

Parkinson's Disease

- * It is a progressive **Movement Disorders**
- * It is one of the most common neurological disorders. [DEPTH OF BIOLOGY]
- * In this Dopamine producing Neurons 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 or α -Synuclein gene

In rare cases — caused by MPTP (a toxic Impurity
[DEPTH OF BIOLOGY] found in recreational drug MPPP)

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

[DEPTH OF BIOLOGY]

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 disappear.

⇒ Under Microscope



Lewy's bodies



which are acidophilic are present in the affected substantia nigra neuron before they die

* Lewy's bodies are round inclusion made of α -synuclein gene.

The function of α -synuclein is unknown as well as the significance of Lewy's body

[DEPTH OF BIOLOGY]

DEPTH OF BIOLOGY

→ The Substantia Nigra actually can be split into two regions - subregions [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.

[DEPTH OF BIOLOGY]

Pars Compacta



It's 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

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

Clinical features :-

① Tremor - Invol. shakiness most noticeable in hands (Pill Rolling Tremor)

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② Rigidity - Refers to the stiffness that can appear as cogwheel rigidity.

③ Bradykinesia - Slow Movement

or Hypokinesia — lessened movement

or Akinesia — Absence of movement

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

④ Postural Instability (late feature) — 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
↓

[DEPTH OF BIOLOGY]

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

• Like prefrontal cortex or dysfunction in other
Neurotransmitters in Acetylcholine

Treatment :- [DEPTH OF BIOLOGY]

* Increase the amount of dopamine signalling in
the brain

* Dopamine itself — ~~*~~ — Blood Brain Barrier
↓
cannot cross the Blood Brain Barrier

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But precursor of Dopamine can cross BBB

levodopa $\xrightarrow{\text{BBB}}$ In Brain levodopa $\xrightarrow[\text{[DEPTH OF BIOLOGY]}]{\text{dopa decarboxylase}}$ Dopamine

Peripheral Dopa Decarboxylase also exist

It can metabolise levodopa $\xrightarrow{\text{into}}$ Dopamine
 $\downarrow$ [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 Anaemia

So, we administer levodopa, carbidopa, adopa decarboxylase Inhibitor that is not able to cross BBB. [DEPTH OF BIOLOGY]

Another strategy $\rightarrow$

Use Amantadine $\rightarrow$ Antiviral Medication
 $\rightarrow$ $\uparrow$ se dopamine Production.

Dopamine Agonist $\rightarrow$ can stimulate dopamine receptors

③ Inhibitors of COMT $\rightarrow$ catecholamines - o-methyl transferase
like tolcapone
enzyme
It degrades dopamine & levodopa

[DEPTH OF BIOLOGY]

④ Selegiline Inhibit $\rightarrow$ MAO-B degrade $\rightarrow$ Dopamine

⑤ Dopamine $\downarrow$ ACTH $\uparrow$

Therefore we give Anticholinergic like
Benztropine — improves tremors

[DEPTH OF BIOLOGY]

⑥ Deep brain stimulation —

Involve an implantable device

that directly sends electrical signals to the
Basal ganglia

Symptoms :- [DEPTH OF BIOLOGY]

$\rightarrow$ like other nervous syst. disease like
Lewy body dementia
Wilson disease

& as side effect of medication Pick disease

$\rightarrow$ Antipsychotic (Haloperidol)

Block dopamine receptors