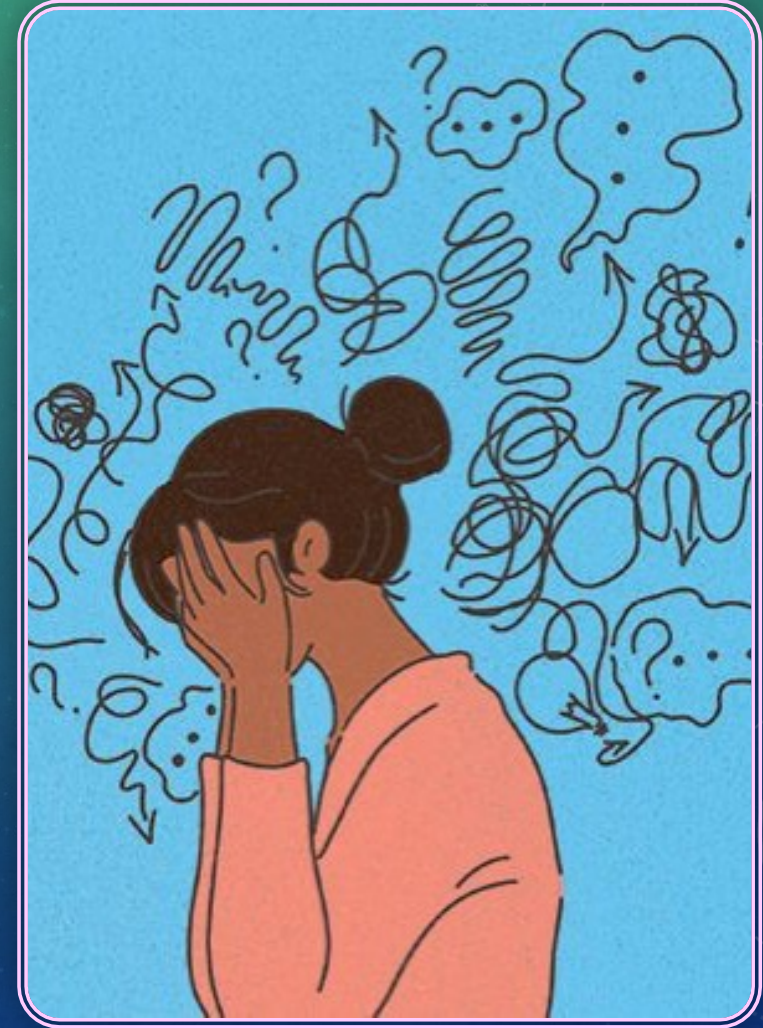
# NONMOTOR SYMPTOMS

- Since dopamine affects more than just the way a person moves, all patients will have concurrent nonmotor symptoms.
- Nonmotor symptoms can – and often do – precede motor symptoms.
- Their impact is often greater than the motor symptoms.
- Treatment for the motor symptoms may exacerbate or worsen the nonmotor symptoms.



# NONMOTOR SYMPTOMS: NEUROPSYCHIATRIC SYMPTOMS

- Neuropsychiatric symptoms affect the person's mood, motivation, and behavior.
- These symptoms include:
  - Depression
  - Anxiety
  - Apathy or loss of motivation
  - Impulsivity
  - Psychosis – hallucinations, illusions, delusions



# NONMOTOR SYMPTOMS: COGNITIVE SYMPTOMS

- Cognitive symptoms affect the way people think.
- These symptoms include:
  - Memory loss
  - Dementia
  - Word-finding difficulty
  - Inattention
  - Slowness of thought



# NONMOTOR SYMPTOMS: DYSAUTONOMIA

- The autonomic nervous system is involved in body processes that do not require the person to think about doing them, such as digestion, managing blood pressure and heart rate, and sweating.
- Dysautonomia results in the following symptoms:
  - Low blood pressure and feeling like one is about to faint when going from a lying or sitting down position to a standing position
  - Constipation and loss of appetite
  - Urinary incontinence
  - Sexual dysfunction such as reduced libido and erectile dysfunction
  - Sweating and dry, flaky skin
  - Drooling



# NONMOTOR SYMPTOMS: ALTERED SENSES

- Parkinson's disease can lead to changes in our senses such as:
  - A loss in sense of smell and taste
  - Numbness and tingling
  - Unexplained pain
  - Fatigue





