CONTROL OF POSTURE & MOVEMENT: BASAL GANGLIA (BG)

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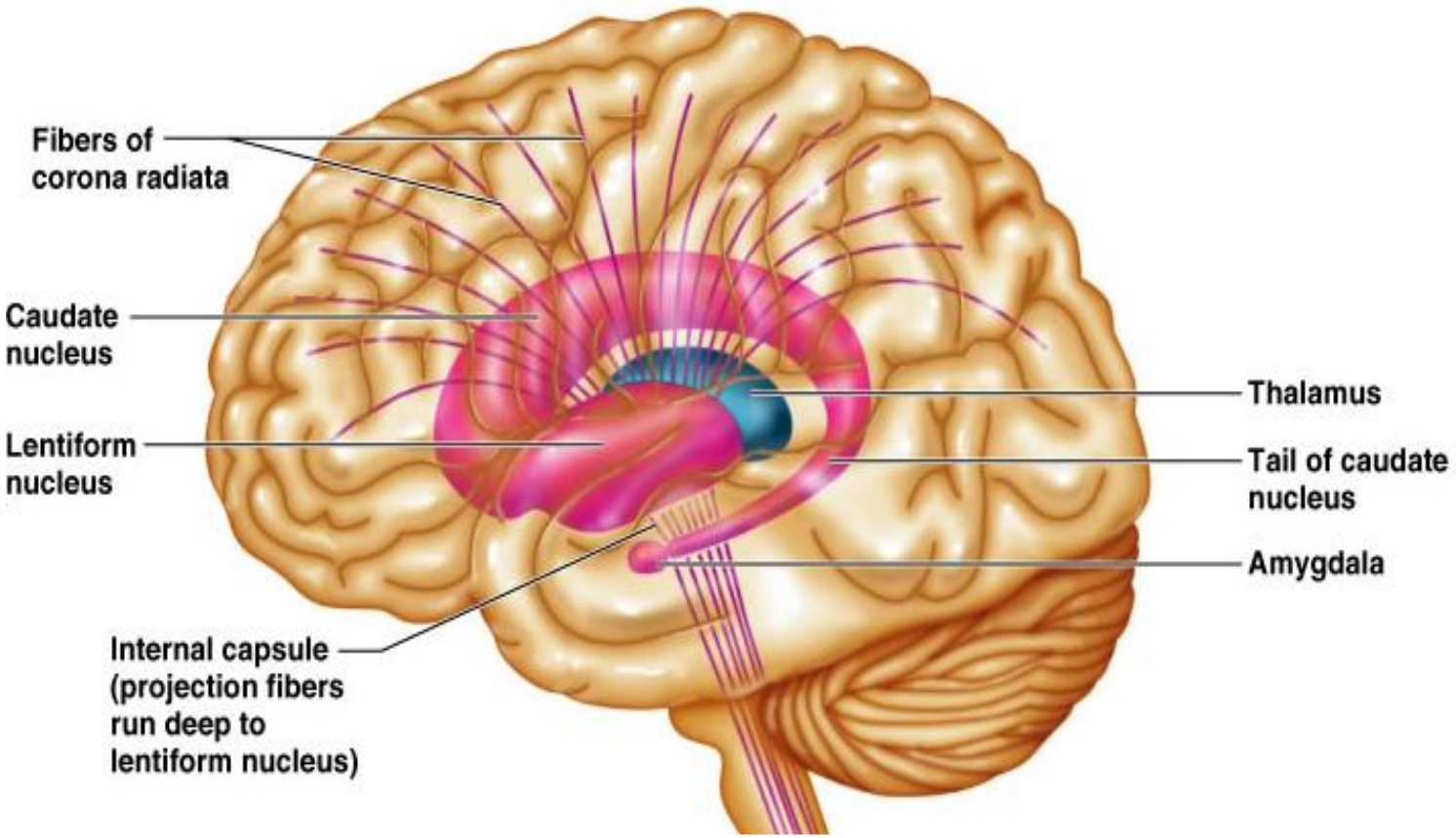
Objectives

By the end of this session students are expected to:

- Name different parts of basal ganglia.
- List important functions of basal ganglia.
- Describe neuronal connections of basal ganglia and their neurotransmitters.
- Describe disorders of the basal ganglia.

Basal Ganglia (BG)

- Putamen
- Globus Pallidus



The term BG (Basal nuclei) refers to a group of several structures deep in the cerebral cortec:

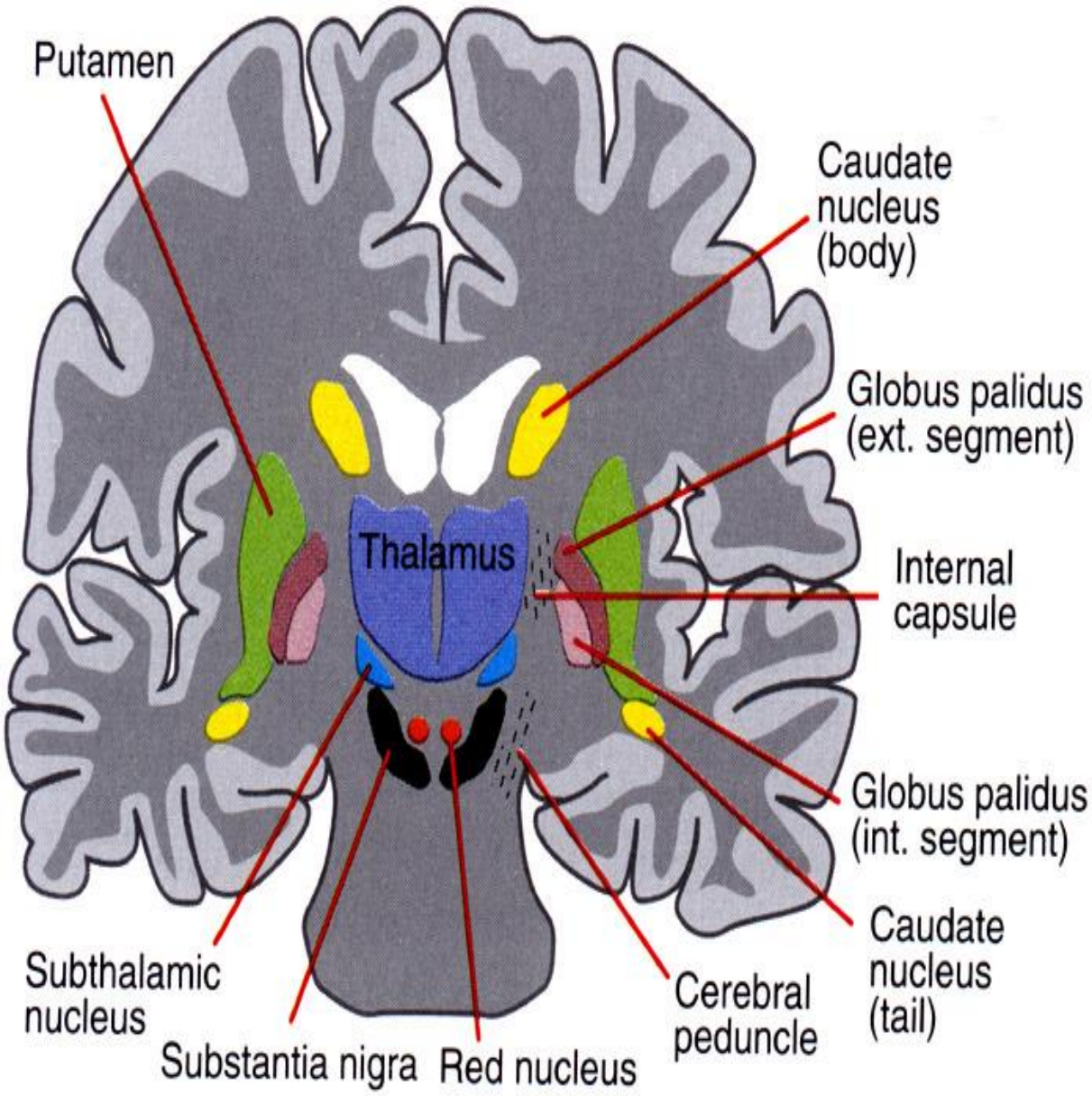
- **Caudate nucleus, putamen, globus pallidus (large masses)**
- **Subthalamic nucleus & substantia nigra** in the mid brain.

