

**431**

**CNS** System  
central Nervous

**Block**

**Physiology Team**

Female Side

Male side

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Revised By :

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# CNS System central Nervous Block

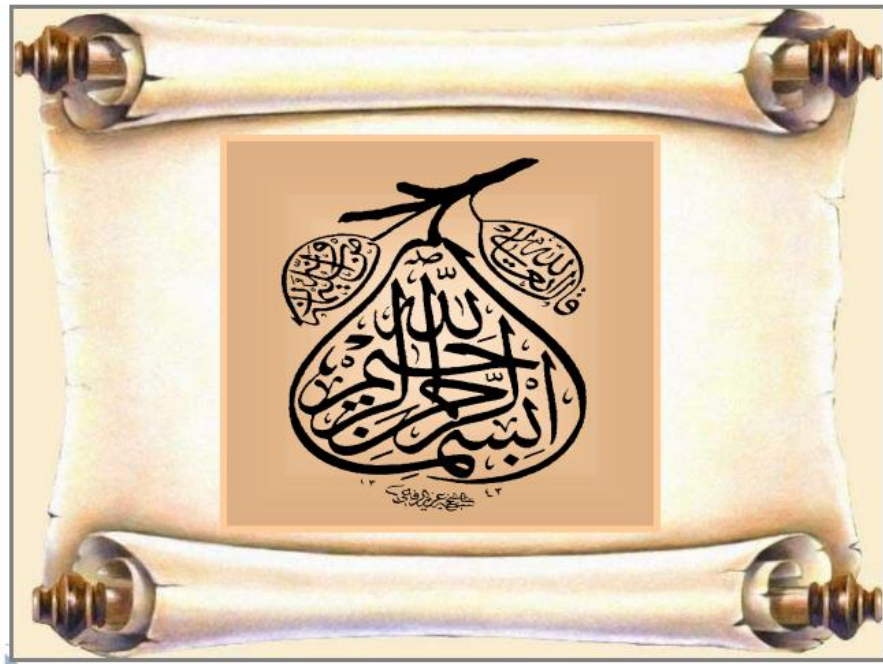
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Team Notes :


# CNS System central Nervous Block

Slide No.( )



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# CNS System central Nervous

## Block

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### Objectives

- ▶ Physiology of basal ganglia and regulatory mechanisms
- ▶ At the end of this lectutre the student should be able to:-
  - ▶ 1-appreciate different nuclei of basal ganglia
  - 2-know different neurotransmitters that have a role in basal ganglia functions
  - 3-know Basal Ganglia connections & their functions
  - ▶ 4-appreciate general functions of basal ganglia
  - ▶ 5-diagnose basal ganglia disorders

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## INTRODUCTION

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- ▶ The basal ganglia (or basal nuclei) are a group of **nuclei** of varied origin.
- ▶ They are situated at the base of the **forebrain** and are strongly connected with the **cerebral cortex**, **thalamus** and other brain areas.
- ▶ The basal gangli functions:
- ▶ voluntary motor control, procedural **learning** relating to routine behaviors or "habits" , eye movements, and cognitive, emotional functions.

### Team Notes :

Located in the interior part of cerebrum near about base.

Motor movement is control by cerebellum and basal ganglia and the differences between them are the basal ganglia have got connections to the cortex directly and indirectly so they control the initiation movement and help for learning motor movement.

Also, they help for planning motor activates and skill downs the process




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- ▶ Experimental studies show that the basal ganglia exert an inhibitory influence on a number of motor systems, and that a release of this inhibition permits a motor system to become active
- ▶ The "behavior switching" that takes place within the basal ganglia is influenced by signals from many parts of the brain, including the prefrontal cortex, which plays a key role in executive functions

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# CNS System

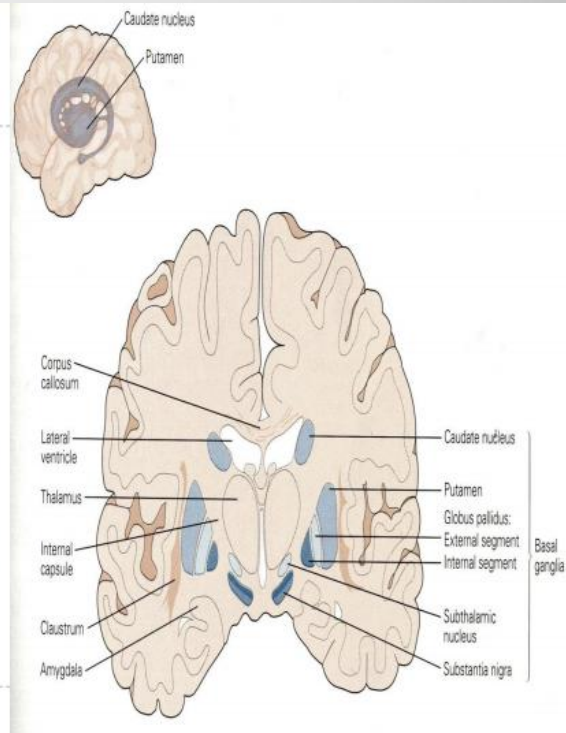
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the four principle nuclei of the basal ganglia are the:

1. striatum
2. globus pallidus
3. substantia Nigra- pars compacta,reticulata
4. subthalamic nucleus



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Notes:

- Anatomically, the Basal Ganglia contains: Caudate, Putamen and Globus Pallidus Nuclei
- Functionally, two nuclei are related to Basal Ganglia: Substantia Nigra and Subthalamic Nucleus.