# NONMOTOR SYMPTOMS: SLEEP DISORDERS

- Parkinson's disease can affect and alter sleep in several different ways:
  - Insomnia
  - Sleepiness
  - Restless Legs Syndrome (RLS)
  - Periodic Limb Movements of Sleep (PLMS)
  - REM-Sleep Behavior Disorder (RBD)
  - Sleep Attacks



# DIAGNOSIS



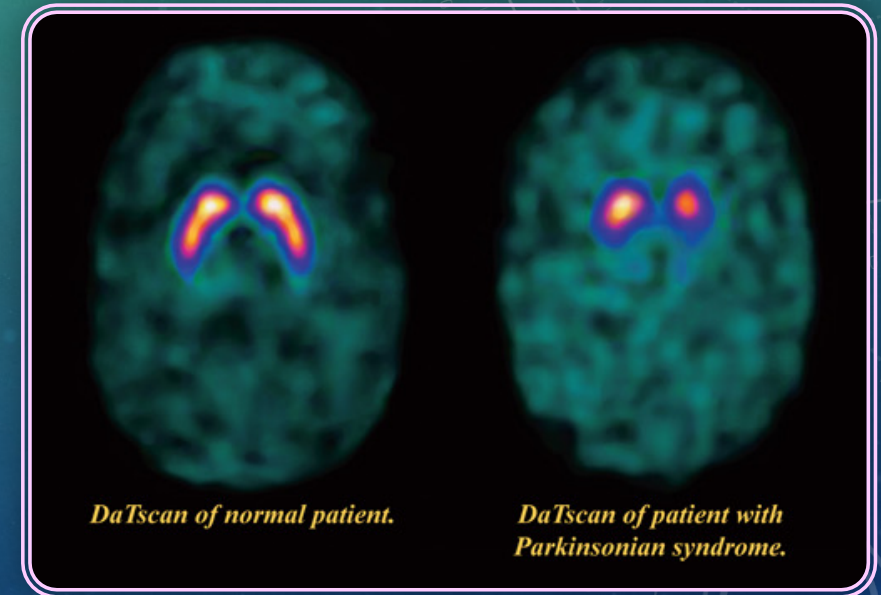
# HOW IS PARKINSON'S DISEASE DIAGNOSED?

- Patients with symptoms concerning for Parkinson's disease should be referred to a neurologist.
- A movement disorders specialist is the best type of neurologist to see because they specialize in diagnosing and managing Parkinson's disease and other diseases that are similar to it.
- The visit with the neurologist will include a thorough medical history and a specialized physical exam.
- These steps alone are enough to make the diagnosis of Parkinson's disease.



