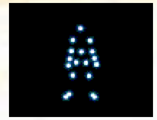
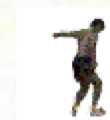


PHYSIOLOGY OF BASAL GANGLIA AND REGULATORY MECHANISMS

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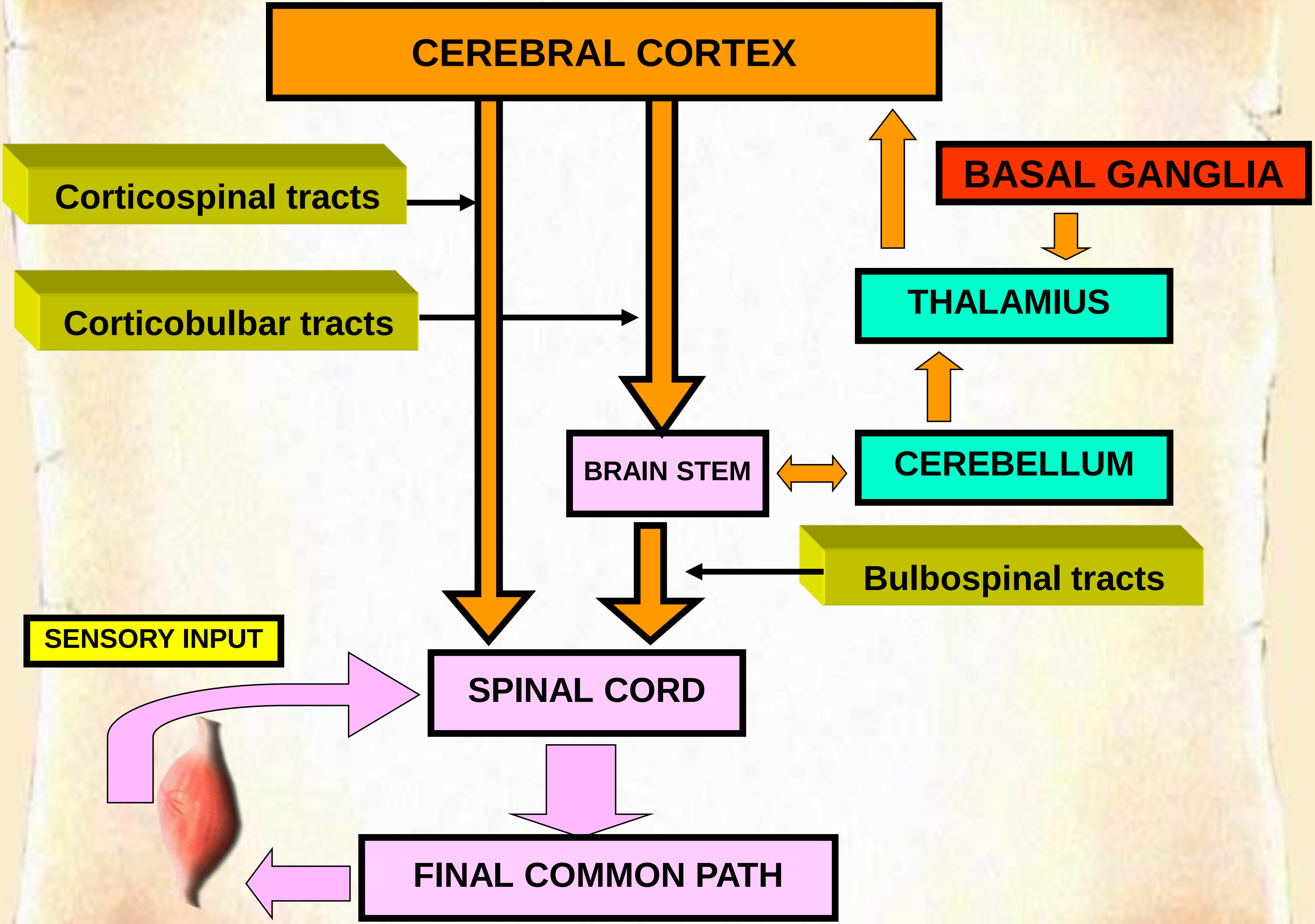
OBJECTIVES

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

- ***Appreciate different nuclei of basal ganglia***
- ***Know different neurotransmitters that have a role in basal ganglia functions***
- ***Appreciate general functions of basal ganglia***
- ***Diagnose basal ganglia disorders***

