PHYSIOLOGY OF BASAL GANGLIA AND REGULATORY MECHANISMS

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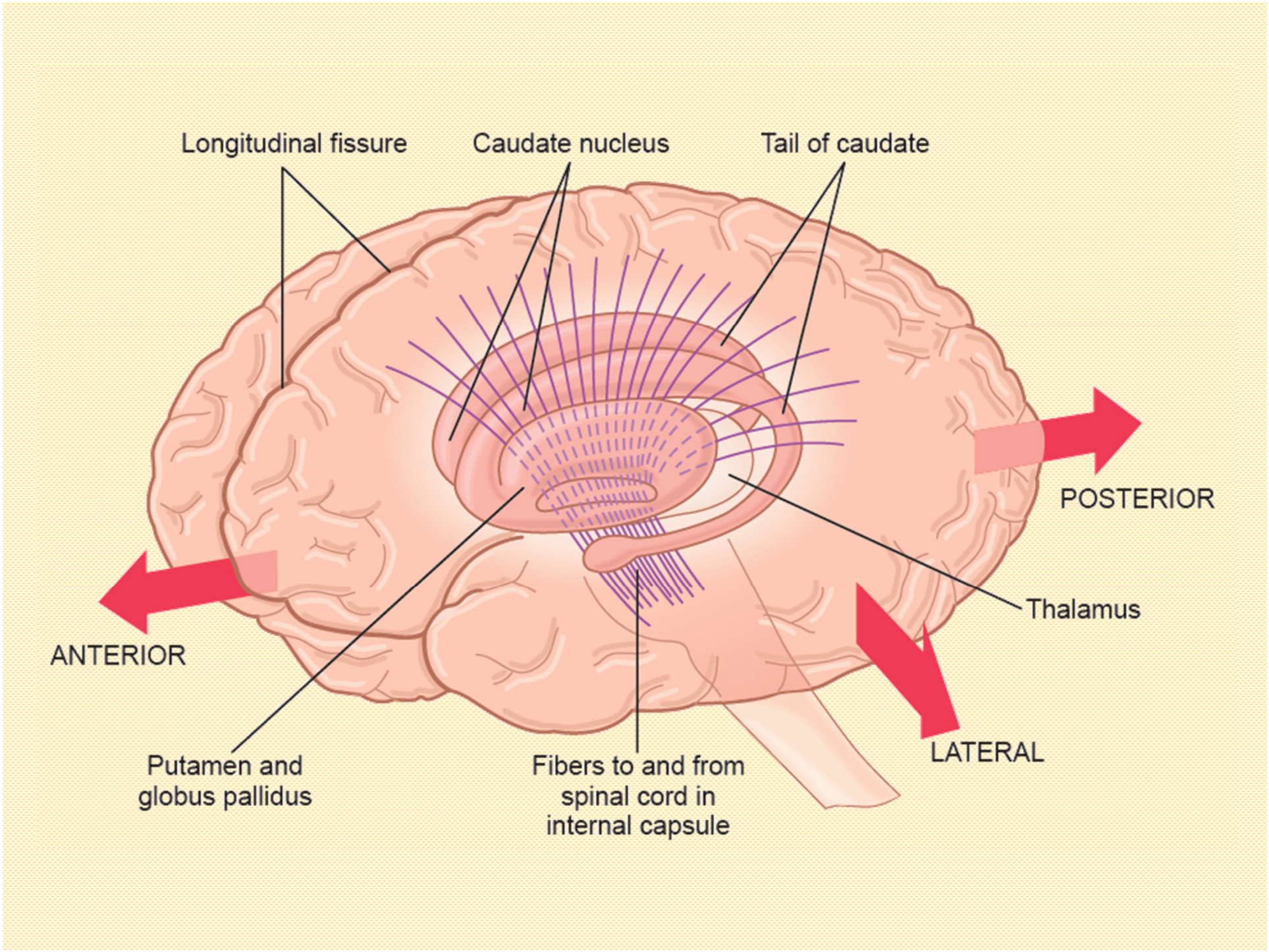
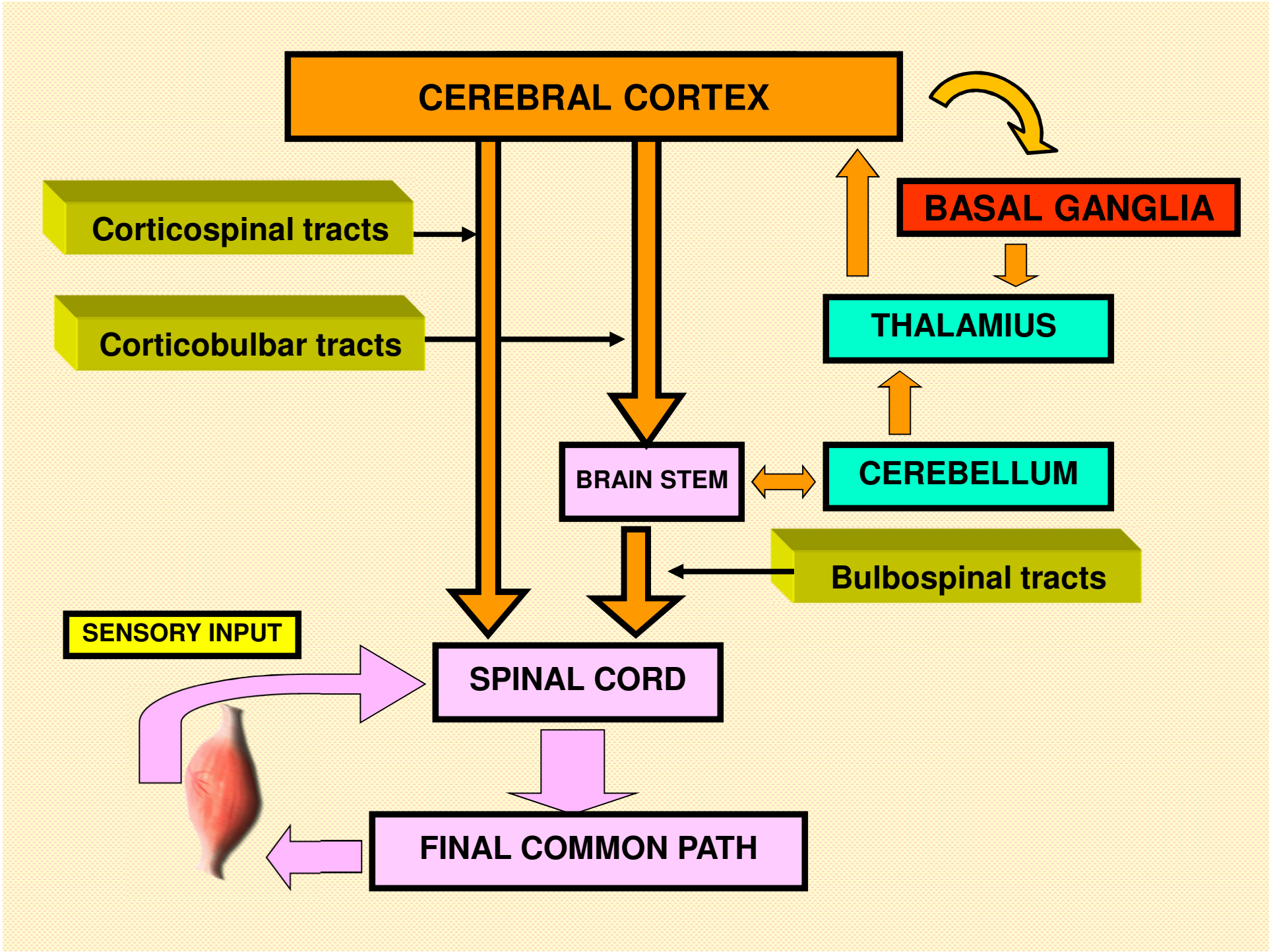
OBJECTIVES

