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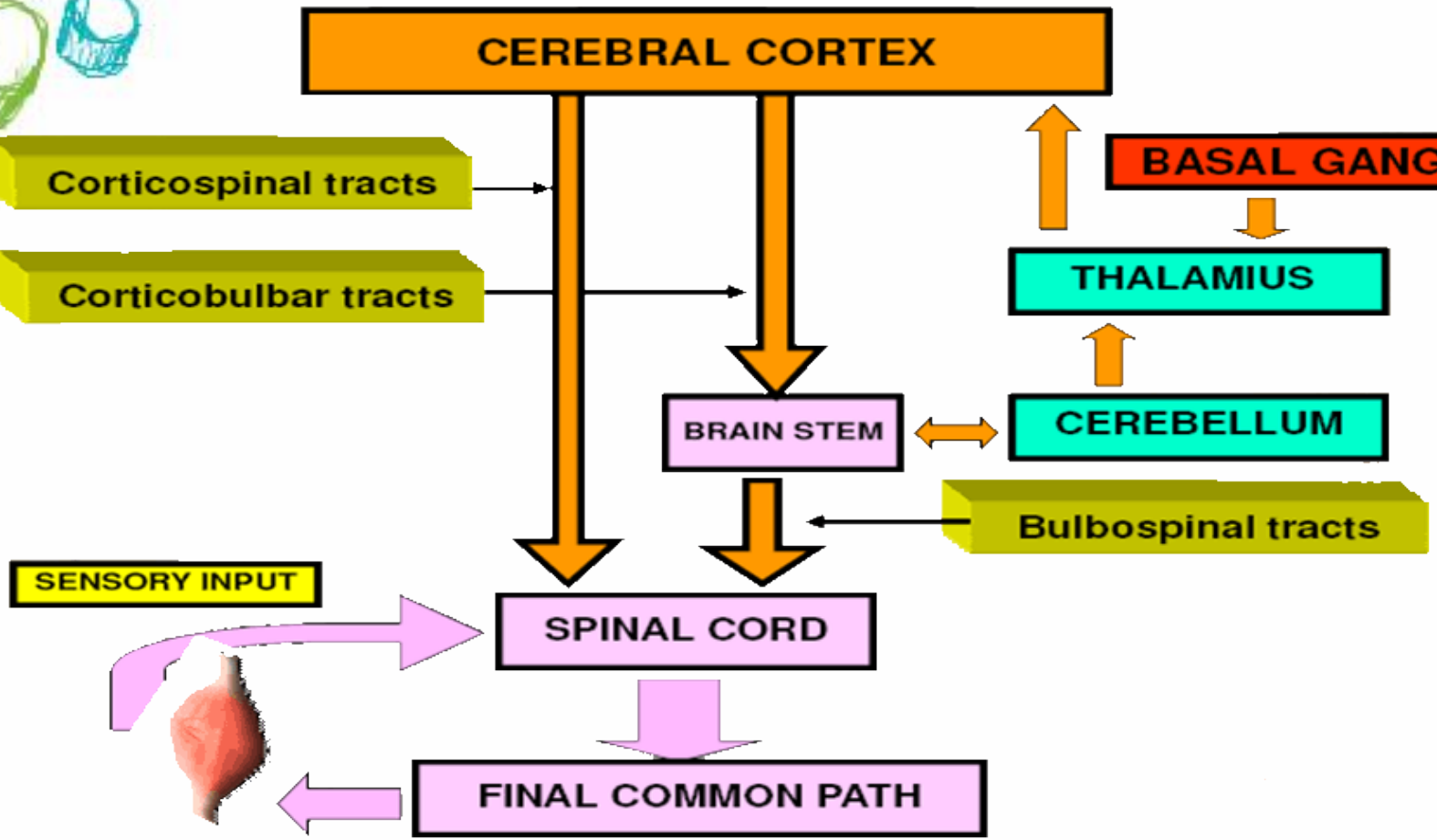
Physiology Of Basal Ganglia And Regulatory Mechanisms..

Done by:

Sarah bin-hussain



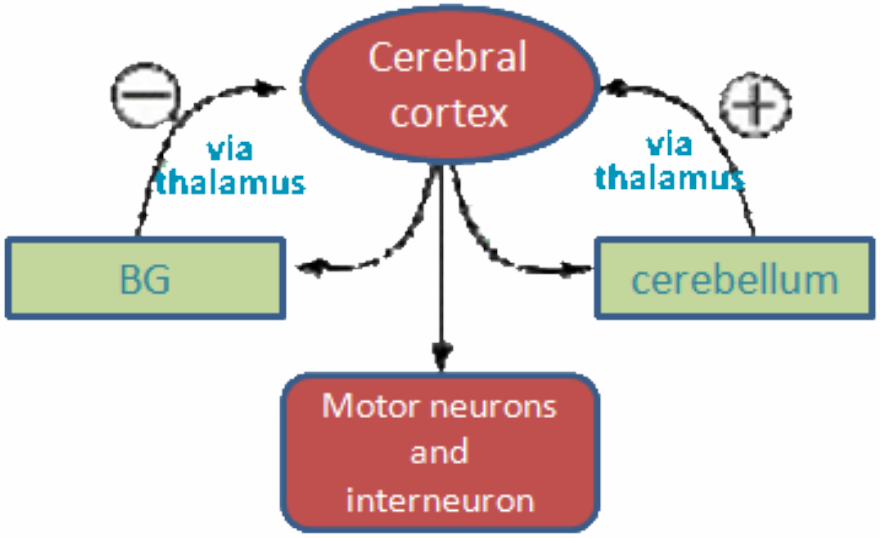
This pic show the motor control of the muscles by **cerebral cortex** through the **SC and brain stem** →these 2 pass the order to final common pathway (alpha neurons) which send the signals to the muscles .