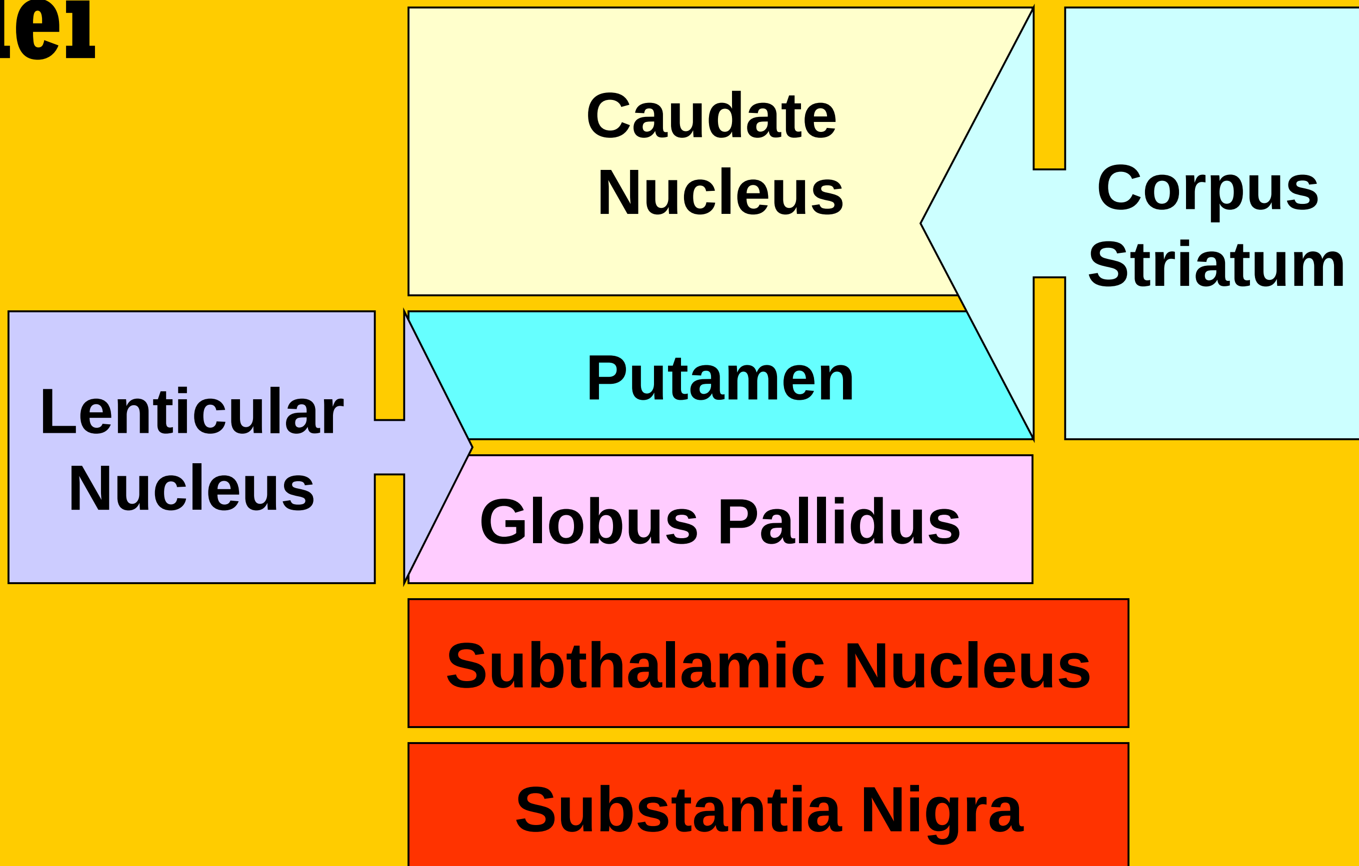
OVERVIEW OF MOTOR ACTIVITY CONTROL


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

BASAL GANGLIA

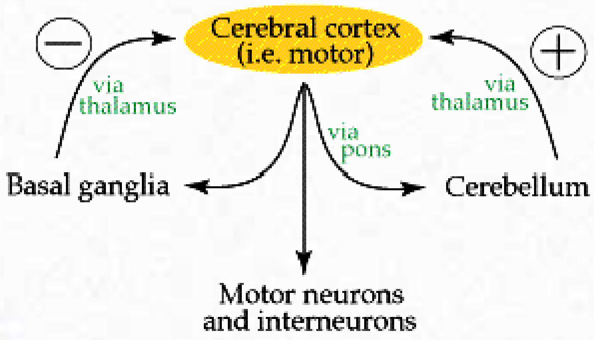
COMPONENTS
FUNCTIONAL ANATOMY

Basal Nuclei

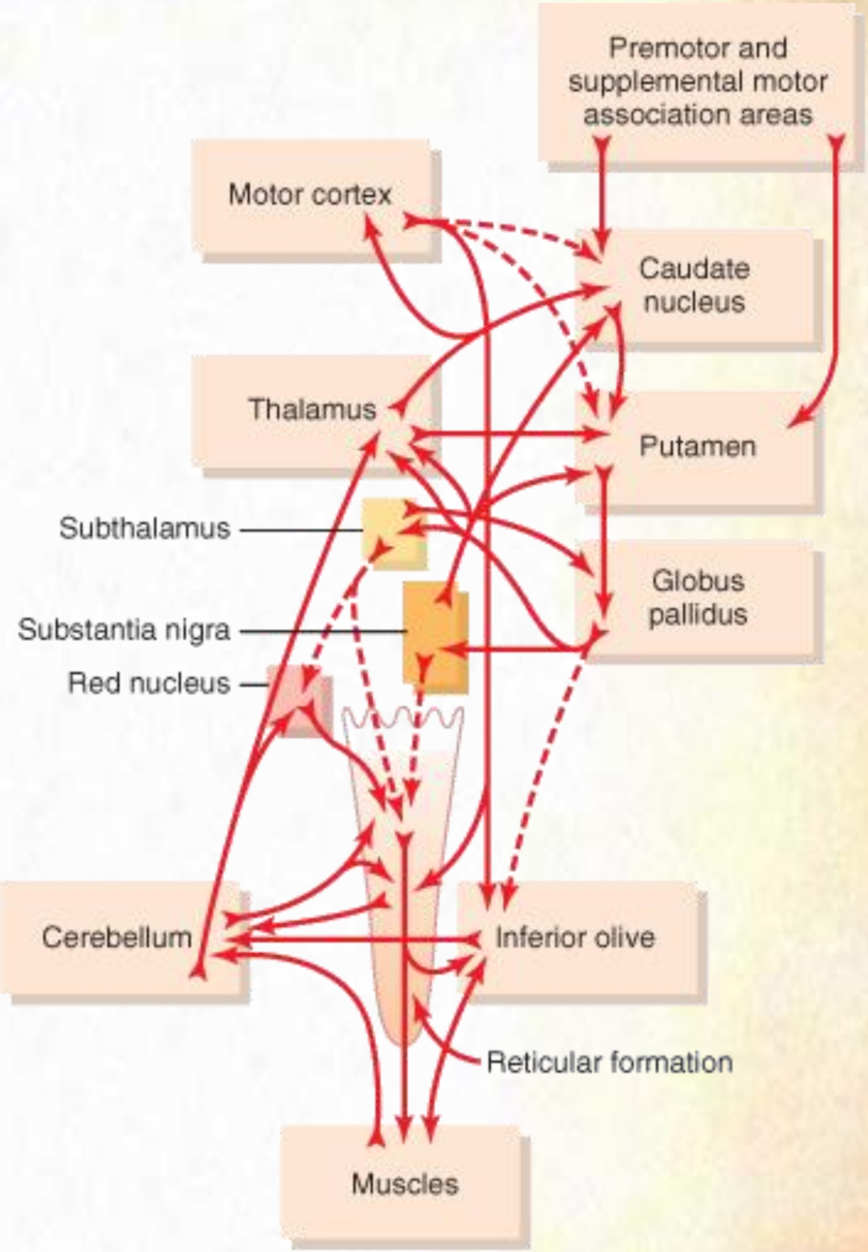


BASAL GANGLIA

CONNECTIONS

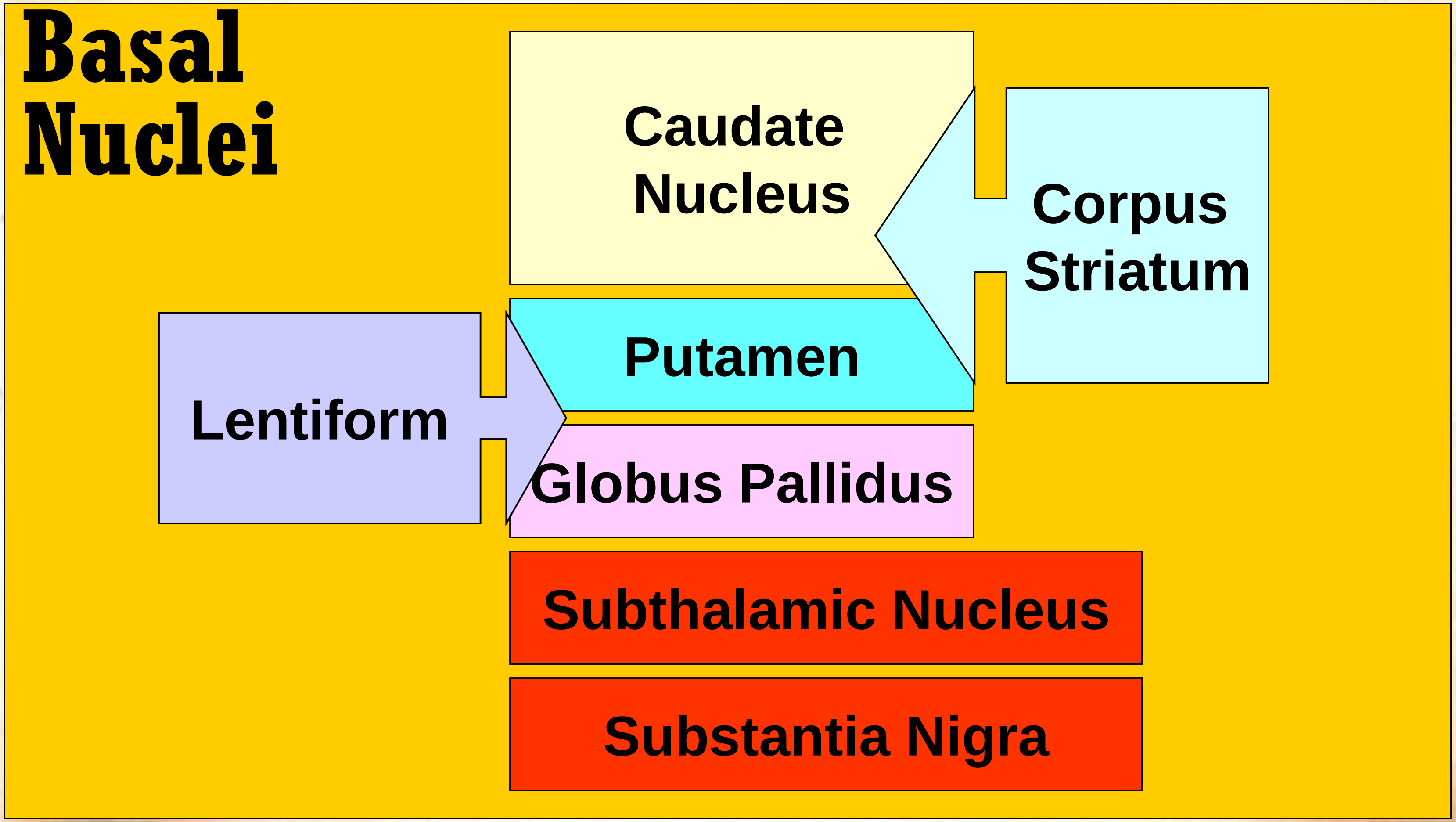


Connections for Motor Control



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

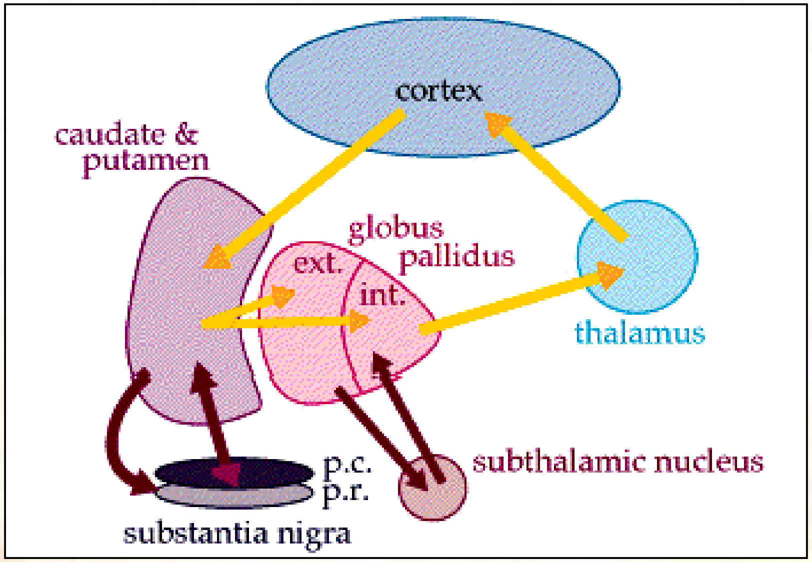
The comes from the cerebral cortex (motor area) and projects to the NEOSTRIATUM