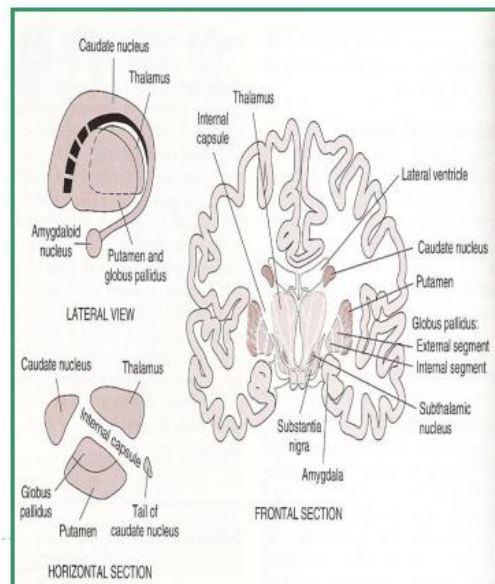
There is an area which has been added to basal ganglia called **nucleus accumbens**. It is located where the head of the caudate and the anterior portion of the putamen meet just lateral to the septum pellucidum. Its function for addicted process. An example if you give some individuals a small dose of drug (Some of them will be addicted to that drug but the other won't.

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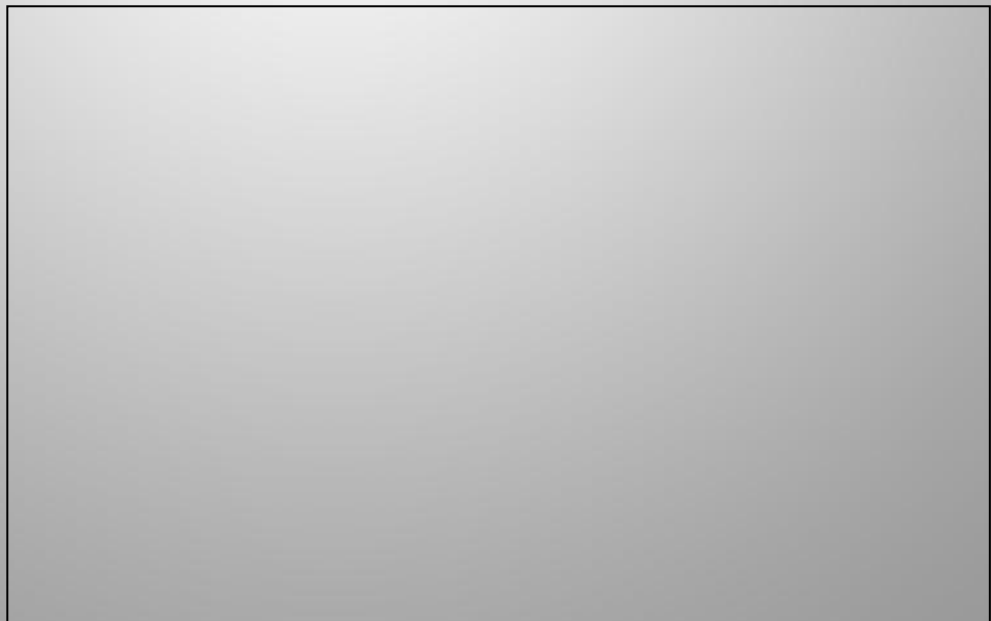
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## The striatum

- ▶ the striatum consists of *three* subdivisions, the:
  1. **caudate nucleus**
  2. **putamen**
  3. **ventral striatum** (which includes the **nucleus accumbens**)
- ▶ a major collection of fibers, called the **internal capsule**, separates the caudate nucleus and putamen



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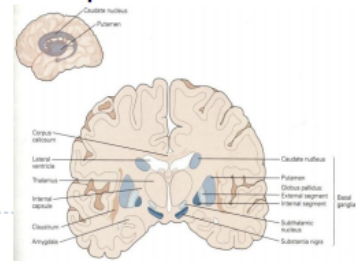


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## subthalamic nucleus

- ▶ The subthalamic nucleus is a diencephalic gray matter portion of the basal ganglia, and the only portion of the ganglia that actually produces an "excitatory," glutamate neurotransmitter.
- ▶ The role of the subthalamic nucleus (STN) is to stimulate the SNr-GPi complex and it is part of the "indirect pathway".



