بِسۡمِ ٱللَّهِ ٱلرَّحۡمَٰنِ ٱلرَّحِيمِ

Basal Nuclei

Dr Zubia Shah

Learning Objectives

- Define Basal Nuclei/Basal Ganglia
- Enumerate the components of Basal Ganglia.
- Describe Basal Ganglia.
- Describe the neural circuits of basal ganglia.
- Enumerate the functions of basal ganglia.
- Describe the disorders of Basal Ganglia.

Basal Ganglia

- masses of **Gray matter** located deep within the cerebral white matter

- **Interconnected** with the cerebral cortex, thalamus, and brainstem, as well as several other brain areas.

- **Motor and Non motor functions**;
  voluntary **motor** movements, procedural learning, habit learning, eye movements, cognition, and emotion

Is It a Misnomer?

Is It a Misnomer?

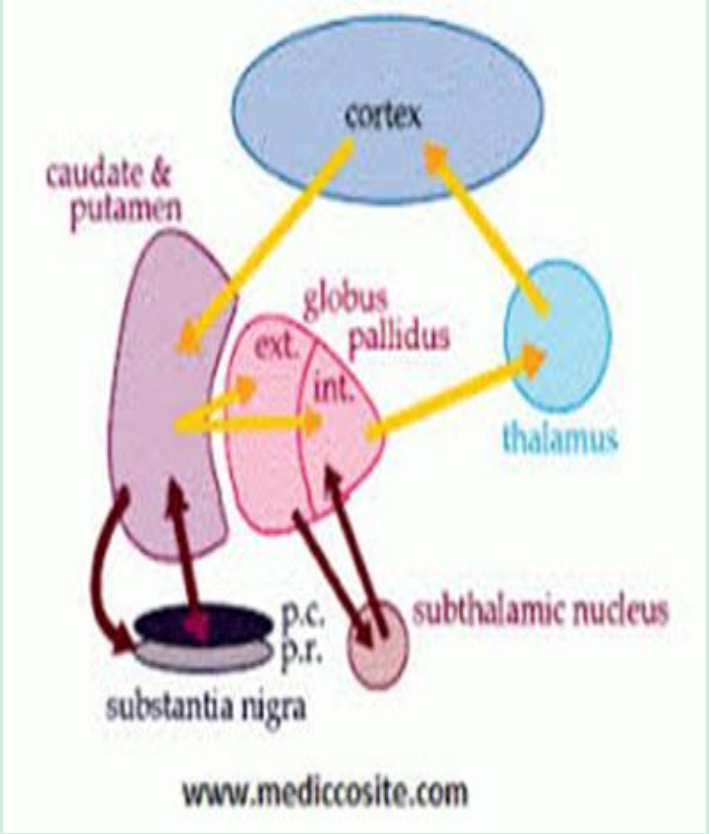
- “**Basal**" as most of its elements are in the **basal** part of the forebrain

- **Ganglia** is a misnomer:

Neural clusters are **called** "**ganglia**" only in the PNS; in the CNS they are **called** "**nuclei’’** surrounded by **white matter**

Parts of Basal Ganglia

1. **Caudate**
2. **Putamen**
3. **Globus Pallidus**
    i. Globus pallidus externa
    ii. Globus pallidus interna
4. **Substantia nigra**
    i. Pars Compacta
    ii. Pars Reticulata
5. **Subthalamic nucleus**



Basal Ganglia

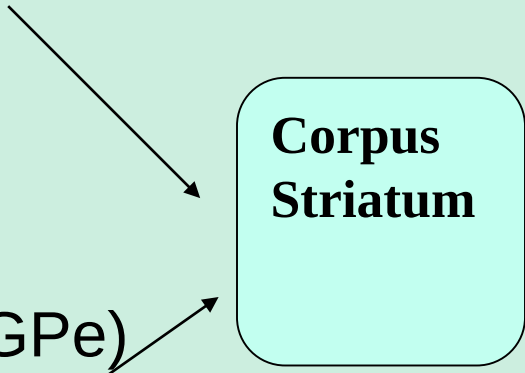
1. Neostriatum
   - Caudate nucleus
   - Putamen

   } Striatum

2. Paleostriatum
   - Globus pallidus external segment (GPe)
   - Globus pallidus internal segment (GPi)

3. Substantia Nigra
   - Pars compacta (SNc)
   - Pars reticulata (SNr)

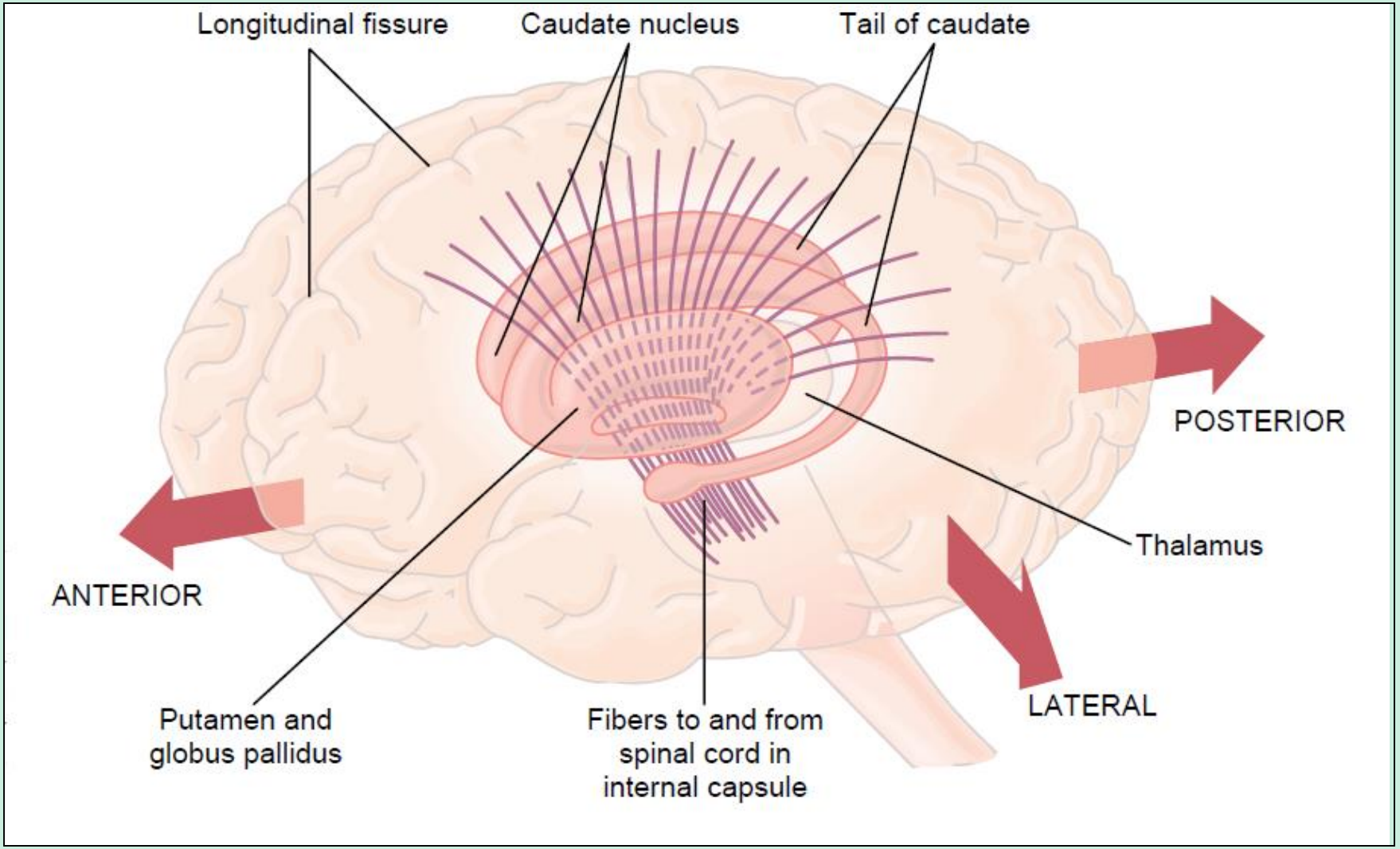
4. Subthalamic nucleus (STN)



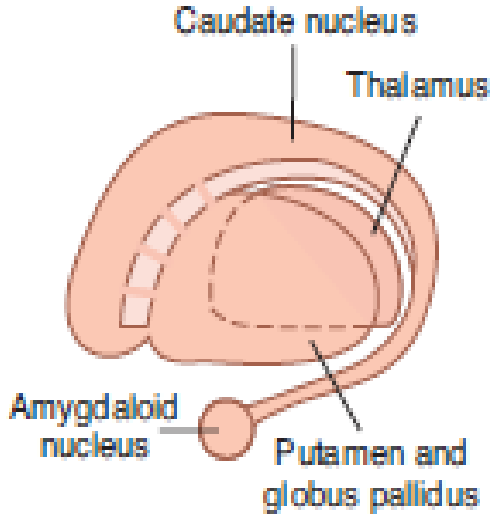
Striatum and Lenticular Nucleus

- Caudate Nucleus + Putamen = Striatum
- Putamen + Globus Pallidus = Lenticular Nucleus