(a term for the caudate nucleus and putamen)

THE MAIN OUTPUT

Is via the thalamus to the cerebral cortex

(motor area)

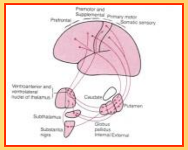


BASIC CIRCUITS OF BASAL GANGLIA

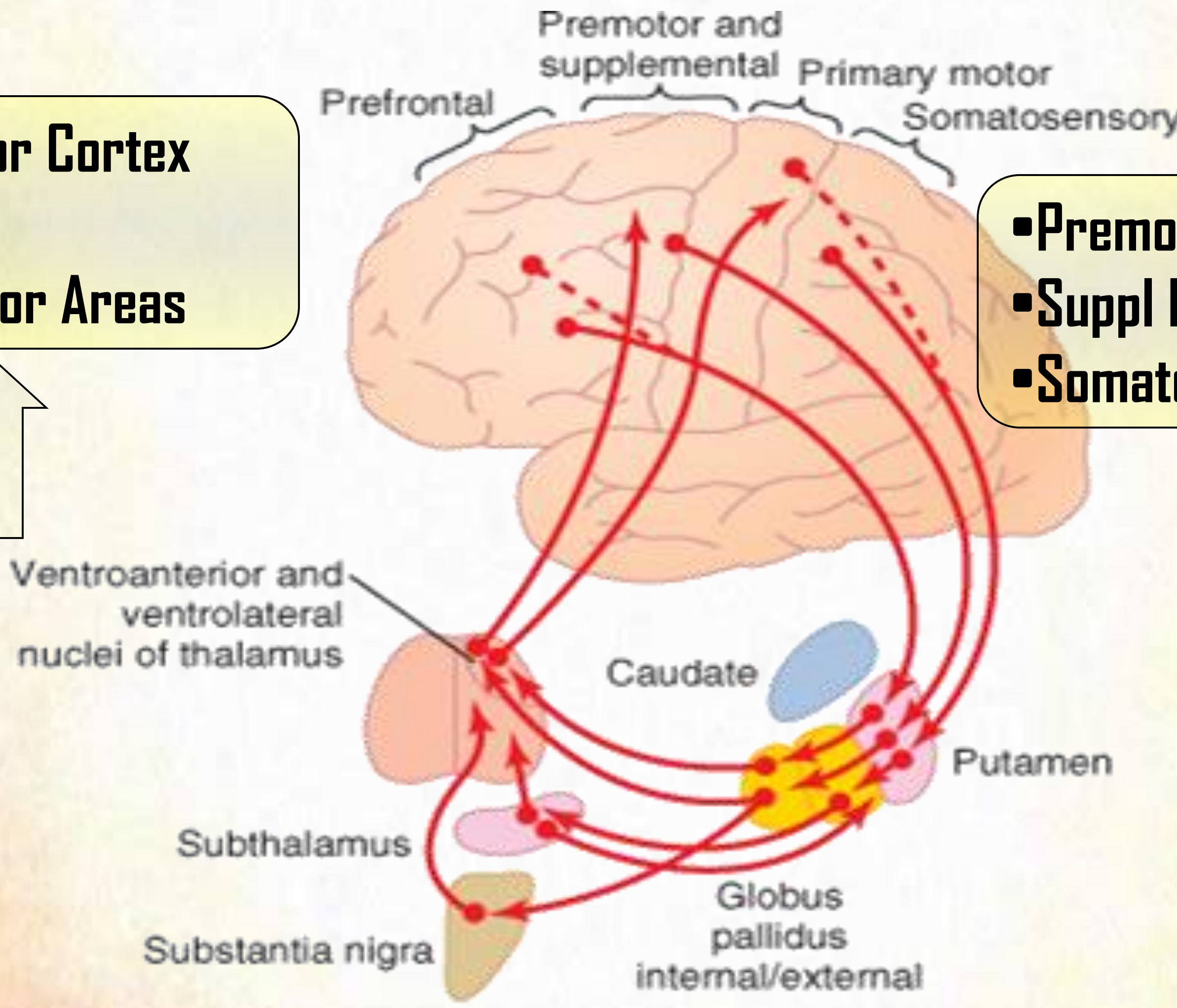
1. **Motor loop (putamen circuit)** concerned with learned movment.
2. **Cognitive loop (Caudate circuit)** concerned with cognitive control of sequences of motor pattern. Basically it is concerned with motor intentions.

   (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



- Prim Motor Cortex
- Premotor
- Suppl Motor Areas



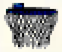
- Premotor
- Suppl Motor
- Somatosensory Cortex

The Putamen Circuit

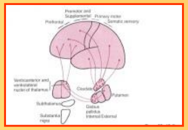
Executes Learned Patterns of Motor Activity