At the end of this lecture the students should be able to:

- Know functional division of basal nuclei (basal ganglia)
- Explain different neurotransmitters that have a role in basal ganglia functions
- Appreciate general functions of basal ganglia
- Diagnose basal ganglia disorders


Longitudinal fissure
Caudate nucleus
Tail of caudate
POSTERIOR
ANTERIOR
Thalamus
LATERAL
Putamen and
globus pallidus
Fibers to and from
spinal cord in
internal capsule

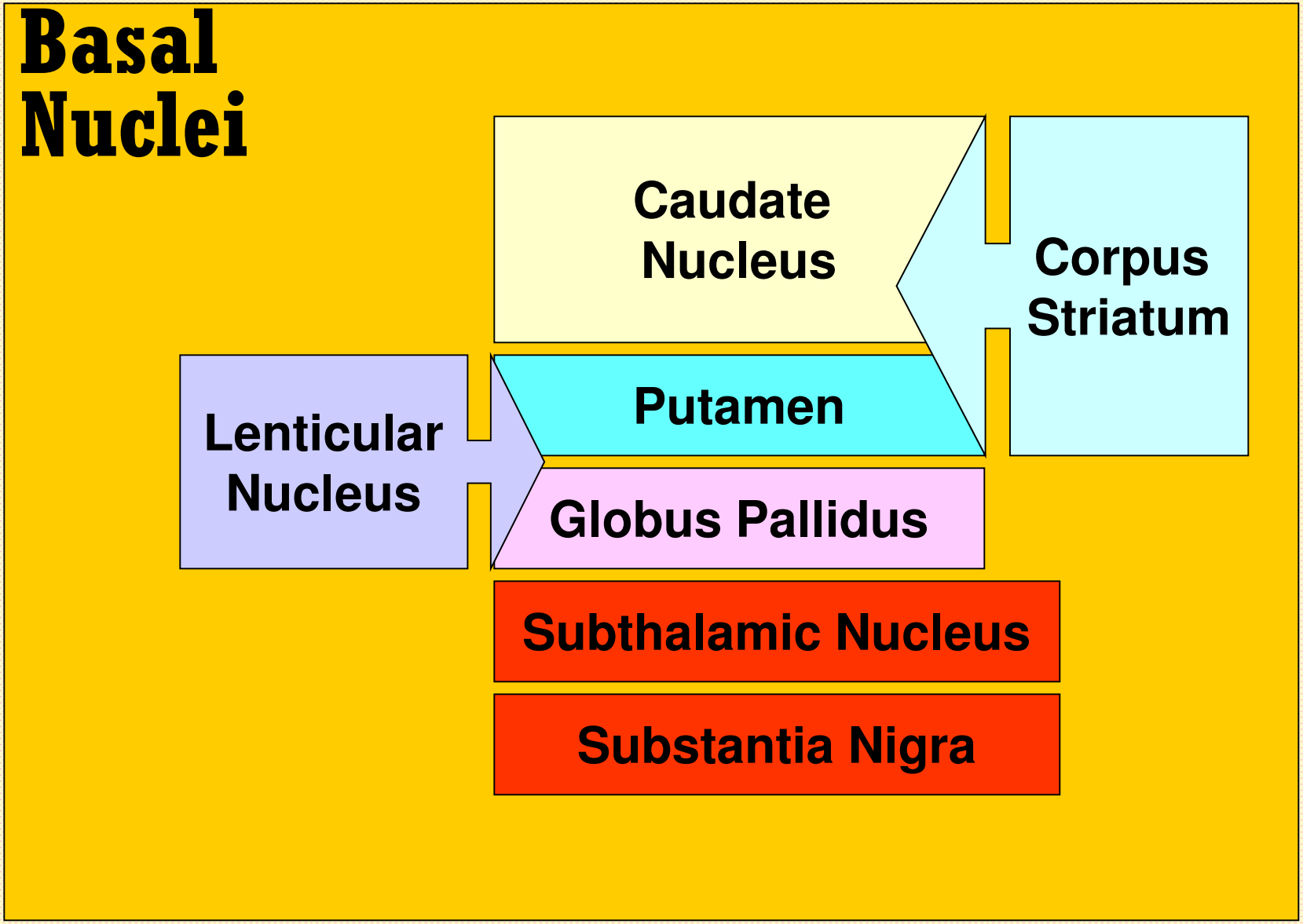
Overview of Motor Activity Control


CEREBRAL CORTEX
BASAL GANGLIA
Corticospinal tracts
Corticobulbar tracts
THALAMIUS
BRAIN STEM
CEREBELLUM
Bulbospinal tracts
SENSORY INPUT
SPINAL CORD
FINAL COMMON PATH

