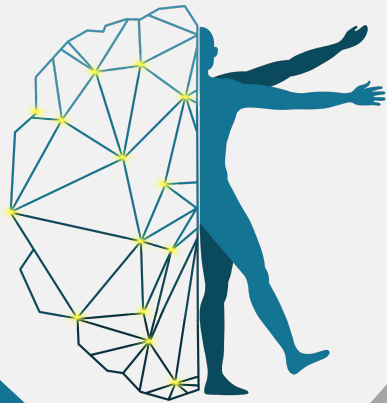
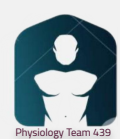


Revised & Approved



Physiology of Basal Ganglia and Regulatory Mechanisms

Objectives:

- ❖ Describe the functional divisions of basal ganglia/**Appreciate different nuclei of basal ganglia.**
- ❖ Enumerate basic circuits of movements control. *
- ❖ Explain Caudate and putamen circuit. *
- ❖ Explain Direct & Indirect Pathways with Neurotransmitters.
- ❖ Appreciate general functions of basal ganglia.
- ❖ Diagnose basal ganglia disorders.

Click **[HERE](#)** to see a video explanation of Basal Ganglia Pathways and Relevant Diseases from a male student.

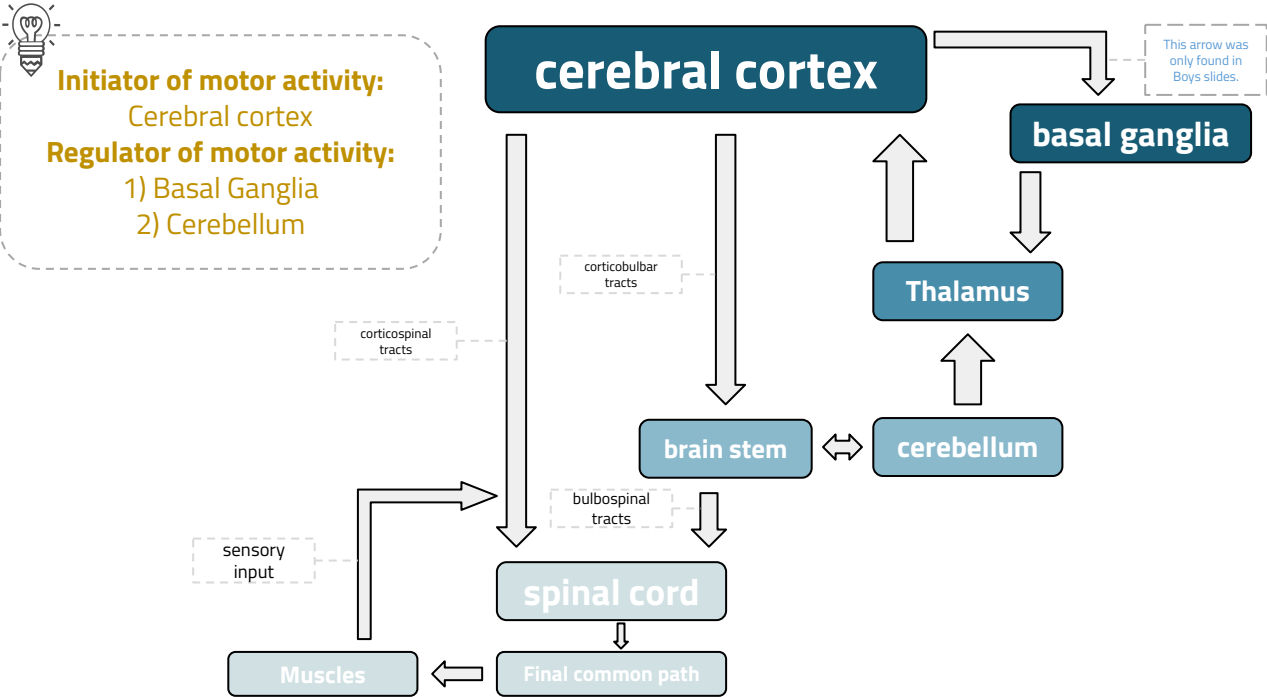
Color index:

- ❖ **Important.**
- ❖ **Girls slide only.**
- ❖ **Boys slide only.**
- ❖ **Dr's note.**
- ❖ Extra information.



