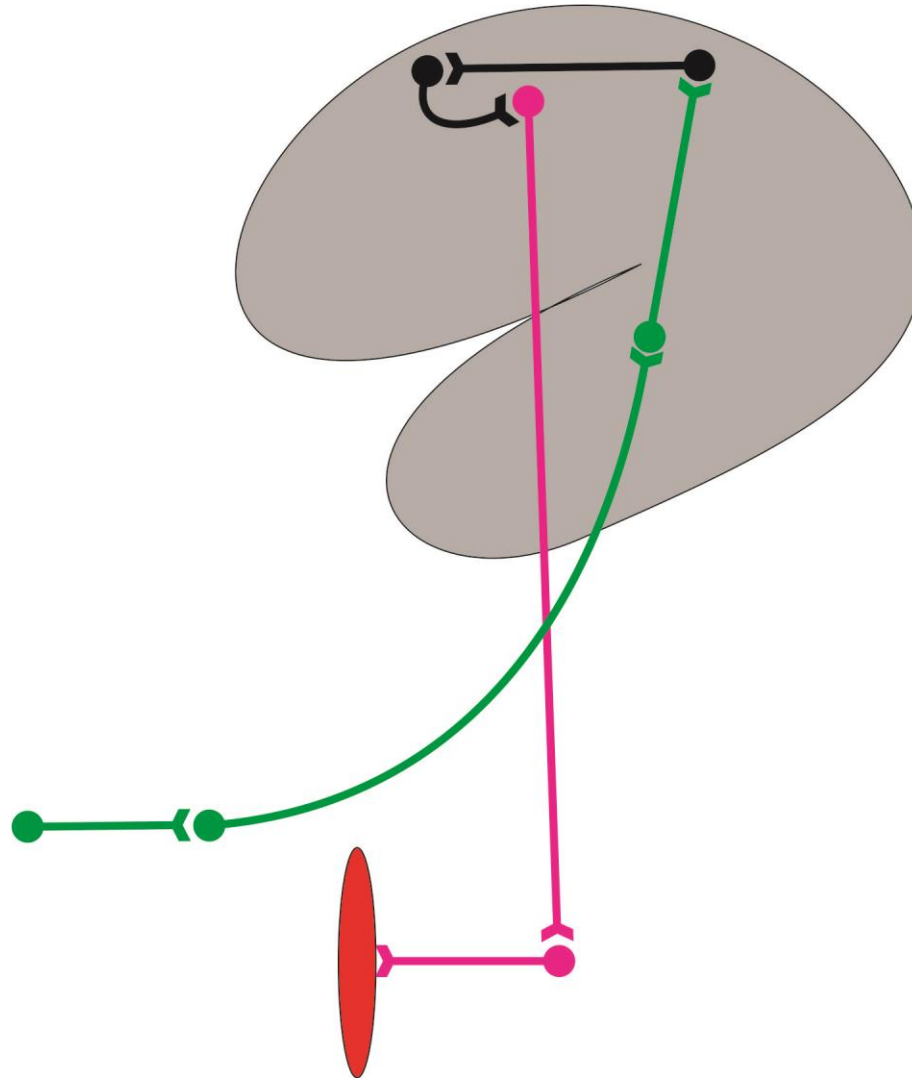


# **Basal Ganglia**

Steven McLoon  
Department of Neuroscience  
University of Minnesota

# Is the nervous system really this simple?

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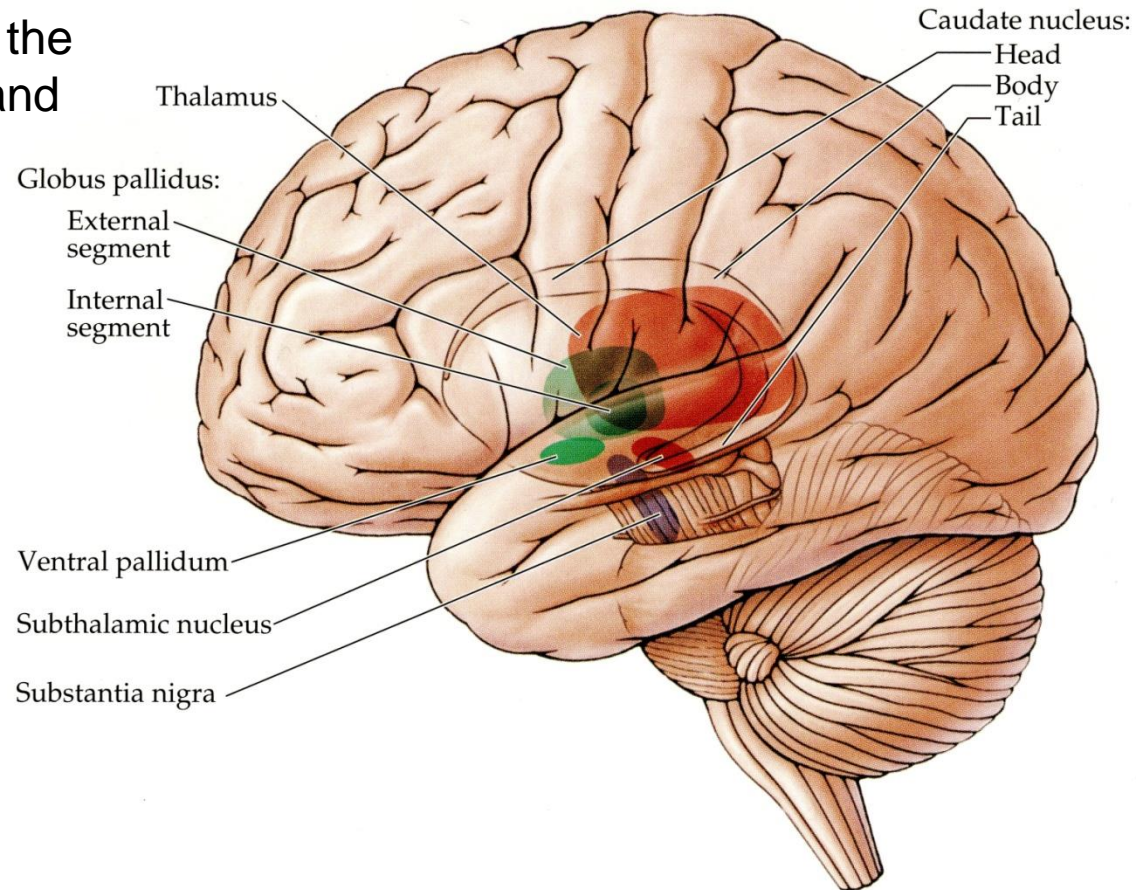


