3rd PBL case:

Parkinson's disease

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This work **DOES NOT** cover the materials discussed during previous lectures. So, please make sure that you go through the learning objectives and fulfill each.

Learning Objectives:

On completion of this PBL package the students should be able to:

1. Describe structures and function of the basal ganglia and its role in control of fine movements.
2. Describe roles of neurotransmitters (particularly dopamine) in the normal function of basal ganglia and control of fine movements.
3. Discuss the pathology and pathogenesis of Parkinson Disease.
4. Use basic sciences to interpret clinical symptoms and signs of an patient with Parkinson Disease.
5. Discuss the biochemical and molecular mechanisms underlying the development of Parkinson Disease.
6. Discuss the pharmacology of drugs used in treatment of Parkinson disease and the mechanisms by which they work.

Parkinson's disease:

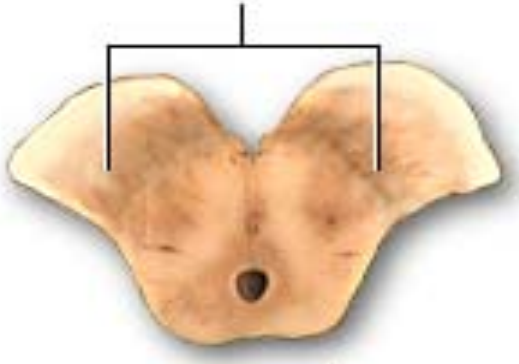
- Is a degenerative disorder of the central nervous system. The motor symptoms of Parkinson's disease result from the death of **dopamine-generating cells in the substantia nigra**, the cause of this cell death is unknown, but several factors appear to play a role, including specific **genetic** mutations and/or **environmental triggers**. (e.g. exposure to certain toxins, oxidative stress…etc)

A short animation video Click here.

Cut section of the midbrain where a portion of the substantia nigra is visible

Substantia nigra

Diminished substantia nigra as seen in Parkinson's disease



New terms:

- **Tremor:** An involuntary trembling of the body or limbs.
- **Stiffness:** Lacking ease or comfort of movement.
- **Cogwheel rigidity:** Rigidity in which the muscles respond with cogwheel-like jerks to the use of force in bending the limb.

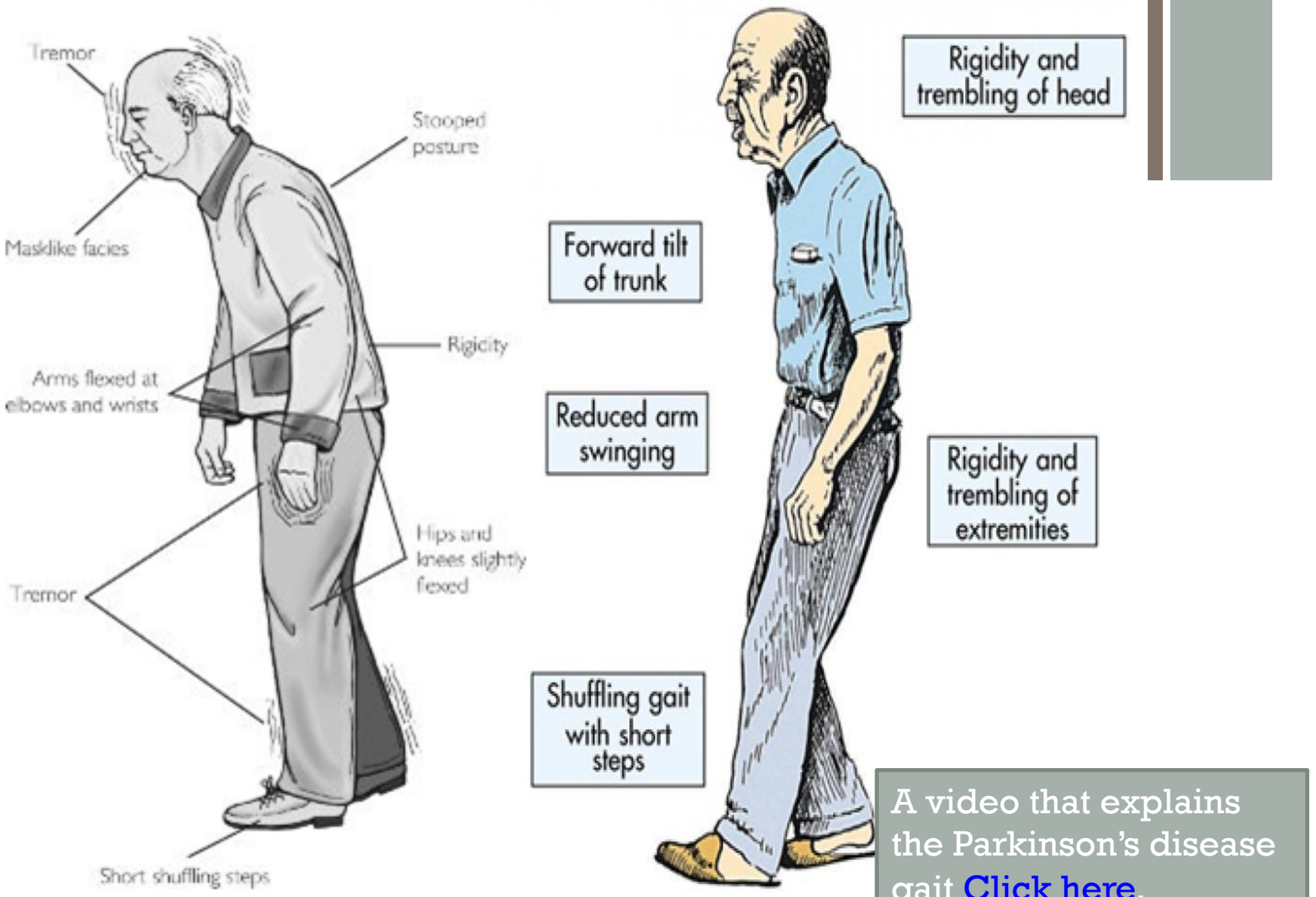
Signs and Symptoms:

- Tremor at rest. *(Static tremor)*
- Stiffness.
- Slow movement.
- Sleeping problem.

(because Dopamine plays a role in regulating sleep-wake cycles in Nucleus Accumbens)

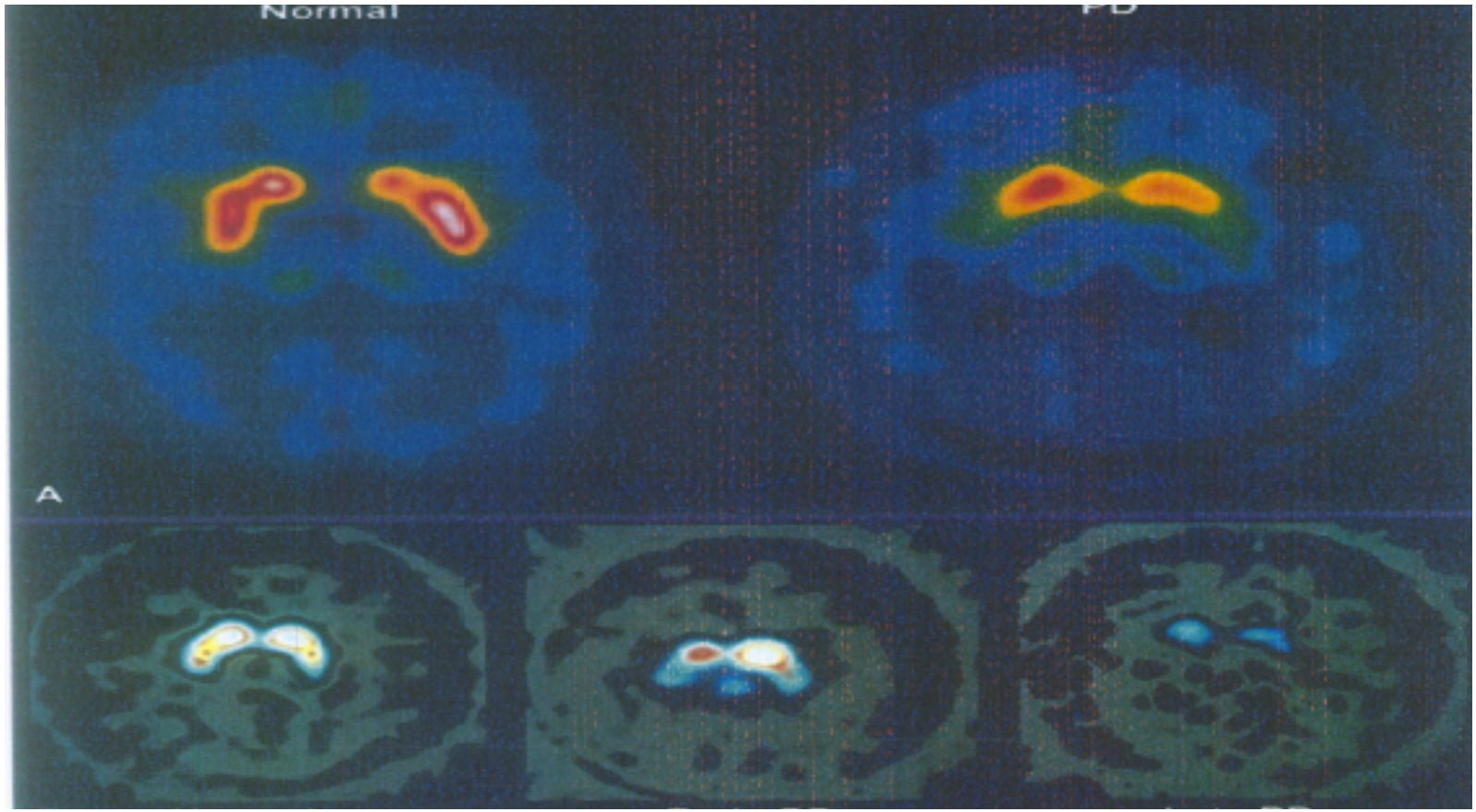
- Decreased facial expression.
- Low tone voice.
- Cogwheel rigidity.
- Serious difficulty in initiating movement. (Akinesia*)
- Postural instability caused by impaired postural reflexes; leading to poor balance.*
- Impaired ability to swallow (Dysphagia).*