- **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.**

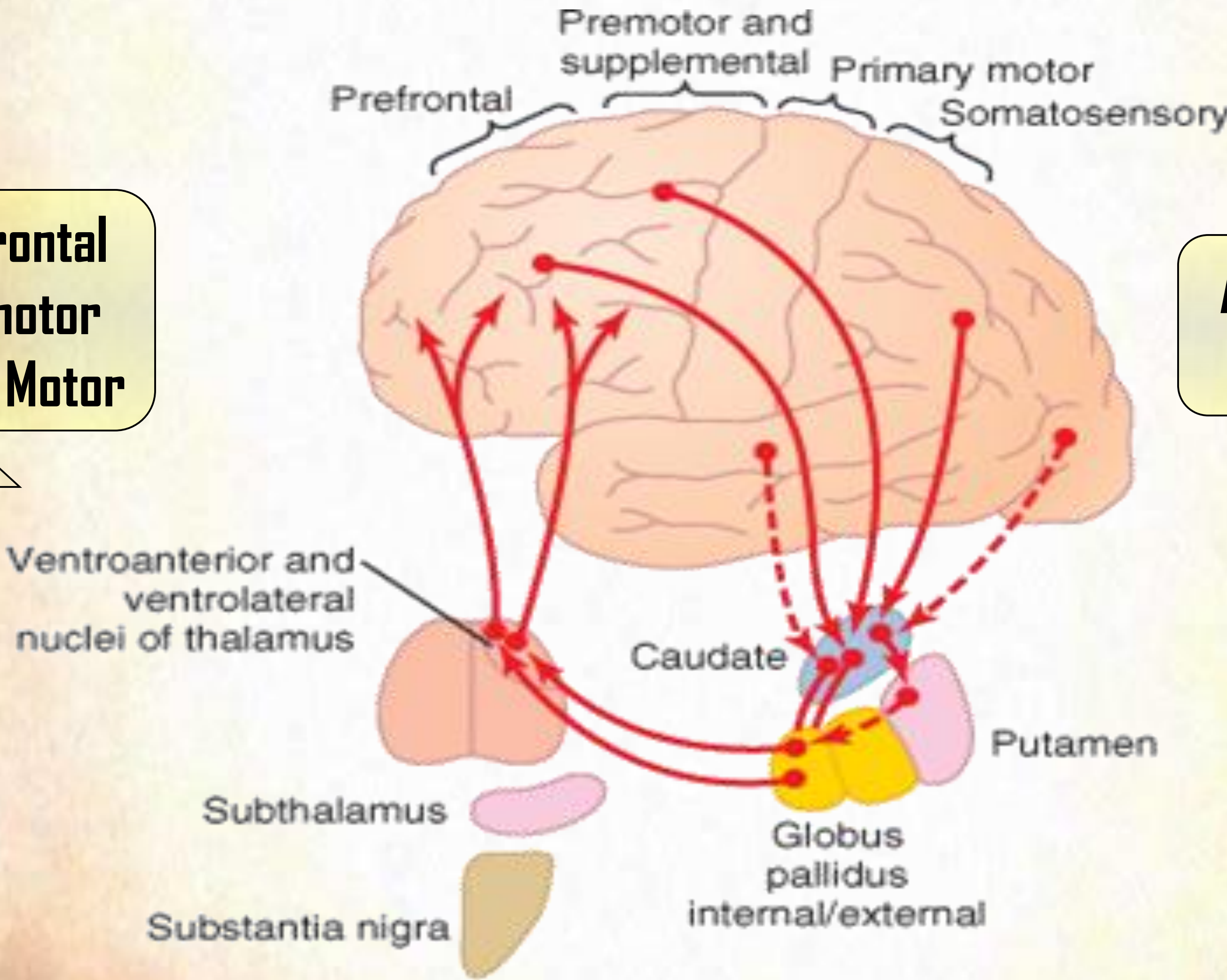


The Caudate Circuit



- Prefrontal
- Premotor
- Suppl Motor



Association Areas

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

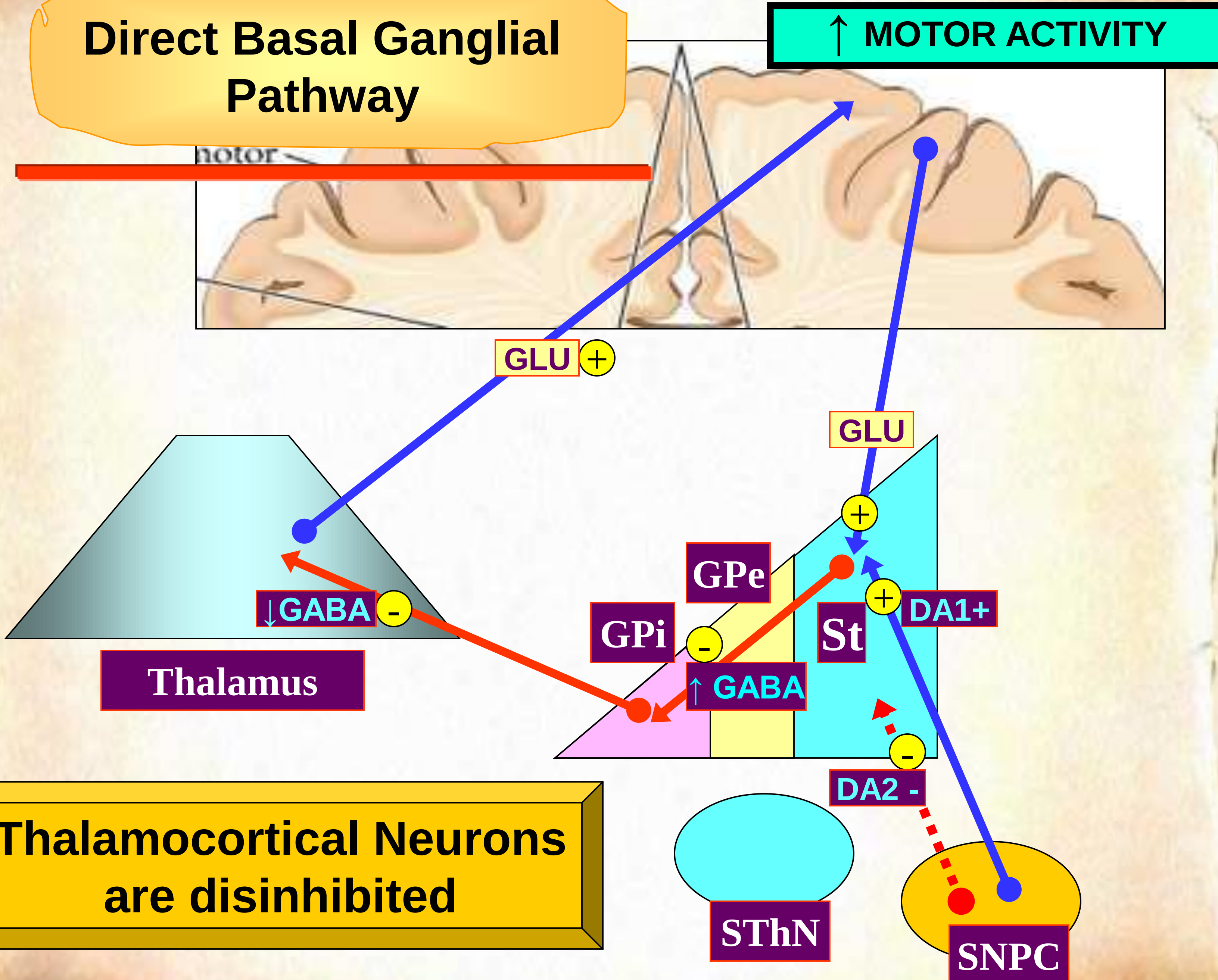
Change the Timing and to Scale the Intensity of Movements

- **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**

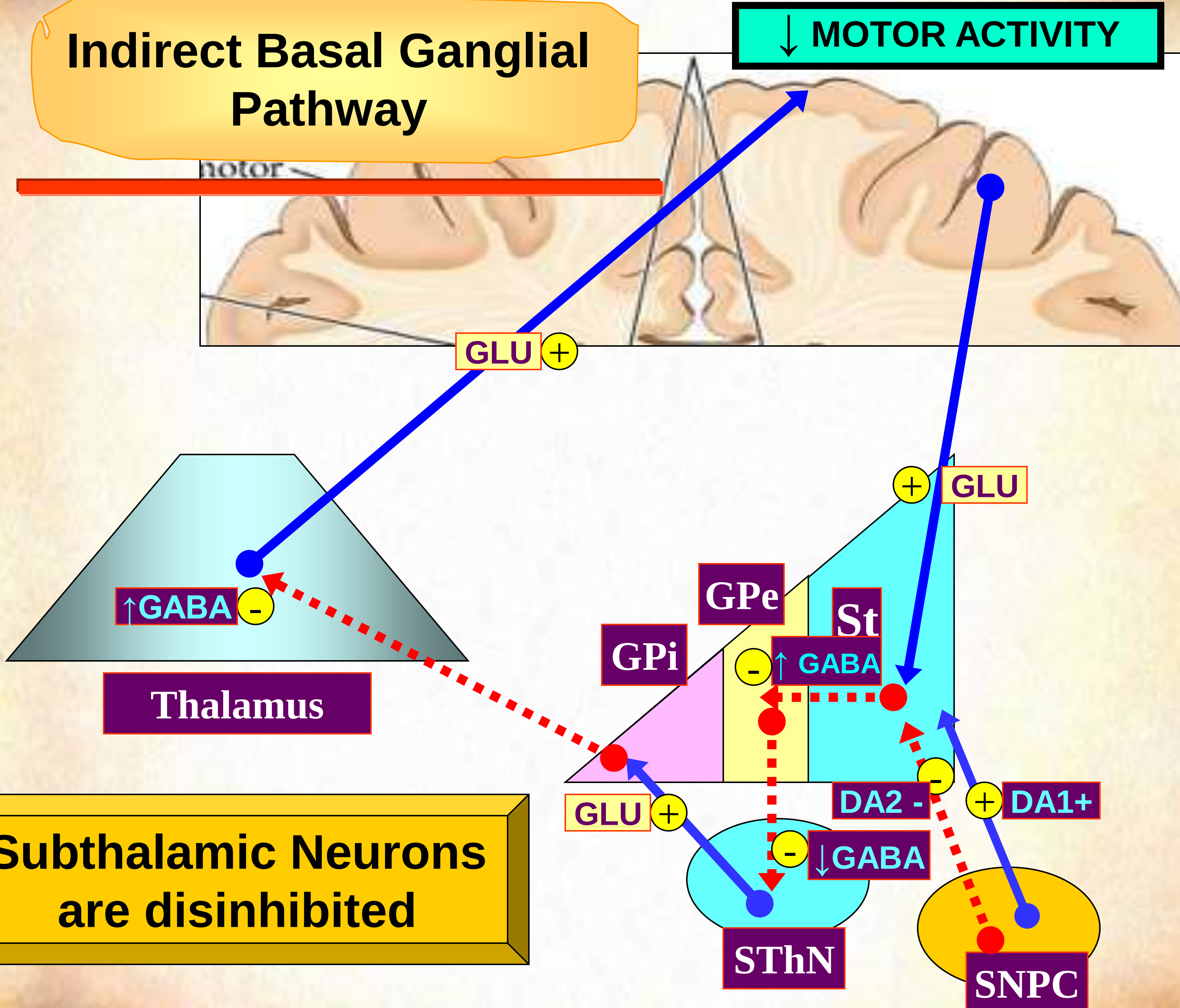
Basal Ganglial Pathways
Direct and Indirect