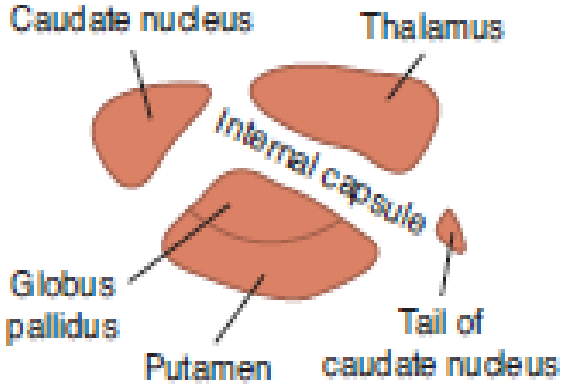
Anatomical Relations of Basal Nuclei



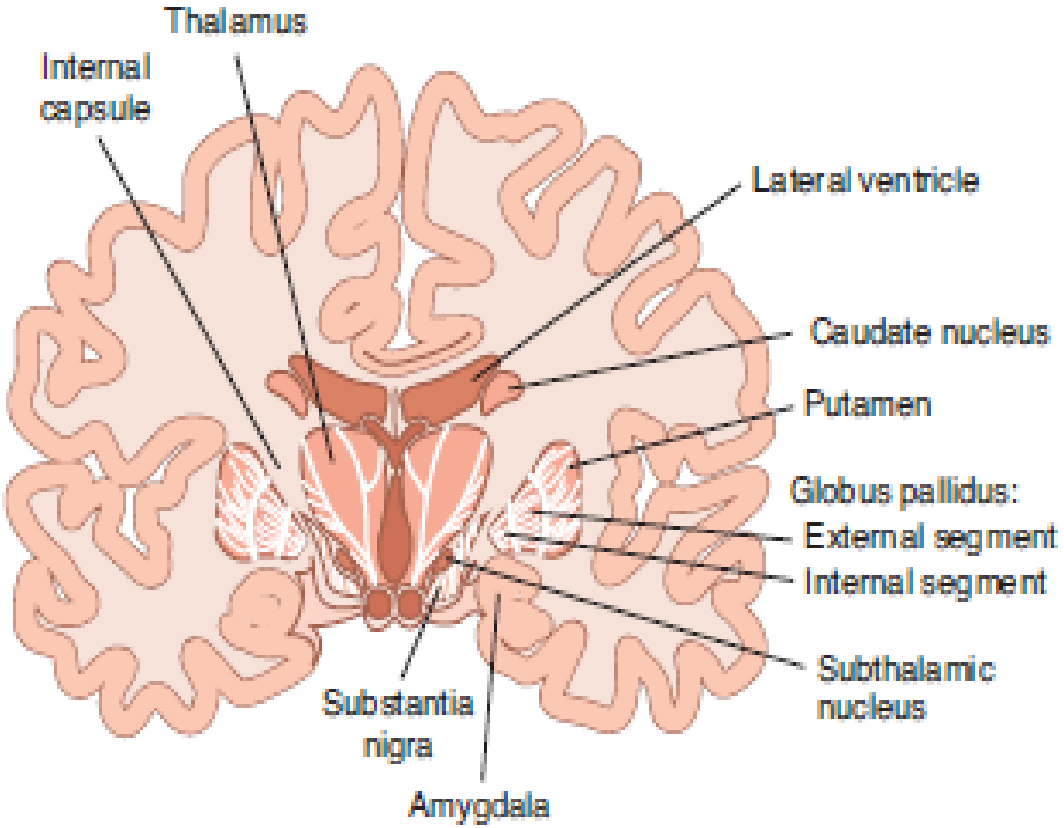
Basal Nuclei



Lateral view

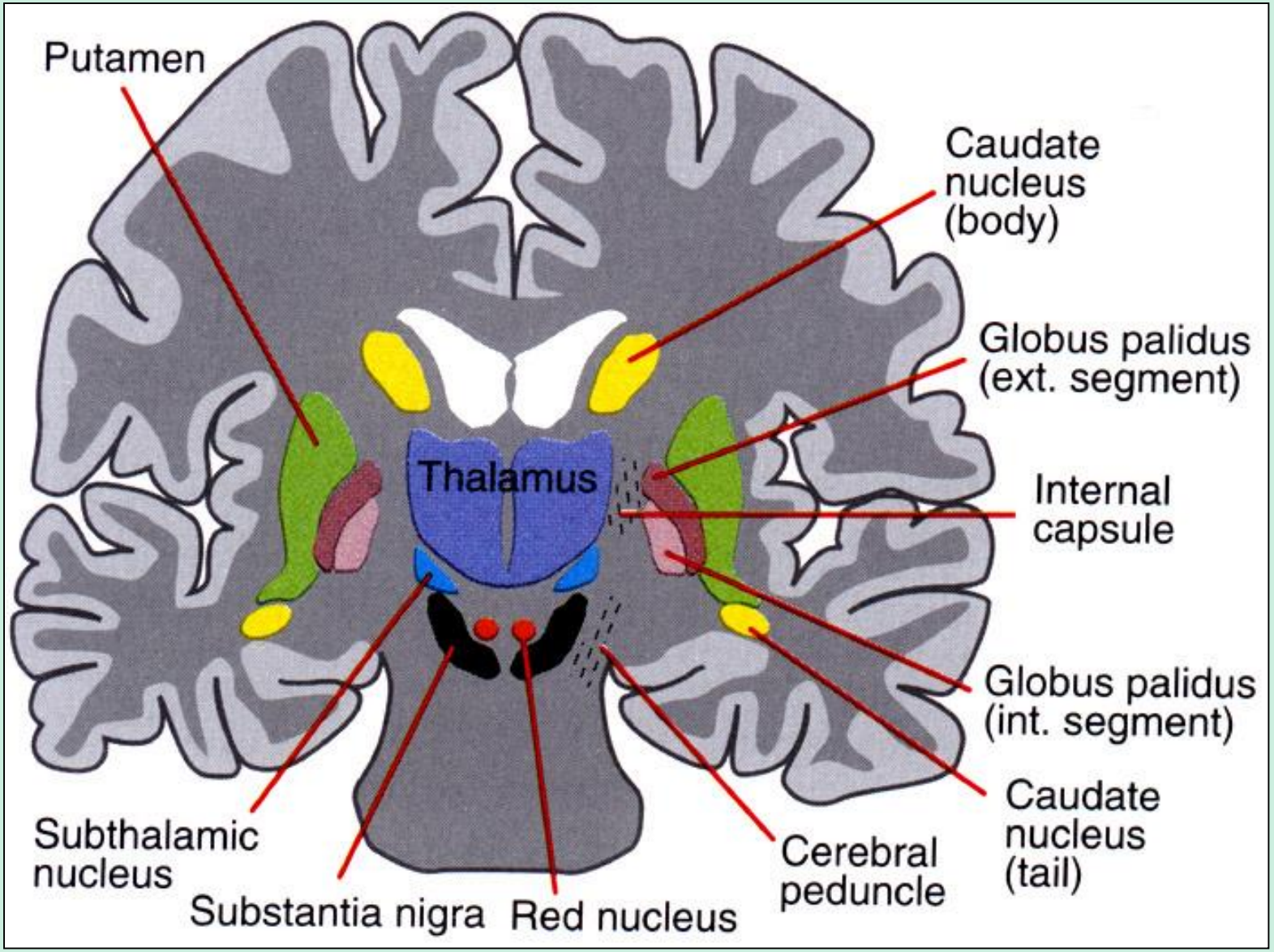


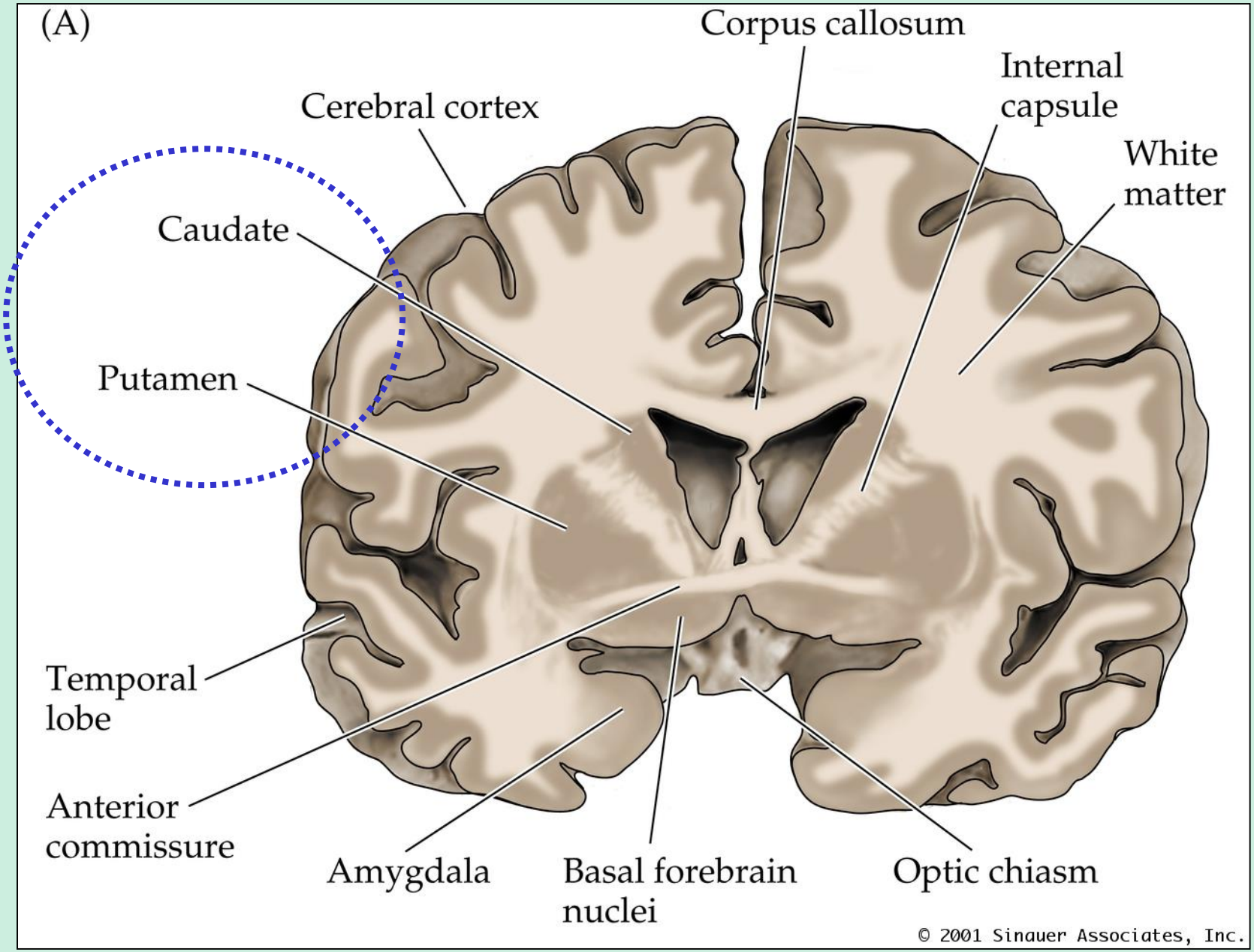
Horizontal section



Frontal section

Where are Basal Nuclei?