### Team Notes :

SNr: substantia nigra pars reticulata

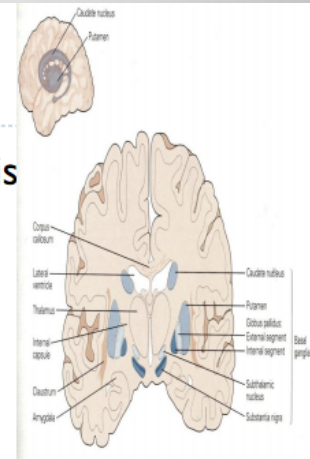
Gpi: internal segment of globus pallidus

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## substantia nigra\_


- a mesencephalic gray matter portion of the basal ganglia that is divided into SNr (reticulata) and SNc (compacta).
- SNr often works in unison with GPi, and the SNr-GPi complex inhibits the thalamus.
- Substantia nigra pars compacta (SNc) however, produces the neurotransmitter dopamine, which is very significant in maintaining balance in the striatal pathway.



### Team Notes :

In Parkinson's disease there is no change in Acetylcholine the change in the dopamine will be reduced. Also, there is lost of cells in substantia nigra





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### **Globus pallidus**

- ▶ The pallidum receives its most important input from the striatum (either directly or indirectly), and sends inhibitory output to a number of motor-related areas, including the part of the thalamus that projects to the motor-related areas of the cortex

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### **Globus pallidus**

- ▶ The external segment, or GPe, receives input mainly from the striatum, and projects to the subthalamic nucleus. The internal segment, or GPi, receives signals from the striatum via two pathways, called "direct" and "indirect". Pallidal neurons operate using a "disinhibition" principle.
- ▶ neurons fire at steady high rates in the absence of input, and signals from the striatum cause them to "pause". Because pallidal neurons themselves have inhibitory effects on their targets, the net effect of striatal input to the pallidum is a reduction of the tonic inhibition exerted by pallidal cells on their targets

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### substantia nigra

One part of substantia nigra, the reticulata (SNr), functions similarly to the pallidum, and another part (compacta or SNc) provides the source of the neurotransmitter dopamine's input to the striatum.

The subthalamic nucleus (STN) receives input mainly from the striatum and cortex, and projects to a portion of the pallidum (interna portion or GPi). Each of these areas has a complex internal anatomical and neurochemical organization

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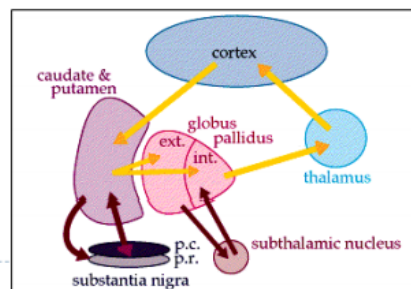
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## MAIN INPUT TO THE BASAL GANGLIA

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

## THE MAIN OUTPUT

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




## Team Notes :

### Notes:

- Motor activity initiation mainly comes from Cerebral Cortex
- Basal Ganglia is connected to the Cerebral Cortex via the Thalamus
- Cerebellum + Basal Ganglia are mainly for correction of movement





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### Neurotransmitters

- ▶ In most regions of the brain, the predominant classes of neurons use **glutamate** as neurotransmitter and have excitatory effects on their targets.
- ▶ majority of BG neurons use **GABA** as neurotransmitter and have inhibitory effects on their targets.
- ▶ The inputs from the cortex and thalamus to the striatum and STN are glutamatergic,
- ▶ but the outputs from the striatum, pallidum, and substantia nigra *pars reticulata* all use GABA.
- ▶ Thus, following the initial excitation of the striatum, the internal dynamics of the basal ganglia are dominated by inhibition and disinhibition.
- ▶ Other neurotransmitters have important **modulatory** effects. The most intensively studied is **dopamine**, which is used by the projection from the substantia nigra *pars compacta* to the striatum, and also in the analogous projection from the ventral tegmental area to the nucleus accumbens.
- ▶ **Acetylcholine** also plays an important role, being used both by several external inputs to the striatum, and by a group of striatal interneurons.
- ▶ striatum has one of the highest acetylcholine concentrations of any brain structure

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### Circuit connections

- ▶ In order to understand the complex circuitry of the basal ganglia, one has to first understand the important participants in this circuit.
- ▶ Parts of the basal ganglia are in direct communication with the thalamus and the cortex. The cortex, thalamus, and the basal ganglia are, therefore, the three main participants in the circuit created by the basal ganglia.

