PARKINSON'S DISEASE

For Class- B.Pharmacy 2nd Semester

Subject- Pathophysiology (BP204T)

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INTRODUCTION:

- Parkinson disease is a slowly progressive , chronic neurological disease that effects a small area of nerve cells in an area of the brain known as the substantia nigra.
- This cells normally produces dopamine, a chemical (neurotransmission) that transmits signal between areas in the brain that when working normally coordinates smooth and balanced muscle movement .
- Parkinson’s disease cause this nerve cells to die and as a result body movement are effected.

HISTORYOF PD:

- In 1817, a detailed medical essay was published on the subject by London doctor, ***Dr. James Parkinson***.
- Jean Martin Charcot was the first to truly recognize the importance of Dr. James Parkinson's and renamed the disease after him as ''Parkinson's disease'' which was formerly named ***paralysis agitation*** (shaking palsy).

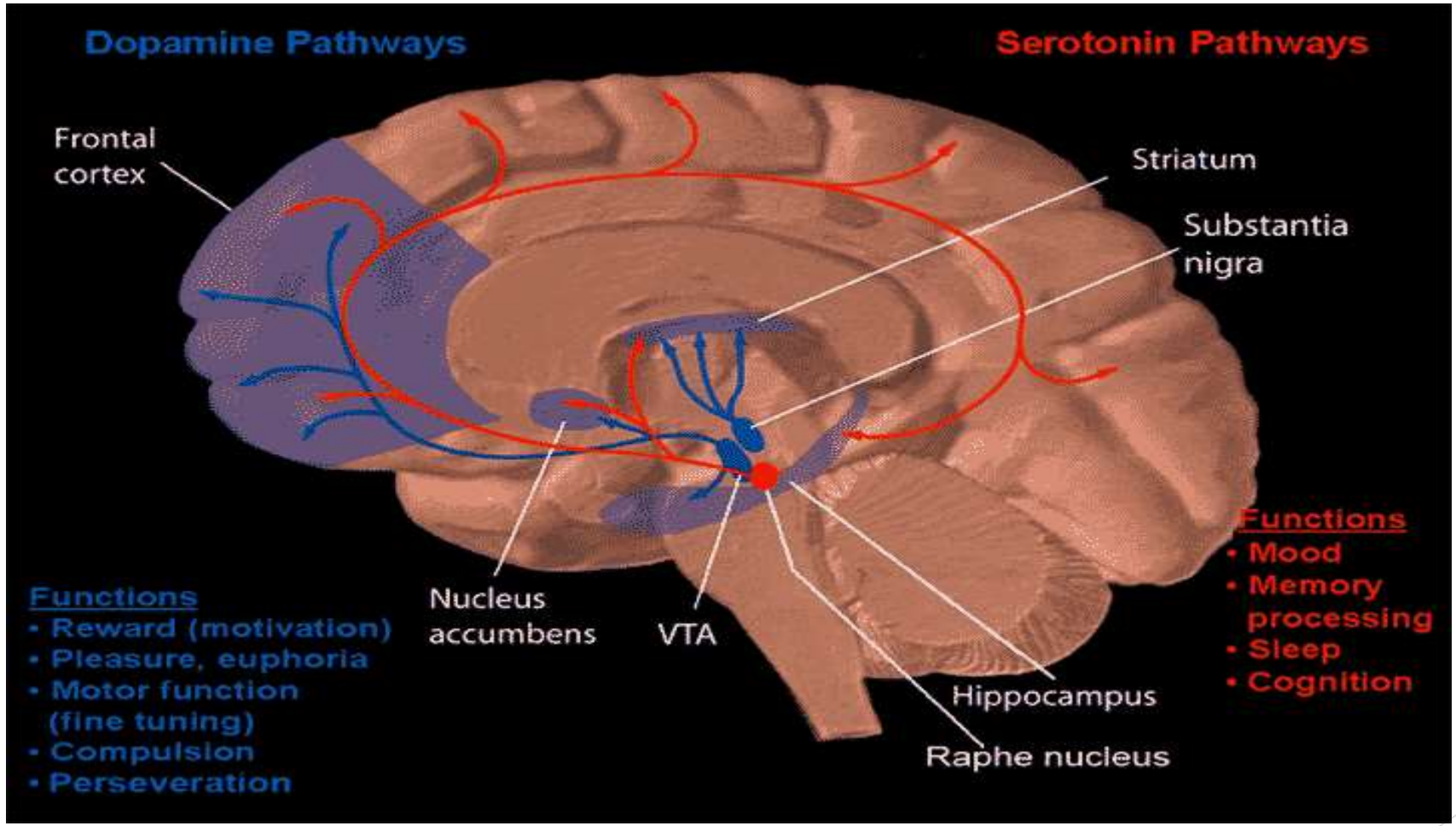
EPIDEMIOLOGY:

- Parkinson disease occurs worldwide and is present in all races.
- Males are more affected than females.
- Prevention of Parkinson disease increase with increasing age of 1% of person from age 60.
- YOPD starts between 21 -40 years of age affecting 5 to 10% of Parkinson disease patients.
- China is the country world largest prevalence of Parkinson disease.
- The incidence and prevalence of Parkinson disease in India is lesser as compared to other country, Rural population had a higher prevalence than urban population 41:14.

DEFINITION:

- Parkinson disease is characterized by tremor at rest, rigidity and slowness or difficulty in initiating and executing movement (Akinesis or Bradykinesis). This combination of clinical features is collectively known as Parkinsonism.
- Parkinsonism is a syndrome with numerous cause of which Parkinson disease is the most common.

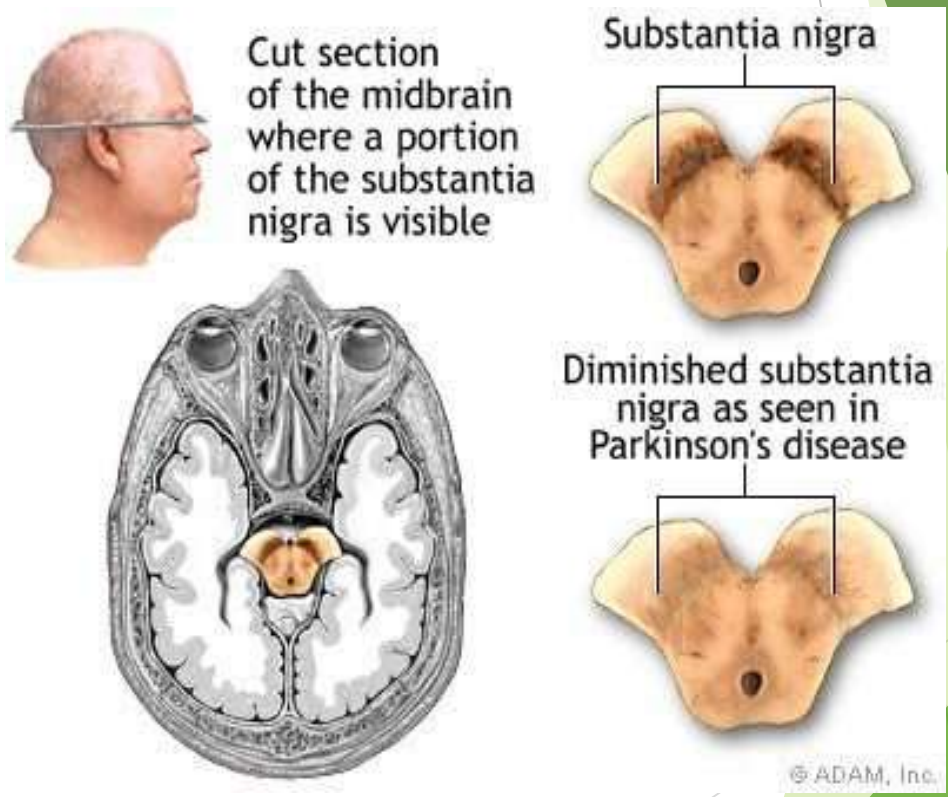
ANATOMY


Dopamine Pathways
Serotonin Pathways
Frontal cortex
Striatum
Substantia nigra
Nucleus accumbens
VTA
Hippocampus
Raphe nucleus
Functions
• Reward (motivation)
• Pleasure, euphoria
• Motor function (fine tuning)
• Compulsion
• Perseveration
Functions
• Mood
• Memory processing
• Sleep
• Cognition