BASAL GANGLIA

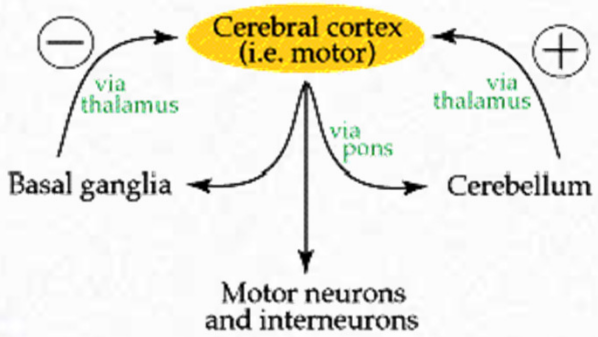
COMPONENTS
FUNCTIONAL ANATOMY

Basal Nuclei

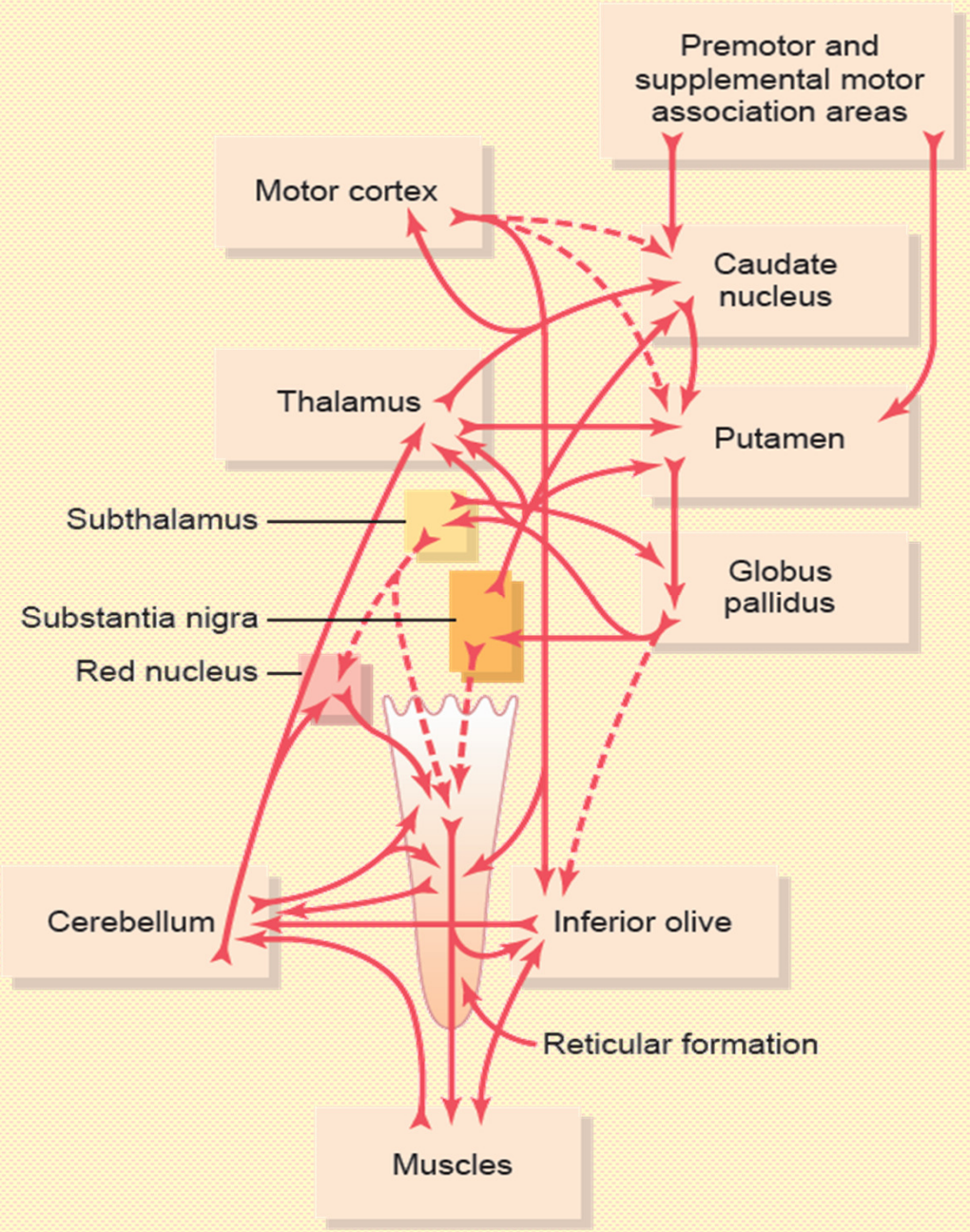


BASAL GANGLIA

CONNECTIONS

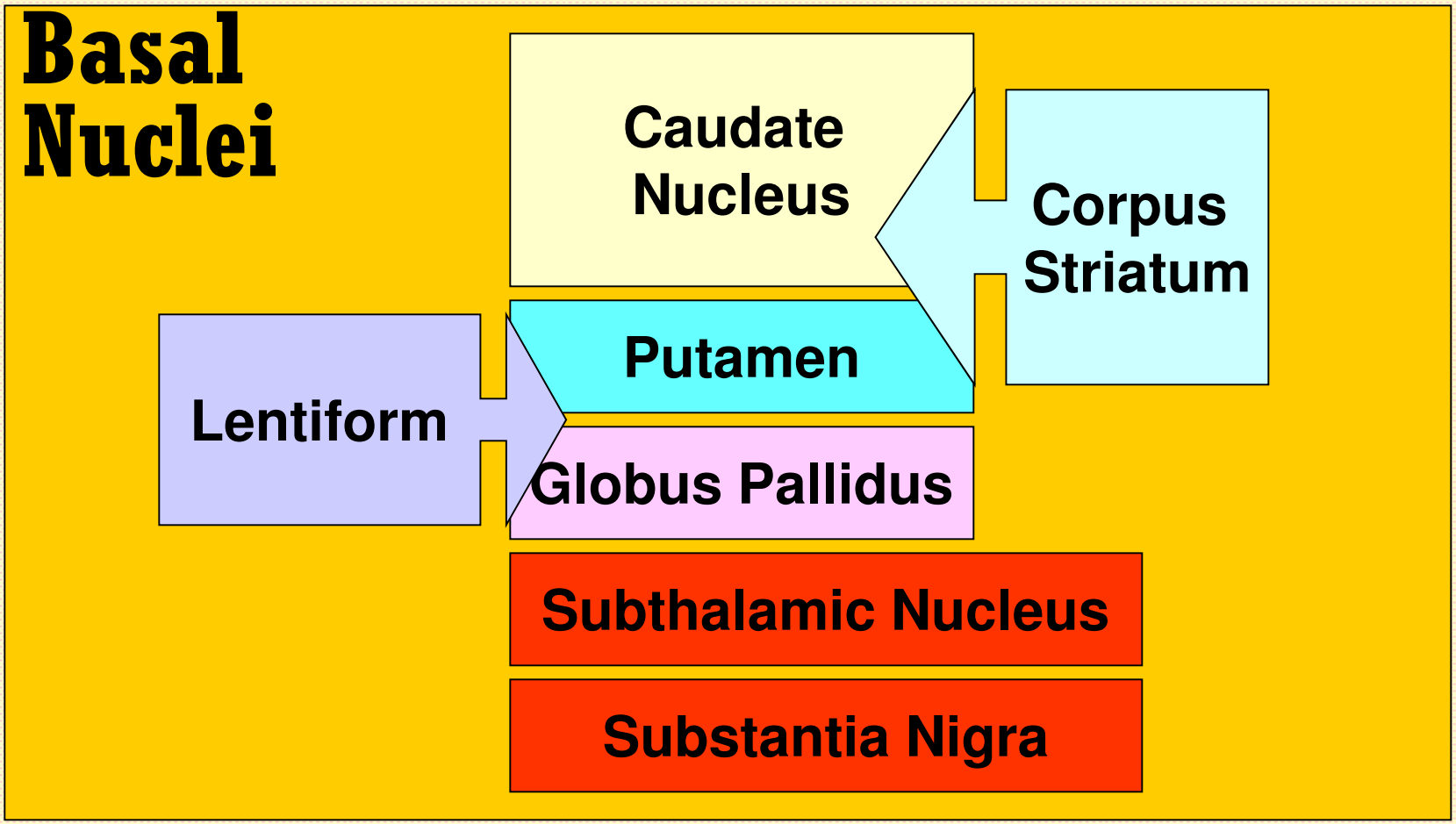


Complex Circuitry of Motor Control



3 Connections to remember

1. Main input to the basal ganglia
2. Main output from the basal ganglia
3. Connections between parts of basal ganglia