# SPECIAL TESTS

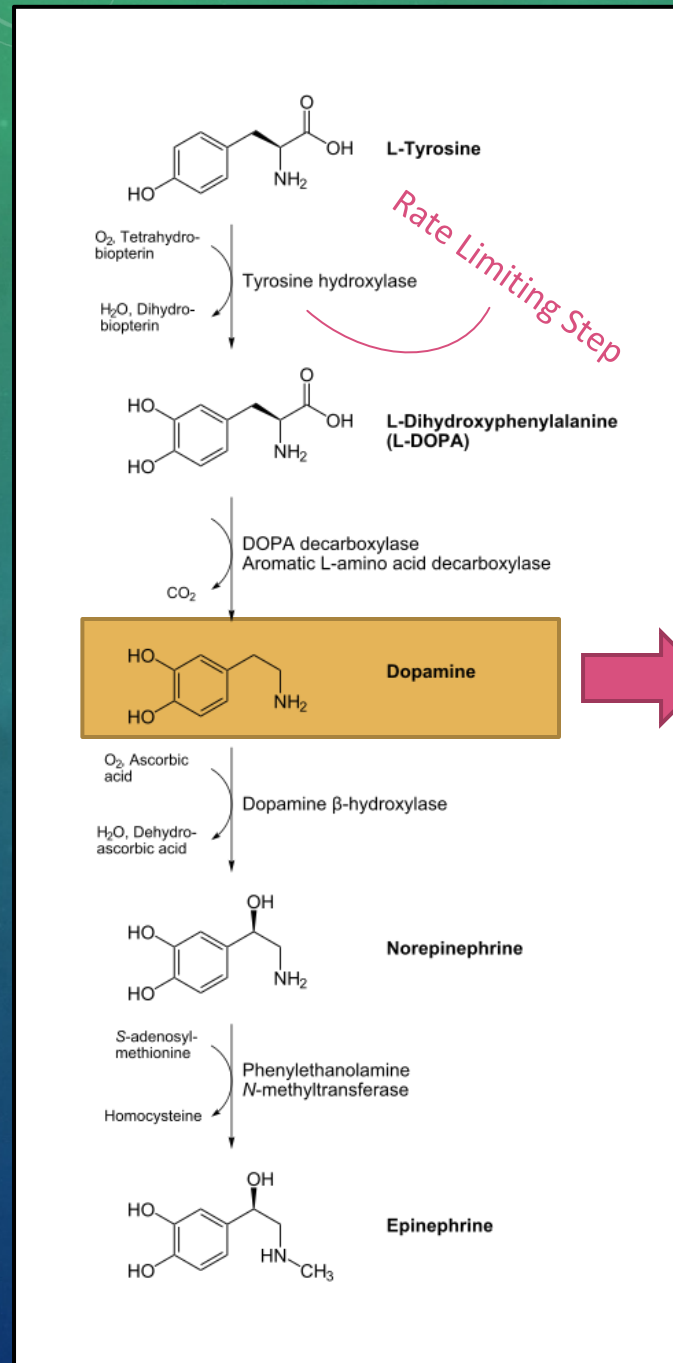
- Sometimes, Parkinson's disease looks like another disease, making it difficult to diagnose right away.
- Occasionally, special tests can be ordered such as a CT or MRI of the brain.
- Other times, a DaTscan is ordered.
- The DaTscan is a type of SPECT scan which uses a radioisotope of iodine called ioflupane ( $^{123}\text{I}$ ).
- Ioflupane binds to dopamine transporters in neurons that create dopamine.
- There is usually an asymmetric loss of ioflupane binding in certain neurodegenerative diseases.
- Certain medicines cause false results in this test and need to be stopped days and sometimes weeks beforehand.



# TREATING MOTOR SYMPTOMS



# SOME CHEMISTRY



Breakdown mediated by:  
-Catechol-O-methyltransferase (COMT)  
-Monamine Oxidase B (MAOB)



# TREATMENT – CARBIDOPA-LEVODOPA

- The main therapy is levodopa which is converted to dopamine in the brain.
- Some symptoms are resistant to levodopa.
- It's most effective at treating akinesia/bradykinesia and rigidity with variable effects on tremor.
- Treatment with carbidopa-levodopa does NOT worsen the disease progression.
- It is available as immediate release, extended release, and orally disintegrating tablets.
- It also comes as an inhaled powder (Inbrija) which is approved for sporadic off episodes in patients who take carbidopa-levodopa.
- **SIDE EFFECTS:** GI upset (typically nausea).
- **COMPLICATIONS:** Dyskinesia, exacerbates orthostatic hypotension, confusion, hallucinations.



# TREATMENT – CARBIDOPA-LEVODOPA

- There is an intestinal gel version (Duopa) which can be administered as a continuous infusion via PEG-J tube.
- This may be useful in patients with symptom fluctuations and frequent off times.
- It can increase “on” time with fewer dyskinesias compared to oral meds in patient’s with advanced disease by lowering the chances of fluctuations of levodopa in the blood.
- Additional side effects to worry about come with PEG-J tube maintenance and risk of infection.





# TREATMENT – DOPAMINE AGONISTS

- **DRUGS:** Pramipexole (Mirapex), ropinirole (Requip), rotigotine (Neupro) – Transdermal, and Apomorphine (Apokyn) – subcutaneously as a rescue med (Kynmobi is the new sublingual form).
- **HOW IT WORKS:** Directly stimulates dopamine receptors.
- **USES:** Can be used alone or in addition to other meds
- They tend to have a longer lasting effect than levodopa but a higher incidence of psychiatric side effects.
- **SIDE EFFECTS:** GI upset, hallucinations, impulse control disorder, “sleep attacks,” leg swelling, exacerbate confusion.