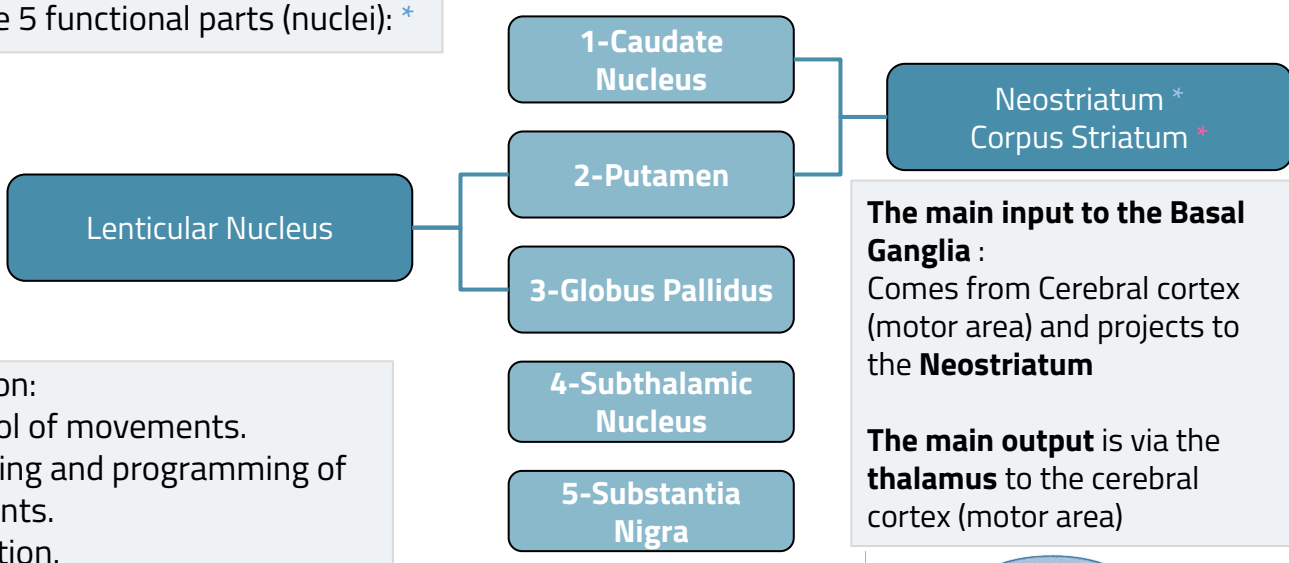
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Overview of motor activity control



Components of functional anatomy

There are 5 functional parts (nuclei): *

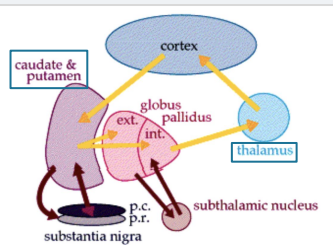


- * Function:
- 1- Control of movements.
 - 2- Planning and programming of movements.
 - 3- Cognition.

The main input to the Basal Ganglia :
Comes from Cerebral cortex (motor area) and projects to the **Neostriatum**

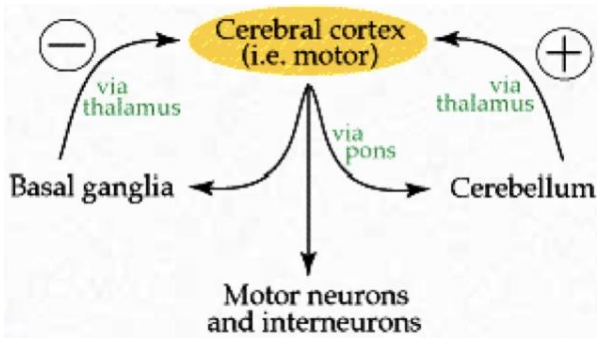
The main output is via the **thalamus** to the cerebral cortex (motor area)

- Corpus striatum = Caudate nucleus + lentiform nucleus. *
- Neostriatum (striatum) = Caudate nucleus + putamen. *
- lentiform= putamen + globus pallidus