Direct Basal Ganglial Pathway



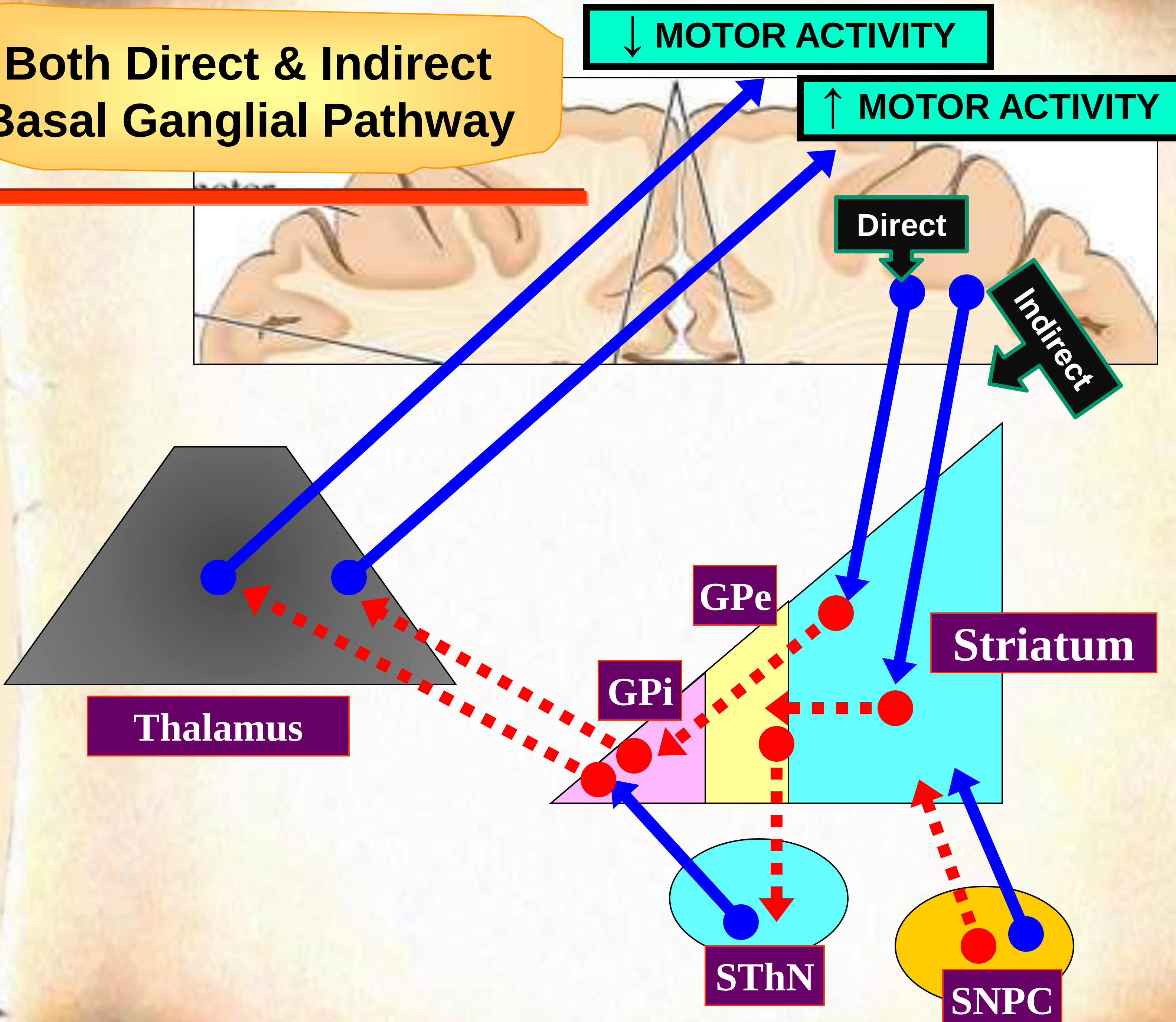
Thalamocortical Neurons are disinhibited