Basal Ganglia (BG)

- Caudate nucleus (yellow) and Putamen (green) are called the striatum (but not internal capsule !!).

- Globus Pallidus (GP) is divided into external (GPe) and internal (GPi) segments

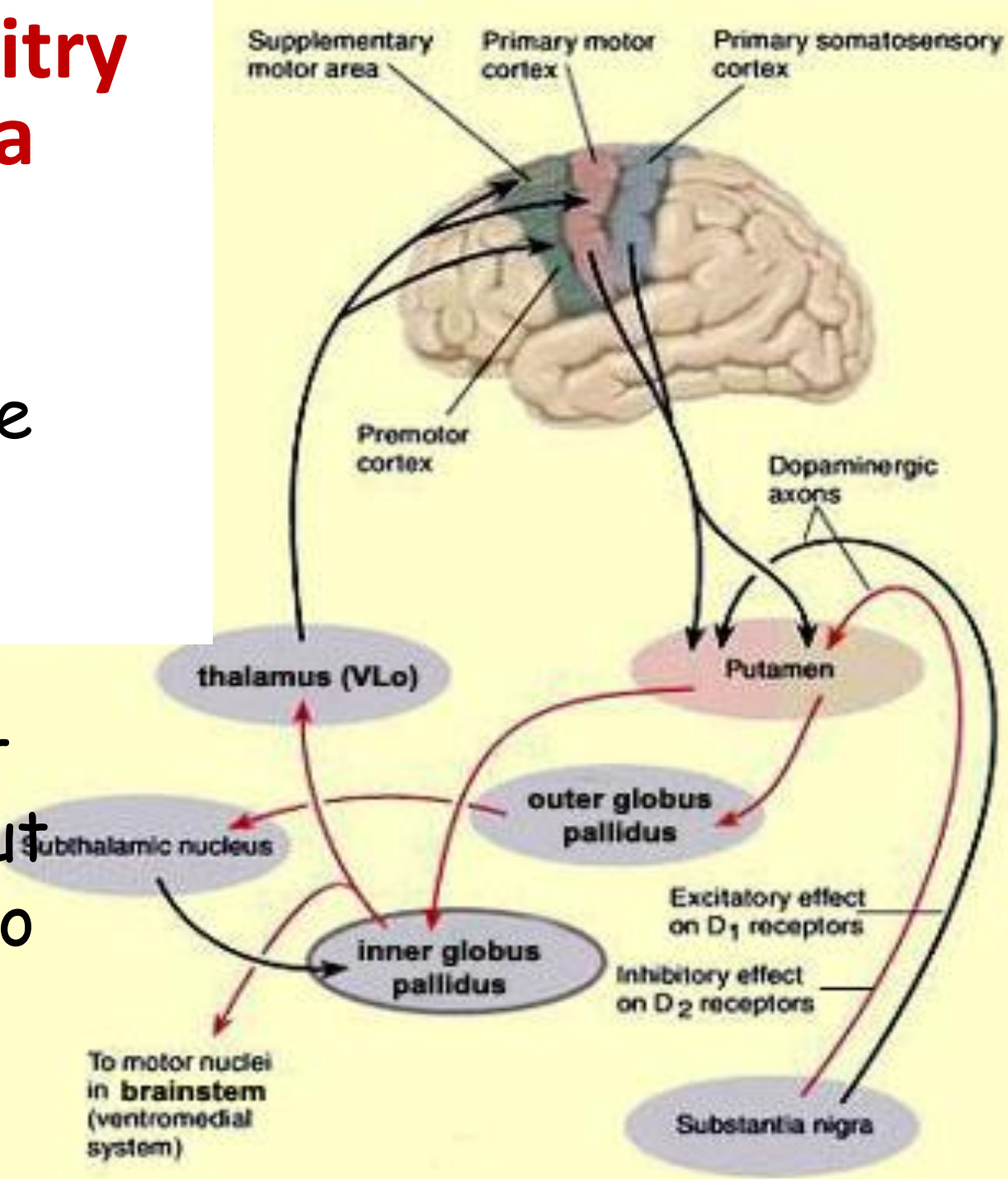
- Substania nigra is divided into pars compacta and pars reticulta