(A)
Corpus callosum
Internal capsule
Cerebral cortex
White matter
Caudate
Putamen
Temporal lobe
Anterior commissure
Amygdala
Basal forebrain nuclei
Optic chiasm
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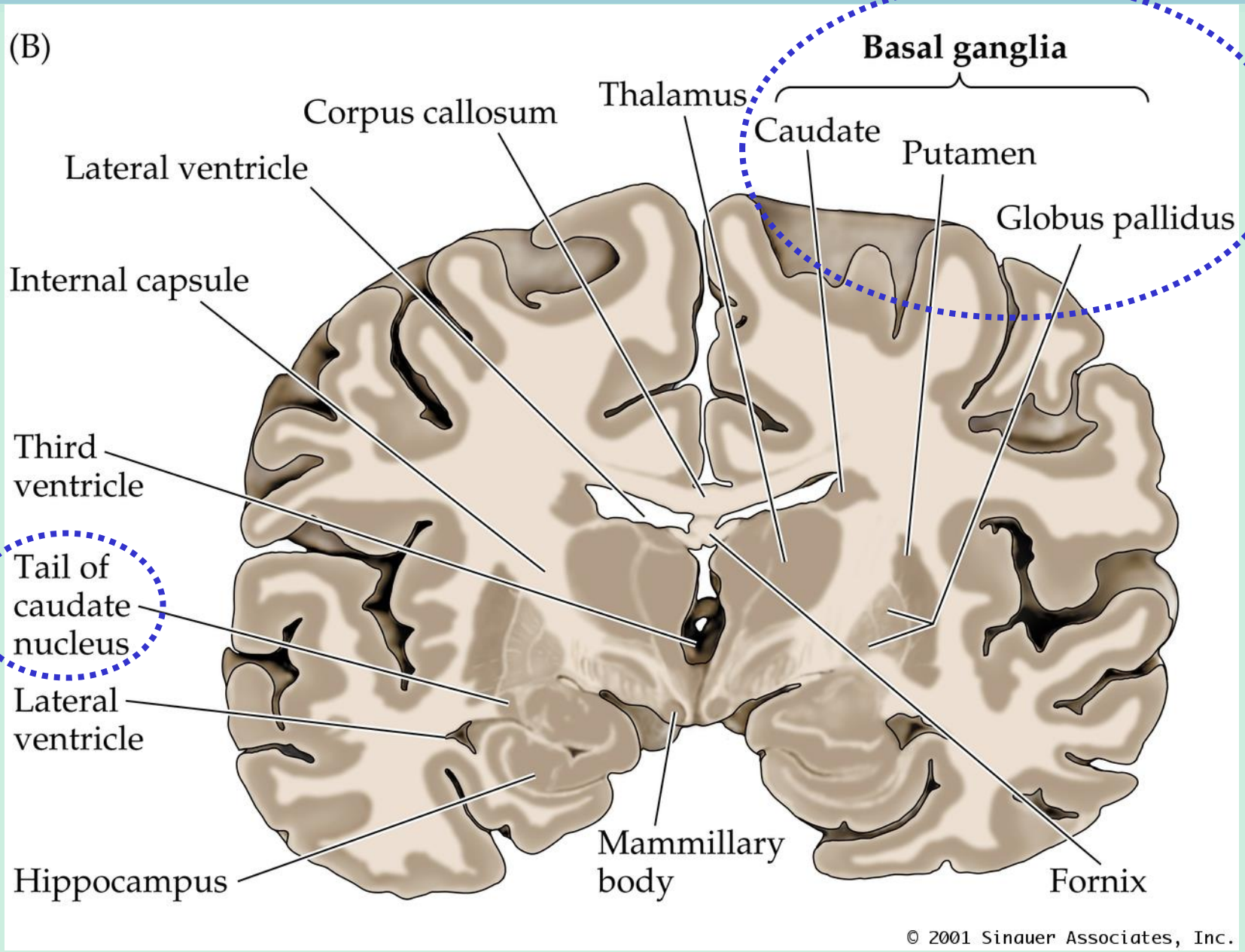
(B)
Basal ganglia
Thalamus
Corpus callosum
Caudate
Putamen
Lateral ventricle
Globus pallidus
Internal capsule
Third ventricle
Tail of caudate nucleus
Lateral ventricle
Mammillary body
Hippocampus
Fornix
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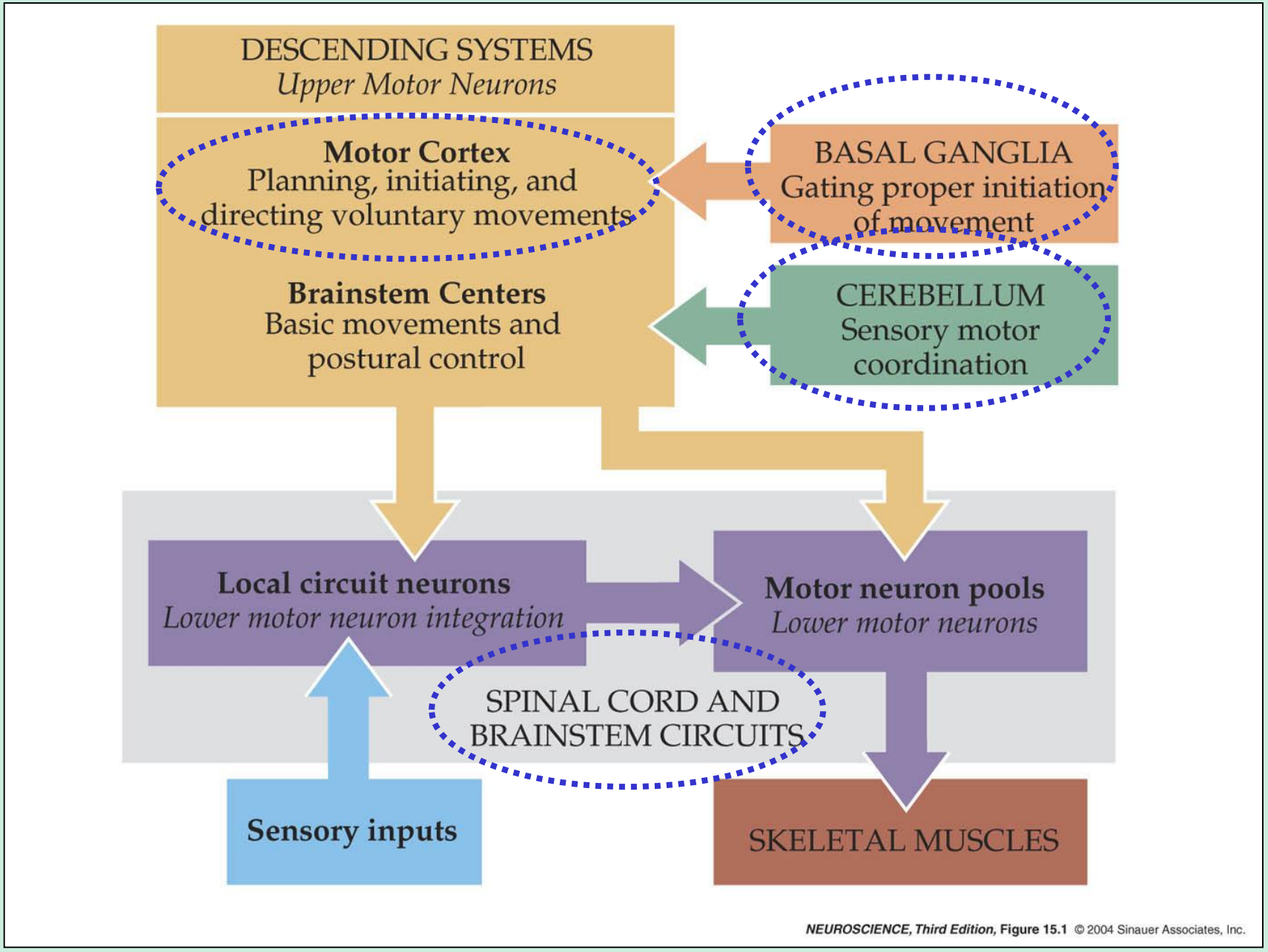
Embryonic Origin

Primary division of the Neural tube	Secondary subdivision	Final segments in a human adult
PROSENCEPHALON	1. Telencephalon 2. Diencephalon	1. **Caudate**, **Putamen** **2. Globus pallidus**, thalamus, subthalamus, hypothalamus, **subthalamic nucleus**
MESENCEPHALON	1.Mesencephalon	**Substantia nigra pars compacta (SNc)**, **Substantia nigra pars reticulata (SNr)**
RHOMBENCEPHALON	1.Metencephalon 2.Myelencephalon	1.Pons and cerebellum 2.Medulla

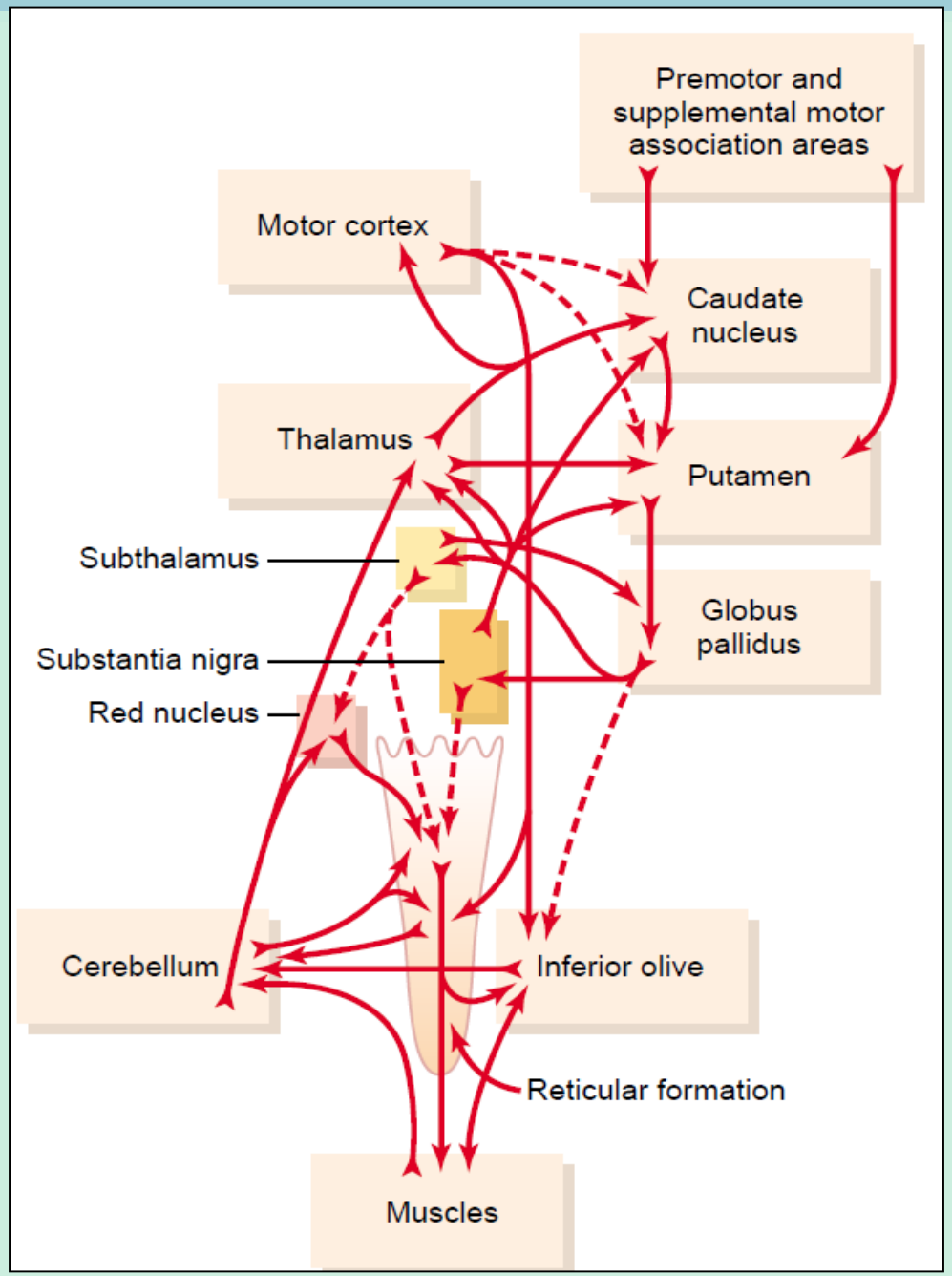
Neural circuits of the Basal Ganglia

Neural Structures Involved In the Control of Movement



NEUROSCIENCE, Third Edition, Figure 15.1 © 2004 Sinauer Associates, Inc.

Relation of Basal Ganglia to Corticospinal - Cerebellar System For Movement Control

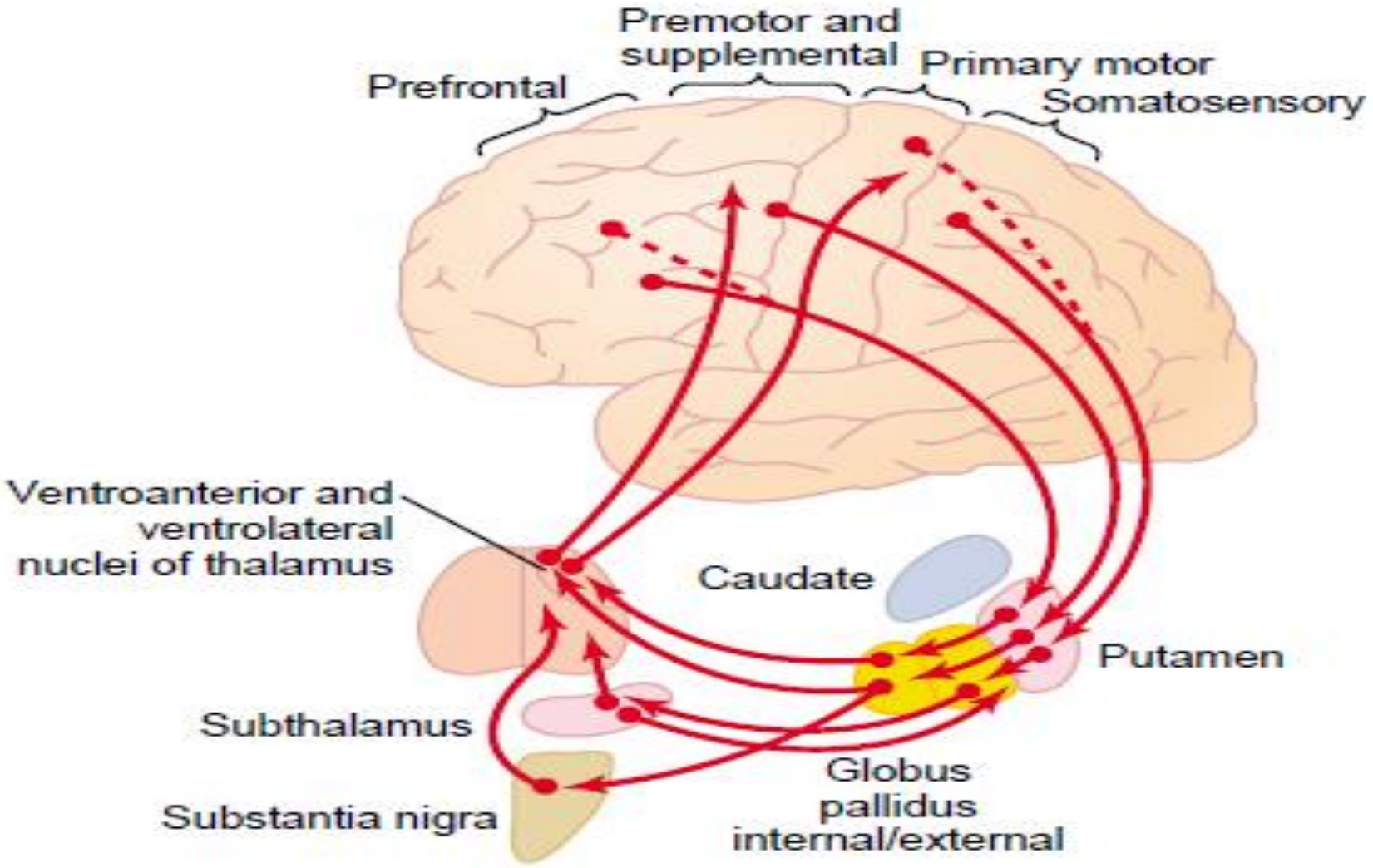


Neuronal Circuitry of the Basal Ganglia

- Anatomical connections between the basal ganglia and other brain elements for motor control are complex
  - 2 circuits

