Parkinson's Disease

* It is a progressive Movement Disorder
* It is one of the most common neurological disorder. [DEPTH OF BIOLOGY]
* In this Dopamine producing Neuron in the substantia Nigra of the brain undergo degeneration
* Adult onset disease and get it more common with age. [DEPTH OF BIOLOGY]

Its cause is still unknown

But in few cases — There might be a genetic cause

↓

like mutation PINK1, PARKIN & α-Synuclein gene

In rare cases — caused by MPTP (a toxic Impurity found in recreational drug MPPP

[DEPTH OF BIOLOGY]

Risk factors — eg- Pesticide exposure, DNA variant in genes like LRRK2

Parkinson disease from the death of dopamine producing or dopaminergic neurons in the

Substantia Nigra

It is a part of the basal ganglia, a collection of brain region that control movement through their connections with the motor cortex.

Black substance

↓

It is darker than other brain region.

*In P.D. these darkened part subst. Nigra gradually dissapear.

⇒ Under Microscope

↓

Lewis bodies

↓

which are acidophillic are present in the affected substantia Nigra neuron before they die

* Lewis bodies are round inclusion made of α-synnuclein gene.

The function of α-synnuclein is unknown as well as the significance of Lewis body

DEPTH OF BIOLOGY

→ The Substantia Nigra actually can be split into two regions — sub regions

[DEPTH OF BIOLOGY]

Pars Reticulata

↓

which receives signals from another part of the basal ganglia called the Striatum

↓

and relay message to the thalamus via neurons such as the neurotransmitter GABA, also known as gamma amino butyric acid.

Pars Compacta

↓

Its the part of the substantia nigra affected in Parkinson's dz-

↓

The pars compacta sends msg. the striatum via neurons such as the neurotransmitter dopamine

↓

help to stimulate the cerebral cortex and initiate movements

[DEPTH OF BIOLOGY]

∴ in P.D patient (low movement state found.)

Clinical features :—

① Tremors — Involuntary shakiness most noticable in hands (Pill Rolling Tremor)

[DEPTH OF BIOLOGY]

② Rigidity — Refers to the stiffness that can appear as cog wheel rigidity.

③ Bradykinesia — Slow Movement

on Hypokinesia — lessened movement

on Akinesia — Absence of movement

all the above 3 are resulted from difficulty in Initiating Movements [DEPTH OF BIOLOGY]

④ Postural Instability (late features) — problem with balance and can lead to falls.

* Now Motor brain function also get affected.

on P.D. →

Depression, Dementia, sleep disturbance and difficulty smelling

↓

These all are because of dysfunction in dopaminergic signalling in other parts of the brain beyond the substantia nigra.

[DEPTH OF BIOLOGY]

- Like prefrontal cortex on dysfunction in other Neurotransmitter is Acetylcholine

Treatment :— [DEPTH OF BIOLOGY]

* Increase the amount of dopamine signalling in the brain

* Dopamine itself —✱—) Blood Brain Barrier

↓

cannot cross the Blood Barrier Barrier

DEPTH OF BIOLOGY

But precursor of Dopamine can cross BBB

Levodopa → (BBB) → In Brain Levodopa —dopadecarboxylase→ Dopamine

[DEPTH OF BIOLOGY]

Peripheral Dopa Decarboxylase also exist

↓

It can metabolise levodopa —into→ Dopamine

↓ [DEPTH OF BIOLOGY]

Before it gets the Blood Brain Barrier and via other through

Enzyme metabolise into other catecholamines (like epinephrine)

which can cause unwanted side effect like :

Asecythremia

So,

we administrate Laveodopa, carbidopa, adopa decarboxylase Inhibitor that is not able to cross BBB. [DEPTH OF BIOLOGY]

Another Strategy →

Use Amantadine ⟶ Antiviral Medication

⟶ ↑se. dopamine Production.

Dopamine Agonist ⟶ can stimulate dopamine receptors

③ Inhibitors of COMT → catecholamines-o-methyl transferase

↓ ↓ enzyme

like Tolcapone → It degrade dopamine & Levodopa

④ Seligitine Inhibit → MAO-B degrade → Dopamine

⑤ Dopamine ↓ ACTH ↑

Therefore we give Anticholinergic like

Benztropine — Improves tremors

⑥ Deg brain Stimulation —

Involve an implantable device

that directly sends electrical signals to the

Basal ganglia

Symptoms :-

→ like other nervous syst. disease like

lewy body dementia

wilson disease

& as side effect of medication Pick disease

→ Antipsychotic (Haloperidol)

Block dopamine receptors.