Neuronal circuitry of Basal ganglia

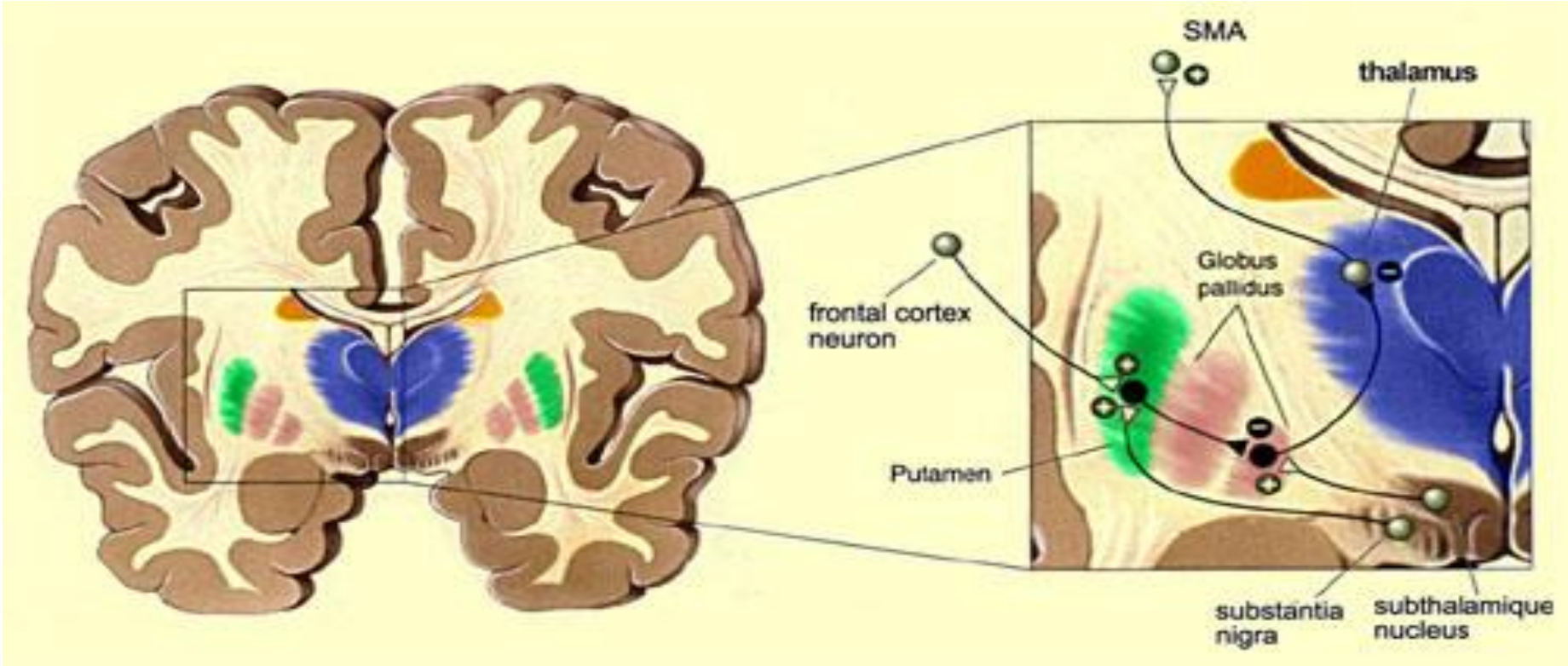
- BG receive most of their input from the cerebral cortex

- Return almost all their output signals back to the cerebral cortex



Neural Connections of Basal Ganglia

- Information from various areas of the cortex passes through the basal ganglia
- Then it returns to the supplementary motor area (**SMA**) via the thalamus



Neural Connections of Basal Ganglia-2

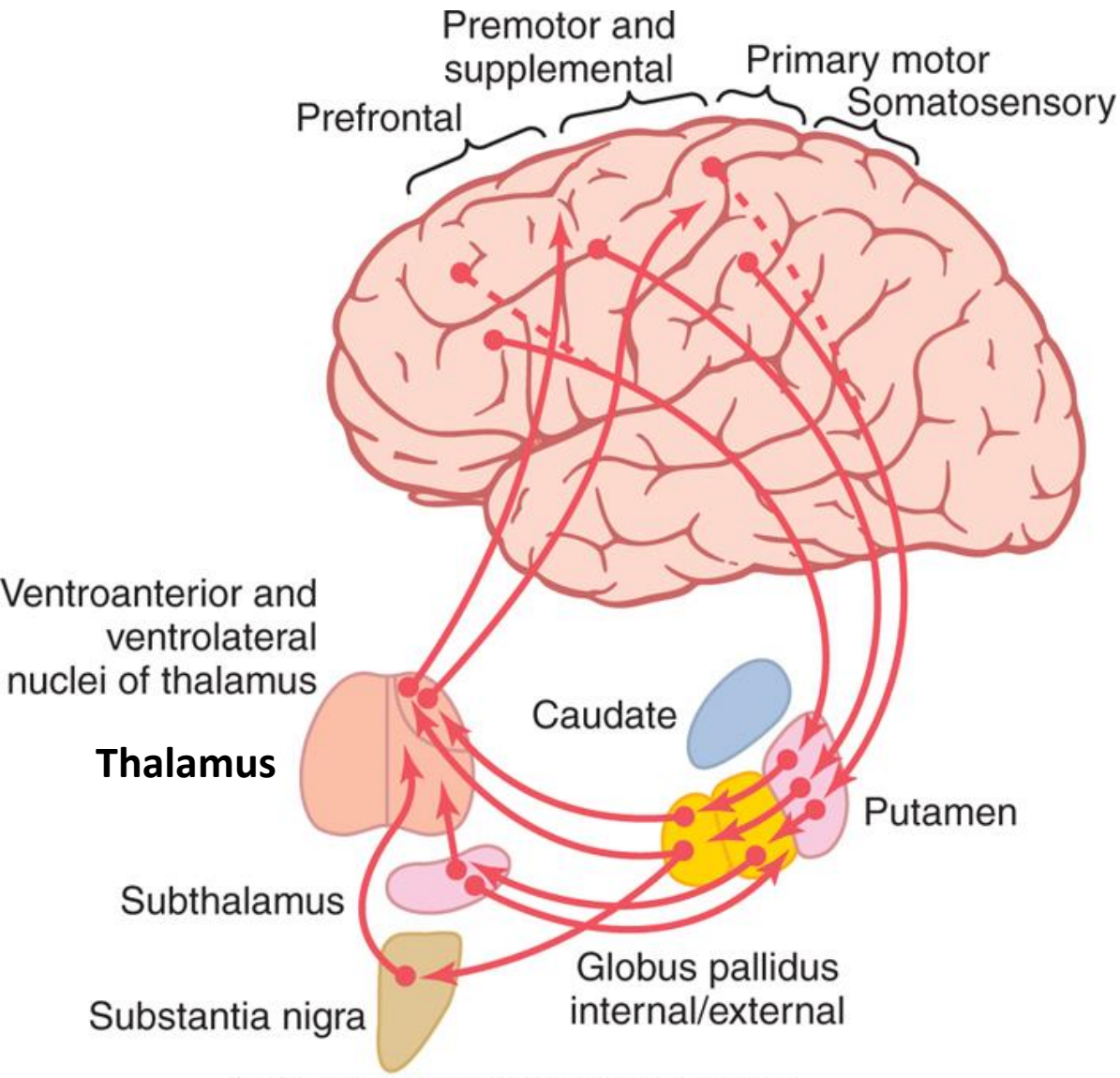
- The BG are connected with cerebral cortex, thalamus and brain stem.
- There are also interconnections between various nuclei of the BG.
- The circuitry of the BG is very complex but is characterized by multiple parallel loops & side chains.