The Putamen Circuit
The Caudate Circuit

The Putamen Circuit



Functions of Putamen Circuit

Function Of Basal Ganglia In Executing Motor Activity– Putamen Circuit

- Writing letters of alphabets→ damage can lead to crude writing
- Cutting paper with scissors
- Hammering nails
- Shooting a basketball through a hoop
- Passing a football
- Throwing a baseball
- Movements of shovelling dirt
- Most aspects of vocalization
- Controlled movements of eyes and any other skilled movement -- subconsciously

Abnormal Function In Putamen Circuit

- Little is known about function of Putamen circuit
- But when a part of circuit is damaged or blocked →

❖**Lesions in Globus Pallidus→ ATHETOSIS – spontaneous and continuous writhing movements of hand, arm, neck or face**

❖**Lesion in Subthalamus → HEMIBALLISMUS – flailing movement of an entire limb**

❖**Lesions (multiple) in Putamen → CHOREA – flicking movements in hands, face and other parts of body**

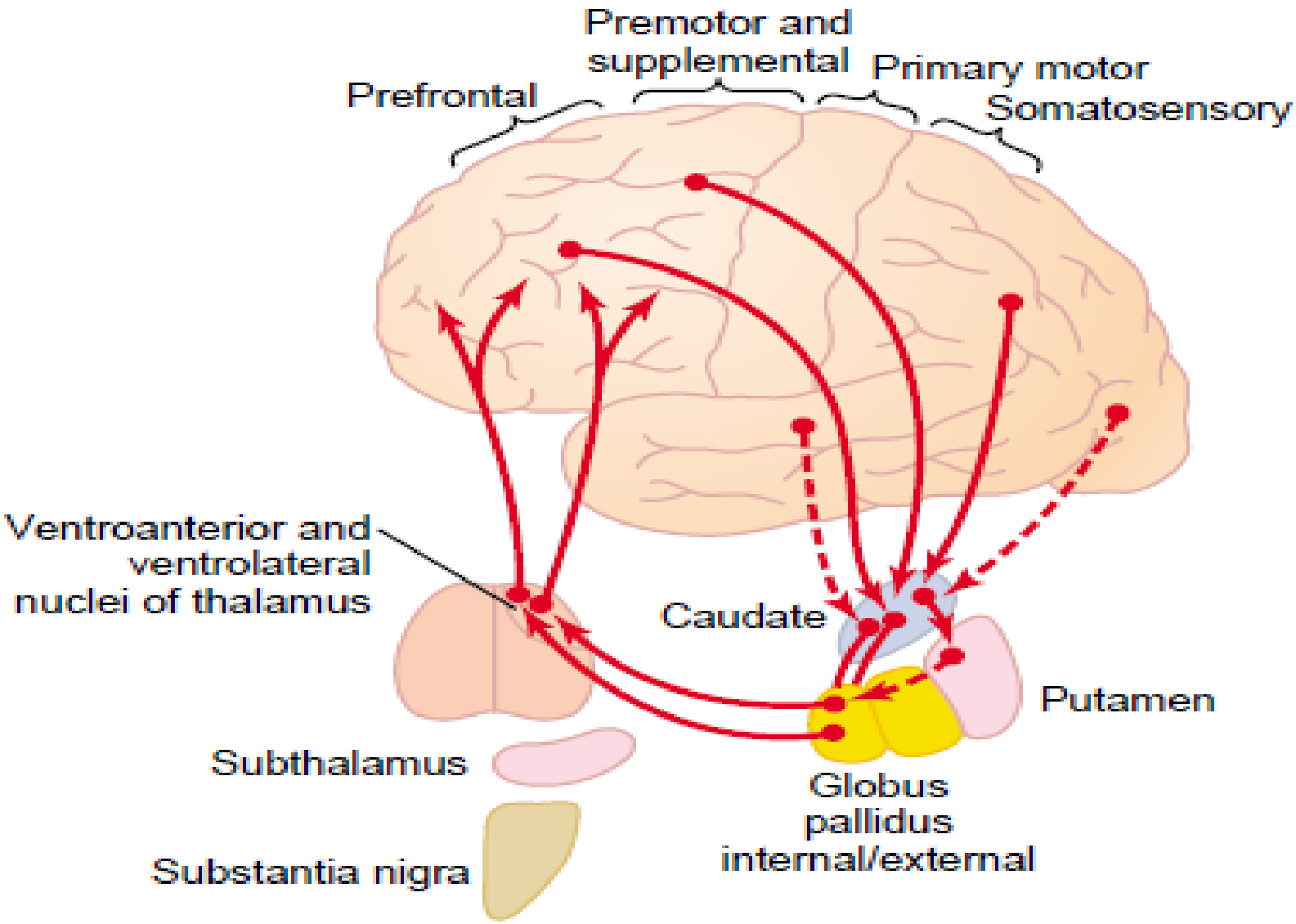
❖**Lesions of Substantia Nigra → PARKINSON'S DISEASE – rigidity, akinesia and tremors**

MCQ

Athetosis results from lesion in

- A. Caudate nucleus
- B. Globus Pallidus
- C. Putamen
- D. Substantia nigra
- E. Subthalamic nucleus

The Caudate Circuit



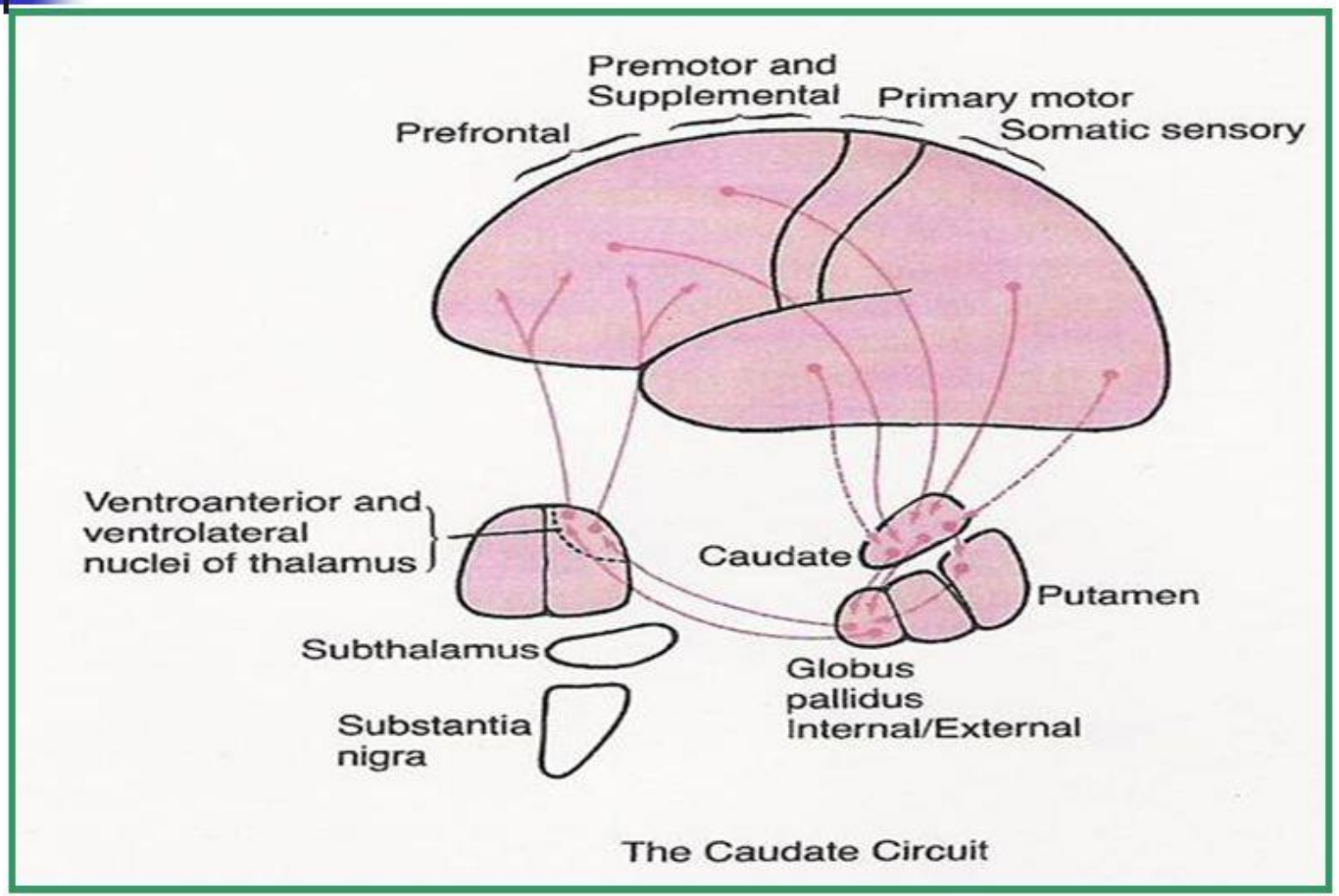
Cognitive Control Of Motor Patterns
The Caudate Circuit

- Caudate nucleus plays a major role in **cognitive control** of motor activity

- Caudate extends to all lobes of cerebrum and gets input from association areas as well

- Signals from cerebral cortex → internal G.pallidus → VA and VL nuclei thalamus → prefrontal, premotor and supplementary motor areas of cerebral cortex that cause sequential motor movement

Cognitive loop (Caudate circuit): Concerned with cognitive control of sequences of motor pattern.
Motor intentions (Cognition means thinking process using sensory input with information already stored in memory)