Indirect Basal Ganglial Pathway

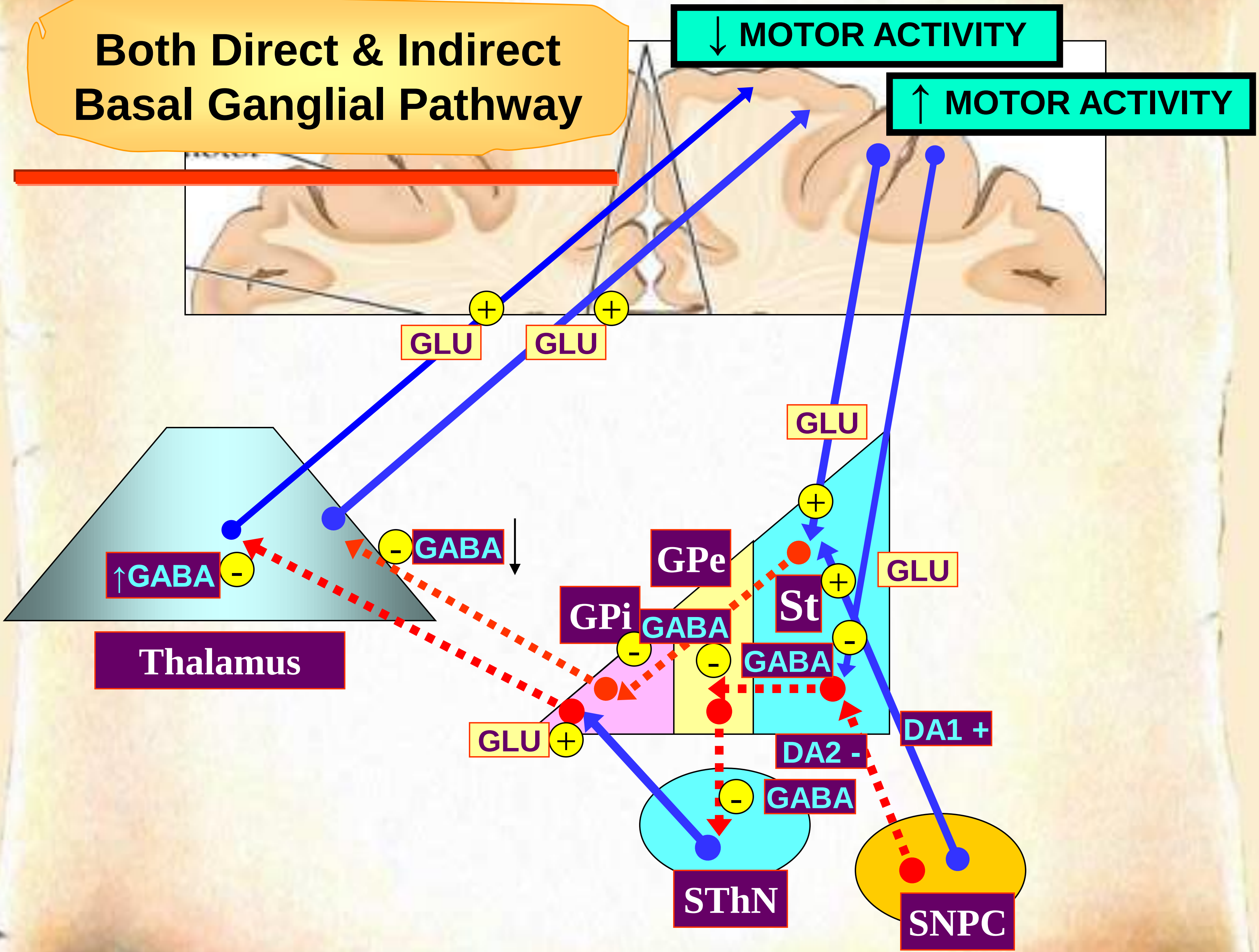


Subthalamic Neurons are disinhibited

Both Direct & Indirect Basal Ganglial Pathway

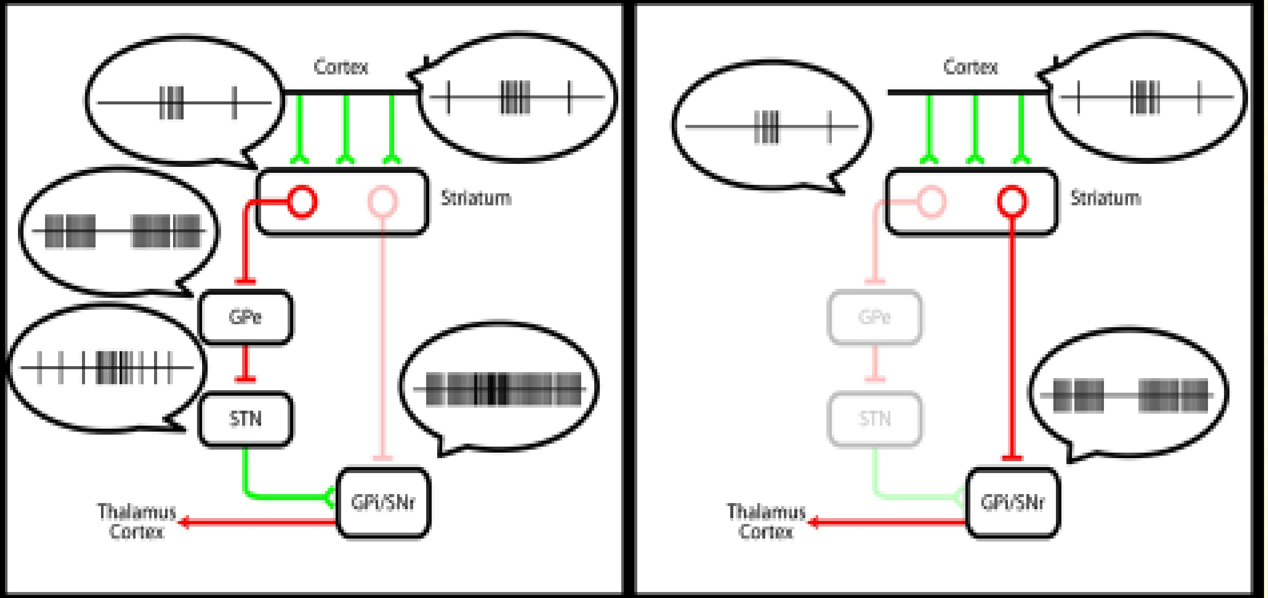


Both Direct & Indirect Basal Ganglial Pathway



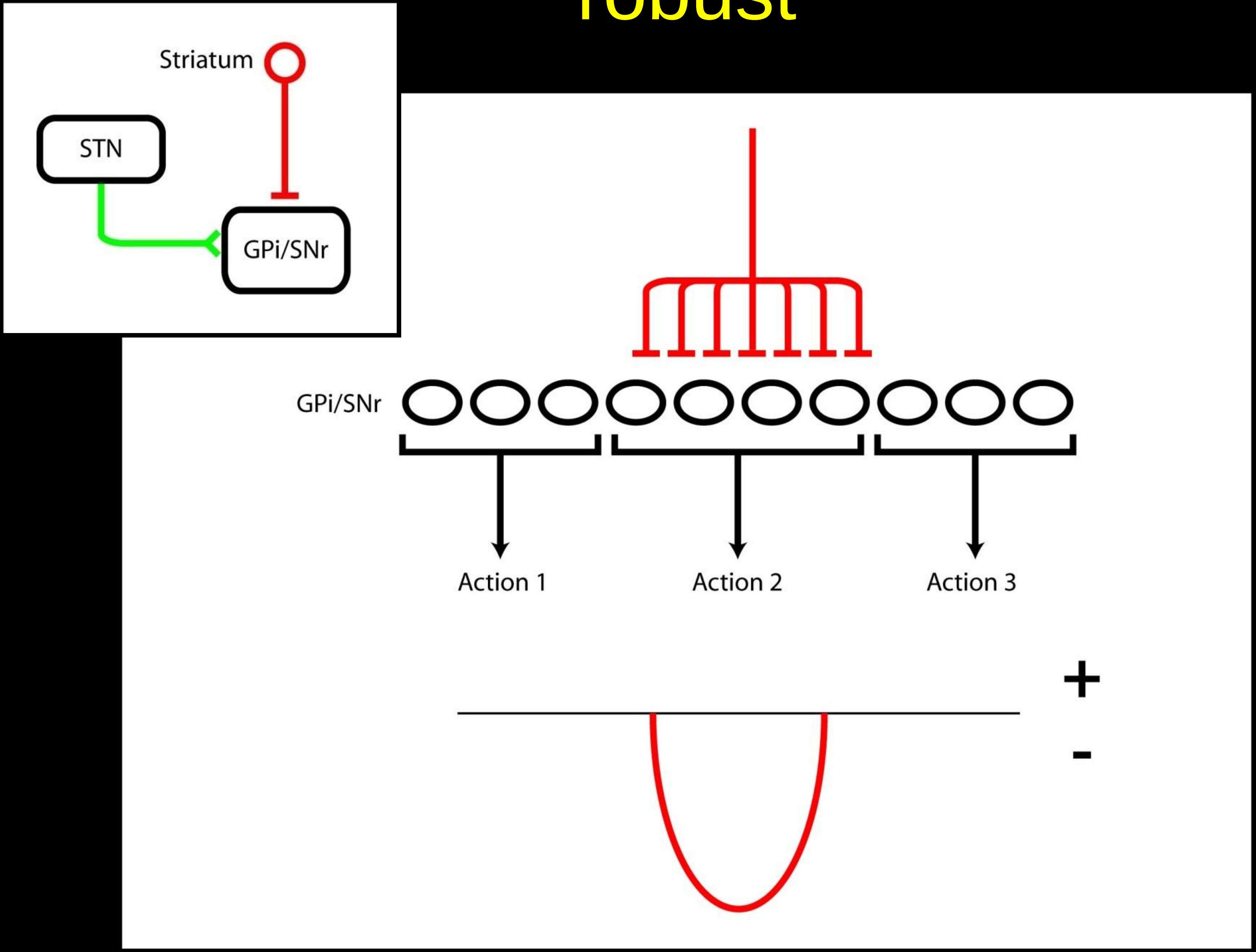
Indirect pathway suppresses action.

Direct pathway facilitates action.

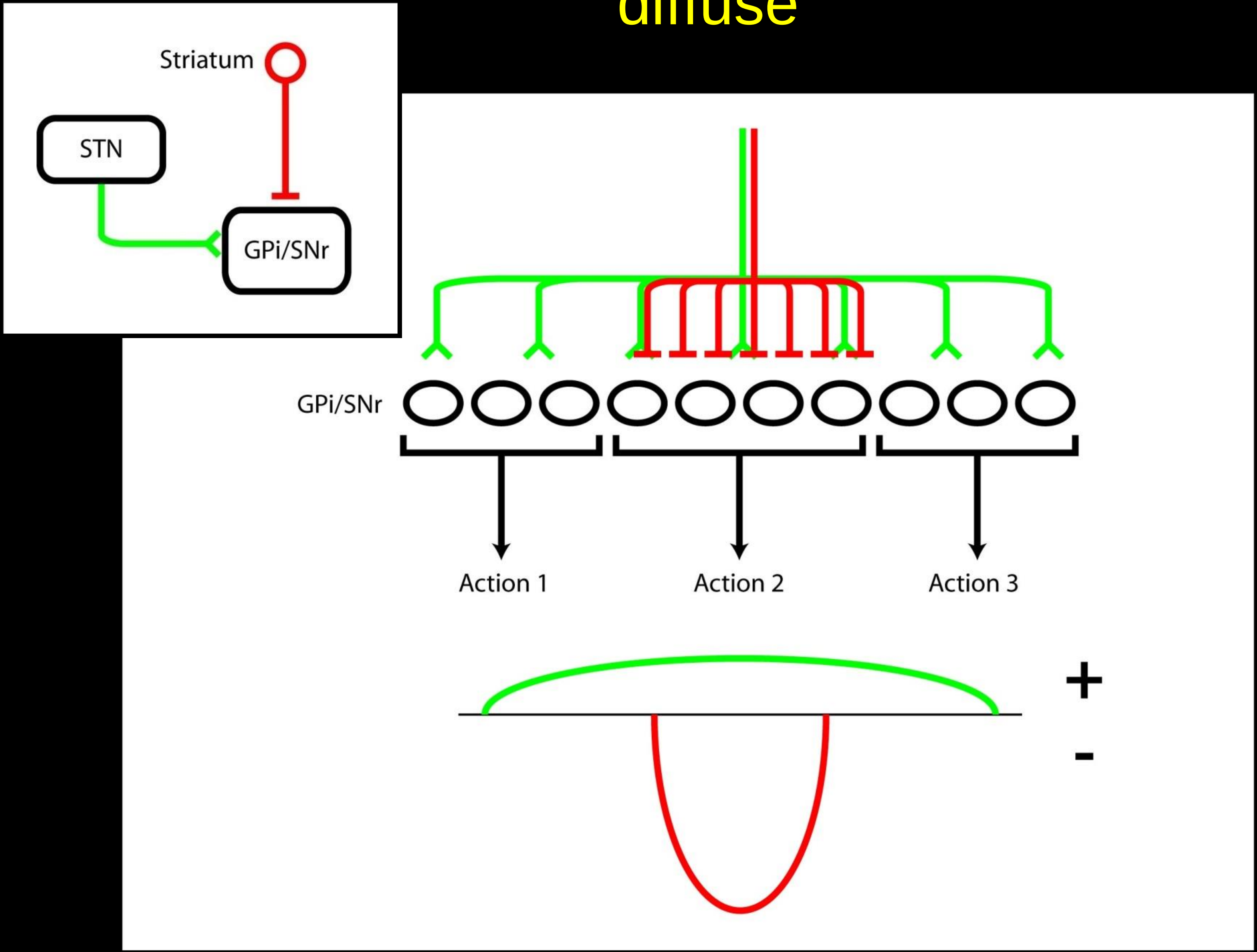


How do they cooperatively regulate motor output?