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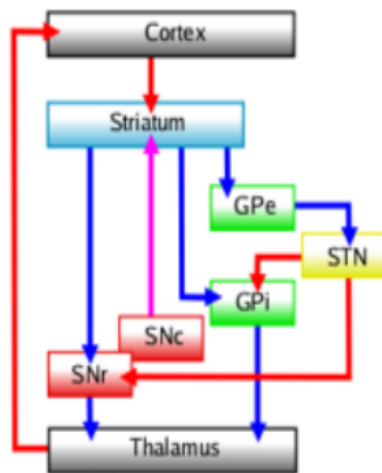
- ▶ These cortical neurons release the neurotransmitter **glutamate**, which is excitatory in nature. Once excited by glutamate, the cells in the striatum project in two different directions giving rise to two major pathways: The "*direct*" and the "*indirect*" pathways:

▶ 1A

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Connectivity diagram showing ▶ excitatory glutamatergic pathways as red, inhibitory GABAergic pathways as blue, and modulatory dopaminergic pathways as magenta. (Abbreviations: GPe: globus pallidus external; GPI: globus pallidus internal; STN: subthalamic nucleus; SNc: substantia nigra compacta; SNr: substantia nigra reticulata)

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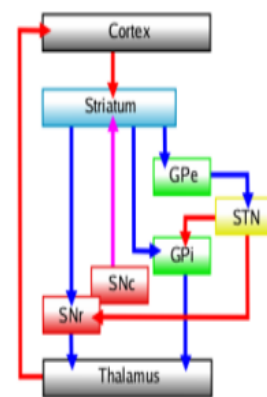


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## direct pathway

- ▶ cortical cells project excitatory inputs to the striatum, which in turn projects inhibitory neurons onto the cells of the SNr-GPi complex.
- ▶ The SNr-GPi complex projects directly onto the thalamus through the inhibitory pathway.
- ▶ This results in a net **reduction** of inhibition of the thalamus via the striatum.
- ▶ The thalamus projects excitatory glutamatergic neurons to the cortex itself.
- ▶ The direct pathway, therefore, results in the excitation of the motor cortex by the thalamus. Once stimulated, the cortex projects its own excitatory outputs to the brain stem and ultimately muscle fibers via the lateral corticospinal tract.



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### **Very Important Note !!!!**

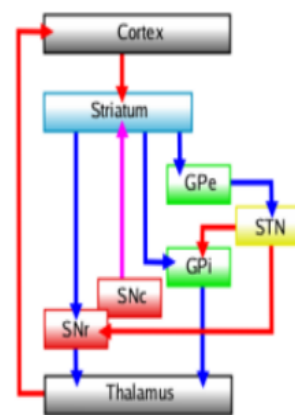
Main function of the **Direct pathway** is to increase muscle activity via **Disinhibition of the Thalamocortical Neurons**

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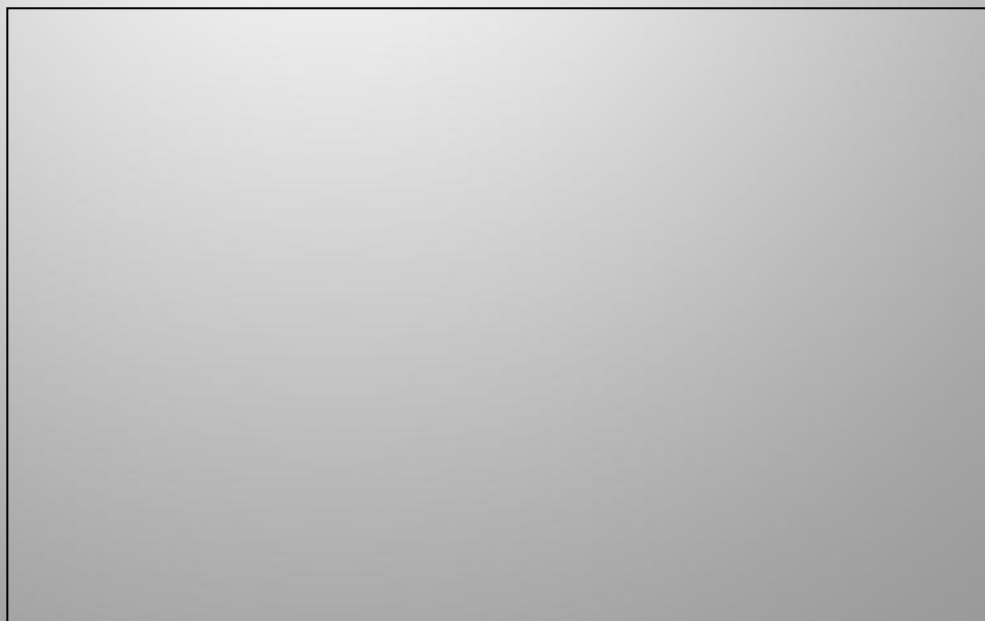
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## indirect pathway

- ▶ Striatum stimulated by the cortex,
- ▶ striatum project inhibitory axons onto the cells of the globus pallidus externa (GPe), which tonically inhibits the subthalamic nucleus (STN).
- ▶ This results in the net reduction of inhibition of the STN. The STN, in turn, projects excitatory inputs to the SNr-GPi complex (which inhibits the thalamus).
- ▶ The end-result is decreased stimulation of the motor cortex by the thalamus and reduced muscle activity.