Neural Connections of Basal Ganglia-3

The basal ganglia are connected with the cerebral cortex through two main circuits:

- **The putamen circuit** for execution of learned patterns of movement.
- **The caudate circuit**. For Cognitive Planning of Motor Patterns

Neuronal Pathways of the Putamen



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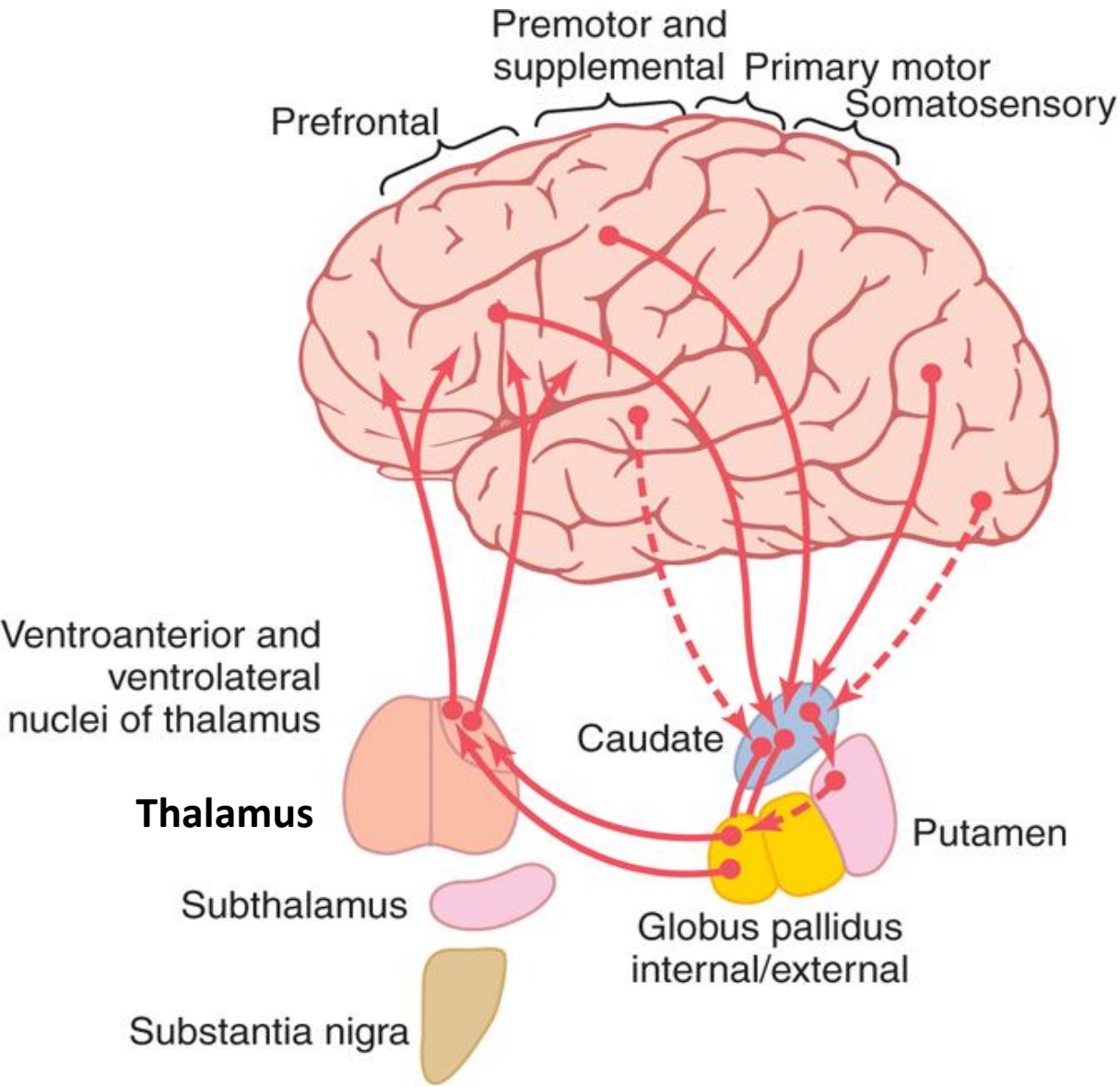
- Mostly from premotor, supplementary motor cortex, and SSC,
- Then to the internal portion of GP, and back to the motor cortex via the thalamus

Neuronal Pathways of the Caudate



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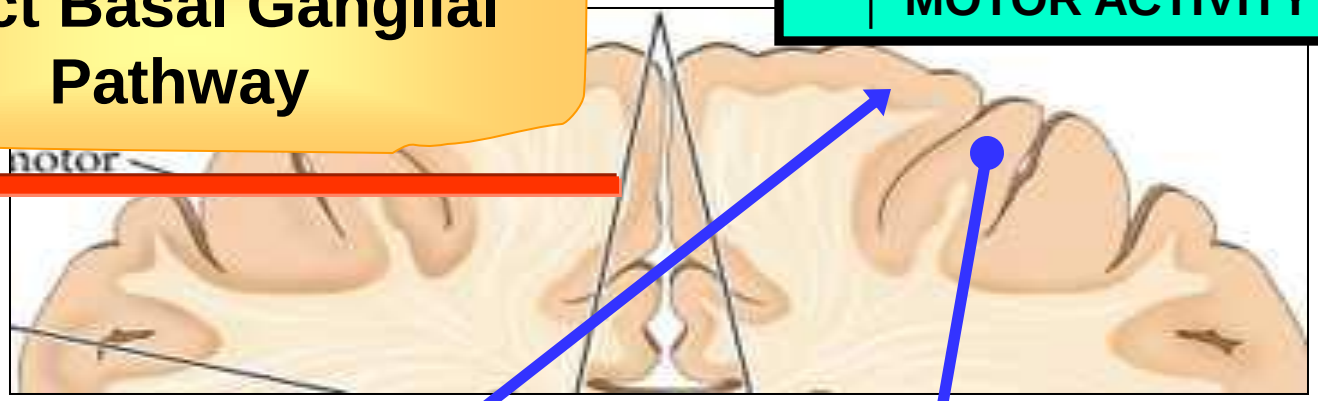
- Mostly from association areas of the cortex
- Mainly areas that also integrate the different types of sensory and motor information into usable thought patterns.