- The substantia nirga is a nucleus in the mid brain which is part of the Basal Ganglia.
- The substantia nigra is made up of two automatically and functionally distinct portion :
  - Substantia nigra pars compacta –more darkened
  - Substantia Nigra pars reticulata –less darken.
- Most of the dopamine neuron of the brain originate in the midbrain and are found in either the substantia Nigra.
- The Dopamine neurons in the substantia Nigra express high level of pigment called Neuromelanin which accounts for thin dark colour .
- The substantia Nigra par compacta contain more dopamine neurons while pars Reticulate contains more GABA neurons .

CLINICAL SIGNIFICANCE:

- Parkinson disease is associated with the death of dopamine Neuron in the substantia Nigra pars compacta which is due to neuro-degeneration .
- when a significant number of this neuron have died, the individual will likely to start to experienced movement –related problems like tremors, rigidity, slowness of movement and postural instability – which are the hall mark symptoms of Parkinson disease.



ETIOLOGY/RISK FACTORS:

- **Advancing age :** Above 60 years mostly seen while young onset Parkinson disease is called a patients develop Parkinson disease between 21-40 years.
- **Sex:** male are more likely to get than female.
- **Family History:** Having one or more close relatives with the disease increase the rise of getting.
- **Low Estrogen Level:** most menopausal women who don't use hormone replacement therapy are more risk of getting the disease.
- **Agricultural work:** exposure to environmental toxin such as pesticide ,herbicides ,inhabits dopamine production and promote free radical damage. these involved in farming and are exposed to such toxins have a greater risk of getting the disease.
- **Low level of vitamins:** researchers de was found that people with low level of vitamin B develop severe Parkinson symptoms.
- **Head Trauma:** Trauma to the head ,neck and upper cervical spine increase the chance of getting Parkinson's.

Genetic Mutation: people who have both young onset Parkinson's disease and a strong family history of the disease are more likely carry genes linked to Parkinson's disease which includes;

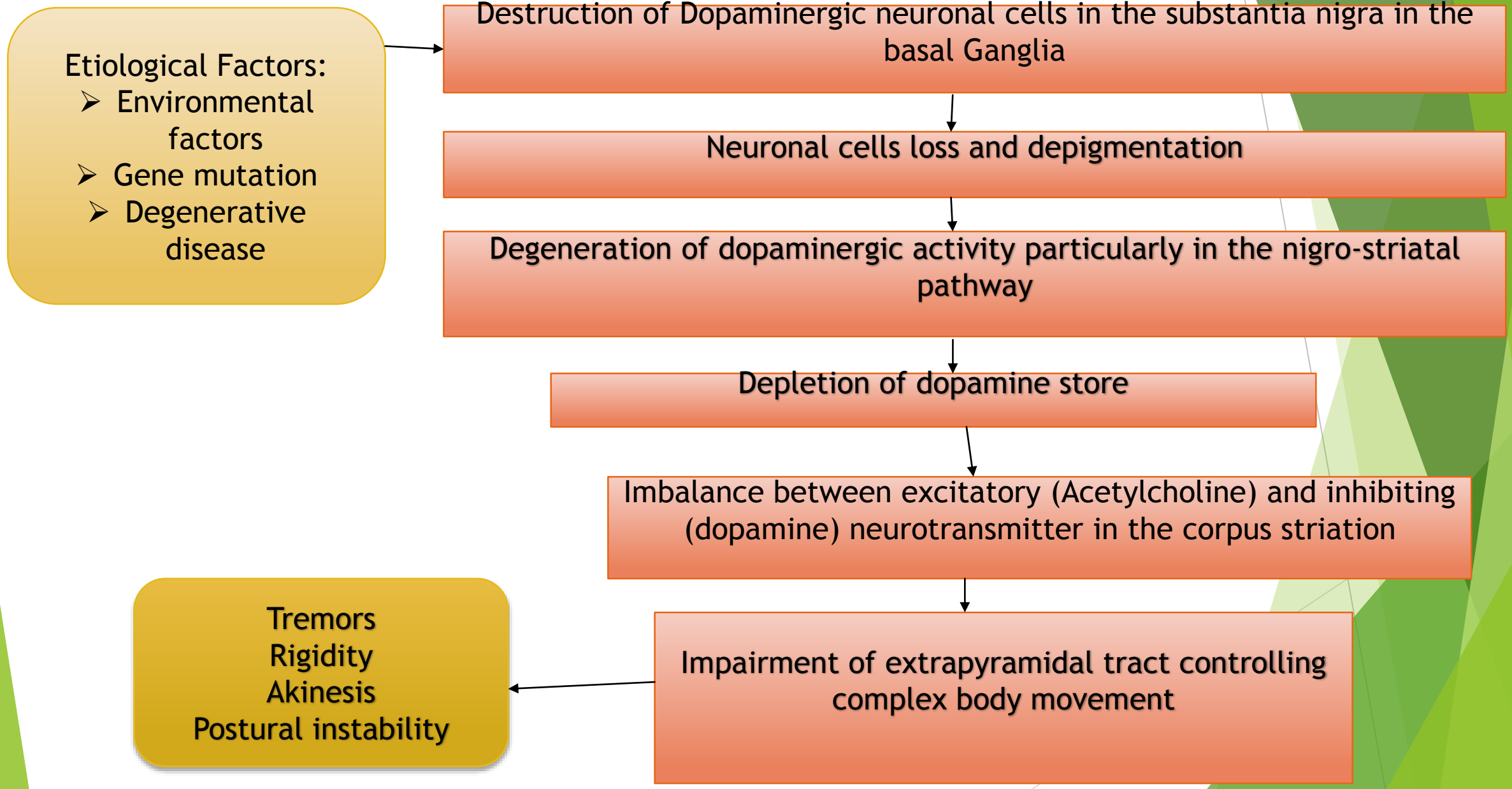
- Alpha Synuclein: Autosomal dominant.
- LRRK2(leucine rich repeat kinesis2): Autosomal.
- PINK1/PARKIN/DJ-1: Autosomal recessive
- GBA(Glucocerebrocidase): Autosomal recessive
- Alpha synuclein and LRRK2 gene mutation is linked with Young onset Parkinson Disease.

