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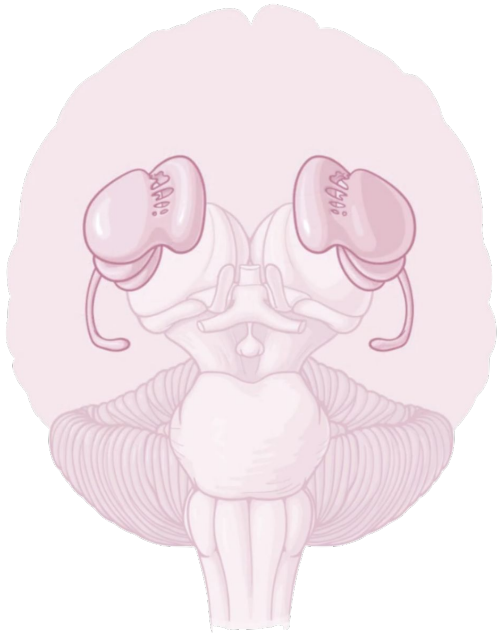

Physiology of basal ganglia and regulatory mechanisms

PHYSIOLOGY
CNS Block
Team 443

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Editing File

Objectives

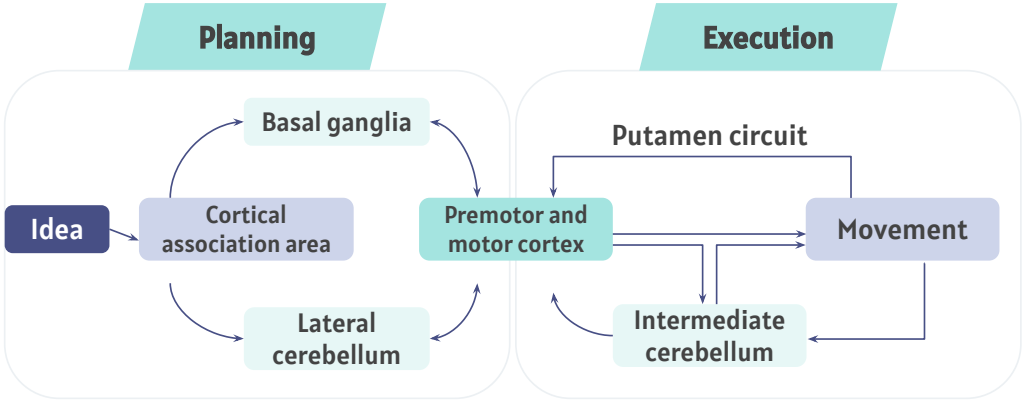
1. Describe the functional divisions of basal ganglia/Appreciate different nuclei of basal ganglia.
2. Enumerate basic circuits of movements control.
3. Explain Caudate and putamen circuit.
4. Explain Direct & Indirect Pathways with Neurotransmitters.
5. Appreciate general functions of basal ganglia.
6. Diagnose basal ganglia disorders
7. Know different neurotransmitters that have a role in basal ganglia functions