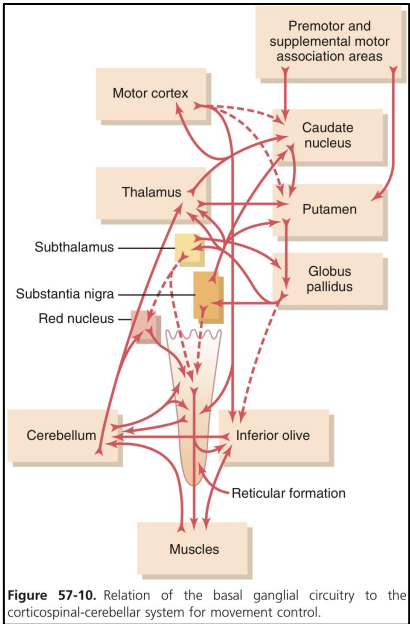
CONNECTIONS

L26



Male doctor explanation

- The cerebral cortex (responsible for initiation of motor activities), it controls the motor neurons and interneurons, it's also connected to cerebellum and basal ganglia (that's responsible for recognition of motor activities) **both of them connected to cerebral cortex by thalamus.**
- **Cerebellum is positive feedback** (usually any lesion leads to **hypotonia** because it's positive feedback),
- **Basal ganglia is negative feedback** (usually any lesion leads to **hypertonia** because it's negative feedback that means inhibitory).



*** There are 3 Connections to remember:**

1

◆ **main input to the basal ganglia. main from cerebral cortex**

2

◆ **main output from the basal ganglia. main to the thalamus**

3

Connections between parts of basal ganglia.

Basic circuits of movement control

1-Motor loop (putamen circuit):

Concerned with **learned movement**. (Not planned movement)

2-Cognitive loop (Caudate circuit):

concerned with **cognitive control** of sequences of motor pattern. Basically it is concerned with motor intention. (**planned movement**)
Note: Cognition means thinking process using sensory input with information already stored in memory.

3-Limbic loop:

involved in giving motor expression to emotions like, smiling, aggressive or submissive posture (Via nucleus accumbens reward circuit) *

4-Oculomotor loop:

concerned with voluntary eye movement (saccadic movement)

1.The Putamen Circuit

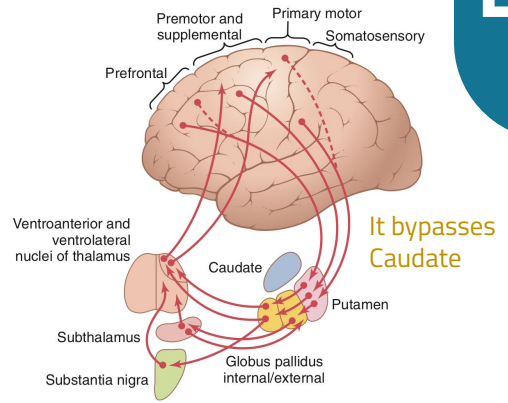


Figure 57-11. Putamen circuit through the basal ganglia for subconscious execution of learned patterns of movement.

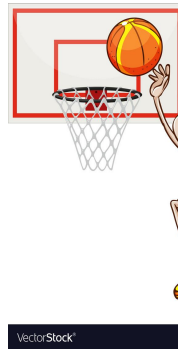
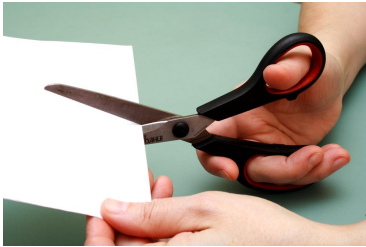
Inputs	Outputs
Somatosensory Cortex	Premotor
Premotor	Supplementary Motor
Supplementary Motor Areas	Primary Motor Cortex

Functions of Putamen Circuit:

-Executes Learned Patterns of Motor Activity:
 ❖ Basal ganglia function in association with the corticospinal system to control complex patterns of motor activity. (performed subconsciously)

-Examples:

- 01 Writing of letters of the alphabet
- 02 Cutting paper with scissors
- 03 Hammering nails
- 04 Shooting a basketball through a hoop
- 05 Passing a football
- 06 Most aspects of vocalization
- 07 the movement of shoveling dirt *
- 08 Throwing a baseball *
- 09 Controlled movement of the eyes *
- 10 Virtually any other of our skilled movement, most of them performed subconsciously *



Most of these activities are performed subconsciously *

2.The Caudate Circuit

Input	Outputs
Association areas	Prefrontal
	Premotor
	Supplementary Motor

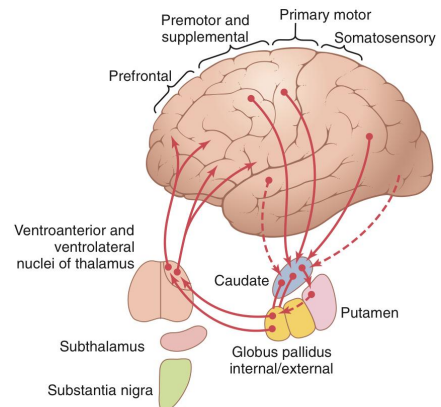


Figure 57-12. Caudate circuit through the basal ganglia for cognitive planning of sequential and parallel motor patterns to achieve specific conscious goals.

*Signals are sent to caudate,, and also some signals are sent to the putamen, but why? because once the movement is planned we need the help of putamen circuit to initiate execute it.
 *Differ from the putamen circuit in that the subthalamic and substantia nigra connection is not involved.

Functions of Caudate Circuit:

1-Cognitive Control of Sequences of Motor Patterns:

- ❖ Cognition means the thinking processes of the brain, using both sensory input to the brain plus information already stored in memory. (Thoughts are generated in the mind by a process called cognitive control of motor activity) *
- ❖ Example: A person seeing a lion approach and then responding instantaneously and automatically by:
 - turning away from the lion.
 - beginning to run.
 - even attempting to climb a tree.
- ❖ Thus, Cognitive control of motor activity determines subconsciously, and within seconds, which patterns of movement will be used together to achieve a complex goal



2-Change the Timing and to Scale the Intensity of Movements:

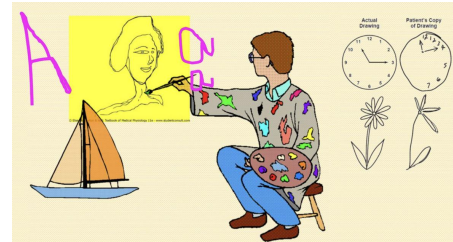
- ❖ Two important capabilities of the brain in controlling movement are:
 - -to determine how rapidly the movement is to be performed
 - -to control how large the movement will be.
- ❖ For instance, a person may write the letter "a" slowly or rapidly. Also, he or she may write a small "a" on a piece of paper or a large "a" on a chalkboard. Regardless of the choice, the proportional characteristics of the letter remain nearly the same.

Damage to Caudate Circuit Results in:

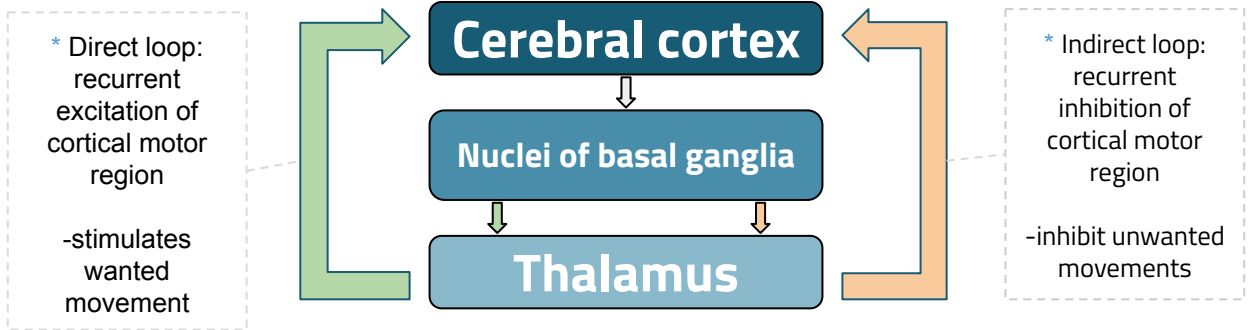
1 Inability to organize pattern of movements to achieve a complex goal. *

2 Inability to write or draw figures with fixed scale. *

3 Loss of timing and scaling of movements. *



Basal Ganglia Neurotransmitters & Pathways (Direct and Indirect)



Eg: Flexing the arm:

- Excite the direct pathway to the Biceps
- Excite the Indirect pathway to the Triceps

Note that when the indirect loop is stimulated it will cause inhibition..