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- ▶ direct pathway:.....
  - ▶ **Cortex** (stimulates) → **Striatum** (inhibits) → **"SNr-GPi" complex** (less inhibition of thalamus) → **Thalamus** (stimulates) → **Cortex** (stimulates) → **Muscles, etc.** → (hyperkinetic state)
- ▶ indirect pathway:
  - ▶ **Cortex** (stimulates) → **Striatum** (inhibits) → **GPe** (less inhibition of STN) → **STN** (stimulates) → **"SNr-GPi" complex** (inhibits) → **Thalamus** (is stimulating less) → **Cortex** (is stimulating less) → **Muscles, etc.** → (hypokinetic state)

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### **Very Important Note !!!!**

Main function of the **Indirect pathway** is to decrease muscle activity via **Disinhibition of the Subthalamic Neurons**



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- ▶ The antagonistic functions of the direct and indirect pathways are modulated by the substantia nigra pars compacta (SNc), which produces dopamine.
- ▶ Special D1-receptors in basal ganglia are excited by dopamine, favoring the direct pathway.
- ▶ D2-receptors in the basal ganglia are inhibited in presence of dopamine and favor the indirect pathway.
- ▶ Through these mechanisms the body is able to maintain balance between excitation and inhibition of motion. Lack of balance in this delicate system leads to pathologies such as Parkinson's disease.

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**Team Notes :**

**The conclusion of both direct and indirect pathways is to make the movement smooth.**





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### Eye movement

- ▶ Eye movement is influenced by an extensive network of brain regions that converge on a midbrain area called the superior colliculus (SC).
- ▶ eye movements begin with activation in the caudate nucleus, which inhibits the SNr via the direct GABAergic projections, which in turn disinhibits the SC

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### **Basic Circuits of basal ganglia**


1. A motor loop (putamen circuit) concerned with learned movement.
2. Cognitive loop (Caudate circuit) concerned with cognitive control of sequences of motor pattern. Basically it is concerned with motor intentions.

(Note: cognition means thinking process using sensory input with information already stored in memory.)

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**Also, the motor loop concerned with the movements we do without thinking (subconsciously)**



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3. Limbic loop: involved in giving motor expression to emotions like, smiling, aggressive or submissive posture.
4. Occulomotor loop concerned with voluntary eye movement [ saccadic movement]

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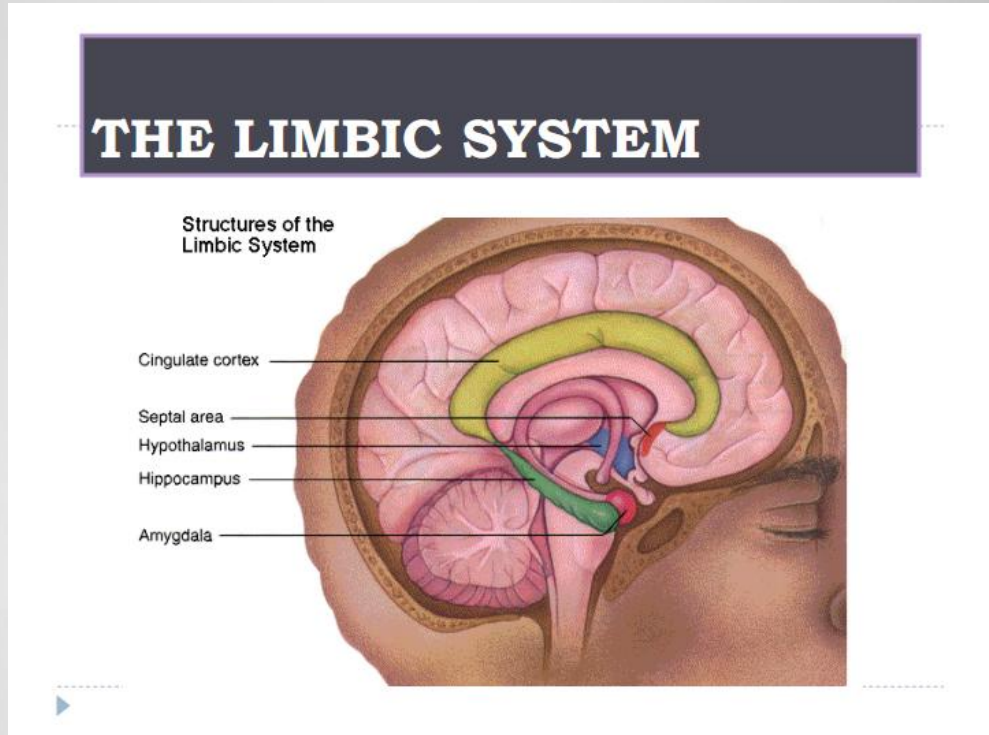
## Team Notes :

There is a mask face in Parkinson's disease due to defecting in limbic loop.