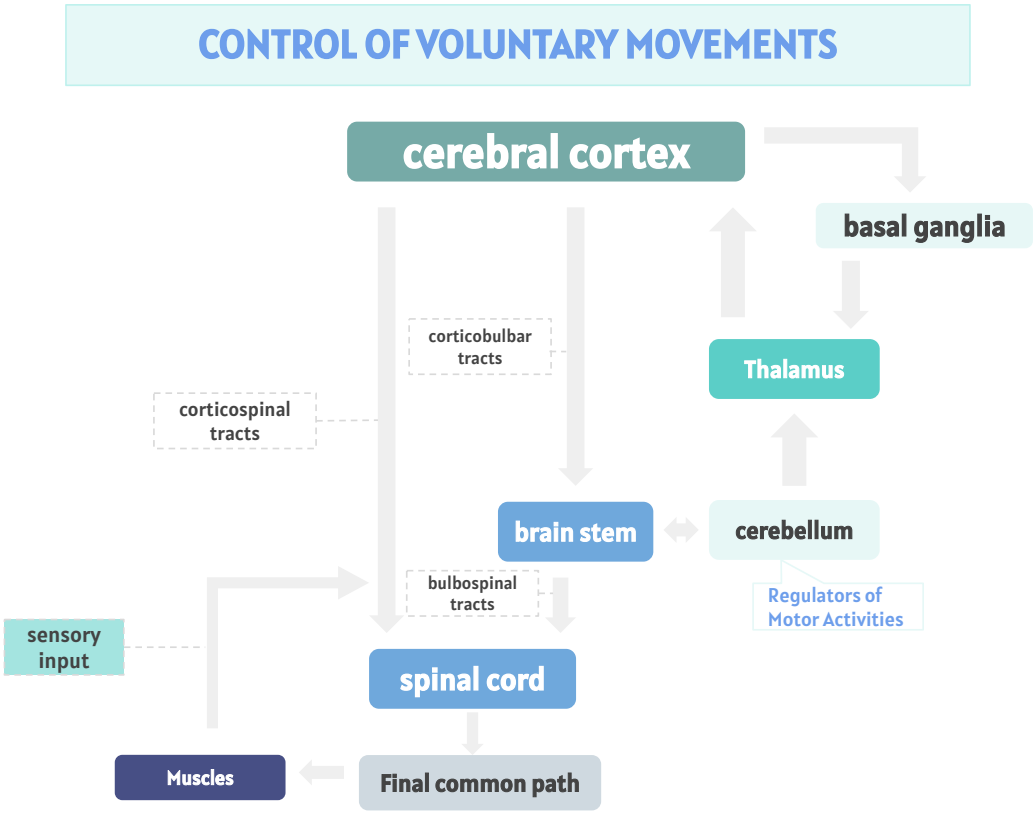
Overview of motor activity control

Male slides

- A learned skilled movement is either:
  1. performed subconsciously
  2. planned cognitively before head.

- When an idea pops in your head it undergoes 2 phases:

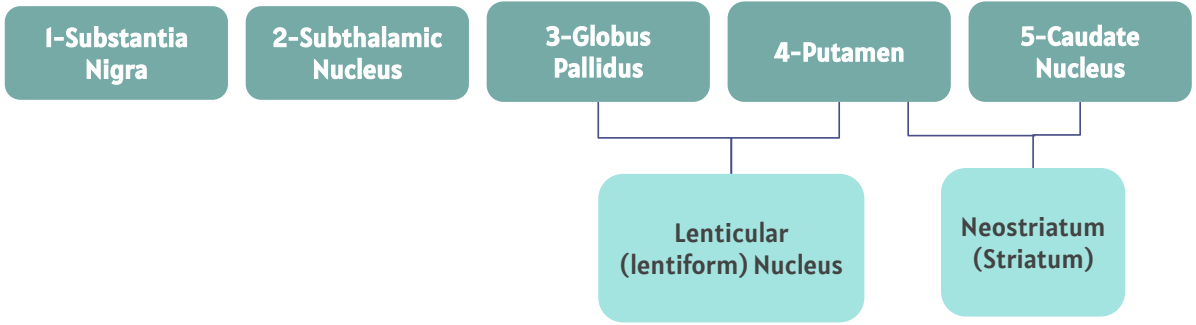


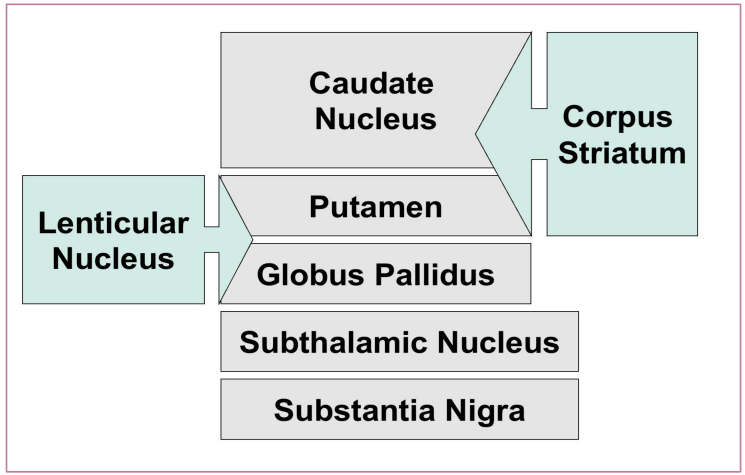


Basal Ganglia Components And Functional Anatomy

Basal ganglia nuclei:

5 functional parts:





- **Function**: movement modulation

Putamen + Globus pallidus = lentiform nucleus.
Caudate nucleus + putamen = Neostriatum (striatum).
Caudate nucleus + lentiform nucleus = Corpus striatum.