this activity is controlled and regulated by 2 regulatory organs :

1- **cerebellum** (control the BS and controle the cortex by thalamus)
2- **basal gangilia** (control the cortex by thalamus)

BASAL GANGLIA

CONNECTIONS



Cerebellum and **BG** control cerebral cortex via thalamus

Components And Functional Anatomy Of Basal Ganglia

Basal ganglia are subcorticle nuclei of grey matter located in the interior part of cerebrum near about base .

Function:

1. Play a major role in the subconscious control of Voluntary motor activities (Plan,Programming - Initiate - Maintain Tone)
2. Regulatory (Cognitive “thinking”- Emotional functions- Voluntary control of eye movement)
3. Procedural learning
4. Routine behaviors (Habits)

Notes:

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

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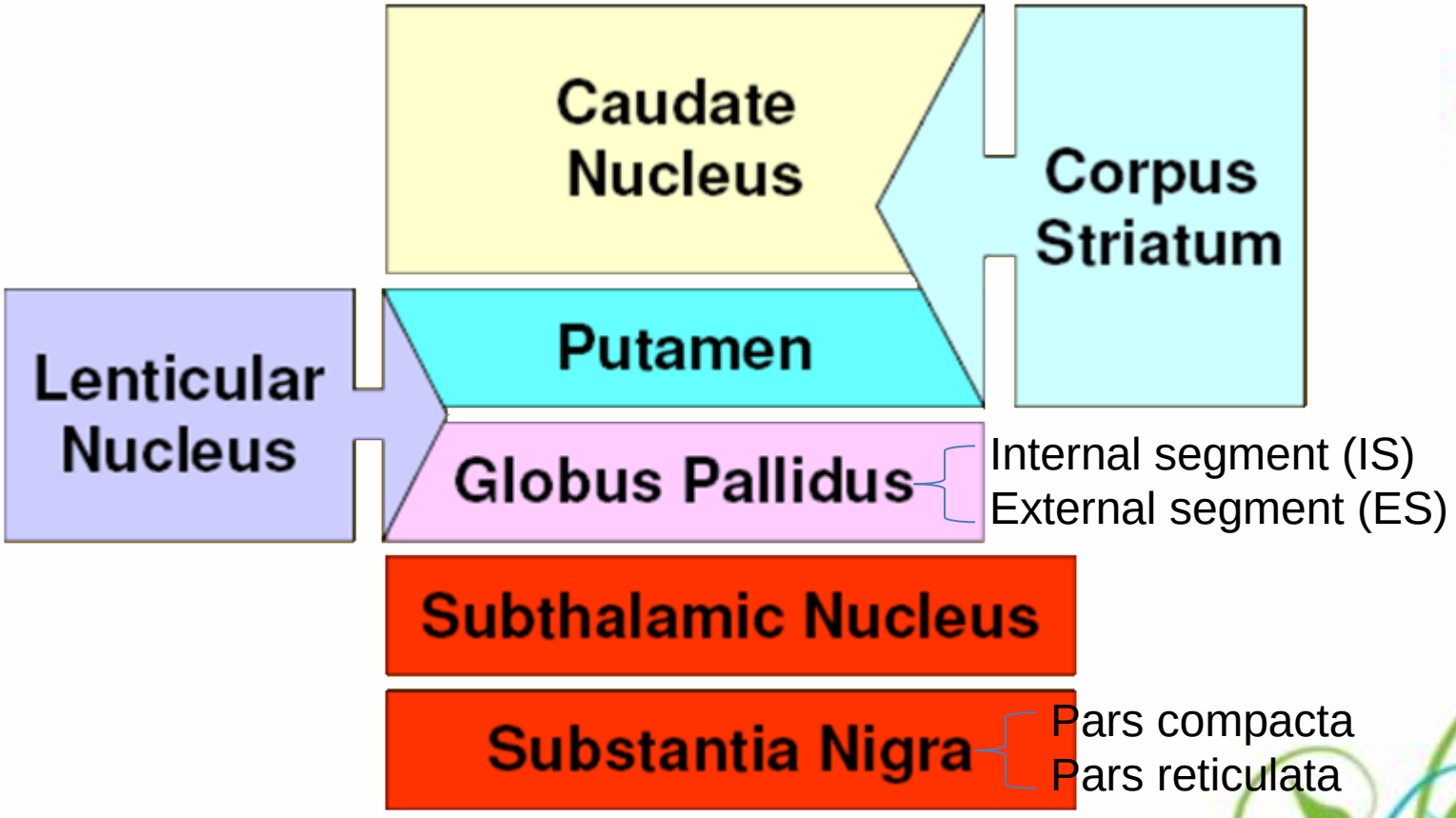
Basal Nuclei:

There are **5** nuclei in the BG:



We called caudate and putamen together = **corpus striatum**
We called putamen and globus pallidus together = **lenticular nucleus**

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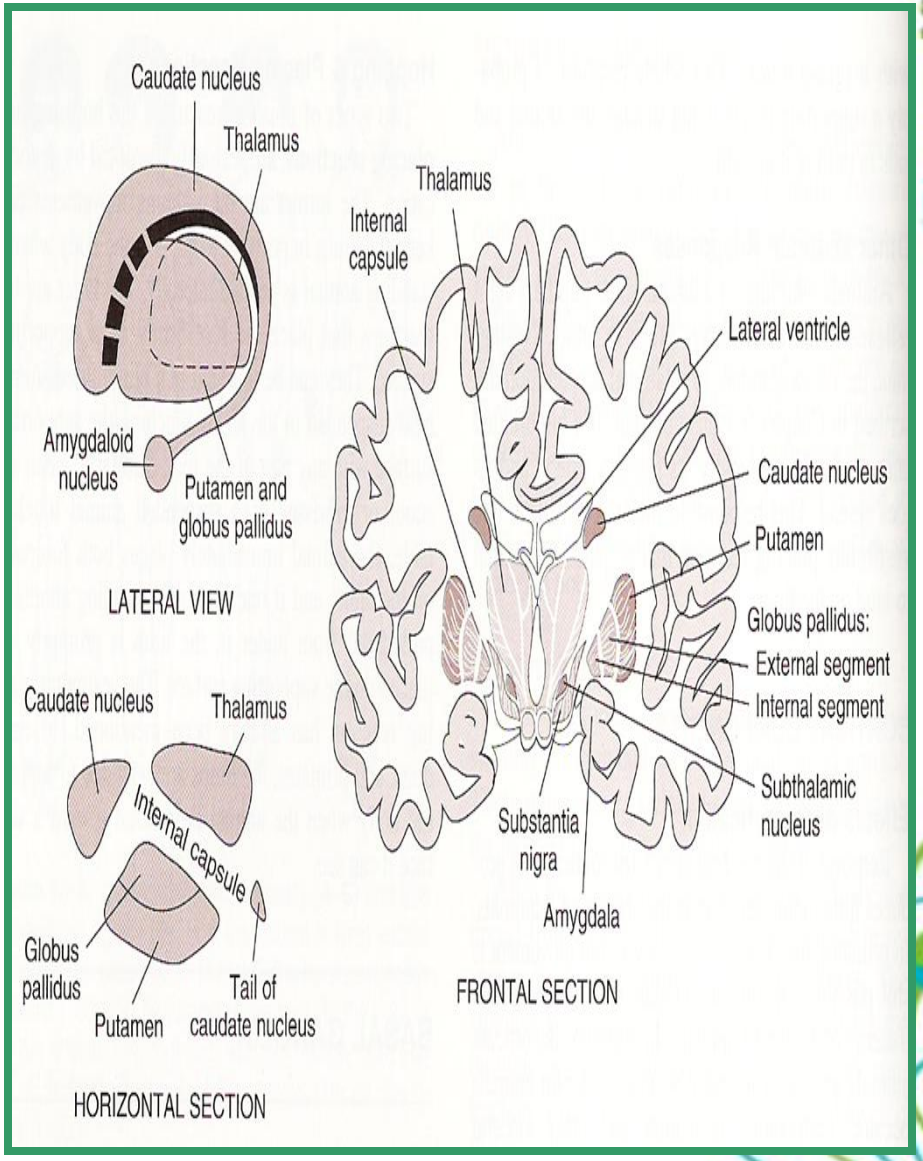
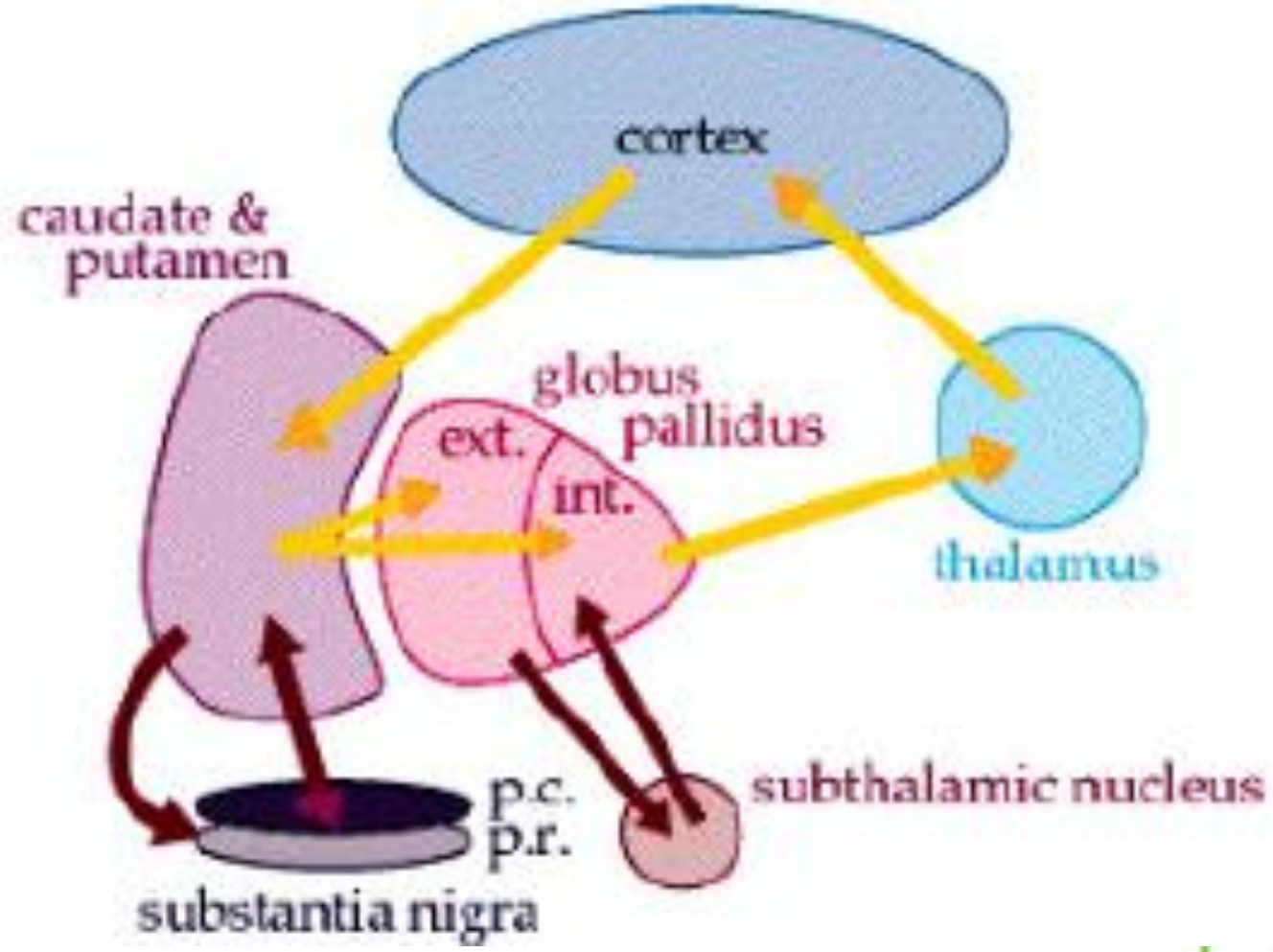
The striatum