The Caudate Circuit

Cognitive Function of Caudate Circuit

- A person on seeing an approaching lion

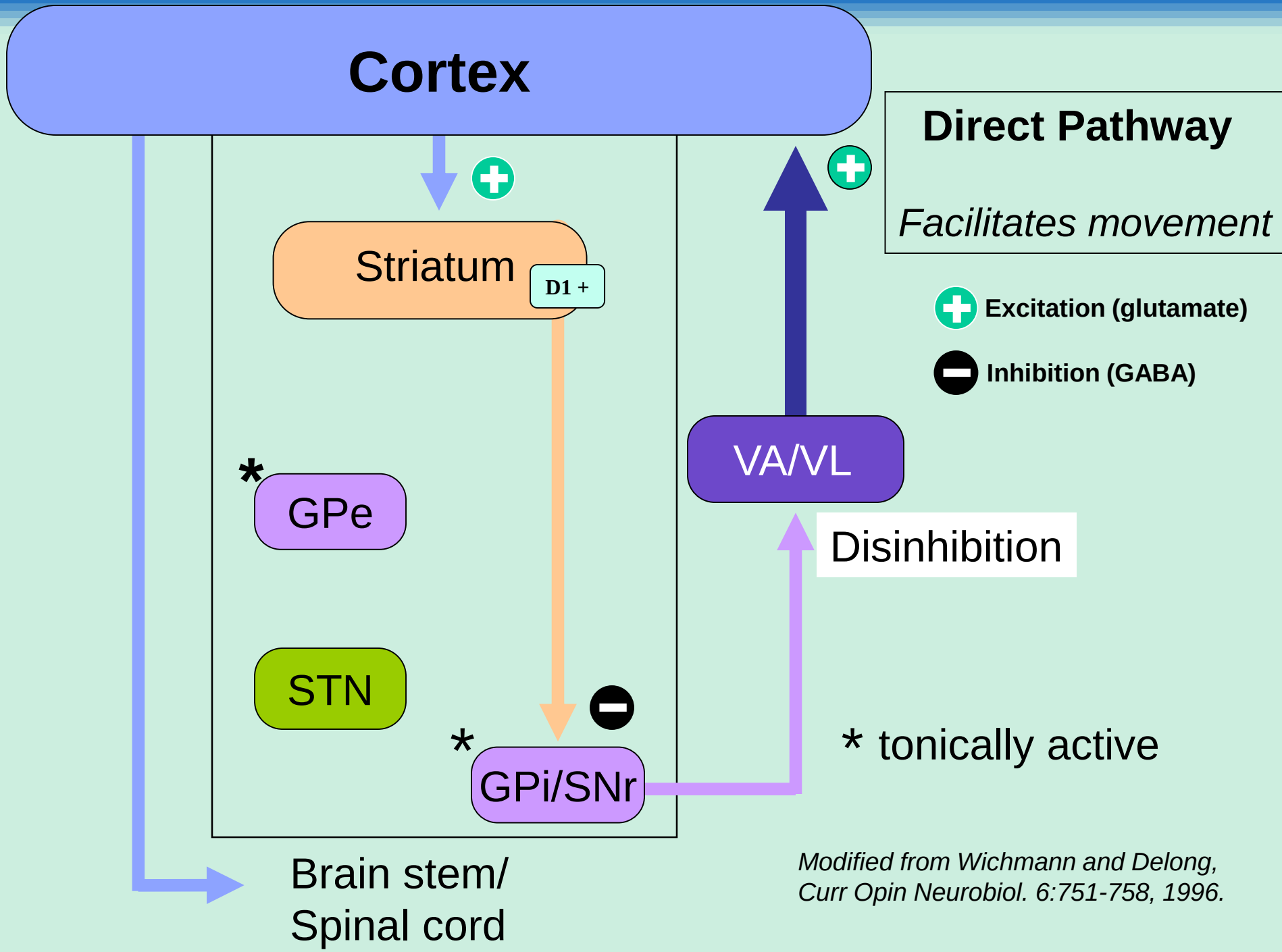
1. Will turn away
2. Begin to run
3. Even attempt to climb something like a tree

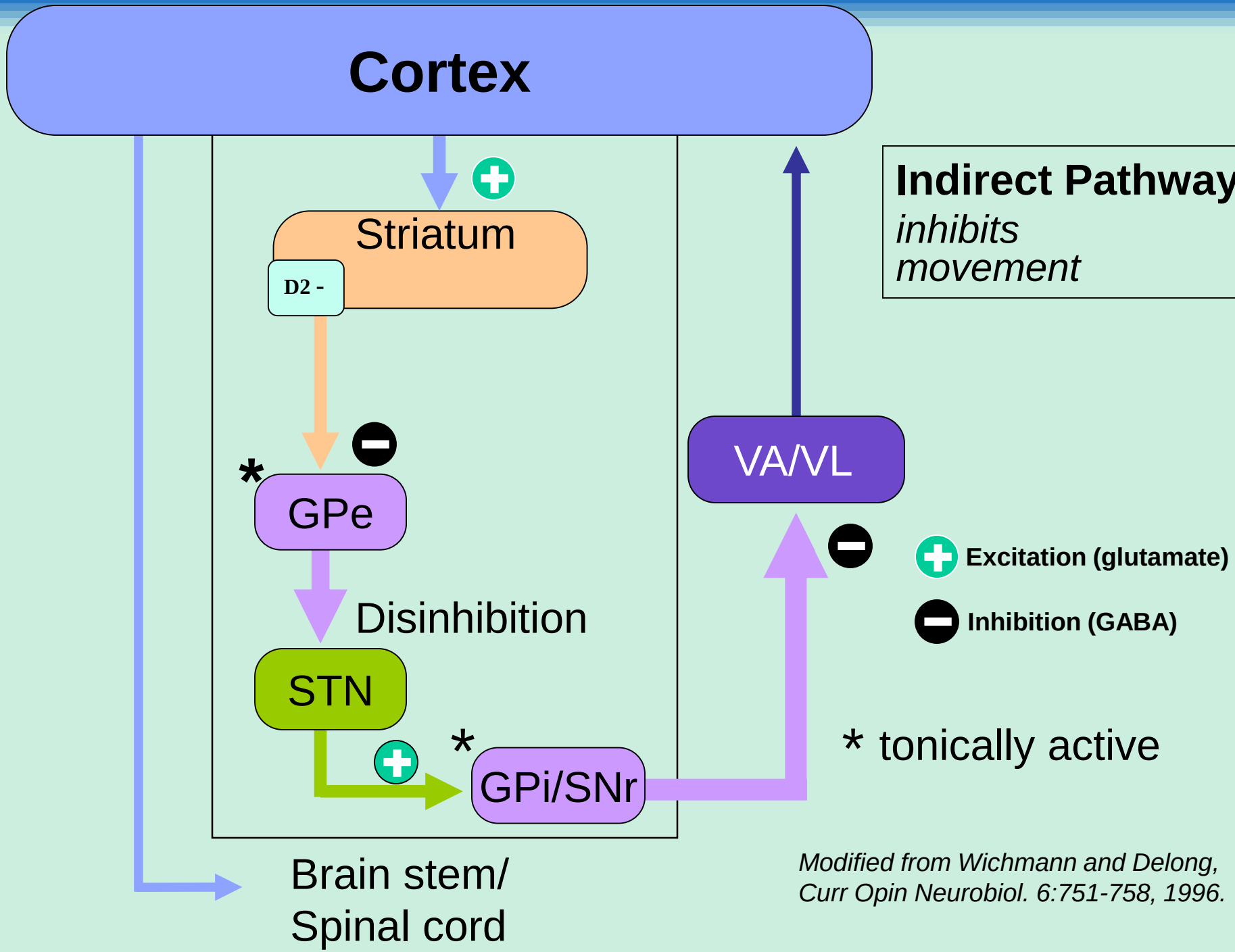
Occurs subconsciously and within seconds

Neural Pathways of Basal Ganglia

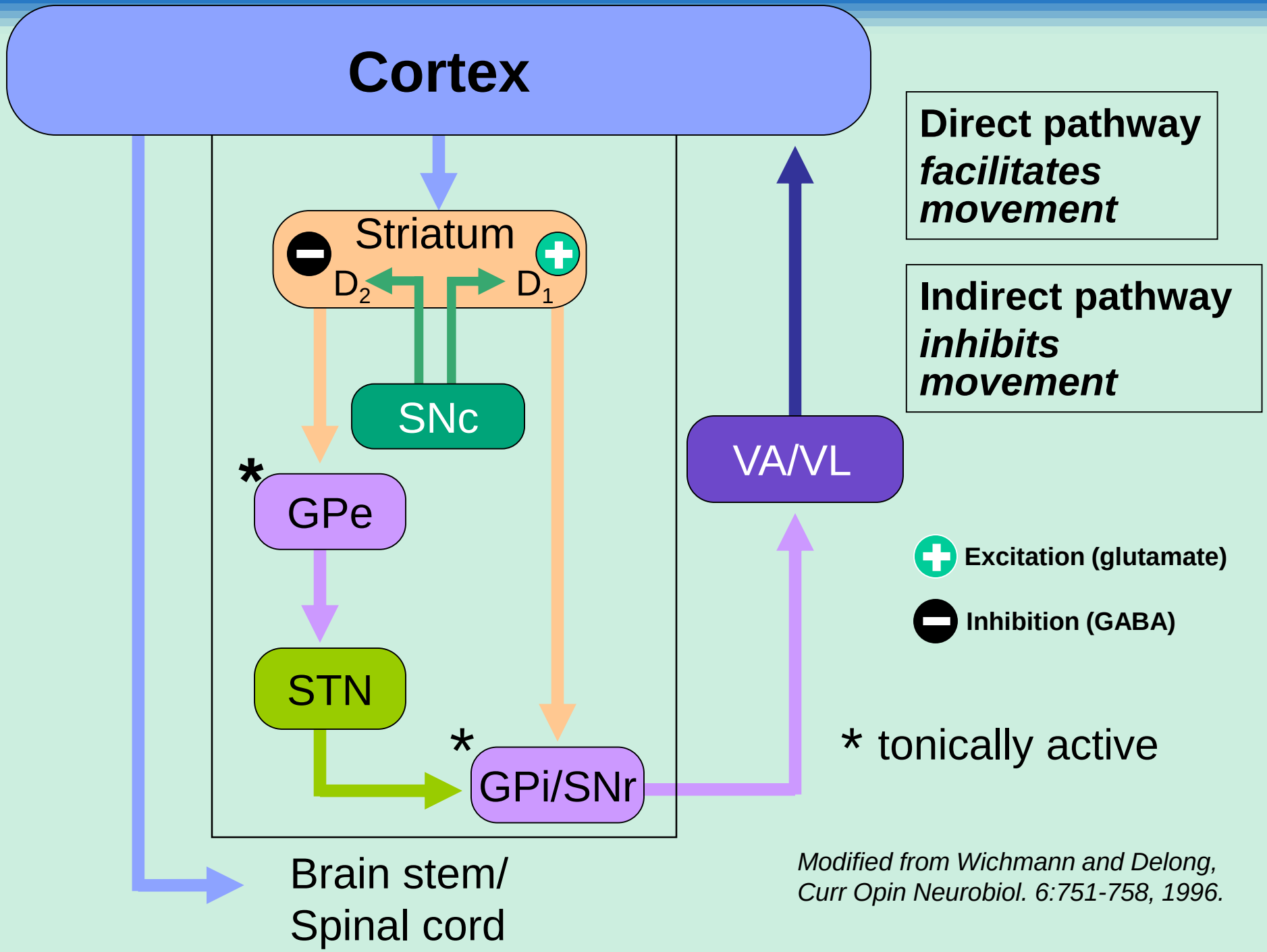
Direct

Indirect


Cortex
Striatum
D1 +
GPe
STN
GPi/SNr
VA/VL
Brain stem/
Spinal cord
Direct Pathway
Facilitates movement
Excitation (glutamate)
Inhibition (GABA)
Disinhibition
* tonically active
Modified from Wichmann and Delong,
Curr Opin Neurobiol. 6:751-758, 1996.



Modified from Wichmann and Delong, Curr Opin Neurobiol. 6:751-758, 1996.