# Basal Ganglia Anatomy

The basal ganglia consist of a number of nuclei in the basal region of the telencephalon, diencephalon and midbrain.

The largest nuclei are:

- Striatum
  - Caudate nucleus
  - Putamen
  - Nucleus accumbens
- Globus pallidus
- Subthalamic nucleus
- Substantia nigra



# Basal Ganglia Anatomy

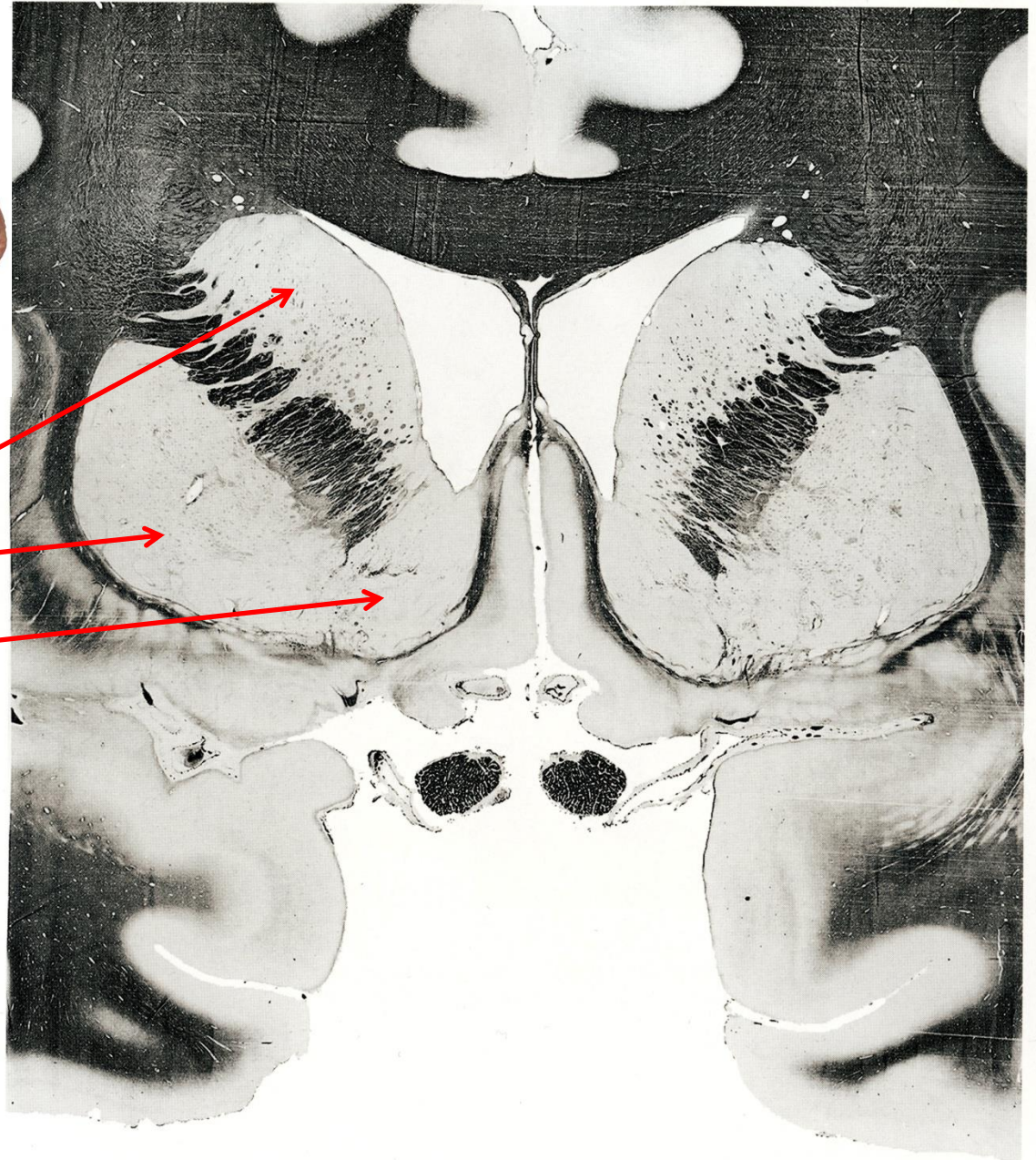
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- The striatum is part of the telencephalon.
- The striatum is composed of three nuclei:
  - caudate nucleus
  - putamen
  - nucleus accumbens
- Anatomically, the striatum is more like one nucleus divided by the internal capsule, which comes together in front of the internal capsule.