Other causes:

- **Secondary Parkinson's:** which are caused by other disorders such as Neoplasm, multiple cerebral infarction and infection of the brain.
- Drug induces Parkinsonism: which are irreversible. causative drugs include : Neuroleptics – haloperidol ,risperidone, olanzapine.

  Antiemetic- metachlopramine, prochlorperazine.
- Parkinson's disease caused by Degenerative disease in which symptoms of Parkinson's disease are combines with neurologic deficit yet patients fail to response to Anti-Parkinson drugs therapy . These disorders include
- Multiple system atrophy (MSA).
- Alzheimer's Disease -often accompanied with mild signs of Parkinsonism.

PATHOPHYSIOLOGY:



SIGNS AND SYMPTOMS:

Four cardinal sign:
- Resting tremor
- Rigidity
- Akinesia
- Postural instability

AKINESIA:
Bradykinesia
Hypokinesia
Hypophonia
Micrographia

Cog-wheeling

DYSAUTONOMIA: it includes
- sweats,facial flushing.
- Dyspnea, urinary frequency, urgency.
- GI dysfunction-constipation.
- Dysphagia
- Orthostatic hypotension and sexual dysfunction

- **POSTURAL DISTURBANCE:** Stooped or fixed positive
- Disequilibrium or postural instability
- Retropulsion –backward motion
- Propulsion – forward motion

Sleep disturbance:
Frequent awakening
Daytimes sleepiness'
Sensory impairment: pain, restlessness and Akathisia.

Cognitive And psychiatric disturbance: Anxiety, Apathy, mental, irritability, impaired executive function, depression psychosis (delusions and Italicization) dementia

STAGES OF PARKINSON’s DISEASE

- Parkinson’s disease is typically classified by the worsenng of clinical manifestation. The modified Hoehn and yohr and scale is one method use to rate the severity of Parkinson’s disease.
- STAGE 0: No evidence of Parkinson’s disease.
- Stage 1: Unilateral involvement .
- Stage 1.5: Unilateral and Axial involvement .
- Stage 2: Bilateral involvement, balance in contact .
- Stage 2.5: Bilateral involvement, recovery on pull test .
- Stage 3: Mild to moderate impairment with postural instability .
- Stage 4: Severe impairment but still able to stand or walk un assisted.
- Stages 5: Confinement to a wheel chair or bed .