MAIN INPUT TO THE BASAL GANGLIA

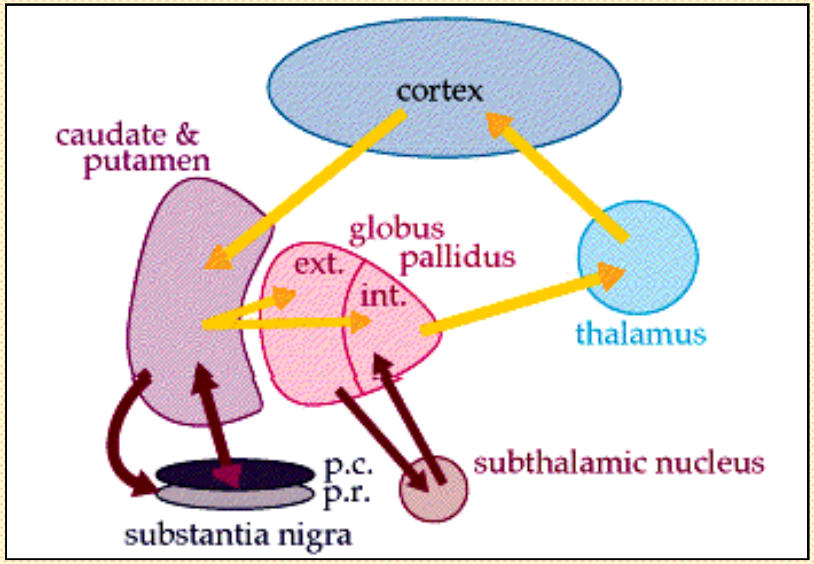
The comes from the cerebral cortex (motor area) and projects to the NEOSTRIATUM

(a term for the caudate nucleus and putamen)

THE MAIN OUTPUT

Is via the thalamus to the cerebral cortex

(motor area)

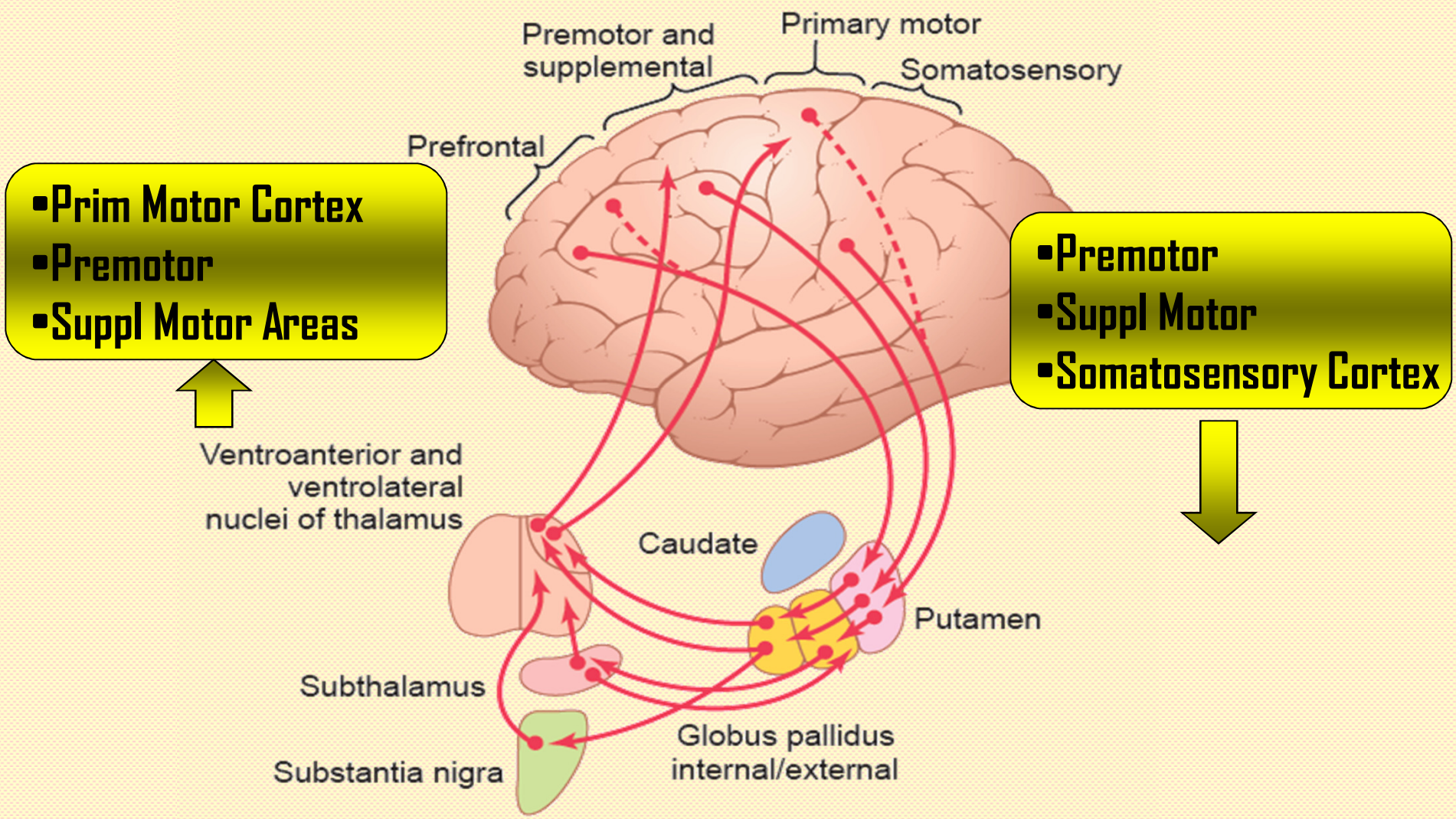


BASIC CIRCUITS OF MOVEMENTS CONTROL

1. **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.