The striatum consists of three subdivisions, :

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**




cortex
caudate &
putamen
globus
pallidus
ext.
int.
thalamus
p.c.
p.r.
subthalamic nucleus
substantia nigra

3 connections to remember:

1- main input to the BG (from cortex)

the main afferent connections to the BG terminate in the NEOSTRIATUM (caudate nucleus and putamen)→they include:

a)- the **Cortico-striatal** projection from all parts of the cerebral cortex (mainly)

b)- centromedian nucleus of the the thalamus to the striatum

2- main output from the BG (via thalamus to cortex"motor area")

a)- internal segment of globus pallidus --inhibitory--> thalamus --excitatory--> motor cortex

b)- Superior colliculus (saccadic eye move.)

3- connections between parts of BG include:

a)- **Dopaminergic nigro-striatal** pathway. (from pars-compacta →to striatum)

b)- **GABAergic striato-nigral** pathway. (from striatum →to pars-reticulata)

c)- from Caudate and putamen → to both segments of globus pallidus.

d)- from Globus pallidus- external segment → to SubThalamic Nucleus →to Globus"both segment" and substantia nigra

Basic Circuits of basal ganglia (function part):

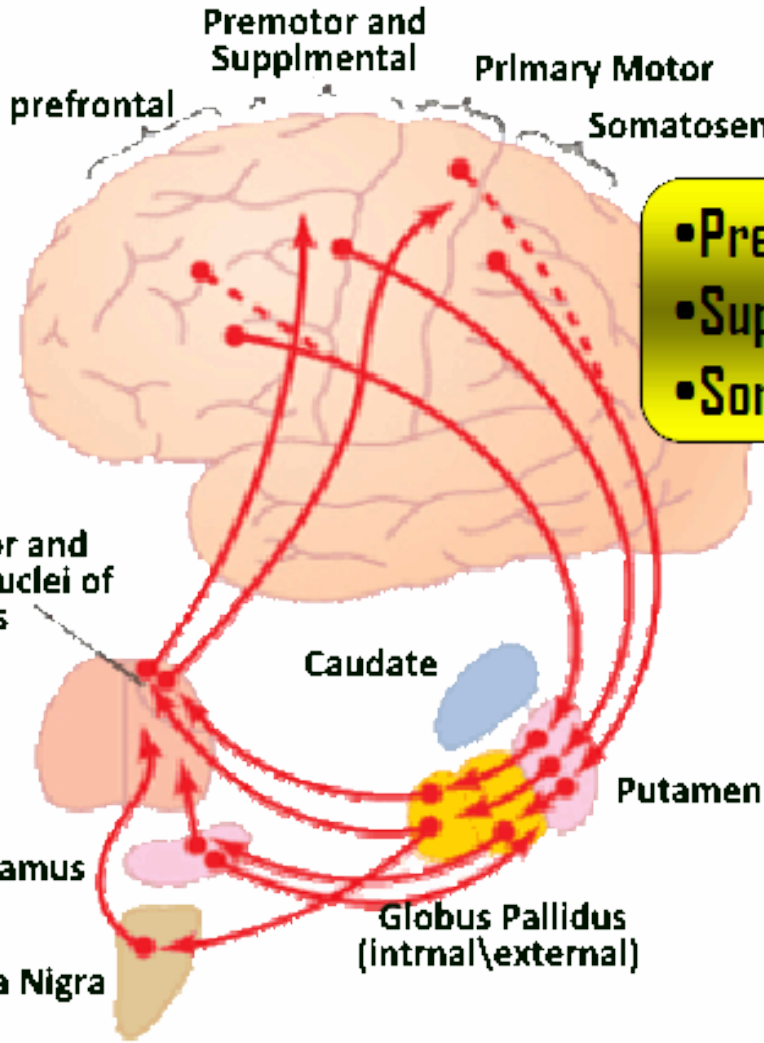