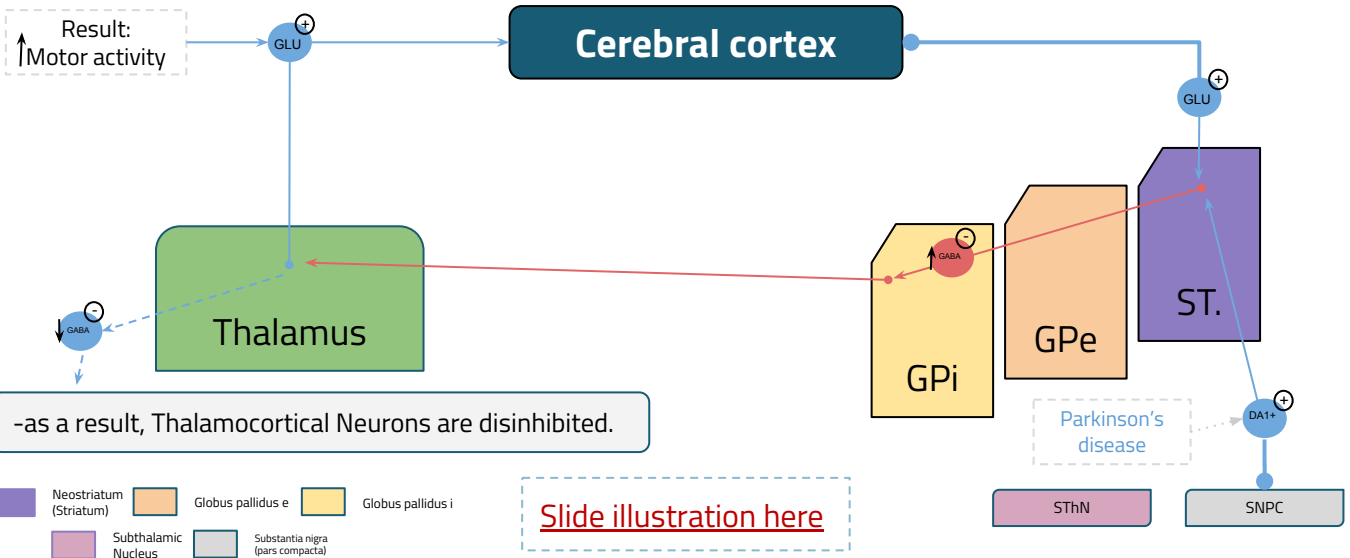
Basal ganglia Nuclei: Striatum (Caudate Nucleus and Putamen), globus pallidus, subthalamic nucleus, substantia nigra. (**movement Modulators**)

Comparison	Direct	Indirect
Type	Excitatory	Inhibitory
Function	movement initiation	movement termination

- ❖ Main circuits of the basal ganglia, The + and – signs at the point of the arrows indicate whether the pathway is excitatory or inhibitory, respectively, in effect.
- ❖ blue arrows refer to excitatory glutamatergic pathways, red arrows refer to inhibitory GABAergic pathways and dopaminergic pathways.
- ❖ Dopaminergic pathways are **excitatory on the direct** pathway and **inhibitory on the indirect** pathway.