DIAGNOSTIC EVALUATION:

- Laboratory test and imaging studies are not helpful in the diagnosis of Parkinson's disease.
- Criteria for making diagnosis of Parkinson's disease include the following

1. Through patients' history and performed complete neurological examination.

2. CT scan or MRI of head to rule out secondary cause.

3. PET-scan to evaluate levodopa uptake and conversion to Dopamine in the corpus Striatum .

4. Present of two or more cardinal features (resting tremors, rigidity, Akinesia, postural instability).

5.Final diagnosis usually made by the pressure of heavy bodies in the brain during Autopsy.

MANAGEMENT:

- There are complete cure for Parkinson's disease.
- Treatment is directed at controlling symptoms and maintaining functional independence.
- There are no medical or surgical approaches that prevent disease progression.
- Care is individualized for each patients based on preventing symptoms and social occupational and social needs.
- Pharmacologic management is the main stay of treatment.

ANTI-PARKINSONISM MEDICATION:

1. **LEVEDOPA (L-Dopa):** it is the most effective agents and the mainstay of treatment, for controlling the symptoms particularly Bradykinesia and rigidity.

- SINEMET: it is made up of Levodopa and carbidopa .Levodopa enters the brain and is converted to Dopamine while carbidopa increase its effectiveness and prevents the side effects of levodopa such as nausea, vomiting.

2. **DOPAMINE RECEPTOR AGONISTS**: this are the drugs that activate or stimulate the dopamine receptors . They mimic or copy the function of Dopamine in the brain. Dopamine agonists can be taken alone or in combination with Levodopa/carbidopa. Most commonly drugs used are

- Ergot derivatives : Bromocriptine or pergolite.
- Non-ergot Derivatives: Ropinirole ,pramipexole.

3. **MONOAMINE OXIDIZED INHIBITORS:** It blocks an enzymes that caused premature of levodopa and are used primarily to treat motors fluctuation associated with levodopa treatment .most commonly drugs used are

- Seligiline
- Rosagiline.

AMANTADINE : it is the most commonly used medication for early onset Parkinson's disease to tract tremor .It reduce dyskinesia's that occur with Levodopa.

COMT INHIBITORS(Catechol-o-methyl-transferase): such is Tolcapone and entacapone response the newest class of Parkinson's drugs .

- It does not have direct effect on Parkinson's disease symptoms
- it prolong the effect of levodopa by blocking its metabolism.

ANTI-CHOLINERGIC: it is helpful in controlling tremors and rigidity.

- It decrease the activity of acetylcholine, a neurotransmitter that regulates movement ,most commonly used are:
- Benzotropine mesylate
- Trihexyphenidyl HCL