1. **A motor loop (putamen circuit):** concerned with learned movment.
2. **Cognitive loop (Caudate circuit):** concerned with cognitive control of sequences of motor pattern. Basically it is concerned with motor intentions.

   (Note: cognition means thinking process using sensory input with information already stored in memory.)
3. **Limbic loop**: involved in giving motor expression to emotions like, smiling, aggressive or submissive posture. (BG has conection with limbic system , when there is a disease in the BG the expression is also affected)
4. **Occulomotor loop**: concerned with voluntary eye movement [saccadic movement]

The Putamen Circuit

- Prim Motor Cortex
- Premotor
- Suppl Motor Areas

output



- Premotor
- Suppl Motor
- Somatosensory Cortex

input

Putamen circuit

has **indirect** connection to cortex via thalamus .

Putamen circuit is **inhibitory**.

- **function:**

Basal ganglia (Putamen circuit)function in association with the corticospinal system to **control complex patterns(Learned \ skilled)of motor activity:**

- **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.

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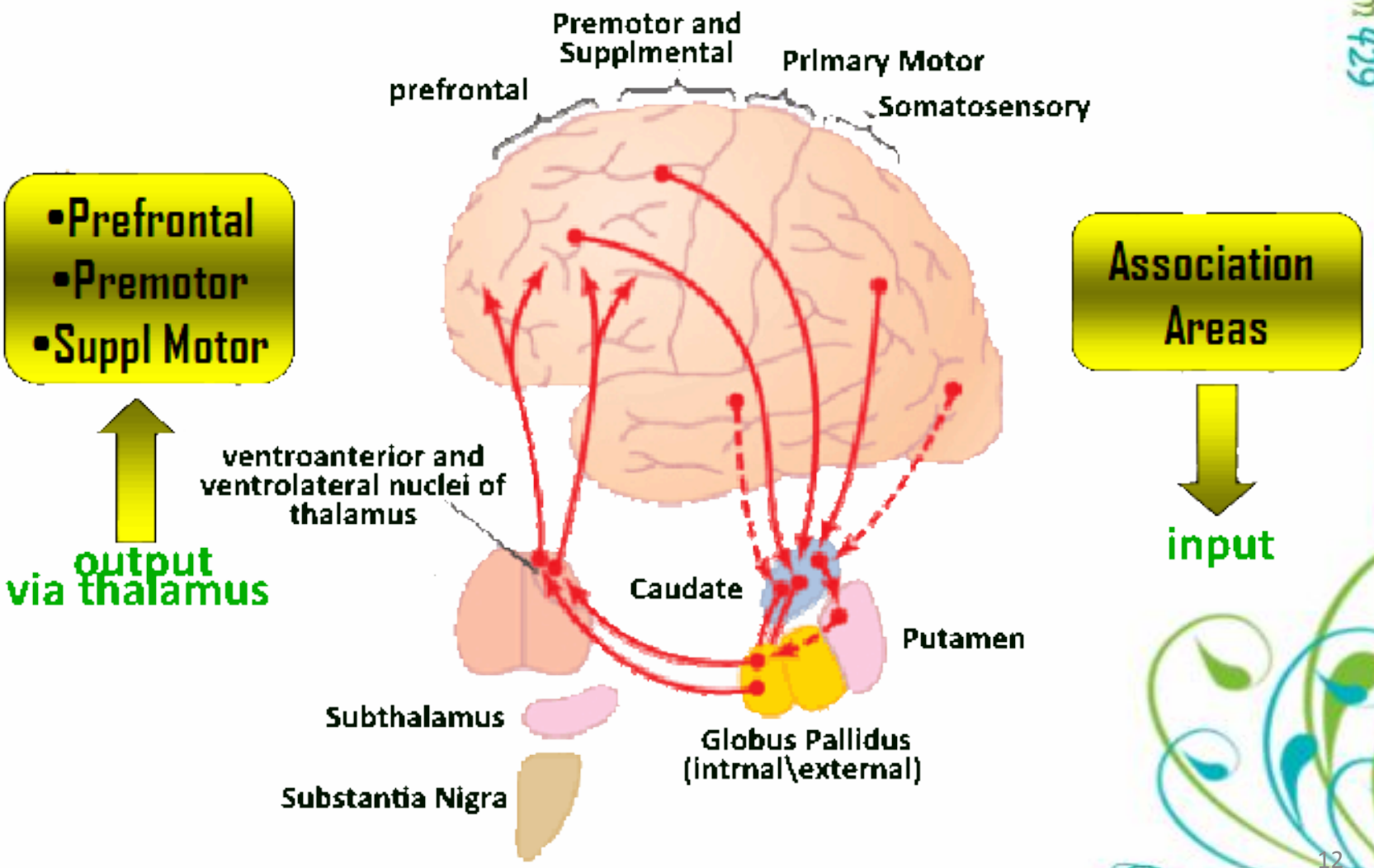
The Caudate Circuit