Basal Ganglia Pathways
Direct and Indirect

Direct Basal Ganglial Pathway



↑ MOTOR ACTIVITY

GLU +

GLU

+

GPe

↓GABA -

GPi

St

+ DA1+

Thalamus

- ↑ GABA

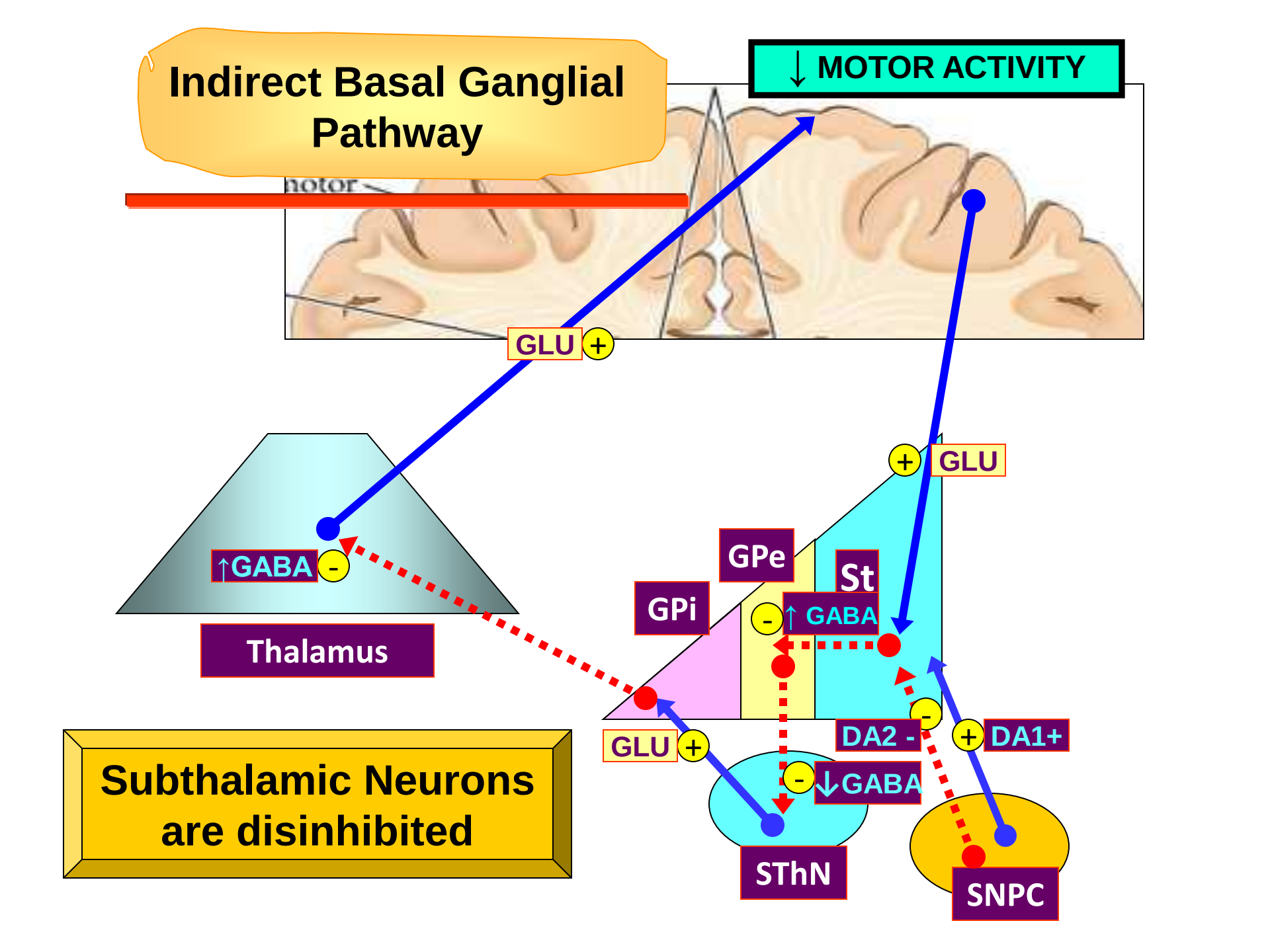
-

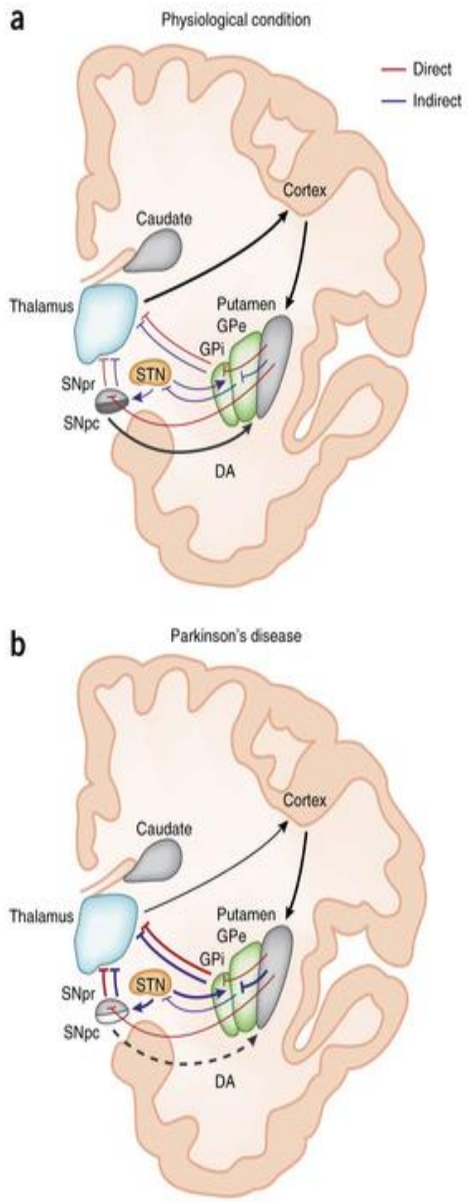
DA2 -

SThN

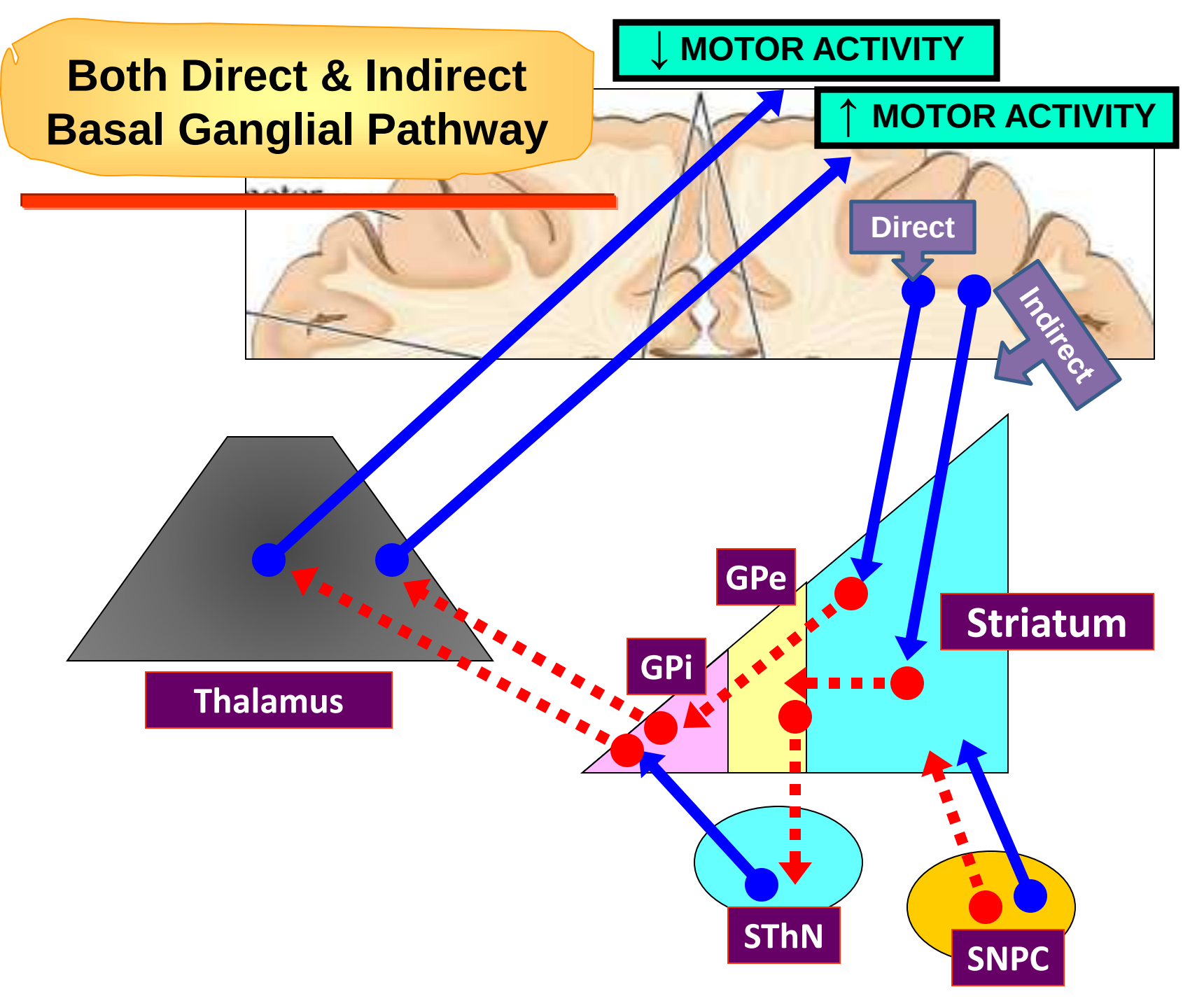
SNPC

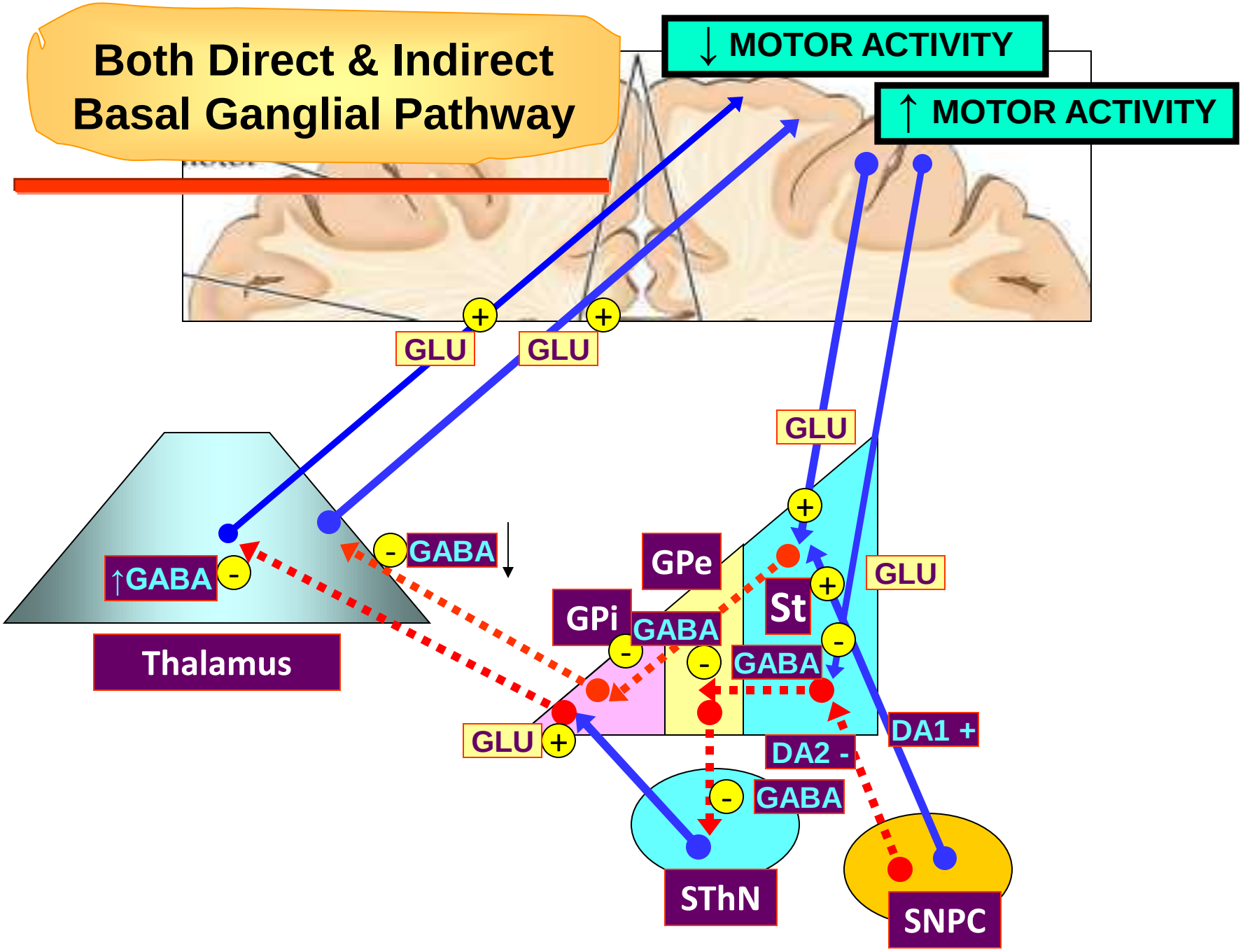
Thalamocortical Neurons are disinhibited


Indirect Basal Ganglial Pathway
↓ MOTOR ACTIVITY
GLU +
↑GABA -
Thalamus
+ GLU
GPe
St
GPi
- ↑ GABA
GLU +
DA2 -
+ DA1+
- ↓GABA
SThN
SNPC
Subthalamic Neurons are disinhibited



In the physiological condition, DA arising from the SNpc is thought to activate D1-expressing striatal MSNs of the direct pathway (red lines) and to inhibit D2-expressing striatal neurons of the indirect pathway (blue lines). The output nuclei GPi and SNpr project to the thalamus, which in turn sends efferents that complete the cortico-basal ganglia-thalamo-cortical loop. (**b**) In Parkinson's disease, degeneration of nigral neurons reduces DA receptor stimulation in striatal MSNs. The imbalance between direct and indirect pathways results into abnormal activation of output nuclei and over-inhibition of thalamic neurons projecting to the cortex


Both Direct & Indirect
Basal Ganglial Pathway
↓ MOTOR ACTIVITY
↑ MOTOR ACTIVITY
Direct
Indirect
Thalamus
GPe
GPi
Striatum
SThN
SNPC


Both Direct & Indirect
Basal Ganglial Pathway
↓ MOTOR ACTIVITY
↑ MOTOR ACTIVITY
GLU
GLU
GLU
↑GABA
GABA
Thalamus
GPe
GPi
St
GABA
GABA
GLU
GLU
DA1 +
DA2 -
GABA
SThN
SNPC

The Putamen Circuit

Executes Learned Patterns of Motor Activity

- Basal ganglia function in association with the corticospinal system to control *complex patterns of motor activity*.
- Examples are:
  - cutting paper with scissors,
  - hammering nails,
  - throwing a baseball,
  - the movements of shoveling dirt,
  - most aspects of vocalization,
  - virtually any other of our skilled movements, most of them performed subconsciously.