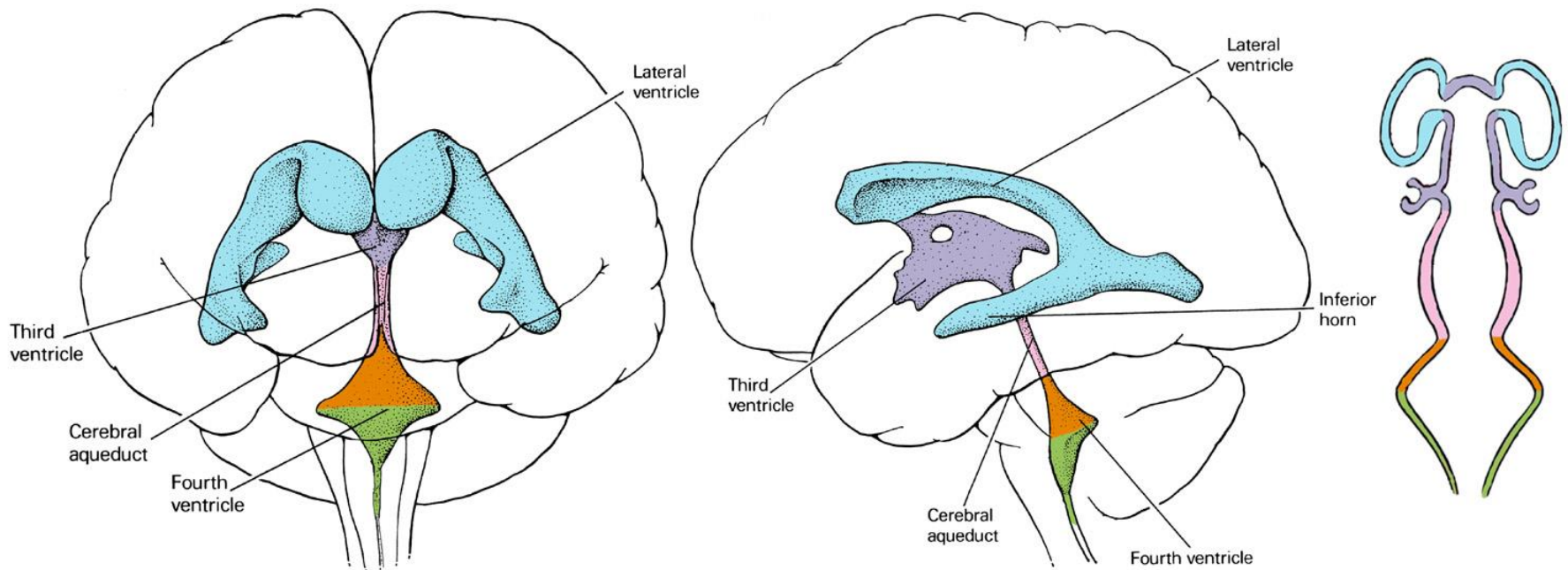
Striatum:

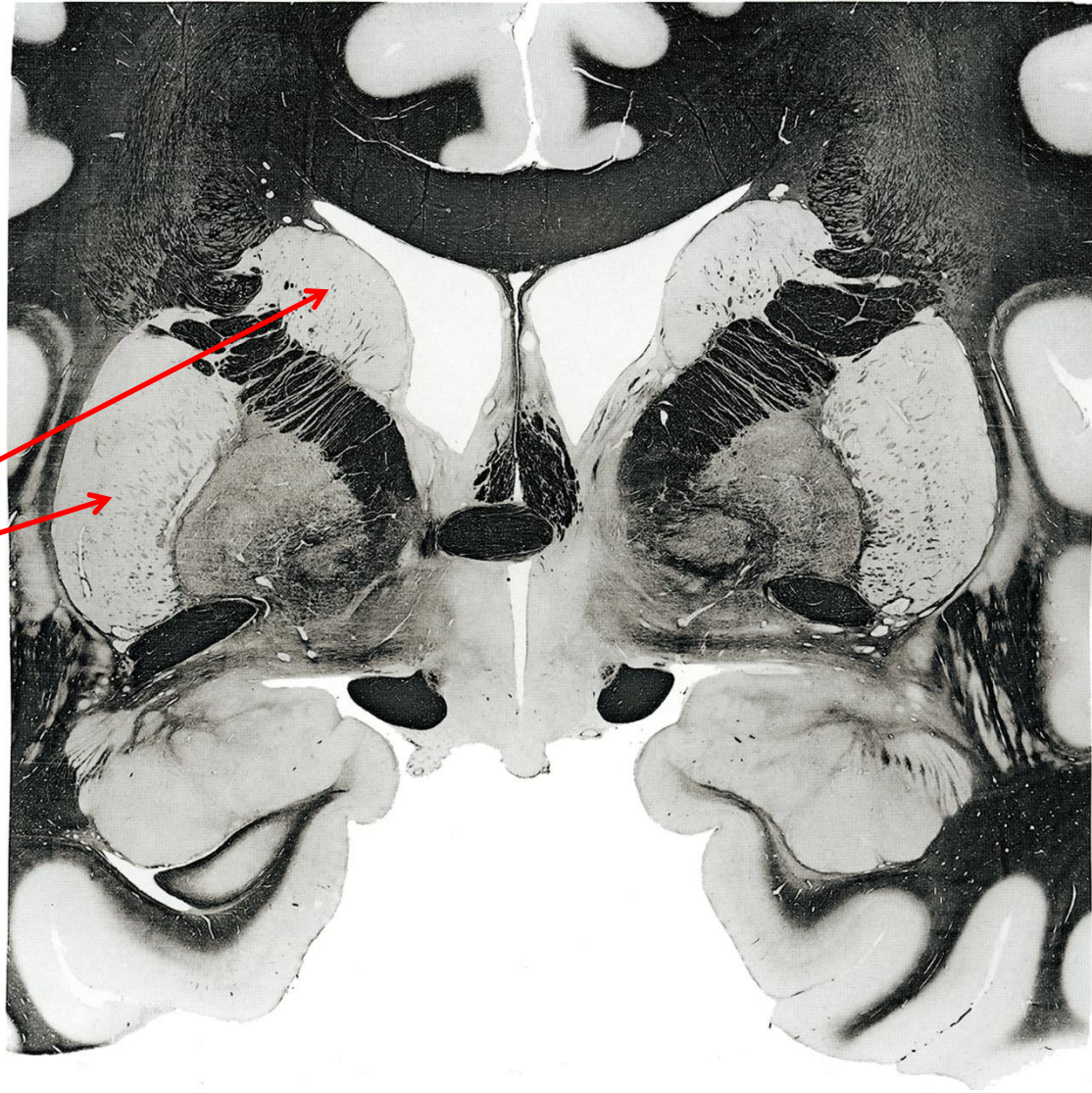
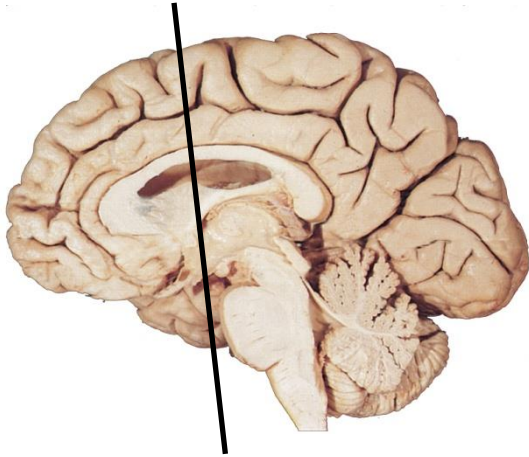
- caudate nucleus
- putamen
- nucleus accumbens