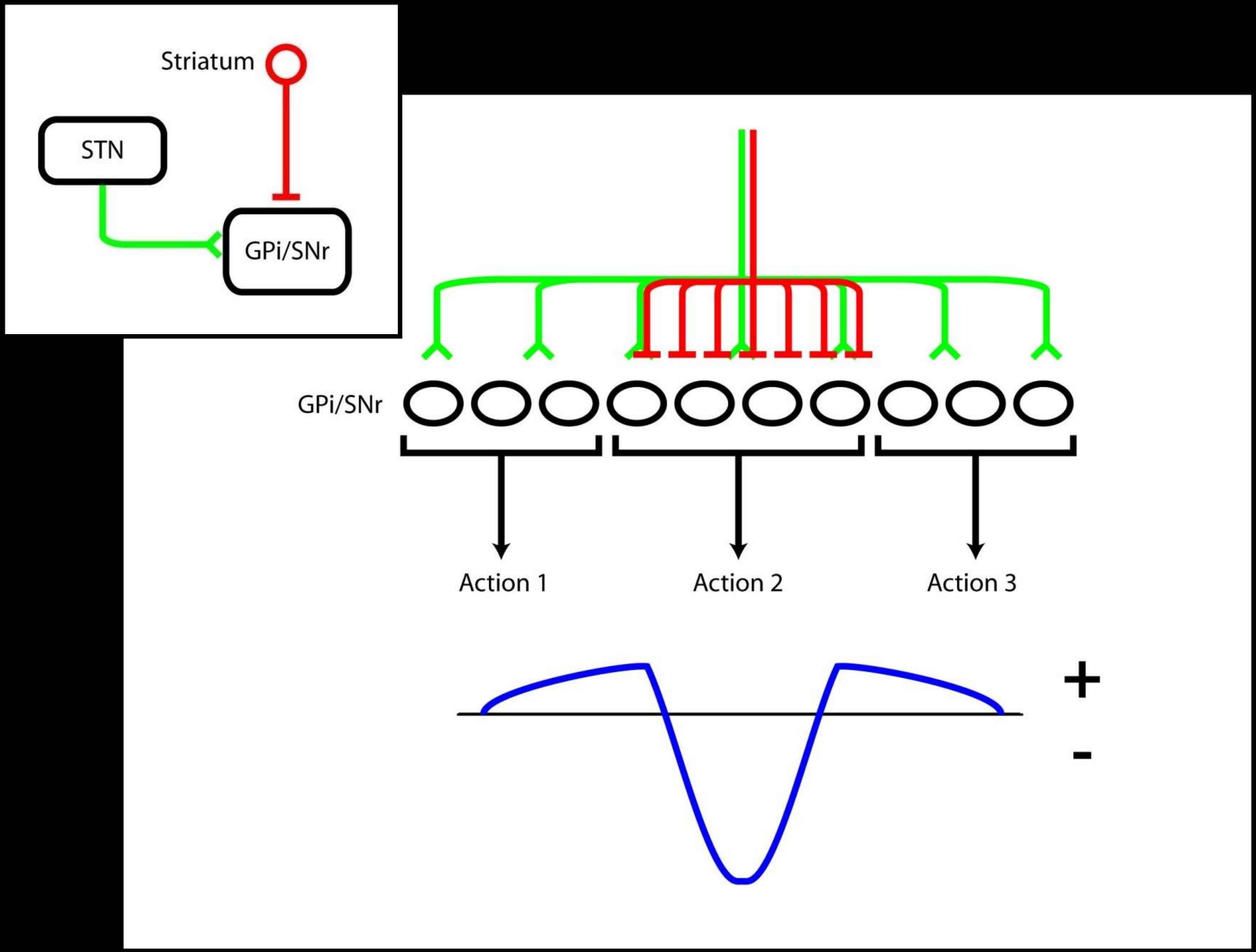
Direct pathway inputs are focused and robust



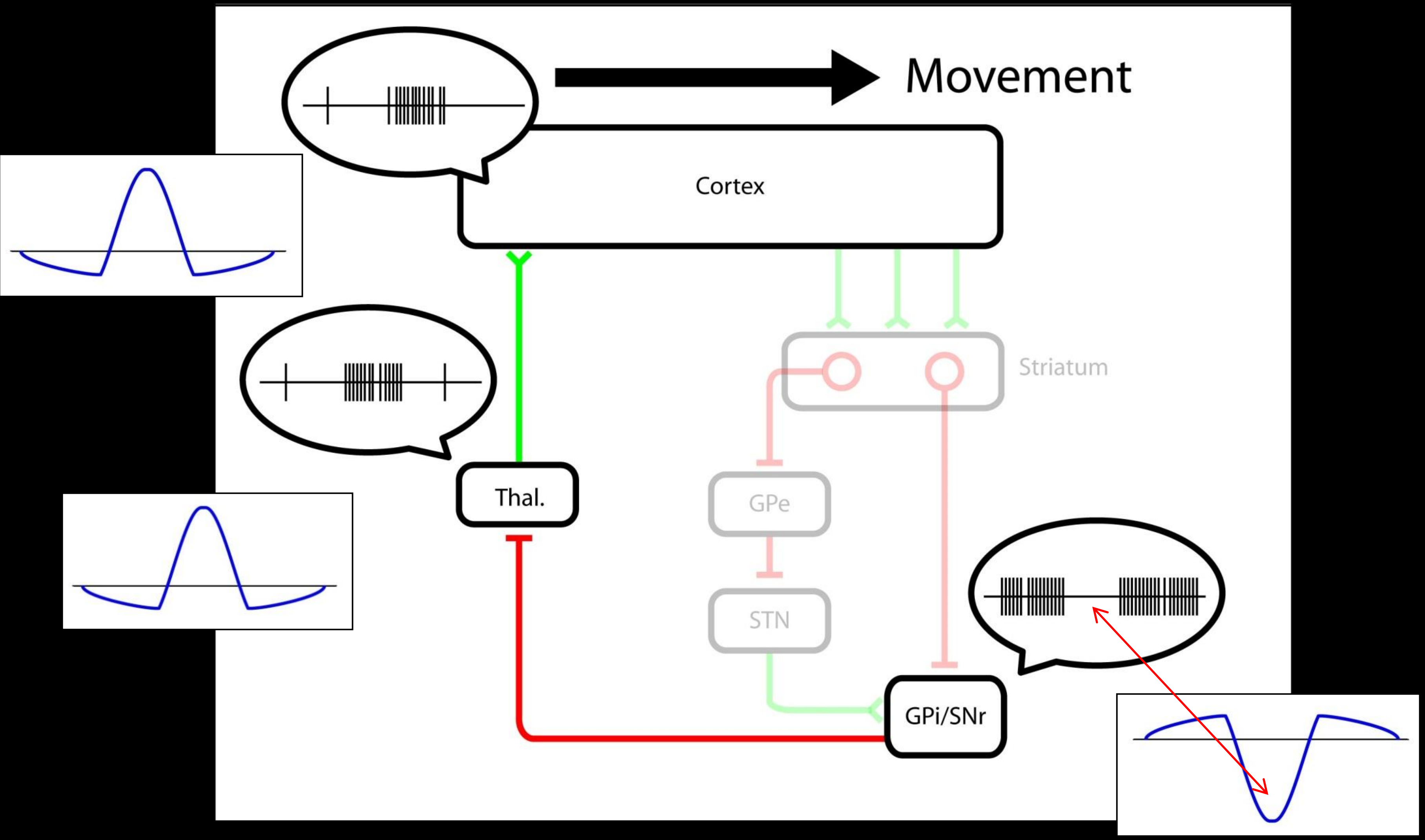
Indirect pathway inputs are widespread and diffuse



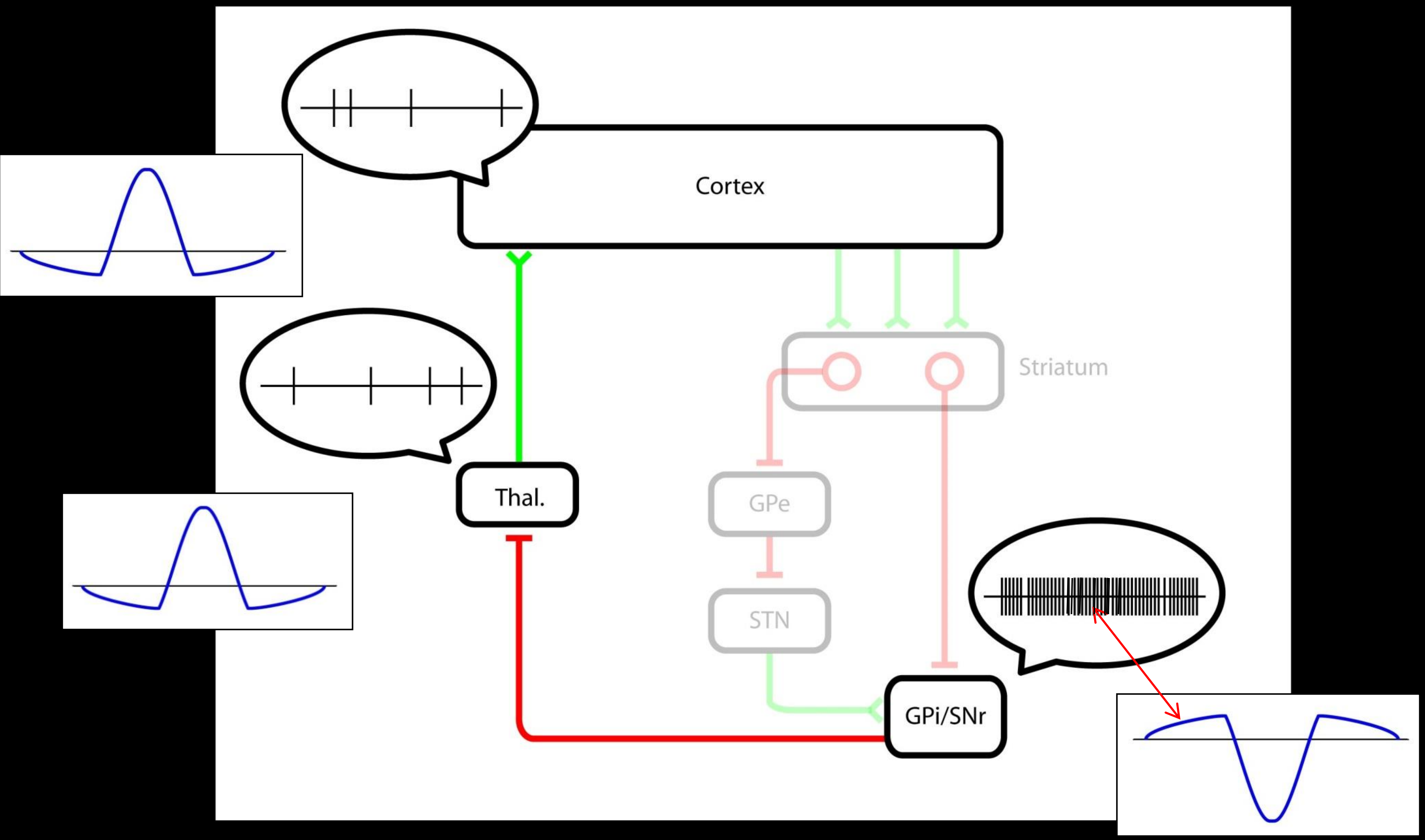
Together, these inputs create a center-surround mechanism for action selection