The Caudate Circuit

Cognitive Control of Sequences of Motor Activities

- Cognition means the thinking processes of the brain, using both sensory input to the brain plus information already stored in memory.
- Example: A person seeing a lion approach and then responding instantaneously and automatically by (1) turning away from the lion, (2) beginning to run, and (3) even attempting to climb a tree.
- Cognitive control of motor activity determines subconsciously, and within seconds, which patterns of movement will be used together to achieve a complex goal

The Caudate Circuit

Control Timing and 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 and

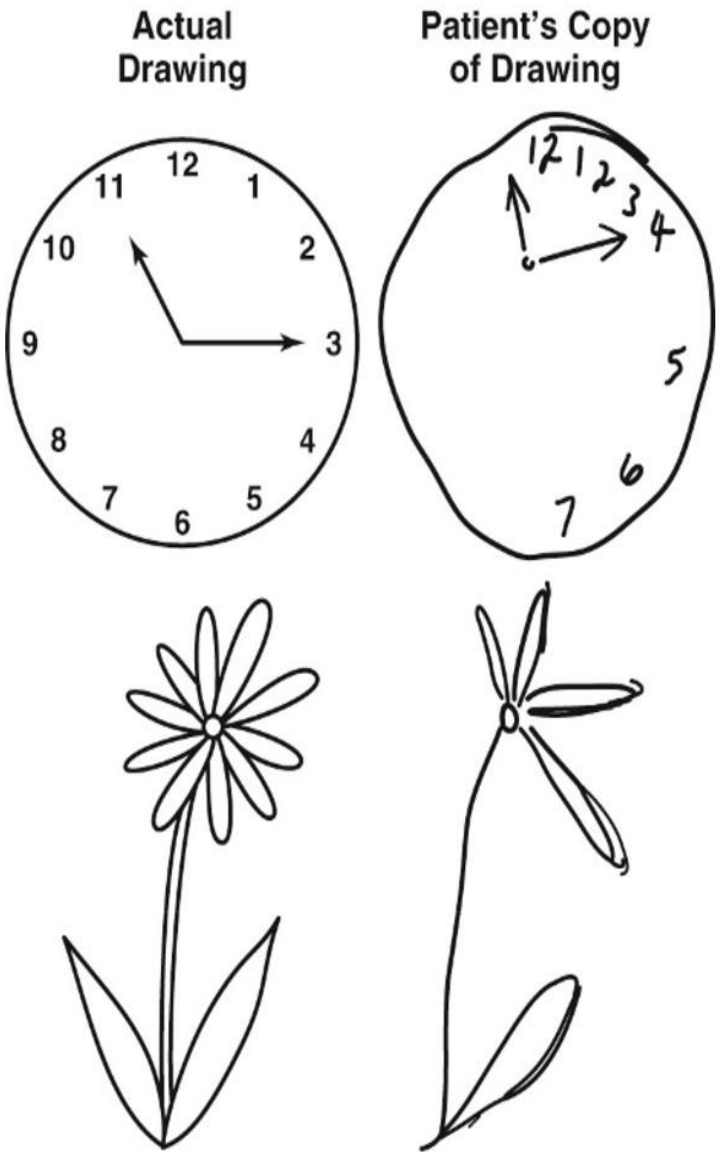
(2) to control how large the movement will be.

• 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 .

Change the Timing and to Scale the Intensity of Movements

Damage of the caudate circuit result 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.