Direct Basal Ganglia Pathway:

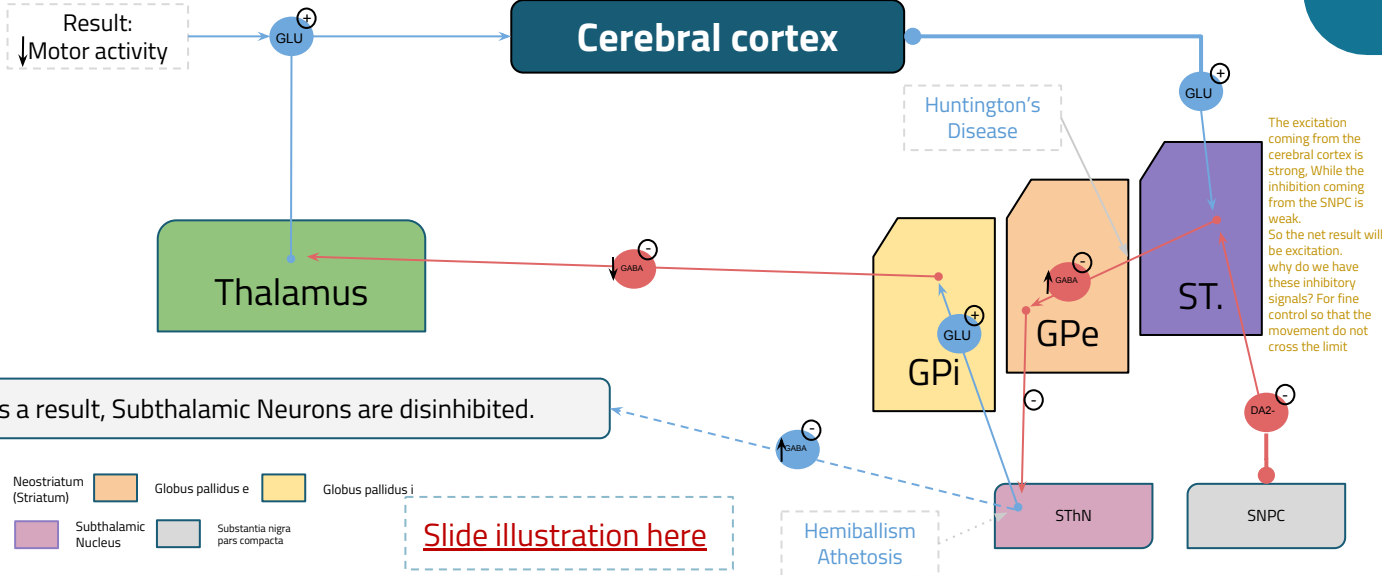
What is the net result of this pathway?
Increase in motor activity



Basal Ganglia Neurotransmitters & Pathways (Direct and Indirect)

InDirect Basal Ganglia Pathway:

What is the net result of this pathway?
decrease in motor activity



Direct and indirect pathways together facilitate action selection:

Comparison	Direct	Indirect
Activation	facilitates movement	suppresses movement
Output	makes focal inhibitory contact on GPi/SNr	makes diffuse, widespread excitatory contact on GPi/SNr
Dopamine effect	<ul style="list-style-type: none"> Facilitates strong, phasic inputs Suppresses weak inputs (through D1 receptors) 	suppresses striatal activity (through D2 receptors)
Co-activation of these pathways facilitates action selection through center-surround mechanism		

Metabolic characteristics:

1 High Oxygen consumption .

2 High Copper content in **Wilson's disease** (Copper intoxication):

- Autosomal Recessive
- Copper binding protein **Ceruloplasmin** is low
- Lenticular degeneration occurs and patient develops choreiform movements and dystonia.

DISORDERS

L26

Basal ganglia disorders:

1-MOVEMENTS:

2-SPEECH.

3-POSTURE.

ATAXIA
(Rate, Range, Force, Direction).

4-Gait.

4-MENTAL ACTIVITY.

5-Others.

1-Movement Disorders:

Hypokinetic *Lesions affect <u>direct</u> pathway Predominately *	Hyperkinetic *Lesions affect <u>indirect</u> pathway predominantly*
<ul style="list-style-type: none"> ❖ Parkinson's Disease ❖ Drug Induced eg; MPTP induced ❖ Dopamine receptor blockers eg; Neuroleptics & antipsychotic drugs 	<ul style="list-style-type: none"> ❖ Chorea:Huntington's Disease ,<i>Saint Vitus Dance (Sydenham's Chorea)</i> ❖ Athetosis ❖ Dystonia ❖ Hemiballismus/Ballismus ❖ Tardive Dyskinesia ❖ Wilson's Disease