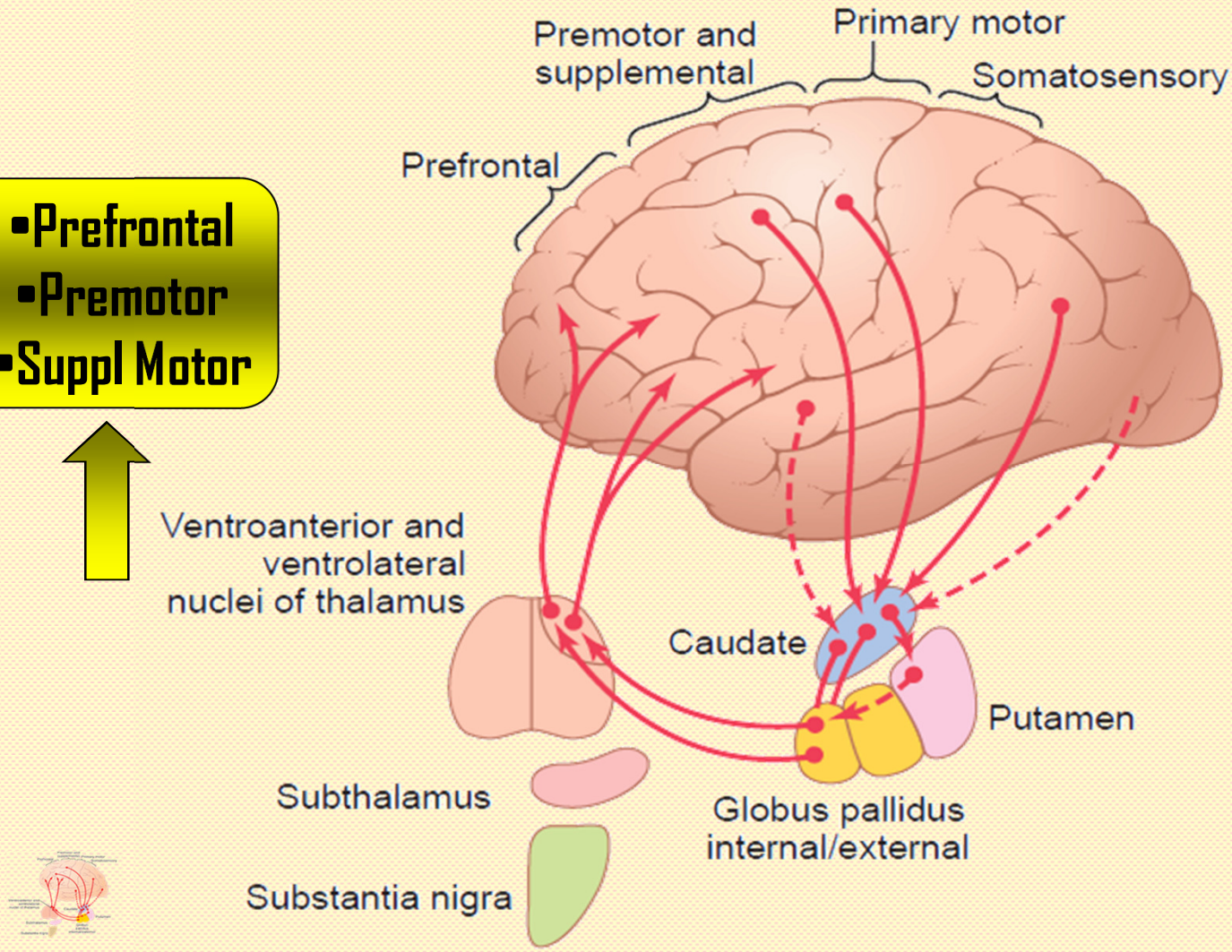
   (Note: cognition means thinking process using sensory input with information already stored in memory.)
3. **Limbic loop** involved in giving motor expression to emotions like, smiling, aggressive or submissive posture.
4. **Occulomotor loop** concerned with voluntary eye movement [saccadic movement]