Basal Ganglia Connections

Connections for \ Complex Circuitry of Motor Control

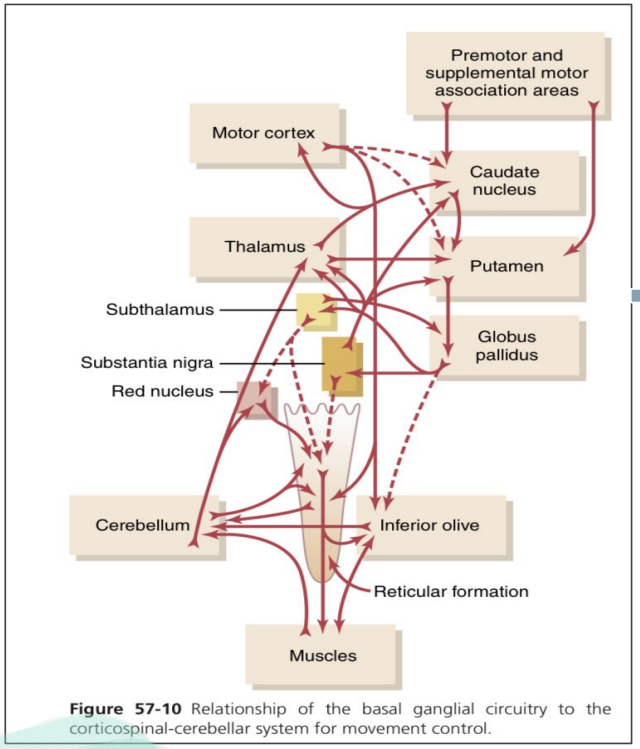
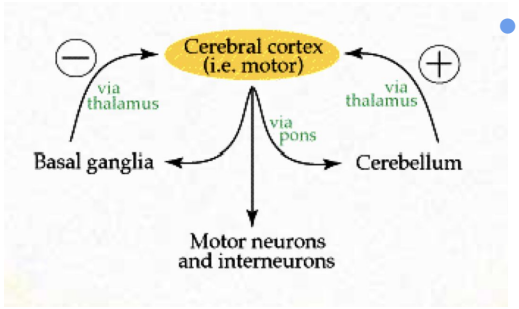


Figure 57-10 Relationship of the basal ganglial circuitry to the corticospinal-cerebellar system for movement control.



- The motor cortex projects to the cerebellum and basal ganglia and receives feedback signals from them. Although cerebellar output is tonically excitatory and basal ganglia output is tonically inhibitory, the balance between these two systems is of pivotal importance for motor control and coordination.

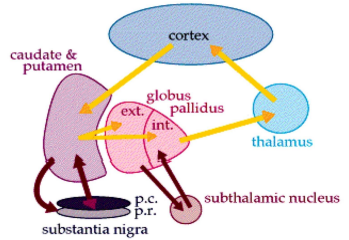
three connections to remember

1- **Main input** to the basal ganglia

comes from the cerebral cortex (motor area) and projects to the **NEOSTRIATUM** (a term for the caudate nucleus and putamen)

2- **Main output** from the basal ganglia

Is via the thalamus to the cerebral cortex (motor area)



3-Connections between parts of basal ganglia

Basic circuits of basal ganglia

Motor loop (Putamen circuit)	Concerned with learned skilled movement that is performed subconsciously without a plan.
Cognitive loop (Caudate circuit)	• Concerned with cognitive control of sequences of motor pattern for planning ahead. • Basically it is concerned with motor intentions. (Note: cognition means thinking process using sensory input with information already stored in memory)
Limbic loop	Involved in giving motor expression to emotions like, smiling, aggressive or submissive posture (Via limbic areas like amygdala and hippocampus)
Oculomotor loop	Concerned with voluntary eye movement (saccadic movement) controlled by Basal Ganglia via superior colliculus.