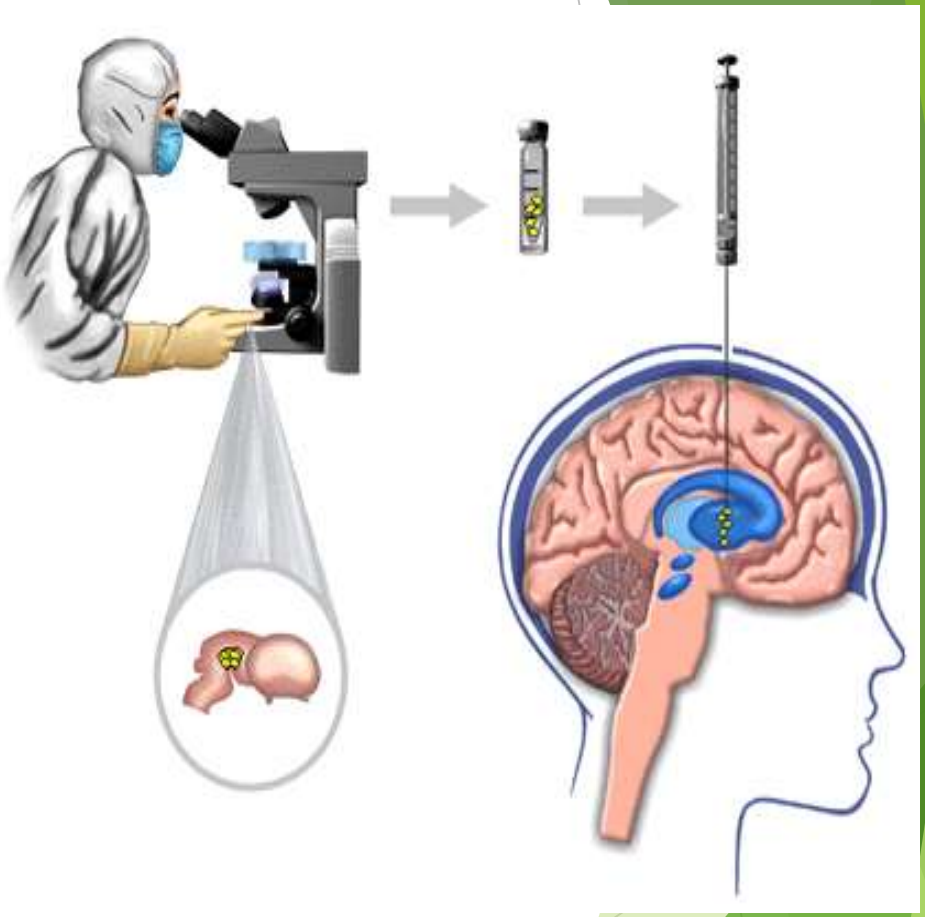
ANTI-DEPRESSANT :

- Amitriptyline is typically prescribe because of its Anticholinergic and Antidepressant effect.
- Serotonins reuptake inhibitors; Fluoxetine Hydrochloride and Bupropion hydrochloride.
- Effective for treating depression in patients with Parkinson's disease.

SURGICAL MANAGEMENT:

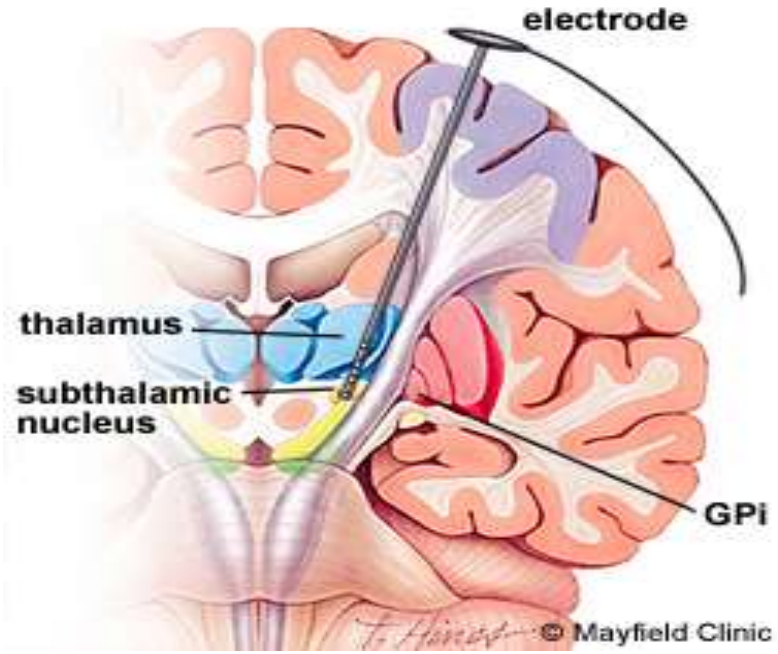
THALATOMY:

- It involves destruction of part of the Thalamus, generally the ventral's intermediates (VIM) to relieve tremor.
- The VIM nucleus is considered the best target for tremor suppression with excellent short and long term tremor suppression in 80-90% of patients with Parkinson's diseases.
- When rigidity and Akinesia are prominent other targets ,deep brain stimulation of both Globus pallidus interna (Gpi) and subthalami nucleus (STN)are preferred.