The Putamen Circuit



The Caudate Circuit

- Prefrontal
- Premotor
- Suppl Motor

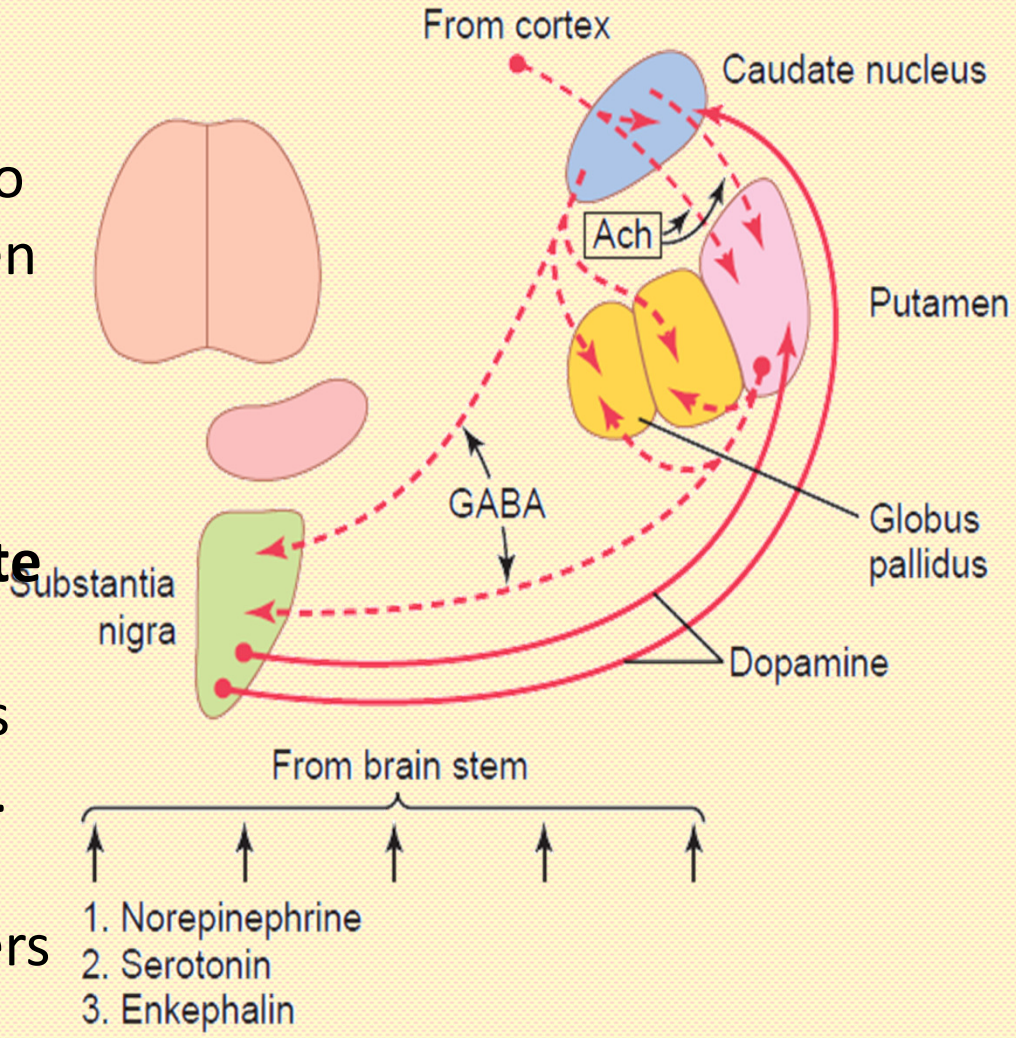


Association Areas

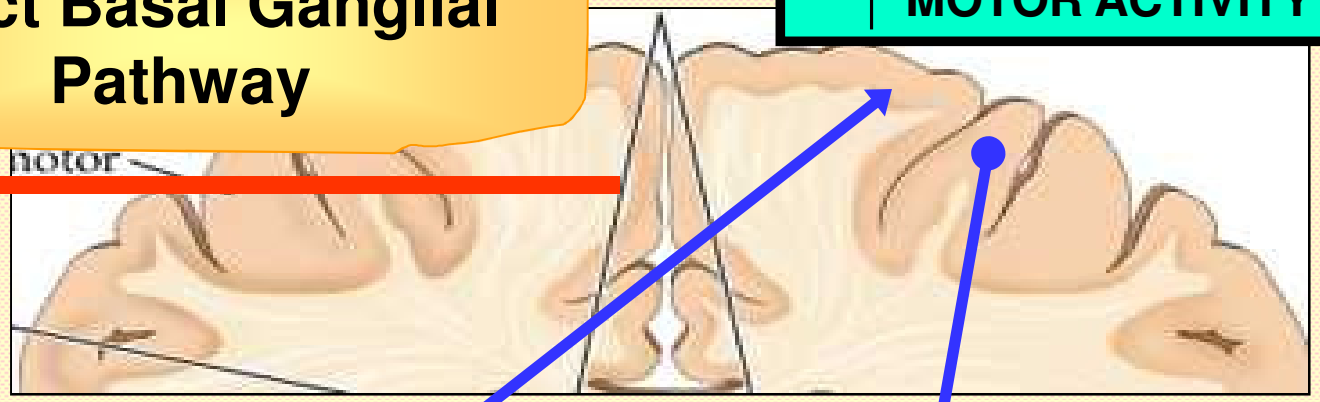
Basal Ganglial Neurotransmitters & Pathways (Direct and Indirect)

Neurotransmitters in Basal Ganglia Circuits

- **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 counter balance DA
- **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.
- **Enkephalin** are also present and may act as co-transmitters



Direct Basal Ganglial Pathway



↑ MOTOR ACTIVITY

GLU +

GLU

+

↓GABA -

Thalamus

GPe

GPi

-

↑ GABA

St

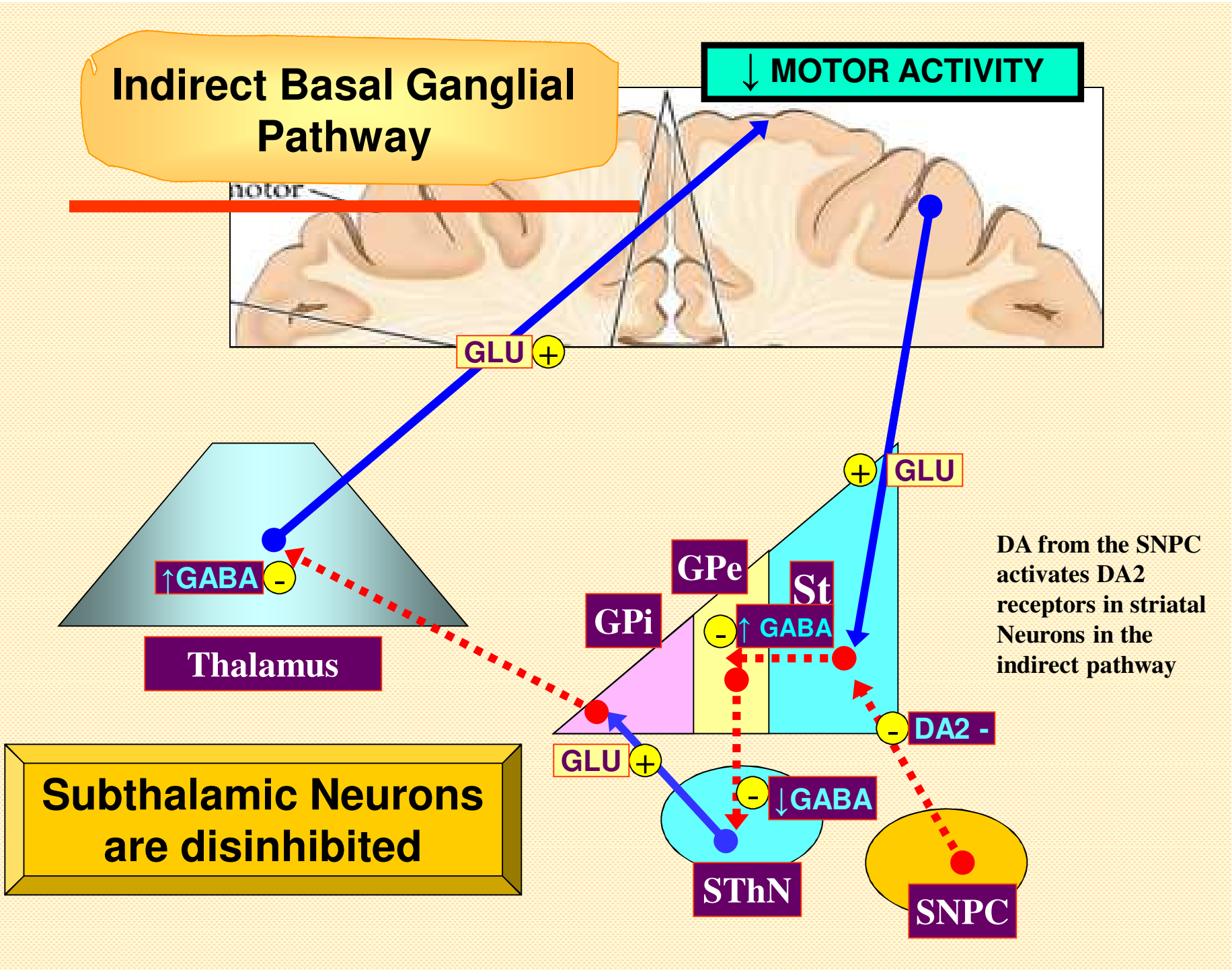
+ DA1+

DA from the SNPC activates DA1 receptors in striatal Neurons of the direct pathway