Caudate circuit :

has **direct** conection to the cortex from thalamus.

Caudate circuit is **excitatory .**

- **function:**

A- Cognitive Control of Sequences of Motor Patterns (instinctive function which works **without thinking and need quick response**)

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) 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.

Cont. Caudate circuit :

B- 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.

	Putamen circuit	Caudate circuit :
Connention	**indirect** connection to cortex via thalamus	**direct** conection to the cortex from thalamus
Function	**inhibitory**	**excitatory**
Function	•control complex patterns(Learned \ skilled)of motor activity:	•Cognitive Control of Sequences of Motor Patterns (instinctive function which works without thinking and need quick response) •Change the Timing and to Scale the Intensity of Movements.
Main input	•Premotor •Suppl Motor •Somatosensory Cortex	•Association Areas
Main output	•Prim Motor Cortex •Premotor •Suppl Motor Areas	•Prefrontal •Premotor •Suppl Motor

Basal ganglia pathways loops

it has 2 pathways loop :

1- direct : ↑ motor activity

2- indirect : ↓motor activity

The **direct** pathway is thought to **facilitate** movements while the **indirect** pathway is thought to **inhibit** unwanted movements.

Imp points to understand the next slides:

Gpi : glopus pallidus internal
Gpe: glopus pallidus external
(+) : excitatory **glutamate**
(-) : inhibitory **GABA**
(-) follow **(-)** → the first inhibit the second so there is no inhibitin (**disinhibited**)

Substantia nigra(pars-compacta)regulate the pathways by (dopaminergic neurons):