The putamen circuit

Inputs	Outputs
2. Premotor cortex	1. Primary motor cortex
3. Supplementary motor area	2. Premotor cortex
4. Somatosensory Cortex	3. Supplementary motor area

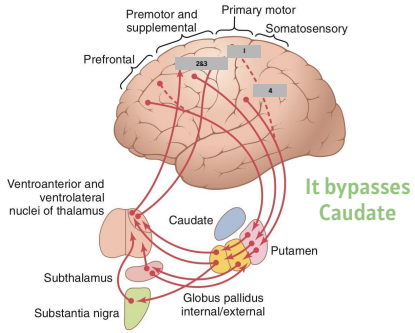


Figure 57-11. Putamen circuit through the basal ganglia for subconscious execution of learned patterns of movement.

Functions of the Putamen Circuit

Executes Learned Patterns of Motor Activity:

- Basal ganglia function \ works in association with the corticospinal system to control complex patterns of motor activity **PERFORMED SUBCONSCIOUSLY.**

- **Examples** are:

  – writing of letters of the alphabet – cutting paper with scissors – hammering nails.
  – shooting a basketball through a hoop – passing a football – throwing a baseball.
  – the movements of shoveling dirt – most aspects of vocalization – controlled movements of the eyes.
  – virtually any other of our skilled movements, **most of them performed subconsciously (Without a plan)**

The caudate circuit

Male slides

- **Functions of the caudate Circuit**

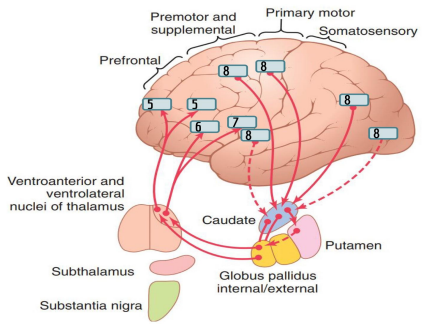
WHICH PATTERNS OF MOVEMENT WILL BE USED TOGETHER TO ACHIEVE A COMPLEX GOAL?

Damage to Caudate Circuit Results in:
- Inability to organize pattern of movements to achieve a complex goal.
- Inability to write or draw figures with fixed scale.
- Loss of timing and scaling of movements.

I. 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:
  (1) turning away from the lion. (2) beginning to run. (3) and 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.

Note that it does not pass through substantia nigra and subthalamus.



Inputs	Outputs
8. Association areas (Association areas provide more understanding of the movement)	**5.** Prefrontal **6.** Premotor cortex **7.** Supplemental motor areas

2. Change the Timing and to Scale the Intensity of Movements

- Two important capabilities of the brain in controlling movement are:
  1. to determine how rapidly the movement is to be performed.
  2. 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.

When the task is no longer novel and becomes automatic, the motor loop "takes over"

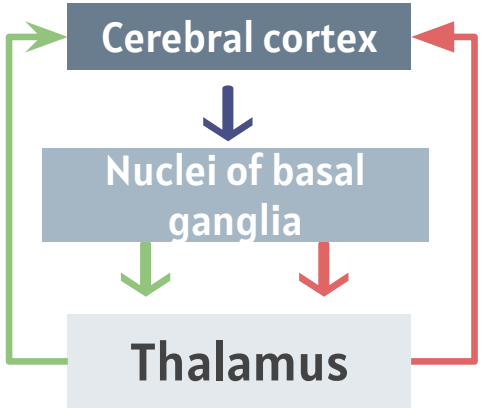
Basal Ganglial NTs & Pathways Direct and Indirect

Male slides

Direct loop:

Recurrent excitation of cortical motor regions

(Stimulates wanted movements)



Indirect loop:

Recurrent inhibition of cortical motor regions

(Inhibit unwanted movements)

Direct	Indirect
Activation of direct pathway facilitates movement	Activation of indirect pathway suppresses movement
Direct output makes focal inhibitory contact on GPi/SNr	Indirect output makes diffuse, widespread excitatory contact on GPi/SNr
Co-activation of these pathways facilitates action selection through center-surround mechanism	

Basal Ganglial Pathways Direct and Indirect

Female slides

	Direct pathway	Indirect pathway
Type	Excitatory	Inhibitory
Pathway	cortex -> striatum -> globus pallidus, pars interna -> thalamus -> motor cortex -> spinal cord / brainstem	cortex -> striatum -> globus pallidus, pars externa -> subthalamic nucleus -> globus pallidus, pars interna -> thalamus -> motor cortex -> spinal cord / brainstem
Function	movement initiation	movement termination