**Saccadic movement:** A rapid intermittent eye movement, as that which occurs when the eyes fix on one point after another in the visual field or the movement of the eye when it makes a sudden change of fixation, as in reading

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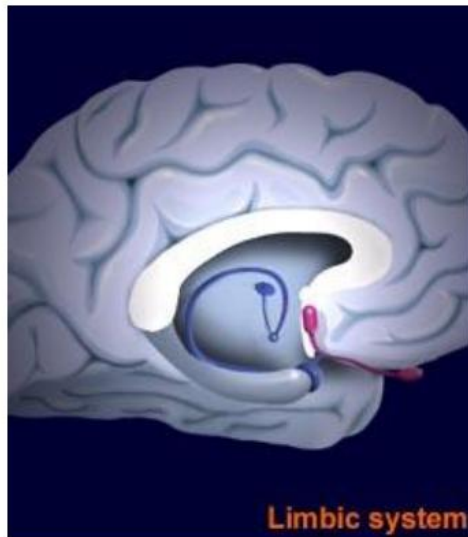
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## FUNCTIONS OF THE LIMBIC SYSTEM



### Cingulate cortex

- Coordination of sensory signals
- Emotion

### Septal area:

- Sexual arousal

### Hippocampus:

- Long-term memory development

### Amygdala:

- Aggression and fear

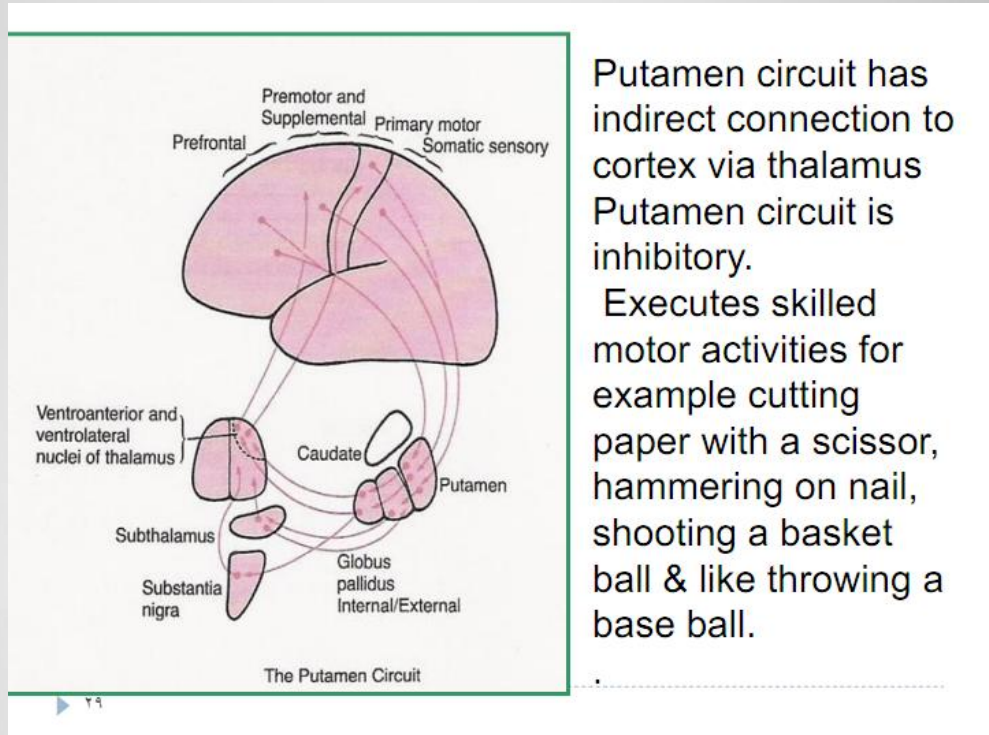
### Hypothalamus:

- Endocrine regulation
- Body temperature
- Regulation of thirst and hunger
- Regulation of circadian rhythms