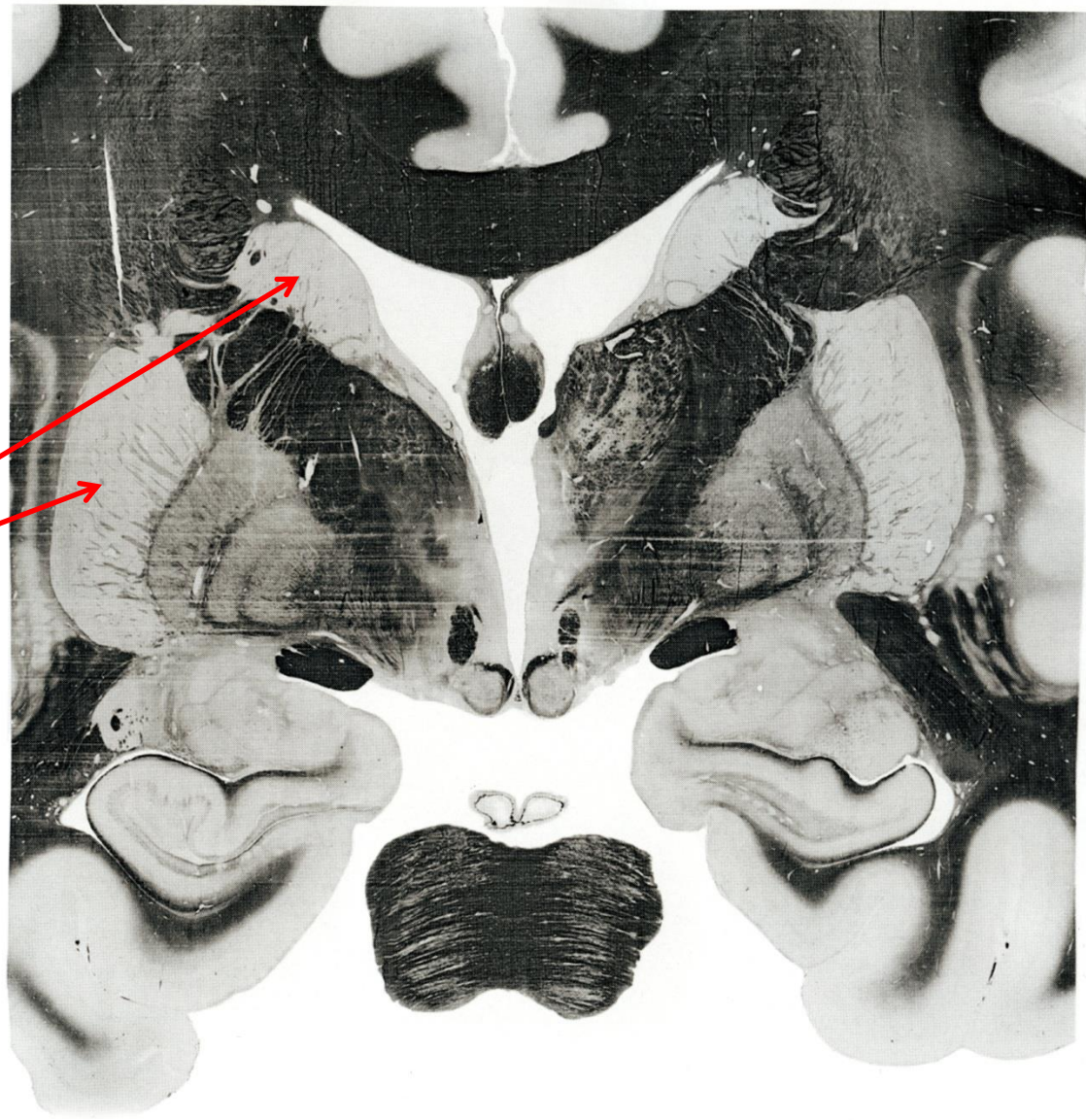
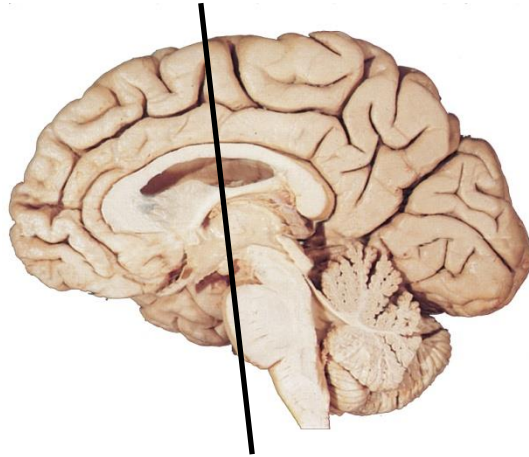
# Basal Ganglia Anatomy

- The caudate nucleus follows the lateral ventricle.