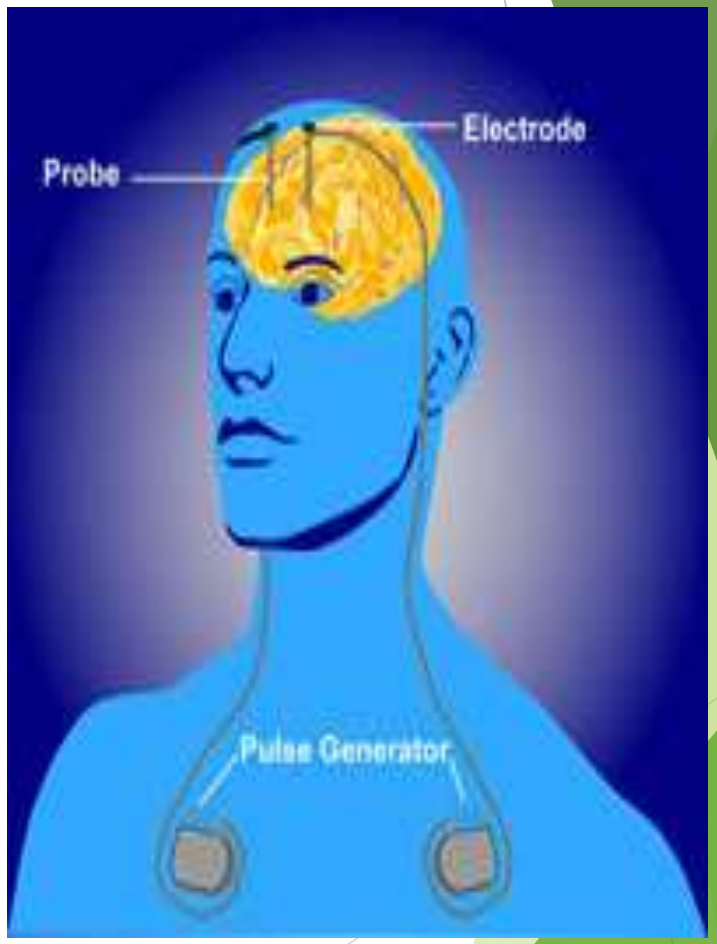
PALLIDOTOMY:

- Pallidotomy is a neurosurgical procedure whereby a tiny electrical probe is placed in the globes pallidus, which is then heated to 80^0C for 60 sec, to destroy a small area of brain cells.
- It is effective for treating in voluntary movements known as Dyskinesia, motor symptoms presented with Parkinson's Disease.



DEEP BRAIN STIMULATION:

- Deep brain stimulation is a neurological procedure which was first approved in 1997 to treat Parkinson's diseases tremor, then in 2002 for treatment of advanced Parkinson's diseases symptoms.
- More recently in 2016 DBS surgery was approved for the earlier stages of Parkinson's for those with at least four years disease duration with motors complication that are not controlled with medications.
- Deep brain stimulation involves the implantation of permanents thin electrodes into selected deep parts of the brain .
- The targets area of the brain depends on the presenting symptoms, the most common targets area are thalamus, subthalamic nucleus(STN)and Globus pallidus in terna(Gpi).



NURSING MANAGEMENT:

Nursing Assessment:

- Obtain a history of symptoms and their effect on functioning, mobility, feeding, communication, and self-care difficulties.
- Assess cranial nerves, cerebellar function (co-ordination) and motor function.
- Observe gait and performance of activities
- Assess speech for clarity and space
- Assess for sign of depression
- Assess family supports and access to social service.

Nursing Diagnosis:

1. Impaired physical mobility related to Bradykinesia, rigidity and tremors
2. Imbalance nutrition less than body requirement related to motor difficulties with feeding, chewing and swallowing
3. Impaired verbal communication related to decreased speech volume
4. Constipation related to diminished motor function and inactivity
5. Ineffective coping related to physical limitation and loss of independence.

CONCLUSION:

- Parkinson's disease is a chronic, progressive neurologic disorders that results from the loss of the neurotransmitter dopamine in a group of brain structures that controls movement.
- The cardinal symptoms are resting tremors, rigidity, Akinesia and postural instability.
- The goal of management is to control the manifestation such as motor and non-motor symptoms with the lowest possible dose of medication in order to avoid side effects.
- Medication selection and dosage depend on the manifestation, age of the client and presence of other medical condition.
- Nursing care should focus on the health assessment, medication instruction and monitoring, liaison with other members of the health care team, and family members and family education.