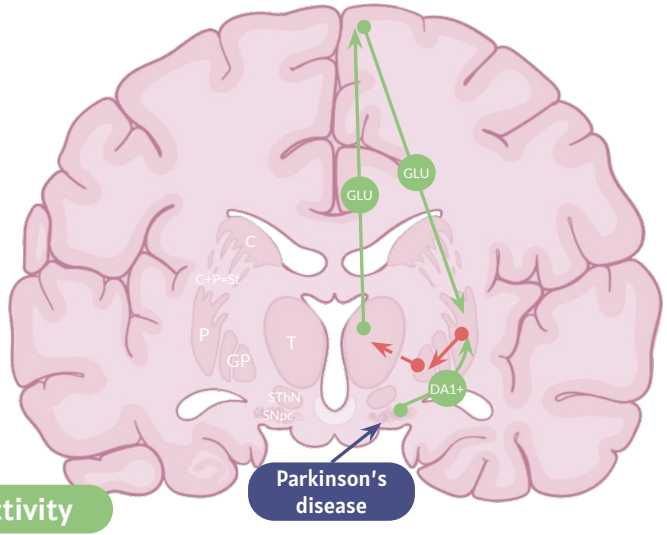
- Main circuits of the basal ganglia The + and – signs at the point of the arrows indicate whether the pathway is excitatory or inhibitory, respectively, in effect. blue arrows refer to excitatory glutamatergic pathways, red arrows refer to inhibitory GABAergic pathways and dopaminergic pathways that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

*Special thanks to **Mansour Aldhalaan** for this amazing slide

Direct Basal Ganglial Pathway

FIVE" Neurons Pathway

Fig key:
C: Caudate
P: Putamen
St: Striatum
T: Thalamus
GP: Globus Pallidus
SThN: subthalamic nucleus
SNpc: Substantia nigra pars compacta



↑ Motor activity

Red arrows secret GABA

Stimulated	السهم المقطع ما يرسل شيء لأن صار له inhibition
Inhibited (won't release NM)	

Thalamocortical Neurons are **disinhibited**

Normally GPi will be secreting GABA which inhibits the thalamus from stimulating the cortex, but when the St. get stimulated it will release GABA to GPi and inhibit it from inhibiting the thalamus.

Click here to see the original picture

Extra

SNpc Substantia nigra pars compacta	Release Dopamine to DI receptors in St. (excitatory)
Cortex	Release Glutamate
Striatum	Release GABA
Inhibit	↑ GABA
GPi	Release GABA
Inhibit	↓ GABA
Thalamus	Stimulate the cortex by Glutamate

↑ Glutamate

Inhibition of an inhibitor = disinhibition (stimulation)
In this case GPi is the inhibitor and this pathway will inhibit it leading to stimulation of the thalamocortical neurons.

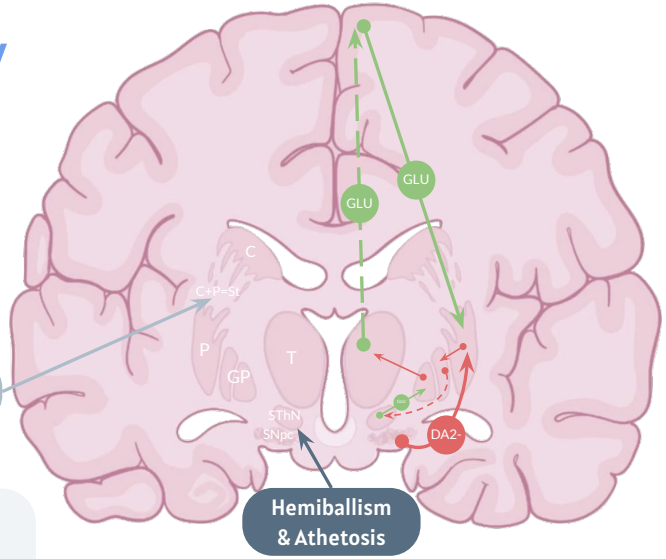
*Special thanks to **Mansour Aldhalaan** for this amazing slide

Indirect Basal Ganglial Pathway

↓ Motor activity

"SEVEN" Neurons Pathway

Fig key:
C: Caudate
P: Putamen
St: Striatum
T: Thalamus
GP: Globus Pallidus
SThN: subthalamic nucleus
SNpc: Substantia nigra pars compacta