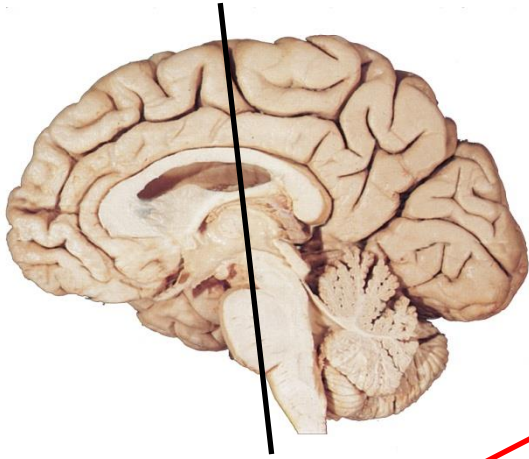


- caudate nucleus
- putamen



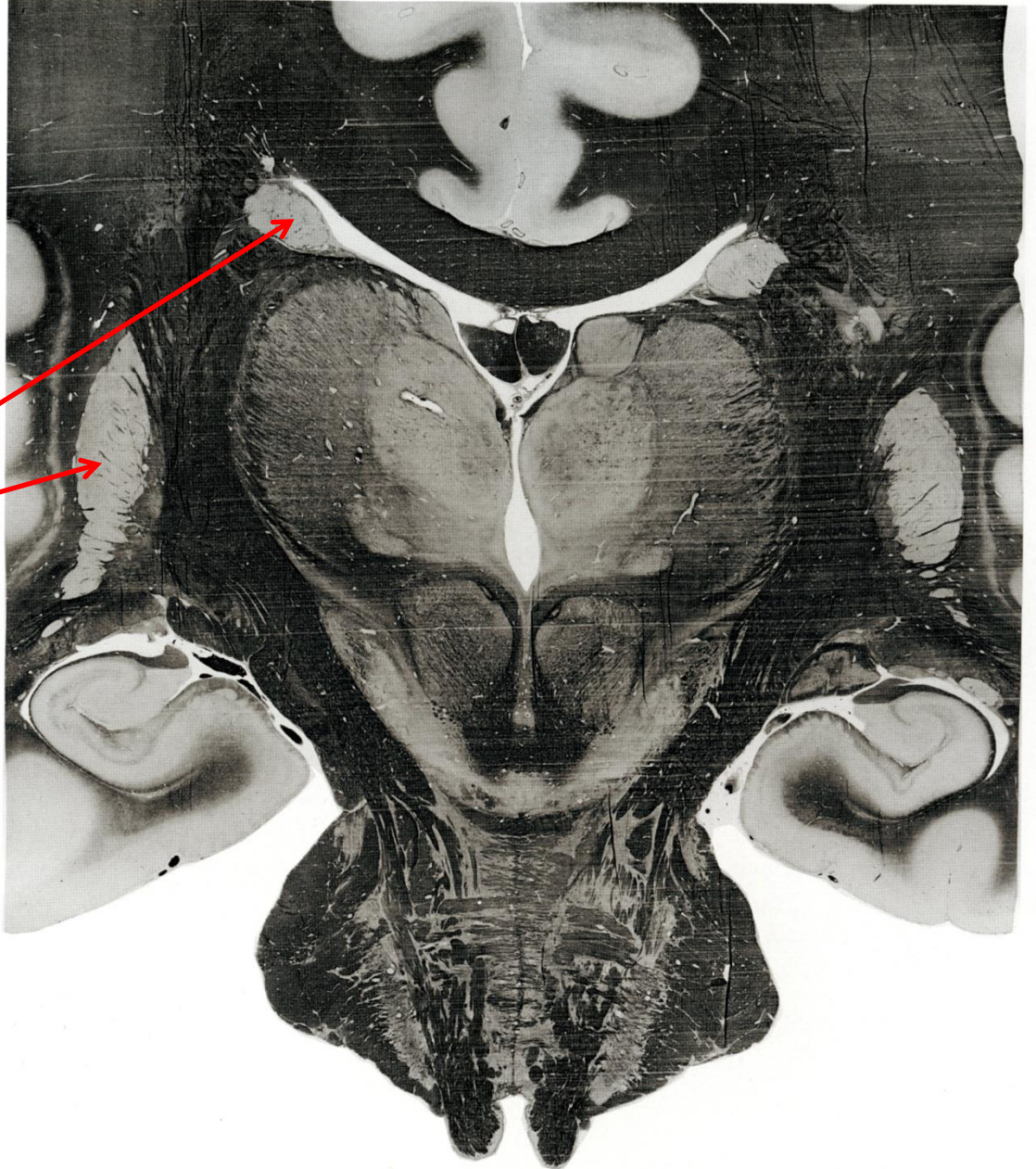
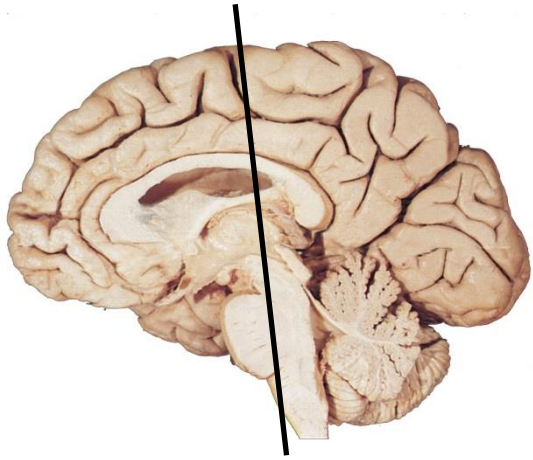
- caudate nucleus
- putamen