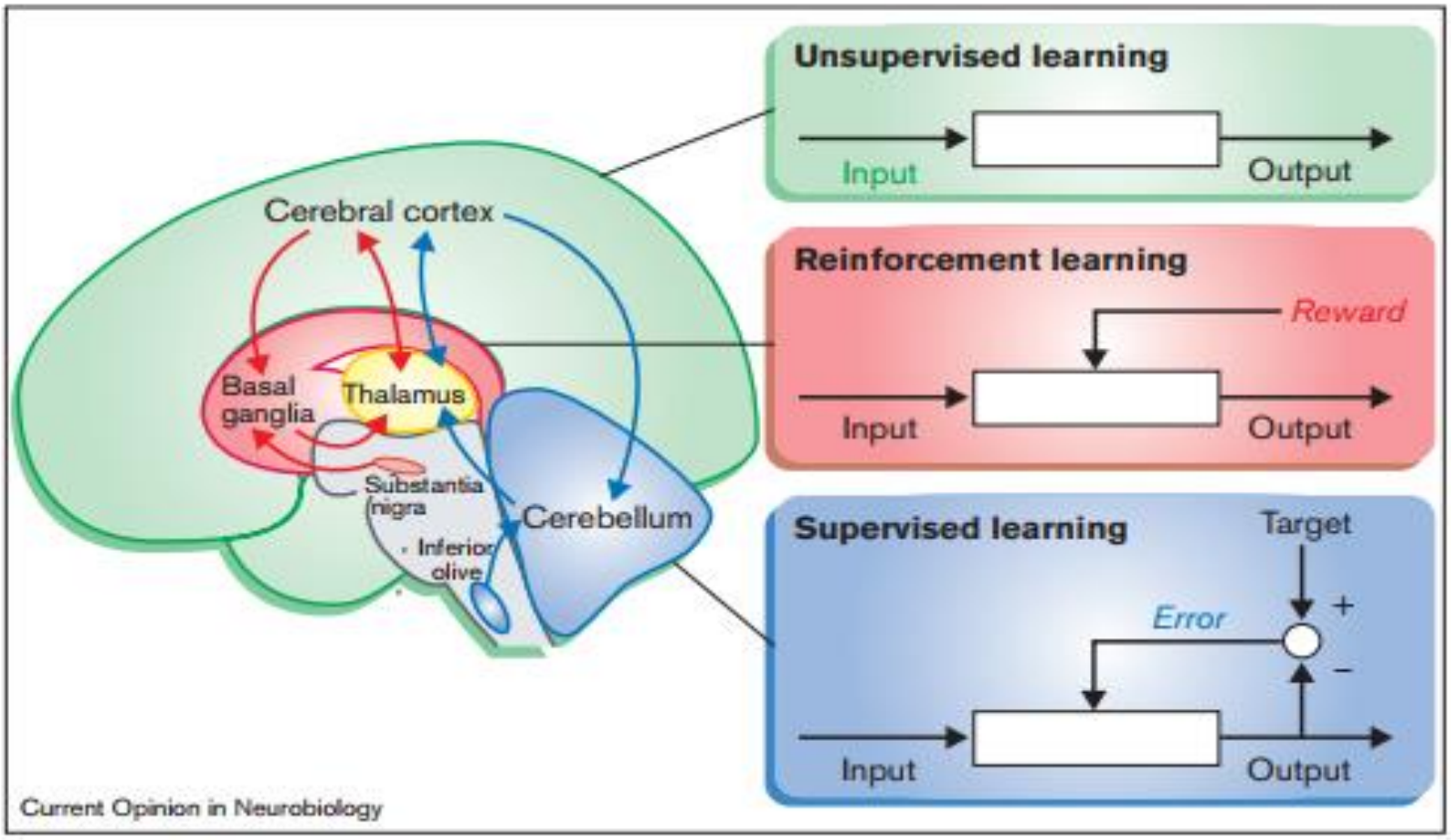

Cortex
Striatum
D2
D1
SNc
GPe
*
STN
GPi/SNr
*
VA/VL
Brain stem/
Spinal cord
Direct pathway
facilitates
movement
Indirect pathway
inhibits
movement
Excitation (glutamate)
Inhibition (GABA)
* tonically active
Modified from Wichmann and Delong,
Curr Opin Neurobiol. 6:751-758, 1996.

Release of DA in substantia nigra, as well as in striatum is required for control of movement by the basal ganglia

Neurotransmitters In Basal Ganglia

- Dopamine
- GABA
- Acetyl Choline
- Glutamate
- Norepinephrine, serotonin, enkephalin

Comparison of Function



Functions of Basal Ganglia (works with Cerebrum)

Complex patterns of motor activity

writing alphabets, cutting paper with scissors, hammering nails, shooting a basketball through a hoop, passing a ball or any skilled movement

Cognitive function

what to do in emergency or any situation

Timing (how rapidly the movement has to be performed) **Scaling the intensity (**and how large the movement will be)

Motor Functions of Basal Nuclei

Complex role in control of movement

1. Inhibiting muscle tone throughout body
   (**Proper Muscle Tone is maintained**)

2. Selecting and maintaining **Purposeful Motor Activity** while **suppressing** unwanted movements

3. Helping **Monitor and Coordinate** slow sustained contractions (**posture and support**)

Non-Motor Functions of Basal Nuclei

- Emotion
- Language
- Decision-making
- Learning
- Memory

Motor Behavior Is Determined By The Balance Between Direct/Indirect Striatal Outputs

Hypokinetic disorders

- **insufficient direct** pathway output
- **excess indirect** pathway output

Hyperkinetic disorders

- **excess direct** pathway output
- **insufficient indirect** pathway output

Parkinson's Disease

Paralysis Agitans

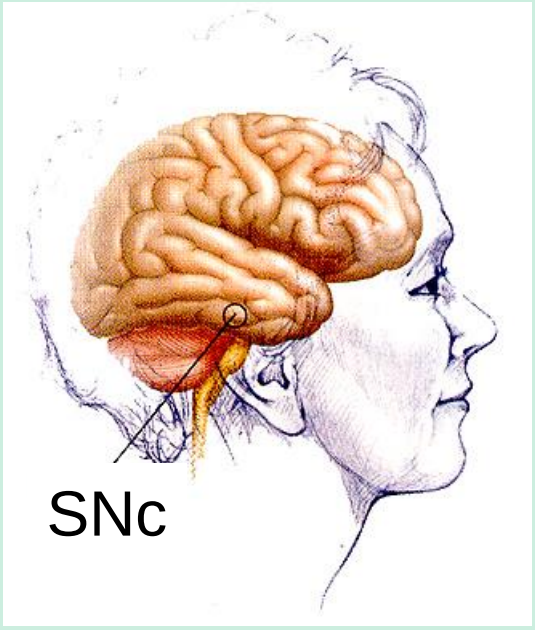
Widespread destruction of **substantia nigra** (**pars compacta)** that sends Dopamine secreting nerve fibers to caudate nucleus and putamen