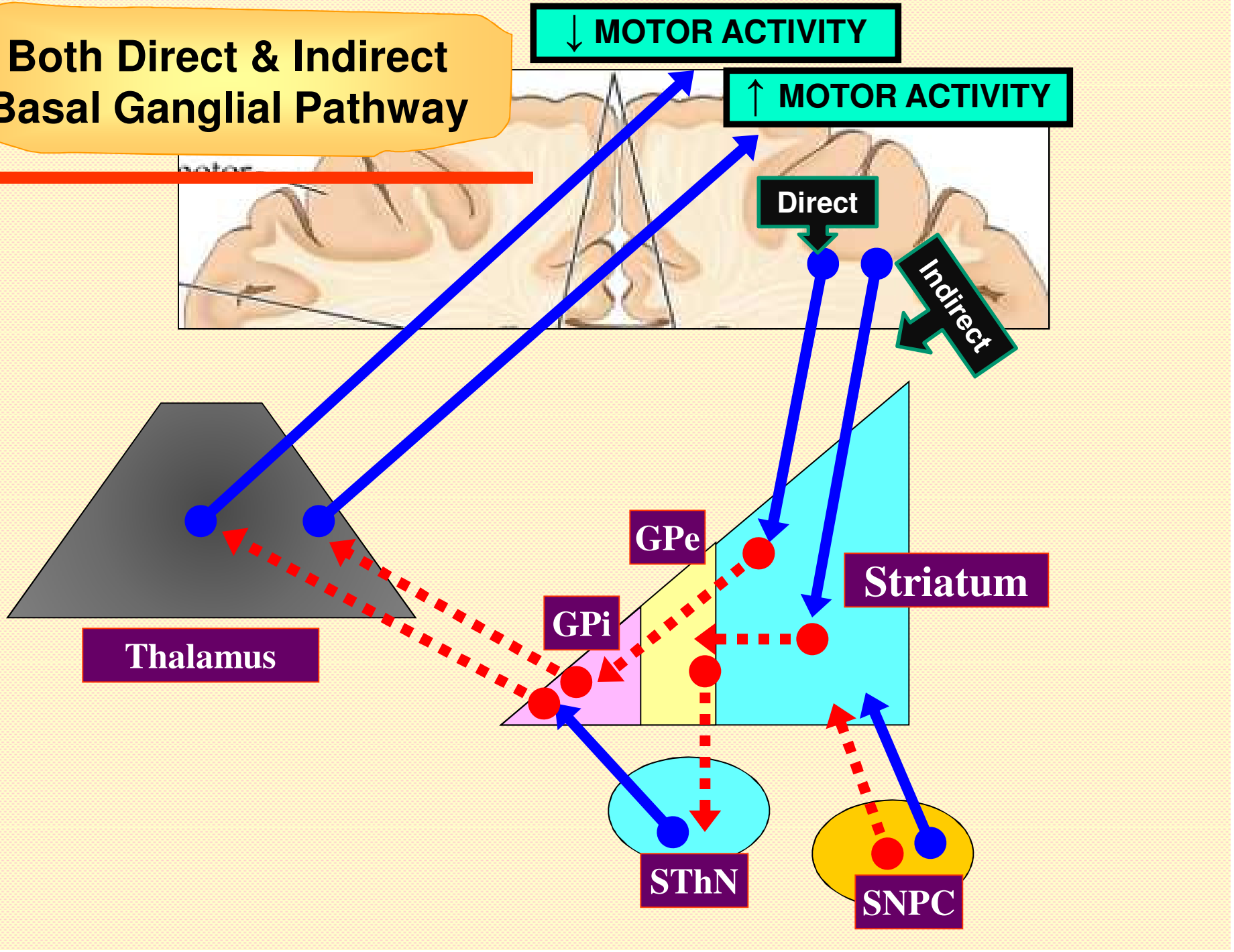
Thalamocortical Neurons are disinhibited

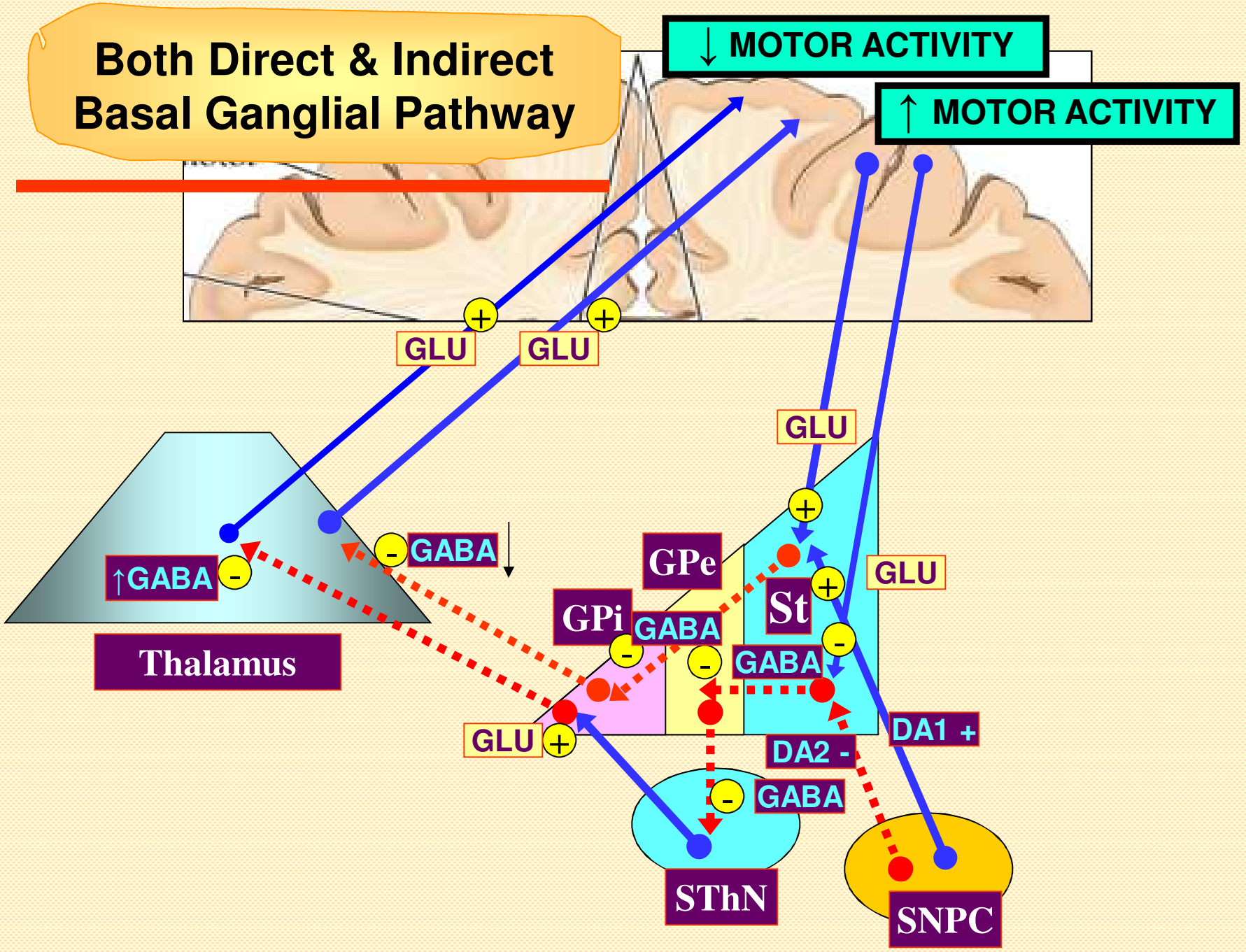
SThN

SNPC


Indirect Basal Ganglial Pathway
↓ MOTOR ACTIVITY
GLU +
GLU +
↑GABA -
Thalamus
GPe
St
GPi
- ↑ GABA
DA2 -
GLU +
- ↓GABA
SThN
SNPC
DA from the SNPC activates DA2 receptors in striatal Neurons in the indirect pathway
Subthalamic Neurons are disinhibited

Both Direct & Indirect Basal Ganglial Pathway




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

BASAL GANGLIA

FUNCTIONS

- Control of movements
- Planning and programming of movements
- Cognitive control in movements

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:
  - 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.