# TREATMENT – COMT INHIBITORS

- DRUGS: Entacapone (Comtan), Tolcapone (Tasmar), opicapone (Ongentys).
- HOW IT WORKS: Reduces the breakdown of levodopa to allow it more time to have an effect.
- USES: An adjuvant to levodopa therapy to improve end-of-dose-wearing-off time.
- SIDE EFFECTS: May increase dyskinesias or amplify any levodopa side effects, discolors urine, diarrhea, and has a black box warning for potential liver toxicity.
- If a patient develops diarrhea, it's not the fun kind that treats their Parkinson's disease constipation, it's the bad kind that requires stopping the medicine.
- COMT = Catechol-O-methyltransferase



# TREATMENT – MONOAMINE OXIDASE-B INHIBITORS (MAO-B INHIBITORS)

- **DRUGS:** Selegiline (Eldepryl, Zelapar), Rasagiline (Azilect), Safinamide (Xadago)
- **HOW IT WORKS:** Each reduces the breakdown of levodopa in slightly different ways to allow it more time to have an effect.
- **USES:** Selegiline is used in addition to levodopa with motor fluctuations. Rasagiline can be used as monotherapy and adjuvant therapy. Safinamide is used for adjuvant therapy for PD with motor fluctuations.
- **SIDE EFFECTS:** Hypertensive crisis, sleep attacks, arrhythmias, hallucinations, extrapyramidal side effects, can amplify levodopa side effects.



# TREATMENT – AMANTADINE (NMDA-R ANTAGONIST)

- DRUGS: Amantadine
- HOW IT WORKS: It is poorly understood but it likely increases the release of dopamine. It also acts as an N-methyl-D-aspartate (NMDA) receptor antagonist.
- USES: Dystonia/dyskinesia, can help with gait freezing.
- SIDE EFFECTS: Livedo reticularis, leg swelling, sleep attacks, lowers white blood cells, dry mouth, constipation, nausea, confusion (especially in the elderly), suicidality, compulsive behaviors.



# TREATMENT - ANTICHOLINERGICS

- **DRUGS:** Trihexyphenidyl (Artane), Benztropine (Cogentin)
- **HOW IT WORKS:** Blocks acetylcholine, another neurotransmitter that contributes to stiffness and tremor.
- **USES:** Medication-resistant tremor and dystonia.
- **SIDE EFFECTS:** Dry mouth, confusion, urinary retention, fatigue, and constipation.