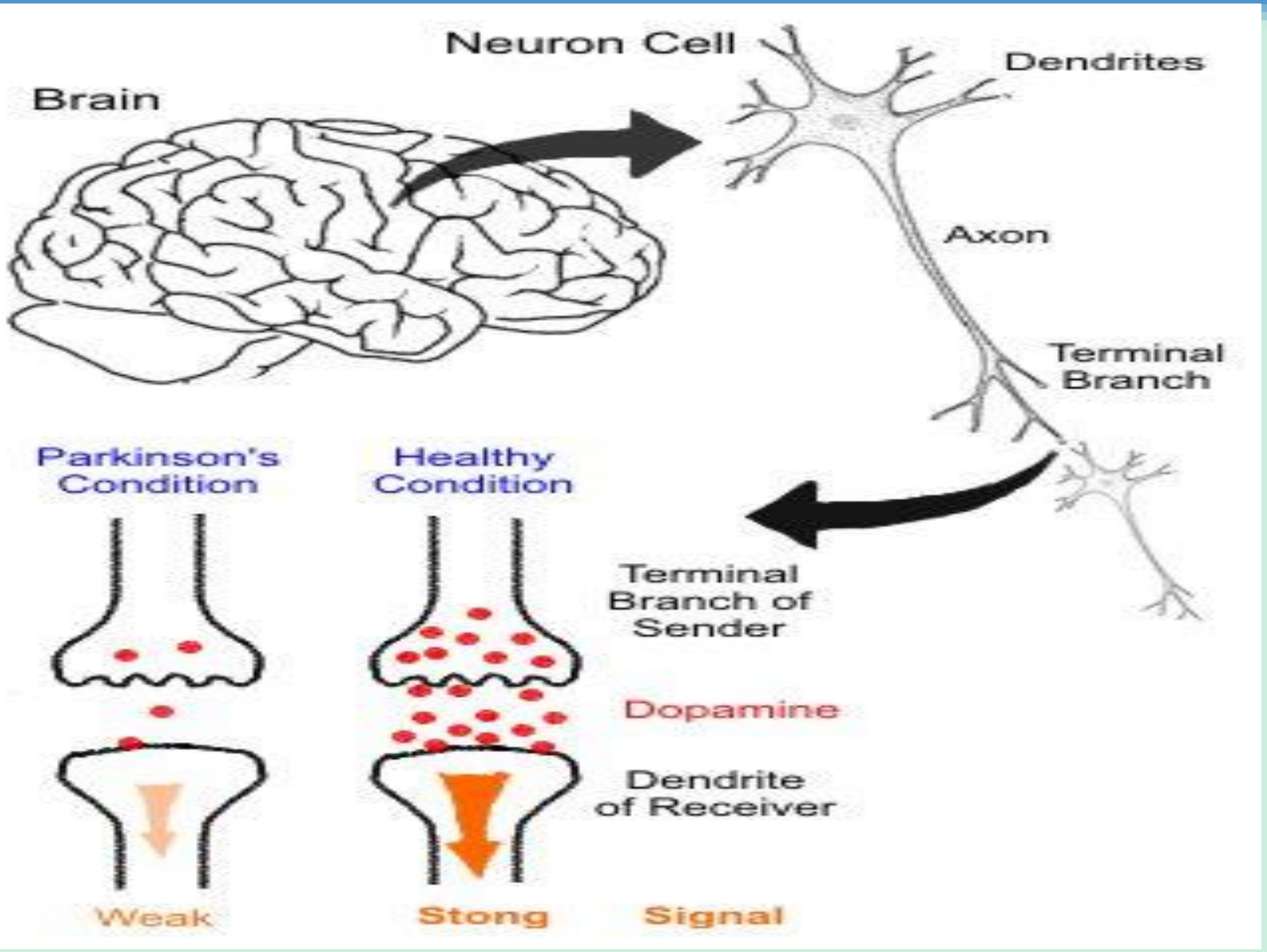
Parkinson's Disease

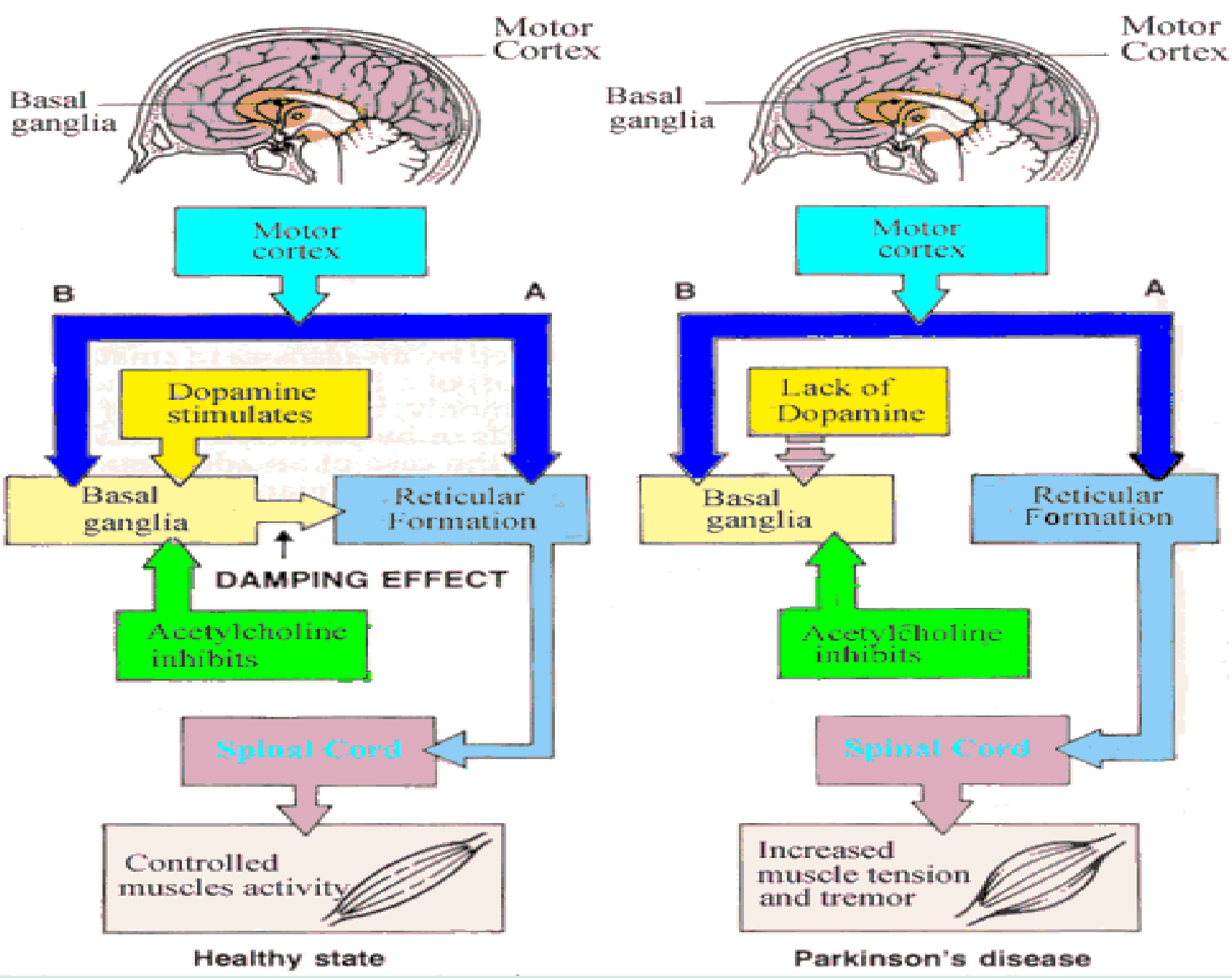
Pathophysiology

Exact cause not known

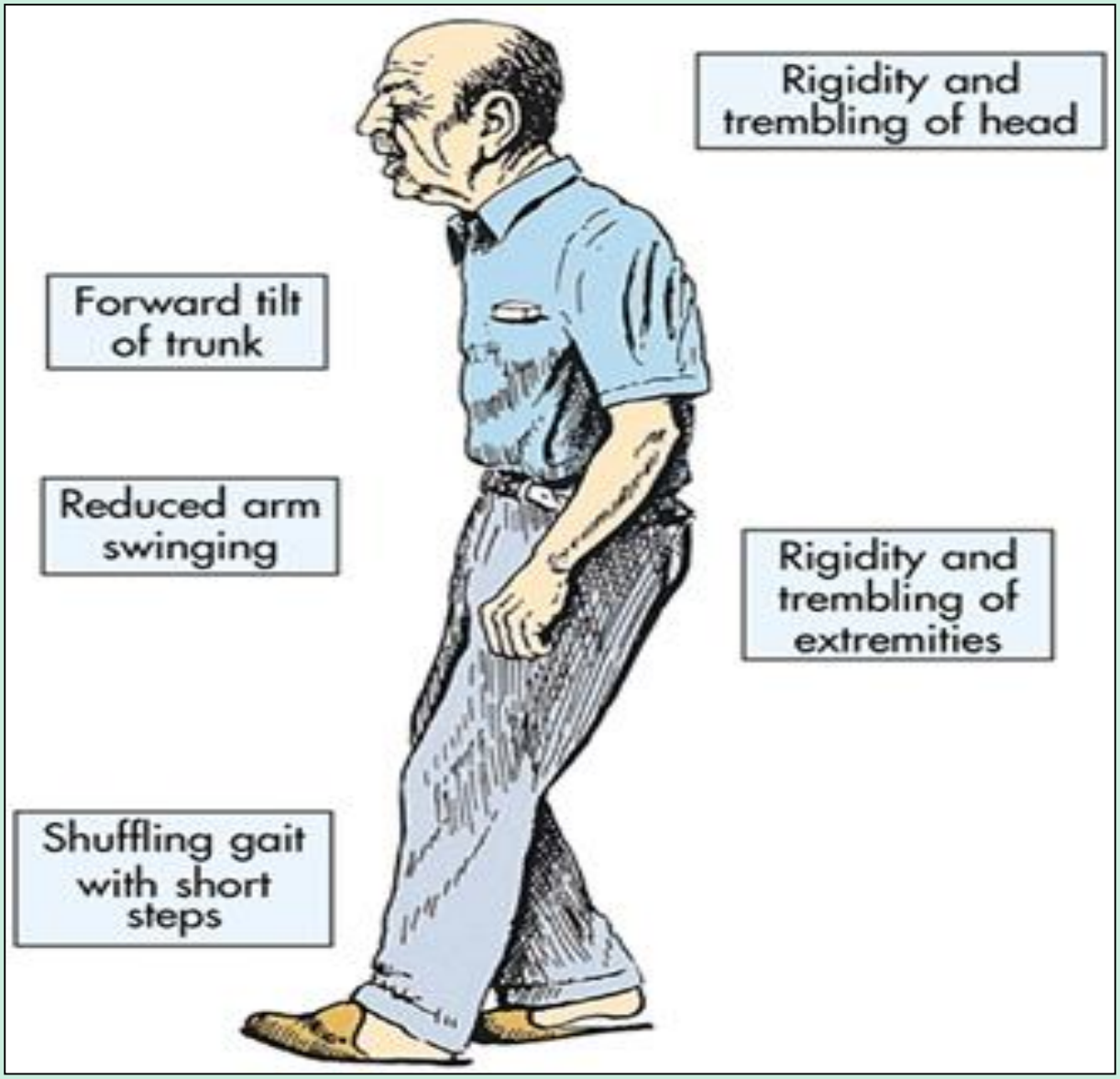
Primary: loss of nigrostriatal DA projection




Neuron Cell
Dendrites
Brain
Axon
Terminal Branch
Parkinson's Condition
Healthy Condition
Terminal Branch of Sender
Dopamine
Dendrite of Receiver
Weak
Stong
Signal


Motor Cortex
Basal ganglia
Motor cortex
B
A
Dopamine stimulates
Basal ganglia
Reticular Formation
DAMPING EFFECT
Acetylcholine inhibits
Spinal Cord
Controlled muscles activity
Healthy state
Motor Cortex
Basal ganglia
Motor cortex
B
A
Lack of Dopamine
Basal ganglia
Reticular Formation
Acetylcholine inhibits
Spinal Cord
Increased muscle tension and tremor
Parkinson's disease

Parkinson's Disease



Signs And Symptoms of Parkinson's Disease

1. Resting Tremor (involuntary)
2. Bradykinesia/ Akinesia (serious difficulty in initiating movement)
3. Rigidity
4. Postural instability by impaired postural reflexes → poor balance
5. Dysphagia, Speech disorders, abnormal gait
6. Depression
7. Dementia

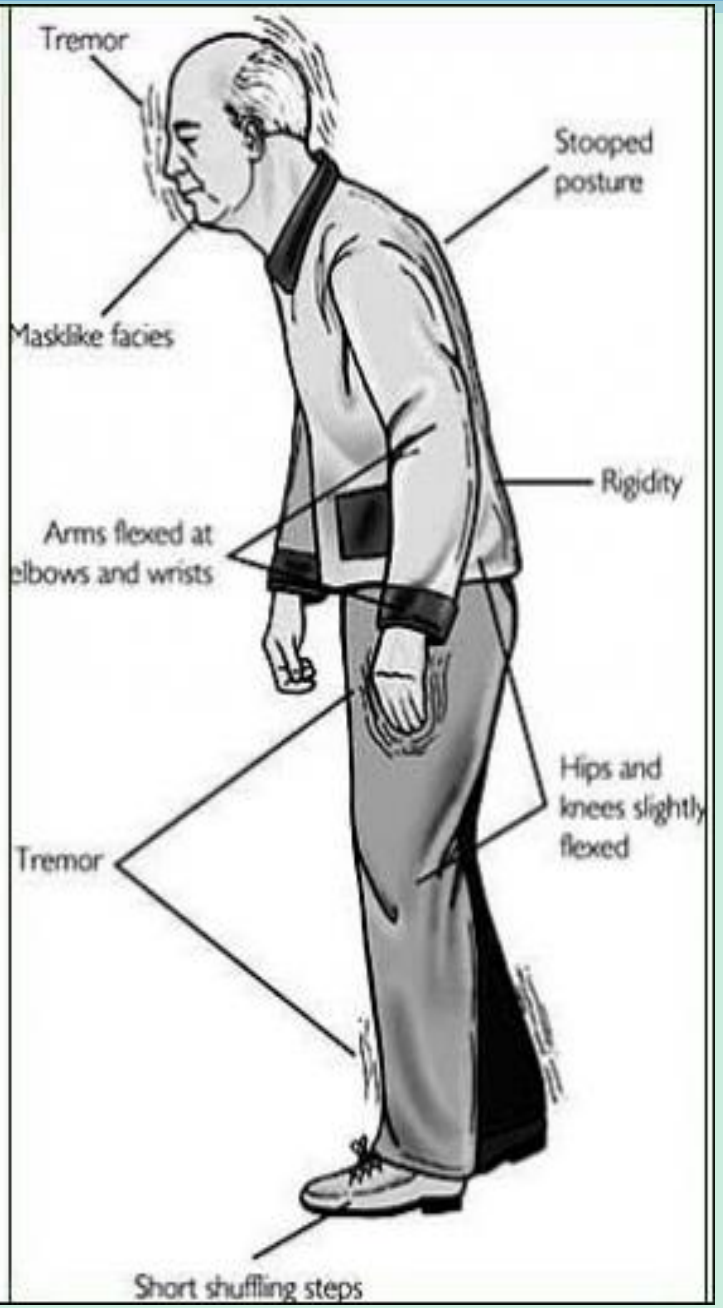
What is Parkinson's Disease?

Parkinson's disease (PD) is chronic and progressive movement disorder, meaning that symptoms continue and worsen over time. Nearly one million people in the US are living with Parkinson's disease. The cause is unknown, and although there is presently no cure, there are treatment options such as medication and surgery to manage its symptoms.

Parkinson's involves the malfunction and death of vital nerve cells in the brain, called neurons. Parkinson's primarily affects neurons in the an area of the brain called the substantia nigra. Some of these dying neurons produce dopamine, a chemical that sends messages to the part of the brain that controls movement and coordination. As PD progresses, the amount of dopamine produced in the brain decreases, leaving a person unable to control movement normally.

The specific group of symptoms that an individual experiences varies from person to person. Primary motor signs of Parkinson's disease include the following.

- **tremor** of the hands, arms, legs, jaw and face
- **bradykinesia** or slowness of movement
- **rigidity** or stiffness of the limbs and trunk
- **postural instability** or impaired balance and coordination



MCQ

The most distressing feature of Parkinson's disease is

- A. Rigidity
- B. Tremor
- C. Akinesia
- D. Depression
- E. Postural instability

Treatment of Parkinson's Disease

- **L Dopa**
- **L Deprenyl** → inhibits MAO that causes destruction of dopamine
- **Transplanted Foetal Dopamine** *Cells*
- **Destroying part of feedback circuitry** to stop abnormal signals to motor cortex

Huntington’s Disease

Huntington’s Disease

Neurodegenerative genetic disorder that affects muscle coordination and leads to

- cognitive decline and
- psychiatric problems

- Typically in mid-adult life, 30 to 40 years (juvenile form atypical in children and adolescence)

- Most common genetic cause of abnormal involuntary writhing movements called CHOREA, so called Huntington's chorea

Huntington's Disease…

- **Prime working years** → deteriorates a person's physical and mental abilities and has no cure
- A child of a parent with HD has a **50/50** chance of carrying the **Faulty gene**
- Today, there are approximately 30,000 symptomatic Americans and more than 200,000 at-risk of inheriting the disease

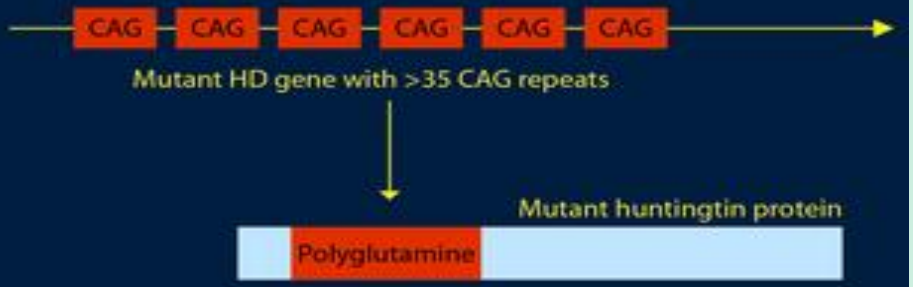
Abnormal Gene in Huntington's Disease

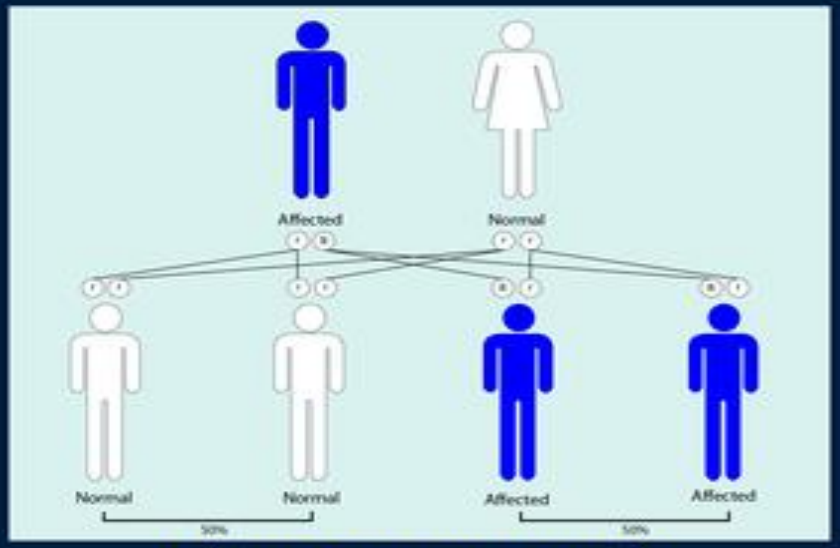
Repeating CAG codons that code for multiple **extra glutamine amino acids** in abnormal neuronal cell protein called Huntingtin