Movement modulation occurs through *disinhibition* of thalamocortical target regions



Competing alternatives are actively inhibited



Why do we need to 'sharpen' selection mechanisms?

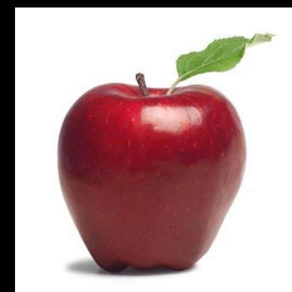
- Multiple/ambiguous stimuli in our environment often demand our attention/action (e.g., visual stimuli)
- However, we're often confined to making a single action to address these stimuli (e.g., a saccade).
- Particularly where conflicting needs are present, action may require active inhibition

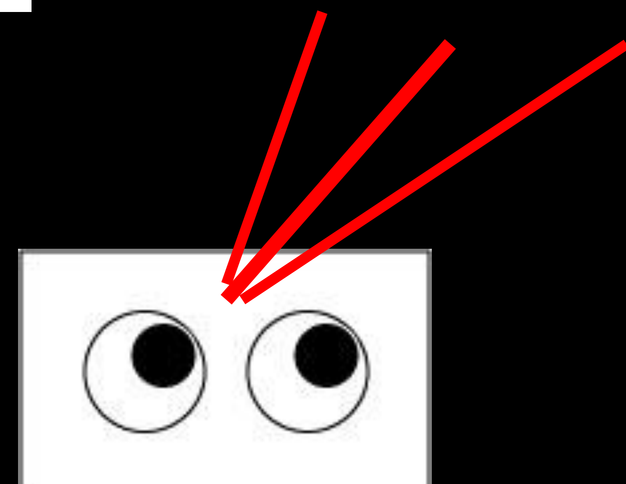
Action selection (in action)

- Multiple/ambiguous stimuli in our environment often demand our attention/action.

- However, we're often confined to making a single action to address these stimuli (e.g., a saccade).

- Selection through surround inhibition likely occurs on large and small scales – i.e., not only saccade left or right, but how far to saccade?





Direct and indirect pathways together facilitate action selection

- 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

Dopamine effects on direct and indirect pathways

- Dopamine signaling through D2 receptors in the indirect pathway suppresses striatal activity
- Dopamine signaling through D1 receptors in the direct pathway:
  - Facilitates strong, phasic inputs
  - Suppresses weak inputs

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

BASAL GANGLIA

FUNCTIONS

- Control of movements
- Planning and programming of movements
- Cognition

BASAL GANGLIA

DISORDERS

MOVEMENTS (ATAXIA Rate, Range, Force, Direction)

SPEECH

POSTURE

GAIT

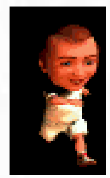
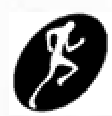
MENTAL ACTIVITY

OTHERS

Movement Disorders

Hyperkinetic

- Hemiballismus
- Huntington's Disease
- Athetosis

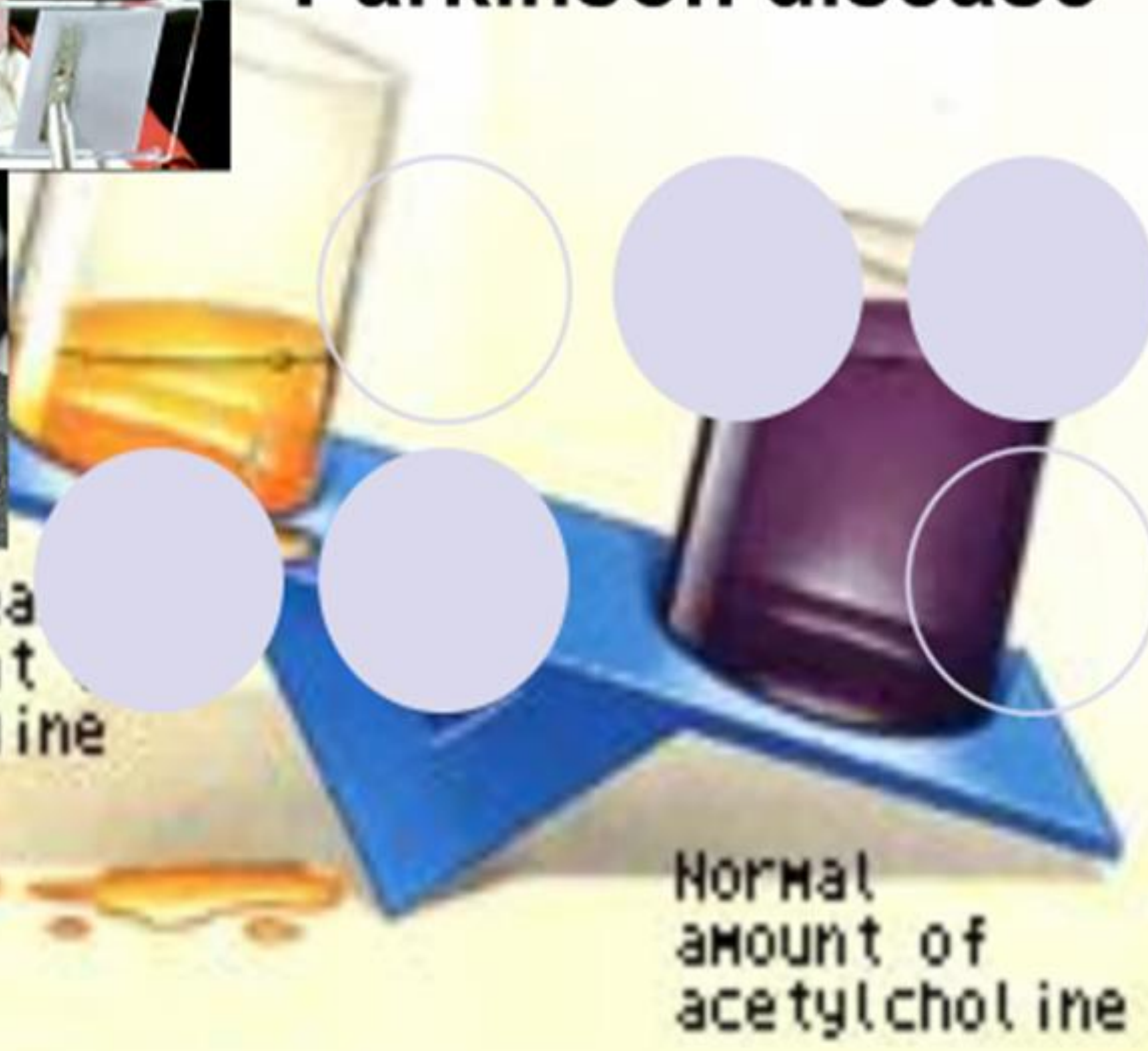





Hypokinetic

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

Movement Disorder	Features	Lesion
Chorea	Multiole quick, random movements, usually most prominent in the appendicular muscles	Atrophy of the striatum. Huntington Chorea
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 disease



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




Parkinson's disease

- Parkinson's disease is characterized by resting tremor, rigidity, akinesia (difficulty in initiation of movement) and bradykinesia (slowness in the execution of movement).
- These symptoms are due to loss of function of the basal ganglia which is involved in the coordination of body movement.

Levodopa

- L-dopa or Dihydroxyphenyalanine
- 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-administrated with L-dopa
- L-dopa exhibits a large first-pass effect
- Only about 1% reaches brain tissue