Subthalamic Neurons are **disinhibited**

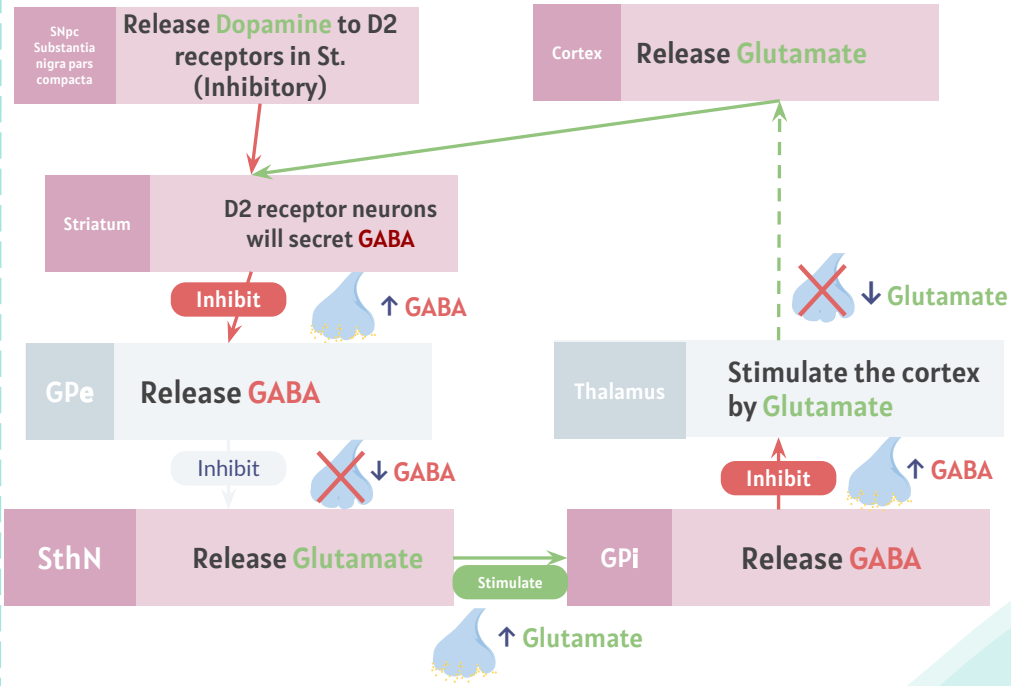
Red arrows secret GABA
Except for SNpc axons which secret Dopamine

Stimulated — السهم المقطع ما يرسل شيء لأن صار له inhibition

Inhibited (won't release NM)

Click here to see the original picture

Extra



Female slides

Dopamine effects on direct and indirect pathways

- Dopamine signaling through D2 receptors in the indirect pathway suppresses striatal activity.

- Dopamine signaling through DI receptors in the direct pathway:
  - Facilitates strong, phasic inputs
  - Suppresses weak inputs

Metabolic characteristics

Related to basal ganglia dysfunction

- Wilson's disease is a rare genetic disorder characterized by excess copper stored in various body tissues, particularly the liver, brain and eyes.
- High Oxygen consumption .
- 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

Female slides

Basal ganglia functions :

1. Control of movements
2. Planning and programming of movements
3. Cognition

Movement disorders

Movement disorder	Lesion	Features
Chorea	- Atrophy of the striatum. - Huntington Chorea - Saint vitus dance (post streptococcal infection)	Multiple quick involuntary, random\ purposeless movements, usually most prominent in the appendicular muscles (pectoral and pelvic girdles)
Athetosis	Diffuse hypermyelination of corpus striatum and thalamus	Slow writhing (twisting) movements,without intervening posture more severe in hands \ more severe in the appendicular muscles
Hemiballismus	Hemorrhagic destruction of contralateral subthalamic n. E.g. Hypertensive patients	Wild flinging movements of half of the body(hip & shoulder girdle)
Parkinsonism	Degeneration of Substantia Nigra	Pill rolling tremor of the fingers at rest, lead pipe rigidity and akinesia
Tardive dyskinesia (Males slides only)	Neuroleptic drugs blocking dopaminergic transmission	Either temporary or permanent uncontrolled involuntary movements of the face, neck and tongue and cogwheel rigidity
Dystonia (Males slides only)	Corpus striatum and thalamus & brainstem	Sustained or repetitive muscle contractions result in twisting or abnormal fixed postures