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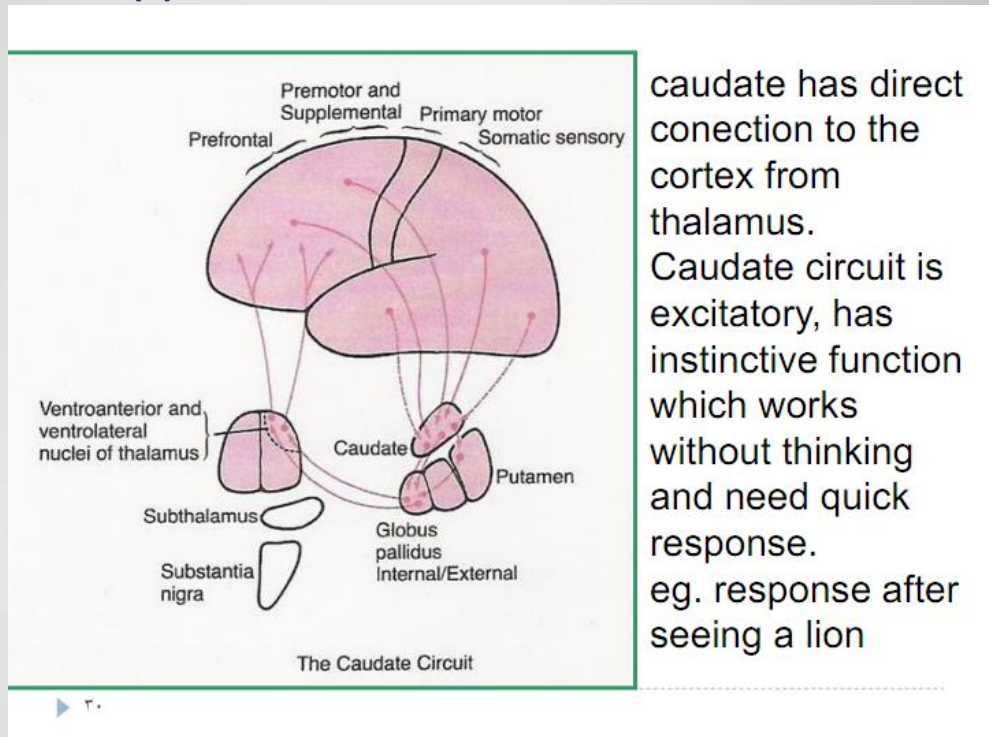
**Putamen circuit is for already learned movement "subconsciously", but if you are doing it for the first time it will be done by the Caudate circuit, then it will be memorized in the Putamen**

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### Neurotransmitters of basal ganglia

1. Dopamine pathway: from substantia nigra to caudate nucleus and putamen.
2. Gama amino butyric acid pathway from caudate nucleus and putamen to globus pallidus and substantia nigra.
3. Acetylcholine pathway from cortex to the caudate nucleus to putamen.
4. Glutamate that provide the excitatory signals that balance out the large no. of the inhibitory signals transmitted specially by the dopamin, GABA & serotonin inhibitory transmitters.

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## FUNCTIONS OF BASAL GANGLIA

- ▶ Voluntary motor activities
- ▶ Regulatory
- ▶ Procedural learning
- ▶ Routine behaviors (Habits)

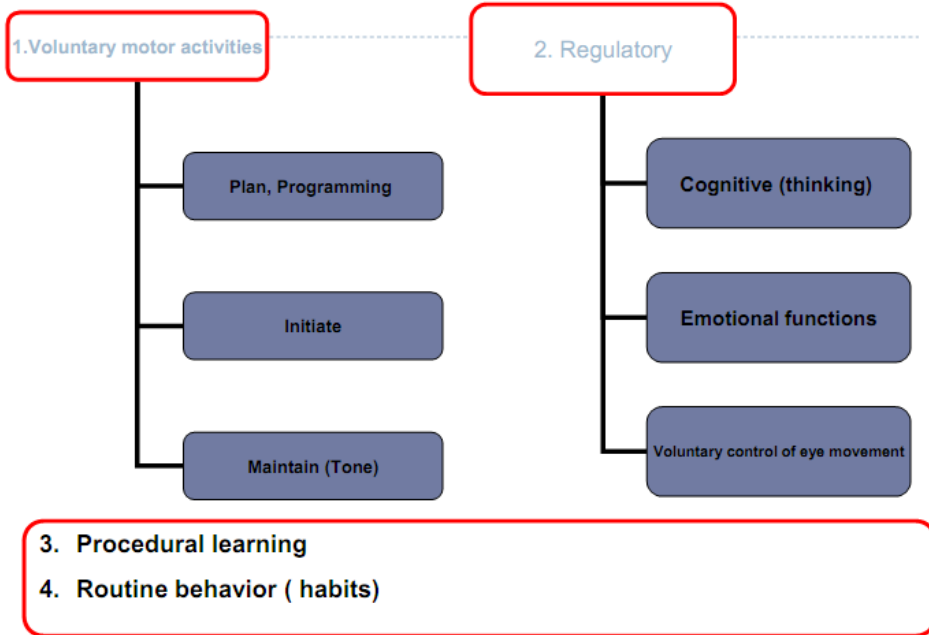
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## FUNCTIONS OF BASAL GANGLIA



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### Functions


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1. Planning & programming (discharge before movement begins) .
2. Motor control of the final common pathway .
3. Muscle tone (lesion increases).
4. Cognitive functions (Frontal cortex) Lesions disrupt performance .
5. Speech , lesion of left caudate results in disturbed speech dysarthria .