*Guyton and Hall textbook of medical physiology pa. 693



A video that explains the Parkinson's disease gait [Click here](#).

Investigations:



The image shows a reduction in uptake of 18F DOPA, and B-CIT uptake by putamen of patients with Parkinson disease, notice that the uptake correlates with the disease progression.

↑Severity = ↓Uptake

Treatment:

- Levodopa. *(because it crosses BBB)*
- Peripheral decarboxylase inhibitor (PDI) e.g. Carbidopa. (it is given to reduce the nausea, vomiting, and to inhibit the peripheral decarboxylation ➔ mask the side effects of levodopa).

Notes:

- **Possible causes of tremor:** Anxiety, thyrotoxicosis, old age, basal ganglia problems.
- **Possible causes of stiffness:** Muscle problem, Impairment of control of muscle tone, Joint problem.
- **Possible causes of slowness of body movement:** Depression, Myopathy, Hyperthyroidism.
- **Dopamine does not cross the blood-brain barrier.**

Remember:

- **Anatomy of the basal ganglia:**

Basal ganglia are a group of interconnected subcortical nuclei that represent one of the brain's fundamental processing units. They are:

Striatum, Globus pallidus, Substantia Nigra (pars compacta,reticulata), Subthalamic nucleus.

- **Basal ganglia's neurotransmitters:**

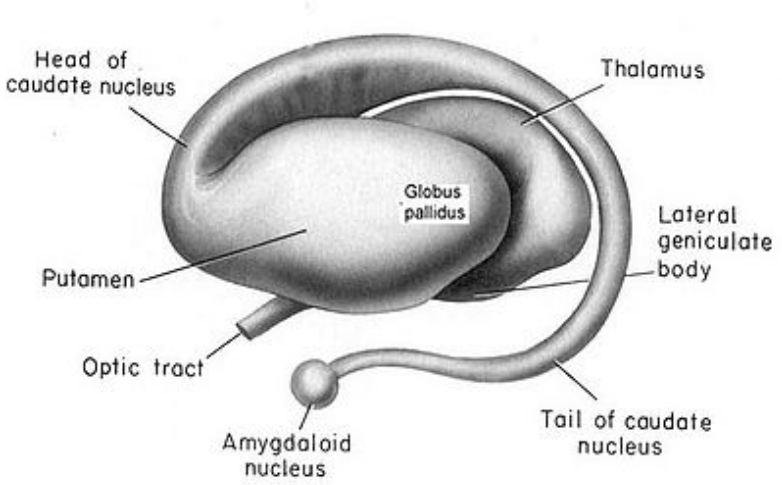
GABA, Dopamine, Acetylcholine, norepinephrine, serotonin and enkephalin.

- **Functions of the basal ganglia:**

✓ Controls Cognition.

✓ Movement Coordination.

✓ Voluntary Movement.



Some Videos Explaining Basal Ganglia:

- http://www.youtube.com/watch?v=-5PXAUdWDgU&sns=em
- http://www.youtube.com/watch?v=TWAKheHlDHs&sns=em
- http://www.youtube.com/watch?v=J56CFExkHgE&sns=em

(Thanks to Lama Al Tawil)

Additional Readings:

- http://en.wikipedia.org/wiki/Parkinson's_disease
- http://www.mayoclinic.com/health/parkinsons-disease/DS00295
- https://www.youtube.com/watch?v=u2RlzL7jJRY
- http://www.dartmouth.edu/~rswenson/NeuroSci/chapter_8C.html

Good luck!