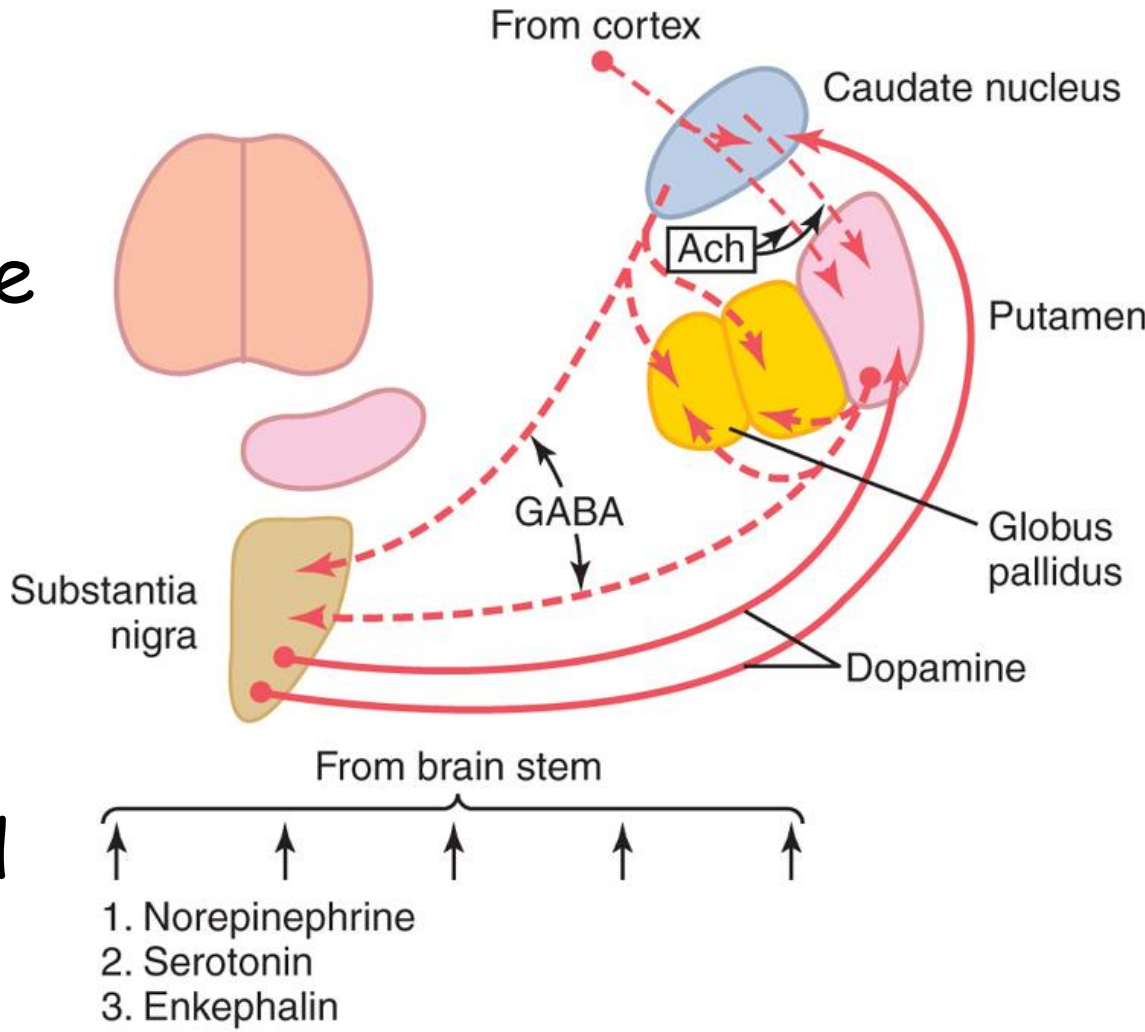

Actual Drawing
Patient's Copy of Drawing
12
1
2
3
4
5
6
7
8
9
10
11

Neurotransmitters of the BG: 1

- **Dopamine:** From SN to Putamen and Caudate nucleus,

- **GABA:** From these nuclei to globos pallidus and SN

- **Acetylcholine:** From cortex to caudate nucleus and putamen



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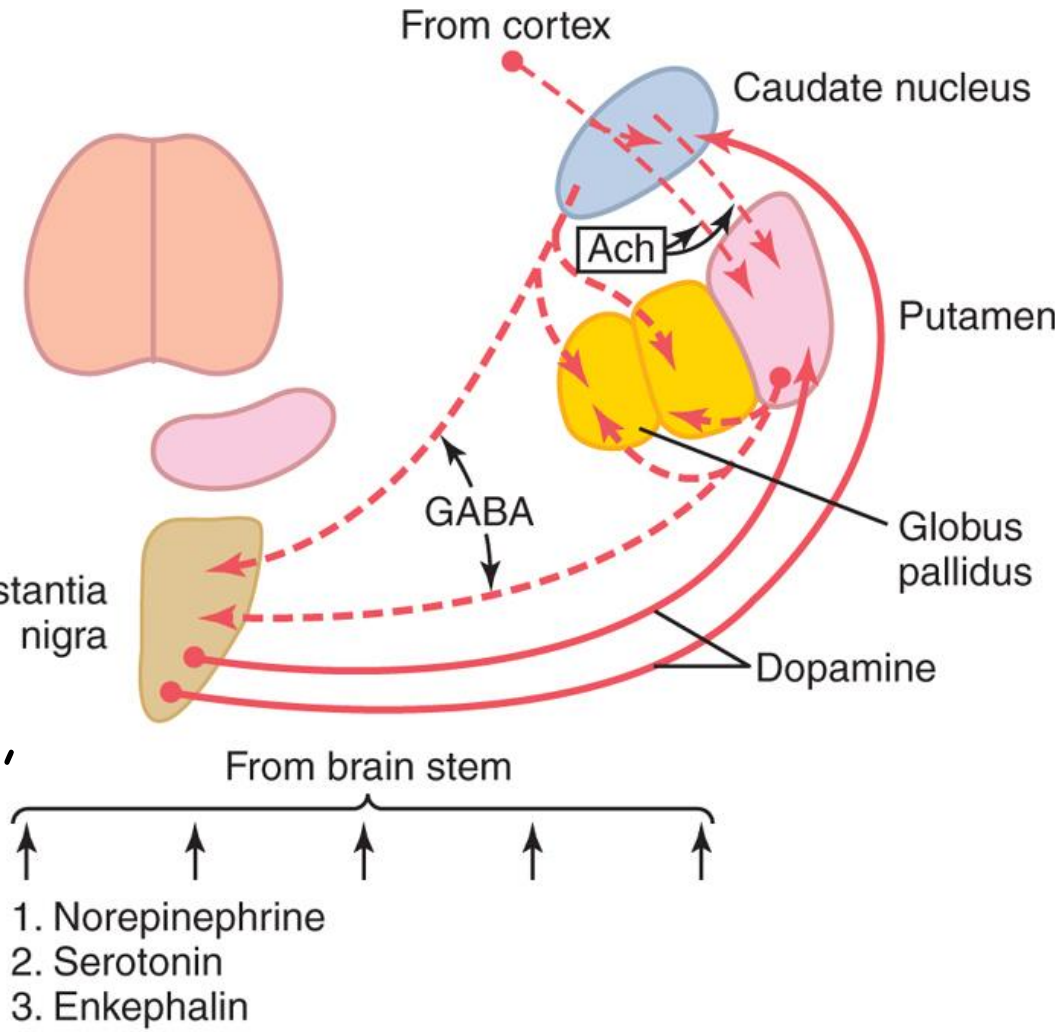
Neurotransmitters of the BG: 2

- **Other neurotransmitters such as SP & Enkephalin** are also present and may act as co-transmitters

- **Several NTs (NA, 5HT, Enk)** from the brain stem

- **Multiple excitatory glutamate** pathways (not shown) that balance the inhibitory effects of GABA, Dopamine and 5HT.

Imbalance of the amount of these NTs result in various BG disorders



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Movement Disorders

Hyperkinetic

- Hemiballismus
- Huntington's Disease
- Athetosis

Hypokinetic

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

Disorders of The Basal Ganglia

Diseases of the BG lead to two general types of disorder:

I. Hyperkinetic: movements are excessive and abnormal:

- **Athetosis** (continuous, slow writhing movements)
- **Chorea** (rapid, involuntary dancing movements)
- **Ballism** (involuntary movement)

II. Hypokinetic:

- **Akinesia** (difficulty in initiating movement)
- **Bradykinesia** (slowness of movement)

Abnormal Function in Putamen circuit

1. Athetosis

- It is characterized by continuous slow writhing (**twisting and turning)** movements of the hand, arm, neck and face.
- There is high degree of hyper-tonia.
- It is due to **degeneration of the globus pallidus.**

Abnormal Function in Putamen circuit

2. Chorea

- Rapid involuntary dancing `jerky` movements of the extremities and facial muscles during rest & increased by muscular activity and emotion.
- Accompanied by hypotonia
- It is due to lesion in the caudate and putamen
- It is explained by loss of GABA-ergic neurons.

Abnormal Function in Putamen circuit

3. Ballismus

- Sudden, intense and violent movements of an entire limb
- It is due to a lesion in the subthalamus
- If only one subthalamic nucleus is destroyed, involuntary movements are confined to the contralateral side (hemi-ballismus)
- The resulting loss of excitatory input to GPi leads to dis-inhibition of the cortical and brain stem motor mechanisms.

Disorders of The Basal Ganglia

Huntington`s chorea:

- It is an inherited autosomal dominant disorder. It occurs in the 3rd to 4th decade of life.
- It is due to mutation in a gene that codes for a protein called huntingtin whose function is unknown (but toxic)
- No treatment is currently available for the fatal disease.

Disorders of The Basal Ganglia

Huntington`s chorea:

- An early sign is a jerky hand when reaching to touch a spot
- Later hyperkinetic movements appear and gradually increase and become incapacitating.
- Speech becomes slurred and then incomprehensible,
- Then a progressive dementia (loss of memory) is followed by death usually within 10-15 years after the symptoms onset.

Disorders of The Basal Ganglia

Huntington`s chorea:

- It is due to selective degeneration of the **GABA-ergic neurons** in the striatum
- This loss of GABA-ergic pathway to the GPe releases inhibition, permitting the hyperkinetic features of the disease to develope

Parkinson's Disease

- 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.

- Five cardinal features
  - Tremor
  - Rigidity
  - Akinesia & Bradykinesia
  - Postural Changes
  - Speech Changes

Movement Disorder	Features	Lesion
Chorea	Multiple quick, random Movements at rest, usually increased by muscular activity & emotion	Degeneration of the striatum.
Athetosis	Slow writhing Movements of hand , neck ,face , & tongue	Damage to the lateral portion of globus pallidus
Hemiballismus	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	Degeneration of Substantia Nigra