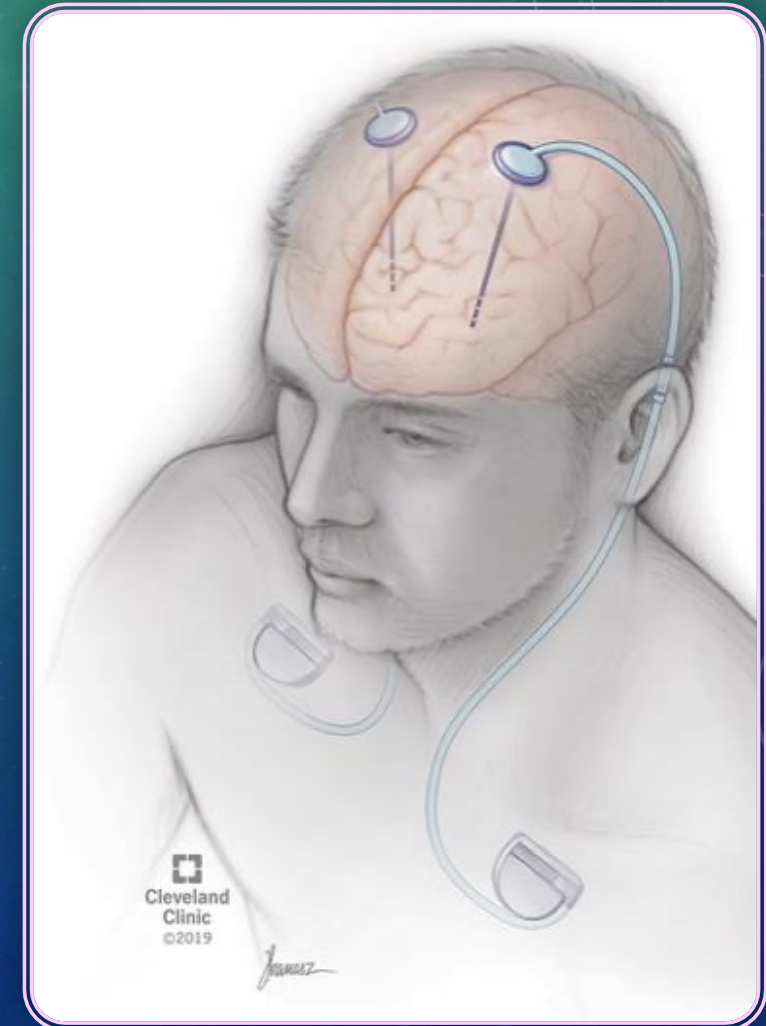
# TREATMENT – ADENOSINE RECEPTOR ANTAGONIST

- DRUGS: Istradefylline (Nourianz)
- HOW IT WORKS: It blocks the Adenosine A<sub>2A</sub> receptor
- USES: An adjuvant to levodopa therapy to improve end-of-dose-wearing-off time.
- SIDE EFFECTS: Dyskinesia, insomnia, hallucinations, nausea, constipation, aggression, impulse control disorder.



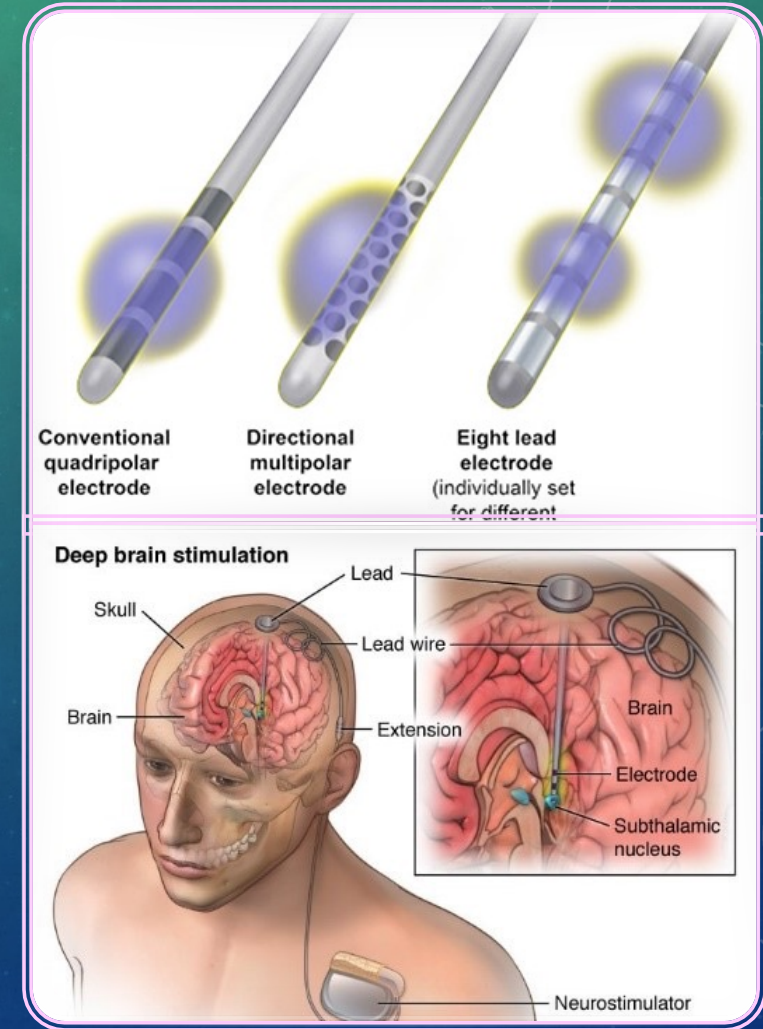
# SURGICAL TREATMENT CONSIDERATION

- Deep Brain Stimulation (DBS) is a surgery that can be offered to some people with Parkinson's disease.
- It can improve tremor, dyskinesia, and motor fluctuations in people who are no longer having success with medical management.
- Patients must be evaluated by a neurologist, neurosurgeon, and often a neuropsychologist.
- It is not offered to people with atypical and rarer forms of parkinsonism, unstable psychiatric disease, advanced Parkinson's disease with significant dementia, comorbidities that preclude surgical candidacy, and advanced age.