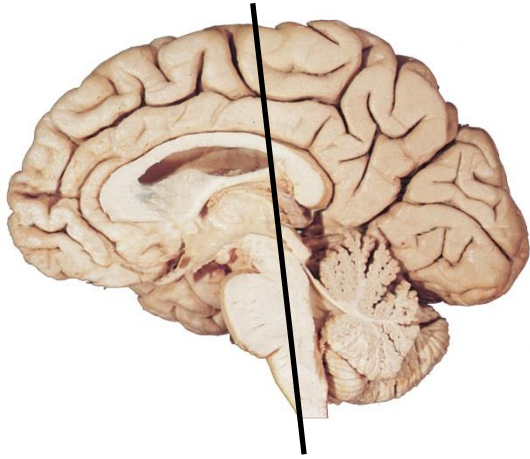


- caudate nucleus
- putamen

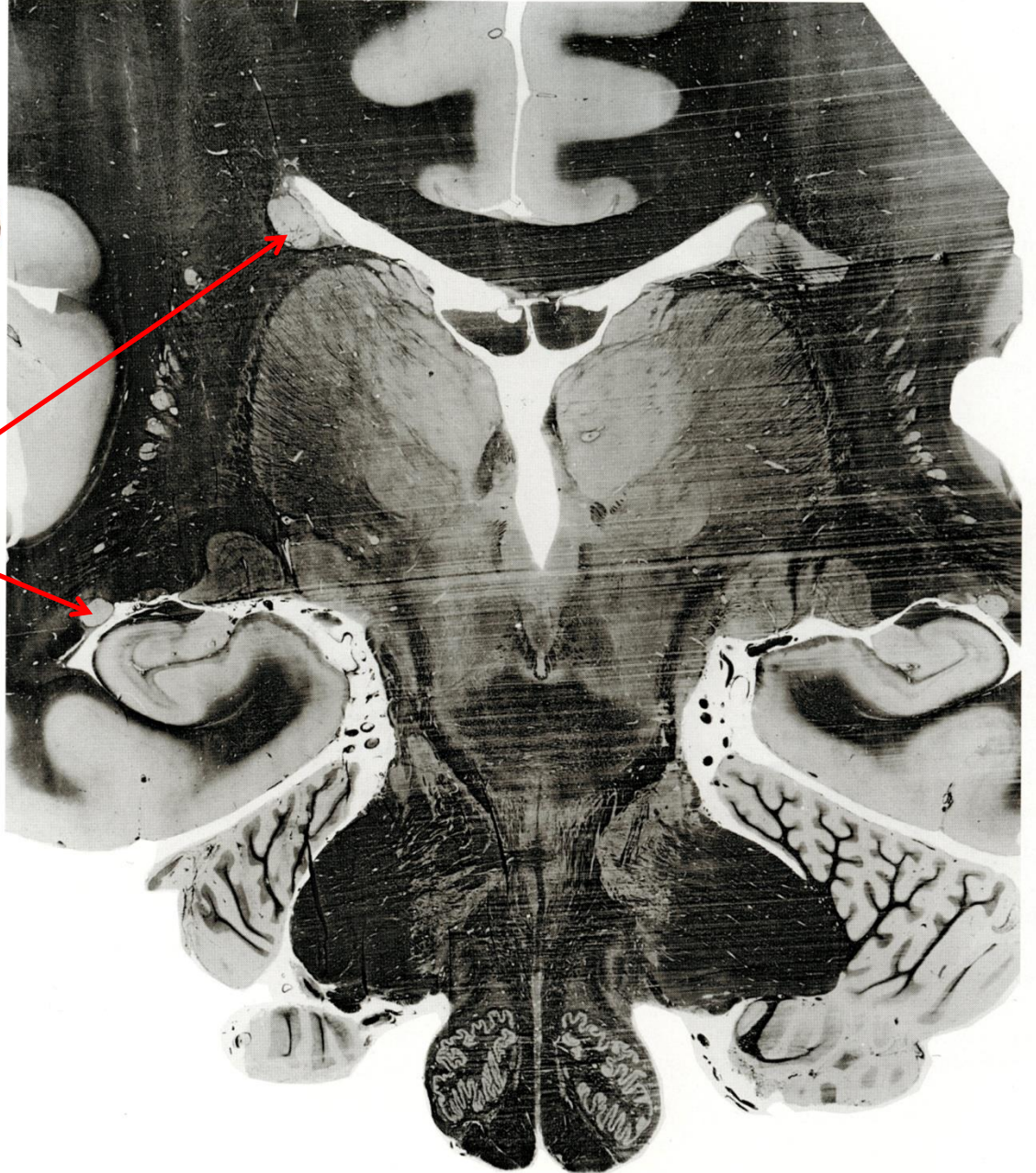




- caudate nucleus
- putamen



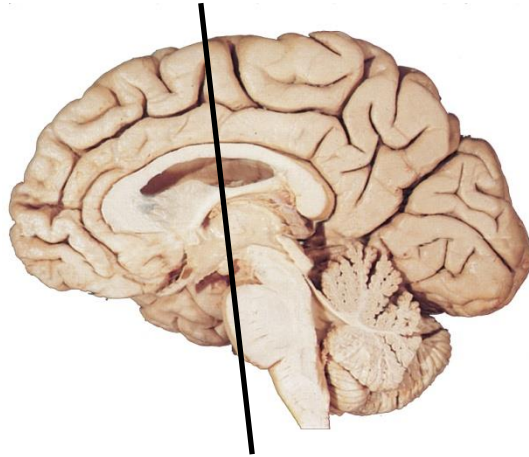
- caudate nucleus



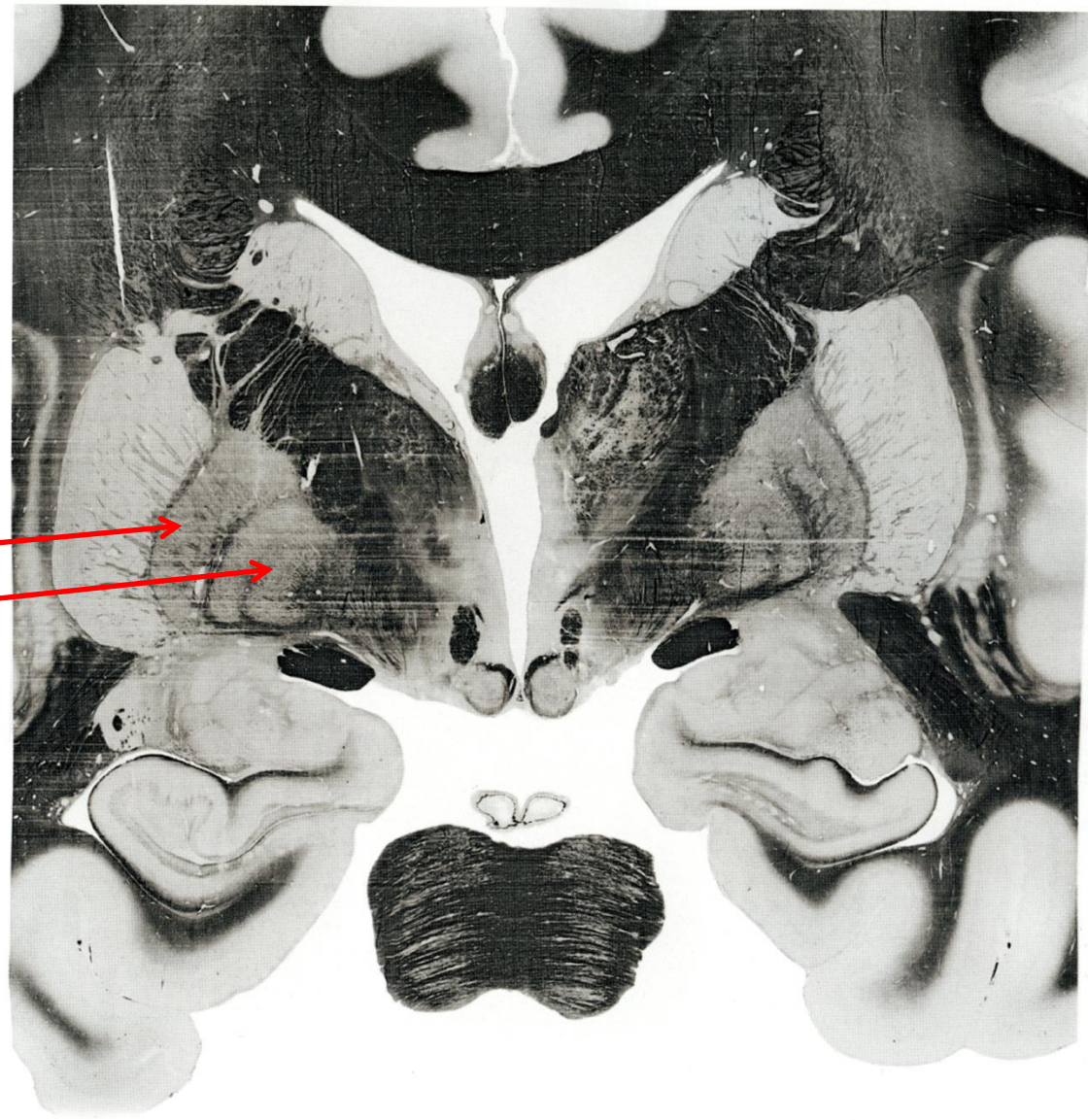
# Basal Ganglia Anatomy

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- Globus pallidus is part of the telencephalon.
- Globus pallidus is positioned just medial to the putamen.
- Globus pallidus has two divisions:
  - external (GPe) – part of the internal basal ganglia circuitry