Huntington's disease

HD gene/*HTT* gene (4p16.3)

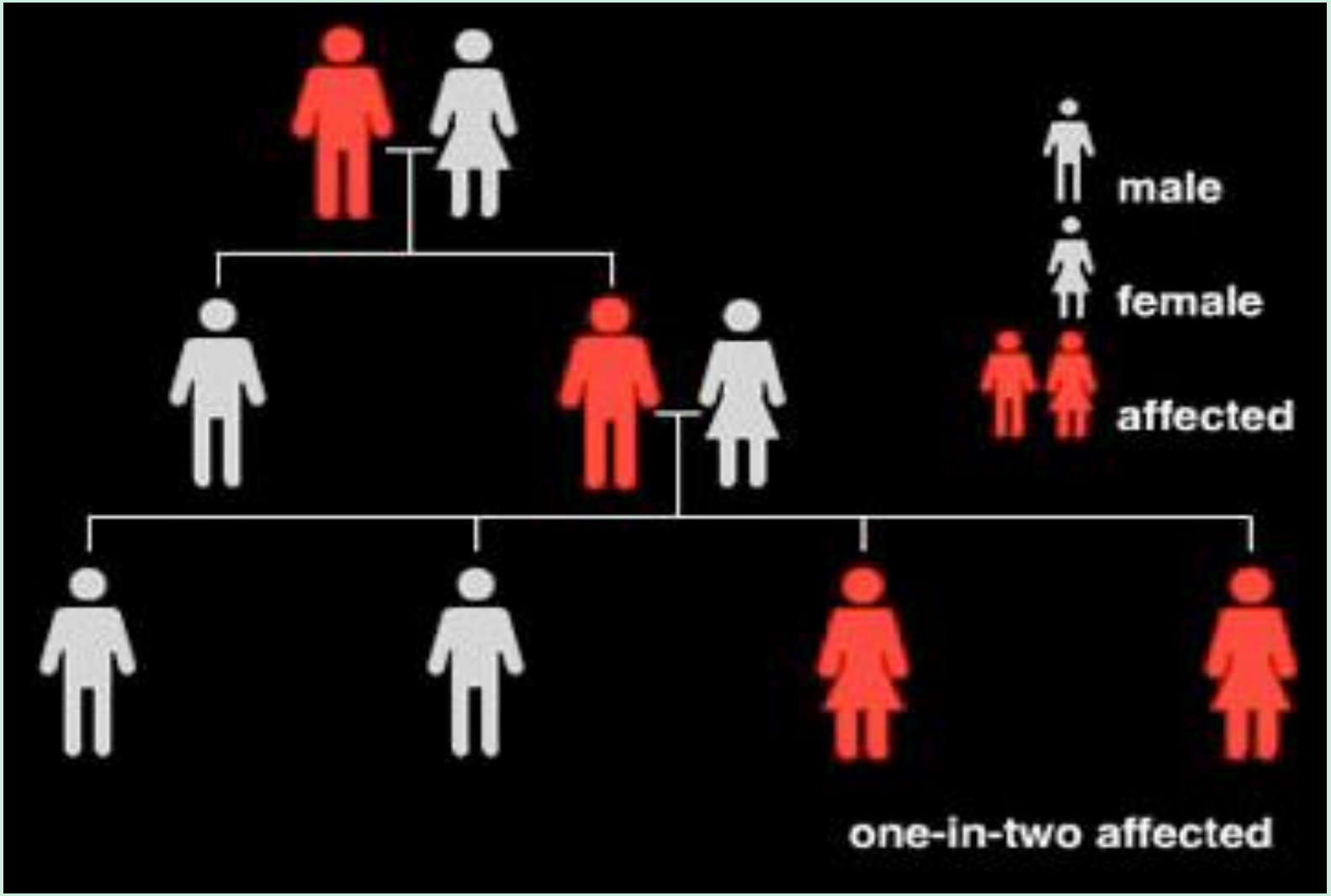
Chromosome 4



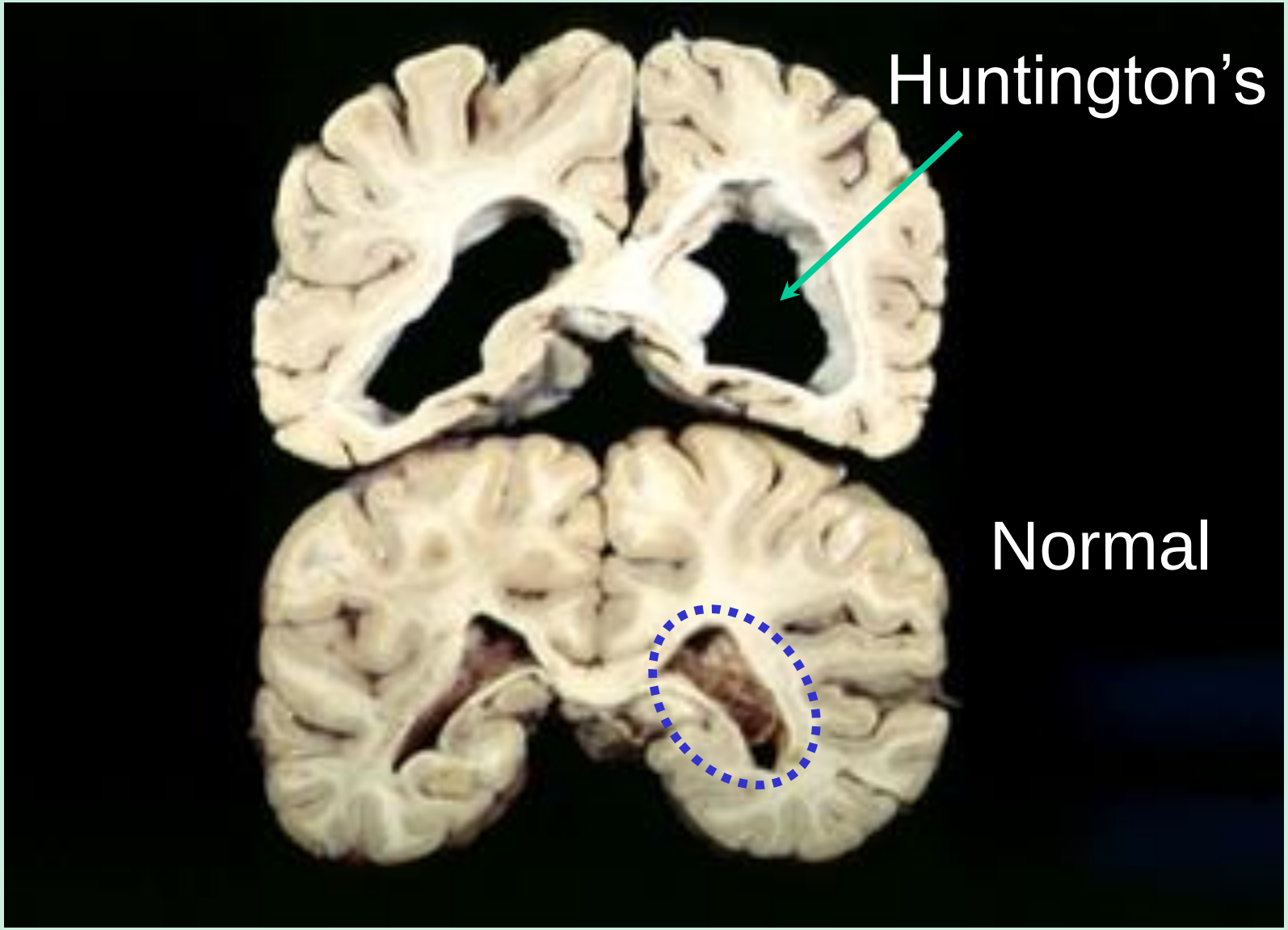


Autosomal Dominant Inheritance

Inheritance of Huntington's Disease



Huntington's disease Pathophysiolology



Pathophysiology of HD

Atrophy of Striatum

Loss of striatal GABAergic neurons in caudate and putamen and Acetyl choline neurons in many parts of brain

GABA inhibits and loss of inhibition → distorted movements

Loss of acetyl choline secreting neurons → Dementia

Abnormal Gene has been found → Abnormal neuronal cell protein called Huntingtin → symptoms

Symptoms And Signs

- Personality changes, mood swings & depression
- Forgetfulness & impaired judgment
- Unsteady gait & involuntary movements **(chorea)**→ starts with flicking movements and progressive severe distortional movements
- Slurred speech, difficulty in swallowing & significant weight loss

Huntington's Disease

- **Etiology**
  - Autosomal dominant progressive chorea and dementia
  - Defective huntingtin protein (chromosome 4)
  - Degeneration of cholinergic and GABA–ergic cells in BG
  - Relative excess dopamine
- **Manifestations**
  - Middle age onset
  - Chorea
  - Violent outbursts, psychosis, withdrawal
- **Treatment**
  - Dopamine antagonists
  - Genetic screening

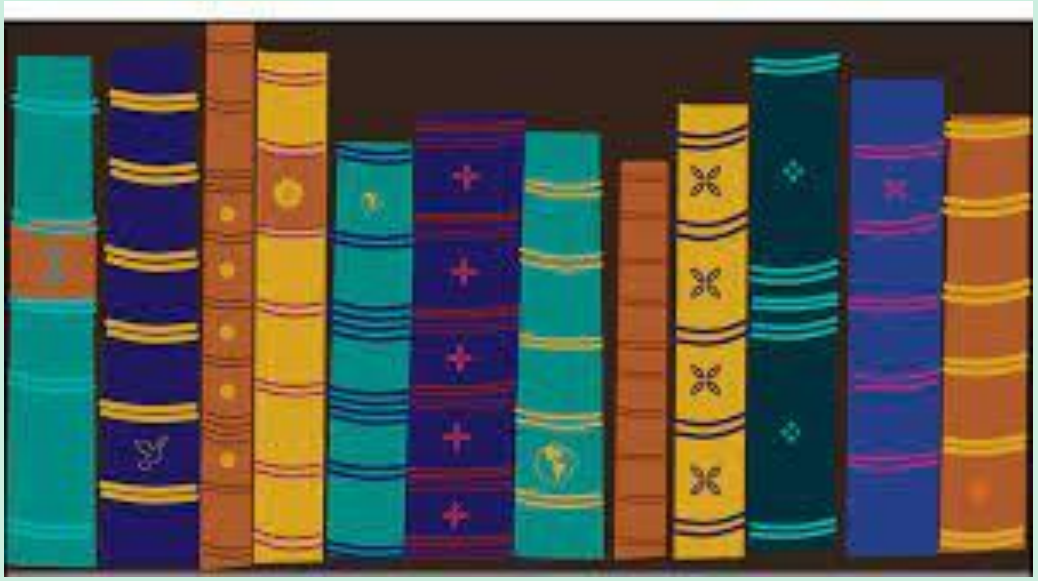
Huntington's Disease

Management of Huntingtin's Disease

- No Cure So far
- Gene therapy
- Genetic Counselling

References

- Guyton
- Lauralee Sherwood
- Henry H. Yin and Barbara J, 2006.
- Gregory *et al.*, 2010.
- Robert *et al.*, 2018




THANK YOU.