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### Disorders of movement in Basal ganglia disease

1. Hyperkinetic – excessive abnormal movement i.e. chorea, athetosis, ballism .
2. Hypokinetic – slow movements i.e. akinesia , bradykinesia .

Team Notes :

#### **Hyperkinetic:**

It means that there's a damage in the Indirect pathway (Responsible for inhibition), and when it is damaged the Direct will take over and this will result in Hyper-activation of muscles

#### **Hypokinetic:**

It means that there's a damage in the Direct pathway (Responsible for excitation), and when it is damaged the Indirect will take over and this will result in Hypo-activation of muscles.





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### HYPERKINESIA

#### I. CHOREA

Rapid involuntary “ dancing” movements .



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See the table blow



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### 2. Athetosis

Continuous , slow writhing movments .

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### 3. Ballism (Hemiballismus)

Involuntary flailing , intense and violent movements .

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### Hypokinesia

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1. Akinesia :  
Difficulty in initiating movement .
2. Bradykinesia :  
Slowness of movement .

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### Parkinson's disease                      Paralysis Agitans

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James Parkinson .

1. Degeneration of dopaminergic nigrostriatal neurons (60-80 %).
2. Phenthiazines(tranquilizers drugs) .
3. Methyl-Phenyl-Tetrahydro-Pyridine (MPTP). The oxidant MPP+ is toxic to SN.

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Cont.

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### Rigidity

agonists and antagonists ( spacticity).

Lead-pipe rigidity

cogwheel -catches


(mixture of tremor and rigidity) .

Tremors . At Rest , 8Hz of antagonists.

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## Features

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Akinesia –Bradykinesia are marked.

Absence of associated unconscious movements(swinging of arms during walking .

Facial expression is masked.


Rigidity

Tremors(static T)

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### Pathogenesis

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Excitation imbalance Inhibition

**loss** of dopamine inhibition of putamen

**increases** in inhibitory output to GBes

**decreases** inhibitory output of STN

**increases** excitatory output GBis

**increases** inhibitory output to thalamus

**reduces** excitatory drive to cerebral cortex

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### Parkinson's Disease: Treatment

- ▶ Drug Therapy
  - ▶ L-DOPA
  - ▶ Cholinergic
  - ▶ Pallidectomy
- ▶ Electrical stimulation of Globus pallidus
- ▶ Tissue transplants

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### Huntington's Disease (Chorea)

- Rare ▶
- onset 30-40s ▶
- early as 20s ▶
- Degeneration of Striatum ▶
- Caudate ▶
- Putamen ▶
- GABA & ACh neurons ▶

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## Huntingtons Disease

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Hereditary , autosomal dominant .

Disease of caudate & putamen.

**Jerky** movement of hands toward end of reaching an object .

**Chorea**


**Slurred** speech and incomprehensive .

Progressive **Dementia** -

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### Cont. Huntingtons

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Loss of GABA – Cholinergic neurons .

The loss of **GABAergic** neurons leads to  
chorea


Loss of **Dopaminergic** neurons leads to  
Parkinson's disease .

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### Summary of functions and disfunctionof basal ganglia

- ▶ It play important motor function in starting and stopping motor functions and inhibiting unwanted movement.
- ▶ It changes the timing and scales the intensity of movements.
- ▶ Putamen circuit is inhibitory. Executes skilled motor activities for example cutting paper with a scissor, hammering on nail, shooting a basket ball & like throwing a base ball.
- ▶ Putamen circuit has indirect connection to cortex via thalamus.while caudate has direct conection to the cortex from thalamus.

▶ 4A

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Cont...

- ▶ Caudate circuit is excitatory, has instinctive function which works without thinking and need quick response. eg. response after seeing a lion.

[Note: effects of basal ganglia on motor activity are generally inhibitory.]

Lesions of the basal ganglia produce effects on contra lateral side of the body

Damage to basal ganglia does not cause paralysis. However it results in abnormal movements

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Movement Disorder	Features	Lesion
Chorea	Multiole quick, random movements, usually most prominent in the appendicular muscles	Atrophy of the <b>striatum</b> . Huntington Chorea
Athetosis	Slow writhing movements, which are usually more severe in the appendicular muscles	Diffuse hypermyelination of <b>corpus striatum and thalamus</b>
Hemiballismus	Wild flinging movements of half of the body	Hemorrhagic destruction of contralateral <b>subthalamic n.</b> Hypertensive patients
Parkinsonism	Pill rolling tremor of the fingers at rest, lead pipe rigidity and akinesia	Degeneration of <b>Substantia Nigra</b>

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## Questions

Q1: which of the following loops is concerned with learned movement?

- 1- Limbic loop
- 2- Motor loop
- 3- Cognitive loop
- 4- Occulomotor Loop

Q2: main function of indirect movement is?

- 1- increase muscle activity
- 2- decrease muscle activity
- 3- maintains muscle activity
- 4- none of these are correct

## Answers

1-2

2-2