a) **D1 receptor → excitatory**
b) **D2 receptor→ inhibitory**

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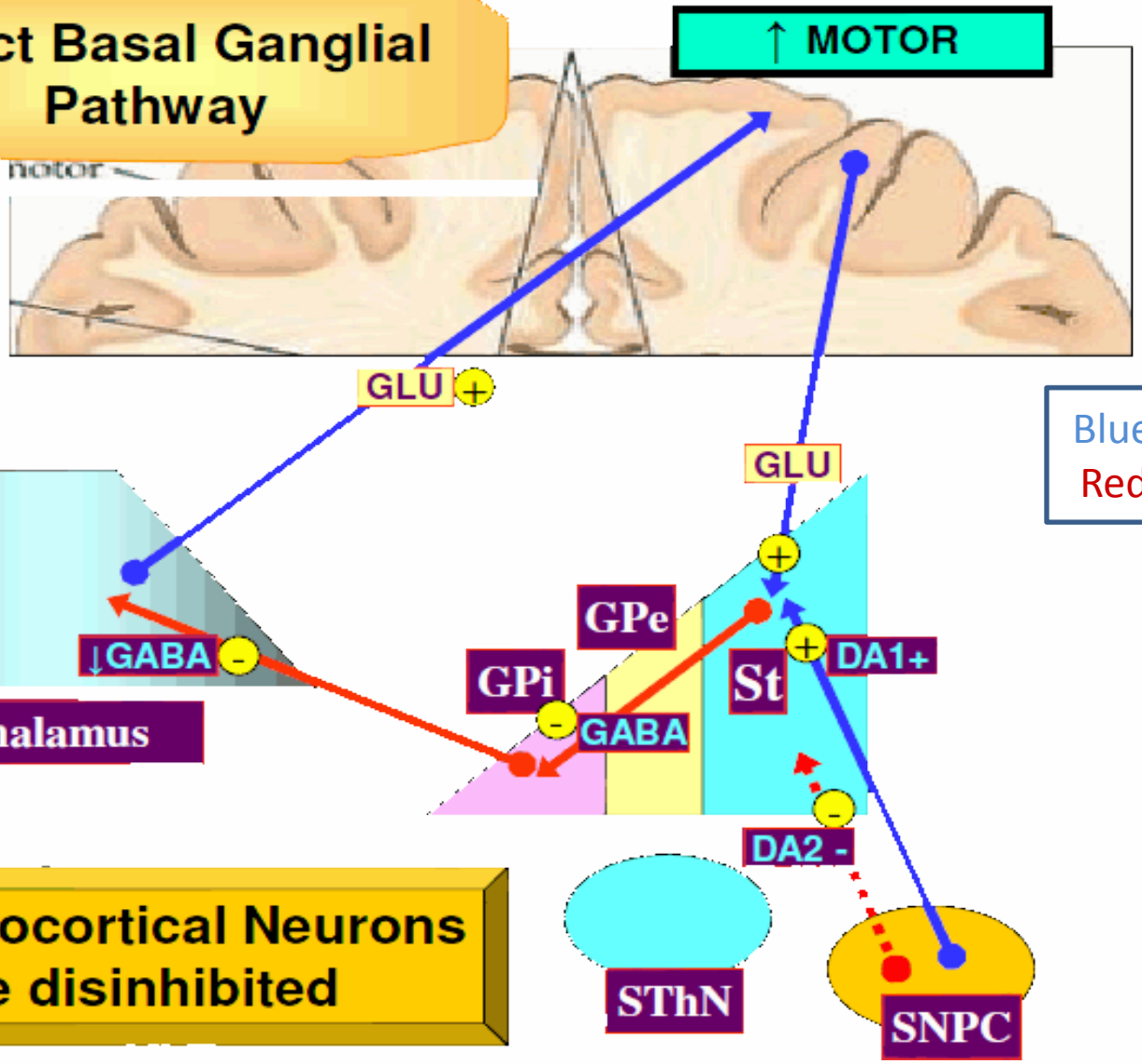
Direct Basal Ganglial Pathway



Blue : excitatory
Red : inhibitory

Thalamocortical Neurons are disinhibited

Cortex (+)→ corpus sriatum (-)→ Gpi (-) →thalamus(+)→ cortex

↑ motor activity

1- direct : ↑ motor activity

Cortex (+)→ corpus sriatum (-)→ Gpi (-) →thalamus(+)→ cortex

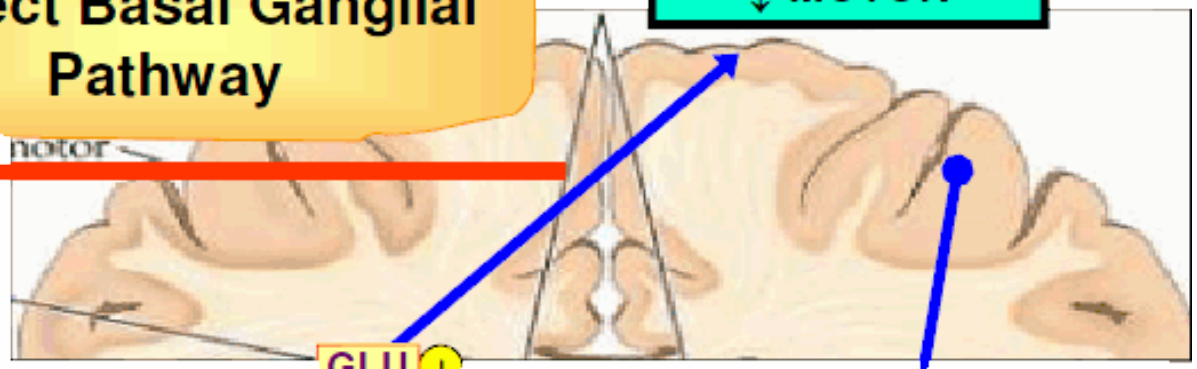
The direct pathway begins with projections from the cortex to the striatum. Striatum neurons projects directly to the Gpi. The Gpi projects to the thalamus which then projects back to the cortex.

1. **The connections from the cortex to the striatum use glutamate and are excitatory.**
2. **The connections from the striatum to the Gpi use GABA as their neurotransmitter and are inhibitory.**
3. **The connections from Gpi to the thalamus use GABA and are inhibitory.**
4. **The connections from the thalamus back to the cortex are excitatory.**

The cortex excites the striatum which then inhibits the Gpi through the direct pathway. The Gpi is normally tonically active and inhibitory to the thalamus. When the Gpi is inhibited, the thalamus is relieved from inhibition (this is called disinhibition) and excites the cortex, thereby reinforcing the desired movement.