The Caudate Circuit

Cognitive Control of Sequences of Motor Patterns

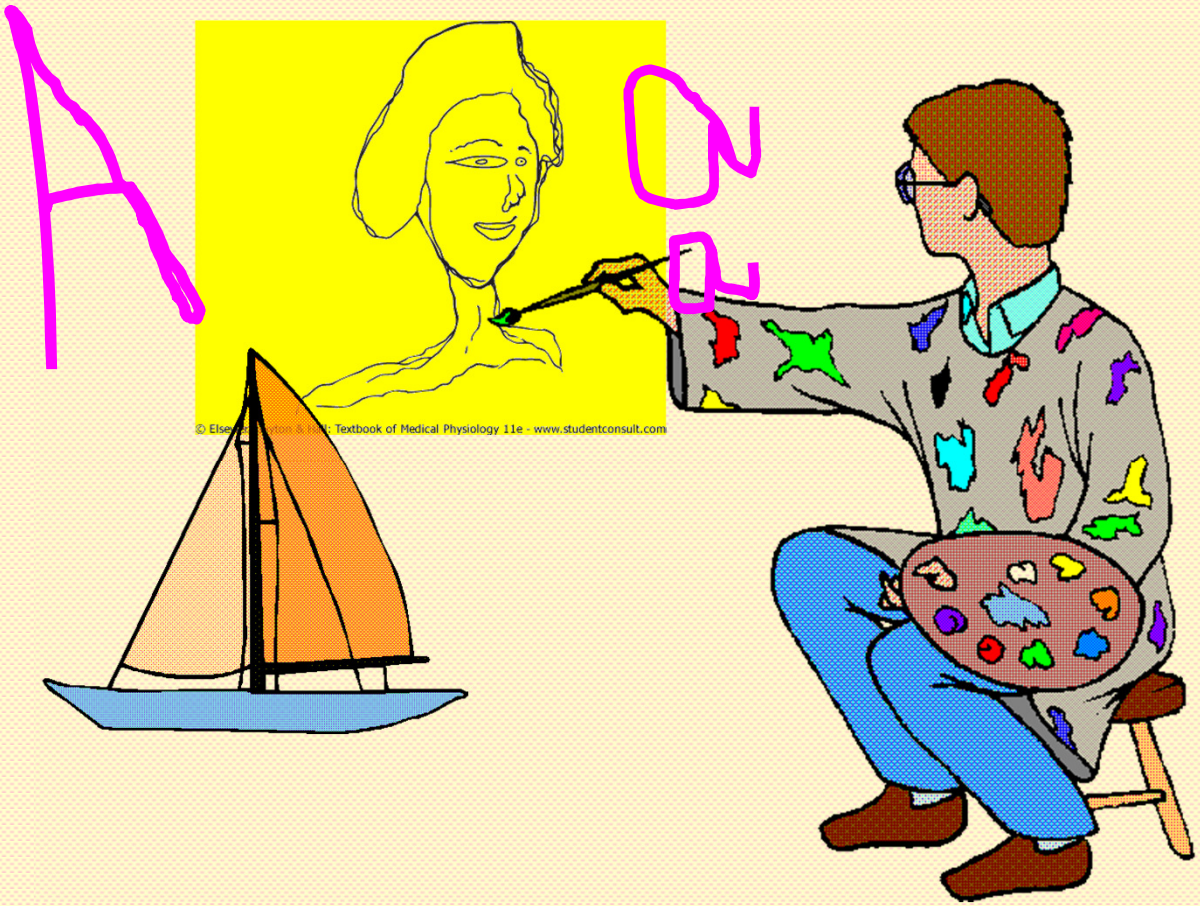
- Cognition means the thinking processes of the brain, using both sensory input to the brain plus information already stored in memory. Thoughts are generated in the mind by a process called cognitive control of motor activity.
- Example:A person seeing a lion approach and then responding instantaneously and automatically by (1) turning away from the lion, (2) beginning to run, and (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

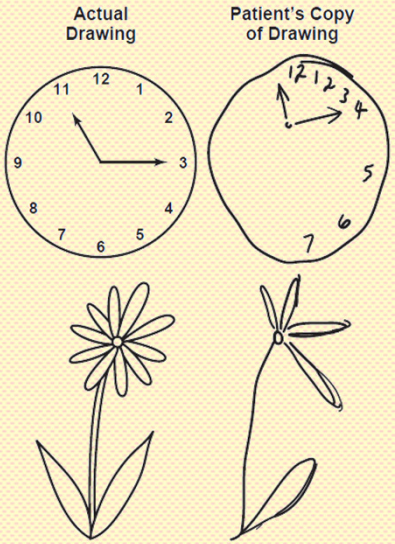
The Caudate Circuit

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 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





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.

BASAL GANGLIA

DISORDERS

MOVEMENTS (ATAXIA Rate, Range, Force, Direction)

SPEECH

POSTURE

GAIT

MENTAL ACTIVITY

OTHERS

Movement Disorders

Hyperkinetic

- Chorea
  - Huntington's Disease
  - Saint Vitus Dance (Sydenham's Chorea)
- Athetosis
- Dystonia
- Hemiballismus/Ballismus
- Tardive Dyskinesia
- Wilson's Disease

Lesions affect Indirect Pathway Predominantly






Hypokinetic

- Parkinson's Disease
- Drug Induced eg; MPTP induced
- Dopamine receptor blockers eg; Neuroleptics & antipsychotic drugs

Movement Disorder	Features	Lesion
Chorea	Multiple quick involuntary, random/purposeless movements, usually most prominent in the appendicular muscles	Atrophy of the striatum. Huntington Chorea **Saint Vitus Dance (post streptococcal infection)**
Athetosis	Slow writhing movements,which are usually more severe in the appendicular muscles	Diffuse hypermyelination of corpus striatum and thalamus
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	Degenration of Substantia Nigra

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

Metabolic characteristics

- 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