Movement disorder	Lesion	Features
Chorea	Atrophy of the striatum . Ex: Huntington's Chorea ,St vitus (post streptococcal infection)	Multiple quick, random movements, usually most prominent in the appendicular muscles
Athetosis	Diffuse hyper myelination of corpus striatum and thalamus	Slow writhing movements, which are usually more severe in the appendicular muscles
Hemiballismus	Hemorrhagic destruction of contralateral subthalamic n. Ex: Hypertensive patients	Wild flinging movements of half of the body
Parkinsonism	Degeneration of Substantia Nigra	Pill rolling tremor (كان المريض يسيج بالمسبحة) of the fingers at rest, lead pipe rigidity and akinesia
* Tardive Dyskinesia *	Neuroleptic drugs blocking dopaminergic transmission	Either temporary or permanent uncontrolled involuntary movements of the face and tongue and cogwheel rigidity

Parkinson's Disease

L26

- ❖ Described by James Parkinson
- ❖ The defect is Degeneration of dopaminergic nigrostriatal neurons (60-80 %).
- ❖ It also can be due to:
 - Phenothiazines (tranquilizers drugs) *
 - Methyl-Phenyl-Tetrahydro-Pyridine (MPTP). The oxidant MPP+ is toxic to Substantia nigra.

It has 5 cardinal features:

- * These symptoms are due to loss of function of the basal ganglia which is involved in the coordination of body movements
1. tremor
 2. rigidity
 3. Akinesia (difficulty in initiation of movements)
 4. Bradykinesia (slowness in executions of movements)
 5. Postural Changes
 6. Speech Changes

- ❖ Loss of dopamine → Lose excitatory effect on direct & lose inhibition of indirect pathway

Treatment:

Girls slides only.

Levodopa (L-dopa or dihydroxyphenylalanine)

- ❖ Biosynthetic precursor of dopamine.
- ❖ Increase dopamine in the brain.
- ❖ Main treatment used to decrease motor dysfunction.
- ❖ Absorbed from proximal duodenum.
- ❖ Protein-restricted diet.
- ❖ Vit B6 should not be co-administered with dopa.
- ❖ L-dopa exhibit a large first pass effect.
- ❖ Only about 1 % reaches brain tissue.

Deep Brain Stimulation (surgery)

- ❖ Brain pacemaker, sends electrical impulses to brain to stimulate the subthalamic nucleus.
- ❖ Improves motor functions and reduce motor complications.
- ❖ Complications include: brain hemorrhage, seizures, death.

Q1: chorea disorder is due to a lesion in :

- A. thalamus
- B. substantia nigra
- C. subthalamic n.
- D. striatus

Q3: which of the following is a Hypokinetic movement disorder :

- A. wilson's disease
- B. dystonia
- C. parkinson's disease
- D. athetosis

Q5: A patient came to the hospital with Wild flinging movements of half of his body , what's the most likely diagnosis

- A. Athetosis
- B. Hemiballismus
- C. parkinsonism
- D. Tardive Dyskinesia

Q2: Corpus striatum is:

- A. caudate nucleus + putamen
- B. lentiform nucleus + substantia nigra
- C. lentiform nucleus + putamen + globus pallidus
- D. caudate nucleus + putamen + globus pallidus

Q4: Concerned with control of sequence of motor pattern :

- A. Motor loop
- B. Limbic loop
- C. Cognitive loop
- D. Oculomotor loop

Q6: The Input of caudate circuit:

- A. Premotor area
- B. Somatosensory cortex
- C. Prefrontal area
- D. Association areas

9: D
5: B
4: C
3: C
2: D
1: D
key:
answer

1- What is the dopamine effects on the Indirect and Direct basal ganglia pathway:

2- Mention 5 basal ganglia disorders :

3- Mention 3 actions that are associated with the Putamen circuit

4- Mention 2 HyperKinetic diseases

A1: Indirect suppresses striatal activity.:

Direct : - facilitates strong input.
- suppresses weak input

A2: movement , speech , posture , gait , mental activity

A3: Cutting paper with scissors, throwing a basketball, writing alphabet letters

A4: Huntington's, Hemiballismus , Athetosis, Dystonia

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