(يعني هنا الـ striatum منعت الـ Gpi انها تمنع الـ thalamus وهذا نسميه "disinhibition")

Indirect Basal Ganglial Pathway



↓ MOTOR

GLU +

Blue : excitatory
Red : inhibitory

↑GABA -

Thalamus

+ GLU

GPe

St

GPi

- GABA

GLU +

DA2 -

+ DA1+

- ↓GABA

STN

SNPC

Subthalamic Neurons are disinhibited

Cortex (+)→ sriatum (-)→Gpe (-)→ STN (+)→Gpi (-) →thalamus(+)→ cortex

↓motor activity

2- indirect : ↓motor activity

Cortex (+)→ sriatum (-)→Gpe (-)→ STN (+)→Gpi (-) →thalamus(+)→ cortex

In the indirect pathway a separate group of striatal neurons projects to Gpe. Gpe then projects to the subthalamic nucleus (STN). The subthalamic nucleus projects to Gpi. The Gpi projects to ventolateral thalamus and the thalamus projects back to the cortex.

1. **The connections from the cortex to the striatum use glutamate and are excitatory.**
2. **The projections from the striatum to the Gpe use GABA and are inhibitory.**
3. **The projections from the Gpe to the subthalamic nucleus also use GABA and are also inhibitory.**
4. **The projection from the subthalamic nucleus to the Gpi is excitatory.**
5. **The connections from Gpi to the thalamus use GABA and are inhibitory.**

Therefore, the cortex excites the striatum which then inhibits Gpe. Since Gpe is inhibitory to the subthalamic nucleus, the subthalamic nucleus now becomes more active and excites the Gpi. The Gpi being more active, then inhibits the thalamus and the thalamus does not excite the cortex. In this way, activation of the indirect pathway by the striatum causes a relative inhibition of movement.

(هنا الـ striatum منعت الـ Gpe انها تمنع الـ STNوهذا نسميه disinhibition ،
بعدين الـ STN حفزت الـ Gpi اللي هي بطبيعتها تمنع الـ thalamus انها تحفز الـ cortex)

Metabolic characteristics

- High Oxygen consumption .
- High Copper content .

In Wilsons disease (Copper intoxication):

✓Autosomal recessive
✓Copper binding protien Ceruloplasmin is low,
✓Lenticular degeneration occures.

Basal Ganglia DISORDERS

- **MOVEMENTS** (ATAXIA Rate, Range, Force, Direction)
- **SPEECH**
- **POSTURE**
- **GAIT**
- **MENTAL ACTIVITY**
- **OTHERS**

Movement Disorders

Hyperkinetic

" Excessive abnormal movement":

- Hemiballismus
- Huntington's Disease
- Athetosis
- Chorea
- ballism

Hypokinetic

" slow movements i.e. akinesia , bradykinesia ":

- Parkinson's Disease
- Drug Induced (Neuroleptics, MPTP)

Note:

akinesia → difficulty in initiating movement

bradykinesia → slowness of movement

Movement Disorder	Features	Lesion
Chorea Rapid involuntry dancing movement	Multiole quick, random movements, usually most prominent in the appendicular muscles	Atrophy of the striatum. Huntington Chorea
Athetosis Continuous, slow writhing movments .	Slow writhing movements,which are usually more severe in the appendicular muscles	Diffuse hypermyelination of corpus striatum and thalamus
Hemiballismus (Ballism) Involuntary flailing , intense and violent movements .	Wild flinging movements of half of the body	Hemorrhagic destruction of contralateral subthalamic n. Hypertensive patients
Parkinsonism	Pill rolling tremor of the fingers at rest, lead pipe rigidity and akinesia	Degenration of Substantia Nigra

Parkinson's Disease (Paralysis Agitans)

- Described by James Parkinson
- Degeneration of **dopaminergic nigrostriatal neurons** (60-80 %).
- Phenthiazines (tranquilizers drugs) .
- Methyl-Phenyl-Tetrahydro-Pyridine (MPTP). The oxidant MPP+ is toxic to SN.

cardinal features

- Tremor (At Rest" static T" , 8Hz of antagonists)
- Rigidity - agonists and antagonists(spacticity) -.
- Lead-pipe rigidity
- cogwheel -catches (mixture of tremer and rigidity) .
- Akinesia & Bradykinesia
- Postural Changes
- Speech Changes
- Absence of associated unconcious movements (swinging of arms during walking .
- Facial expression is masked.

Cont. Parkinson's Disease

- **Pathogenesis (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

- **Treatment :**
  - **Drug Therapy**
    - L-DOPA
    - Cholinergic
    - Pallidectomy
  - **Electrical stimulation of Globus pallidus**
  - **Tissue transplants**

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Hemiballismus

- Injury usually to STN.
- Decreased inhibition (Indirect Pathway).
- **Characterized by:** uncontrolled flinging.
- **TX:** Dopamine Antagonist

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Huntington's Disease

- Hereditory , autosomal dominant
- Rare onset at 30-40s as early as 20s
- Disease of **caudate & putamen**(Degeneration of Striatum).
- Early, Jerky movement of hands toward end of reaching an object
- Later, hyperkinetic choreiform movements(**Chorea**) appear and gradually increase until they incapacitate the patient
- Slurred speech and incomprehensive
- Progressive Dementia
- Loss of **GABA – Cholinergic neurons** (GABA & ACh neurons)

Remember!

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

Loss of **Dopaminergic** neurons leads to→**Parkinson"s disease .**

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Summary :

- 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.
- 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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