Basal ganglia disorders

- **Movement disorder** (Ataxia Rate, Range, Force, Direction).
- Speech
- Posture
- Gait
- Mental activity

Movement disorders

Hyperkinetic Lesions affect indirect pathway predominantly	Hypokinetic Lesions affect direct pathway predominantly
• Chorea -Huntington's Disease -Sydenham's Chorea (Saint Vitus Dance) • Athetosis • Dystonia • Hemiballismus/Ballismus • Tardive Dyskinesia • Wilson's Disease.	• Parkinson's Disease • Drug Induced e.g. (Neuroleptics, MPTP) • Dopamine receptor blockers eg; Neuroleptics & antipsychotic drugs

Parkinson's Disease

Described by James Parkinson

- Degeneration of dopaminergic nigrostriatal neurons (60-80 %).
- Phenothiazine (tranquilizers drugs).
- Methyl-Phenyl-Tetrahydropyridine (MPTP). The oxidant MPP+ is toxic to SN.

5 cardinal features (TRAPSO):

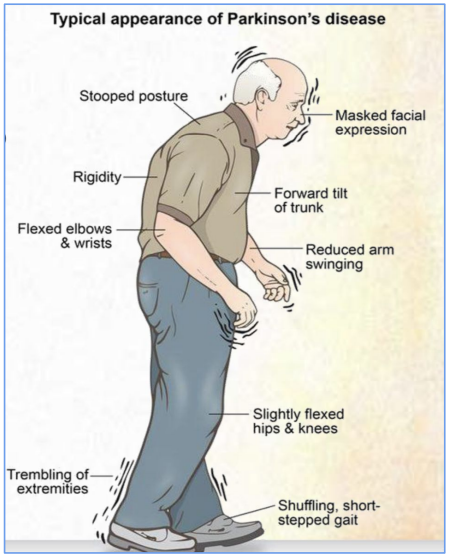
– Tremor (resting tremor, pill rolling)
– Rigidity (Lead pipe)
– Akinesia (difficulty in initiation)& bradykinesia (slowness in the execution of movements)
– Postural Changes (Stooped,Simian)
– Speech Changes (Dysarthria/monotonous/slow)
– Others (Depression, Dysphagia)

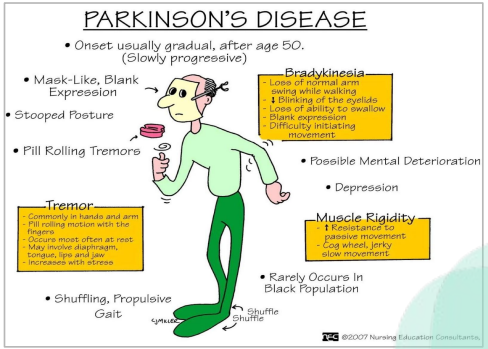
These symptoms are due loss of function of basal ganglia which is involved in coordination of body movements.
(Loss of dopamine = loss of excitatory effect on direct pathway and lose inhibition of indirect pathway)

Treatment of Parkinson's Disease

Female slides

Levodopa	Deep brain stimulation (surgery)
• 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 L-dopa. • L-dopa exhibit a large first pass effect. • Only about I % reaches brain tissue. - why we don't give dopamine directly ? Bcuz it will beakdown in the blood before reaching the brain.	• 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. -The patient will respond better to the treatment if was treated during early stages of the disease.





1-B
2-D
3-D
4-C

TEST YOURSELF !

1-Putamen circuit is

A)Cognitive loop

B)Motor loop

C)Limbic loop

D)Occulomotor loop

2-What are the components of Neostriatum

A)Putamen and Subthalamic nucleus

B)Putamen and Globus pallidus

C)Caudate and Globus pallidus

D)Caudate and putamen

3-What is a characteristic feature of Parkinson's disease?

A)Loss of cognition

B)Loss of balance

C)Spasticity is prominent feature

D)Difficulty initiating movements

4-Which one of the following structures is affected in parkinsonism?

A)Caudate nucleus

B)Lateral thalamus

C)Substantia nigra

D)Globus pallidus

SAQ

1-Mention 3 neurotransmitters in the direct pathway

Glutamate, GABA, Dal

2- What's the result from stimulating the direct pathway

Increase motor activity

3-Mention 4 features patient may have with parkinson's disease

Tremor
Rigidity
Bradykinesia
Postural changes

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