# DEEP BRAIN STIMULATION (DBS)

- It involves a neurosurgical procedure in which a metal wire, called a lead or electrode, is placed in a specific target of the basal ganglia or thalamus.
- An implantable generator is also placed in the chest and acts as the battery for the electrode.
- A neurologist then programs the DBS in the outpatient setting to attempt to achieve maximal benefit from the DBS with the fewest side effects.





# SURGERY AND DBS SIDE EFFECTS

- Complications from the brain surgery include: heart attack, pneumonia, clots in the leg veins, clots in the blood vessels of the lungs, bleeding in the brain, stroke, seizures, infections, and hardware malfunction.
- Side effects from the DBS include abnormal sensations such as numbness or tingling, slurred or altered speech, uncoordinated movements, and changes in mood.
- Additionally, the implantable generators need to be replaced every few years though some of the newer generators are rechargeable.



# TREATING NONMOTOR SYMPTOMS



# PSYCHOSIS AND DEMENTIA

## For Psychosis:

- Always get checked for an infection first.
- Review the medicines. Medicines like sedatives, anti-anxiety medications, antidepressants, and pain medications can contribute to psychosis and may need to be reduced or stopped.
- The antiparkinsonian medications may need to be reduced or stopped if it's safe to do so.
- People may need to be started on an antipsychotic medication.

## For Dementia:

- Some people may benefit from a cholinesterase inhibitor such as donepezil or rivastigmine.
- There may be some benefit from memantine.



# INSOMNIA AND FATIGUE

- Avoid naps during the day and have a set sleep and wake time.
- Sometimes stimulants during the day or sleep aids at night can help.



# NAUSEA, CONSTIPATION, DIFFICULTY SWALLOWING

For nausea:

- Ondansetron can be helpful. Other medicines for nausea can make Parkinson's disease worse.

For constipation:

- Dietary changes can help including: more water, more fiber.
- Medicines like psyllium (Metamucil), methylcellulose, docusate, bisacodyl, and senna can help for less severe constipation. Suppositories may be needed for more severe constipation.

For difficulty swallowing:

- Antiparkinsonian medication can help.
- Swallow rehabilitation
- Feeding tubes may be helpful in the setting of severe disease.



# LOW BLOOD PRESSURE WHEN CHANGING POSITION

- Avoid, reduce, or stop medicines that lower BP like alcohol, beta-blockers, narcotics, diuretics, sedatives, muscle relaxers, some antipsychotics, and antiparkinsonian medications.
- Increase fluid and salt intake.
- Compression stockings and exercise.
- Never lie flat; use pillows to prop the head up at bedtime.
- Medicines that raise the blood pressure.



# MANAGEMENT



# DISEASE MANAGEMENT

- The initial focus should be on dopamine replacement with some combination of carbidopa-levodopa and other medicines.
- Levodopa does not worsen the disease progress; early symptom onset and high doses of levodopa (required in late disease) are what lead to motor fluctuations and dyskinesias.
- Dopamine agonists, MAO-B inhibitors, or anticholinergic medications can be initiated in patients younger than age 70. However, these drugs are more likely than levodopa to cause cognitive side effects in the elderly.
- Long-term aerobic exercise may slow down disease progression: core strength training, tai chi, yoga, boxing, and dance and music therapy.





# RESOURCES

- American Parkinson's Disease Association: <https://www.apdaparkinson.org/>
- National Parkinson's Disease Foundation: <https://www.parkinson.org/>
- National Institute of Health: <https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Hope-Through-Research/Parkinsons-Disease-Hope-Through-Research>
- Davis Phinney Foundation: <https://davisphinneyfoundation.org/>
- Lee Silverman Voice Treatment (LSVT LOUD): <https://www.lsvtglobal.com/>
- Rock Steady Boxing: <https://www.rocksteadyboxing.org/>
- Physical Therapy and Occupational Therapy
  
- Research and Clinical Trials:
- For current clinic trials (national): <https://clinicaltrials.gov>
- Parkinson's Study Group: <http://www.parkinson-study-group.org/>
- Michael J. Fox Foundation: <https://www.michaeljfox.org/>



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QUESTIONS?