  - internal (GPi) – part of the basal ganglia output system



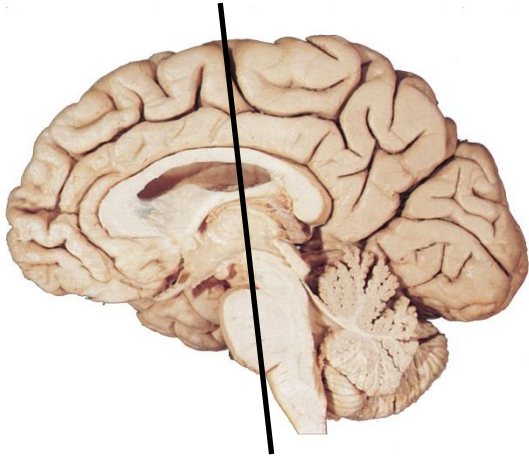
- GPe
- GPi



# Basal Ganglia Anatomy

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- The subthalamic nucleus is part of the diencephalon.
- The subthalamic nucleus is positioned just below the thalamus and above the substantia nigra in the midbrain.



- subthalamic nucleus

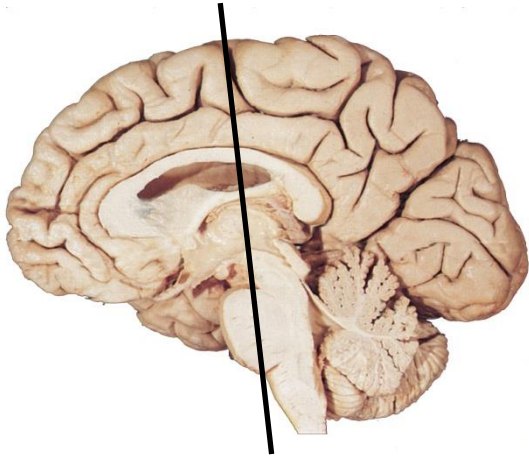


# Basal Ganglia Anatomy

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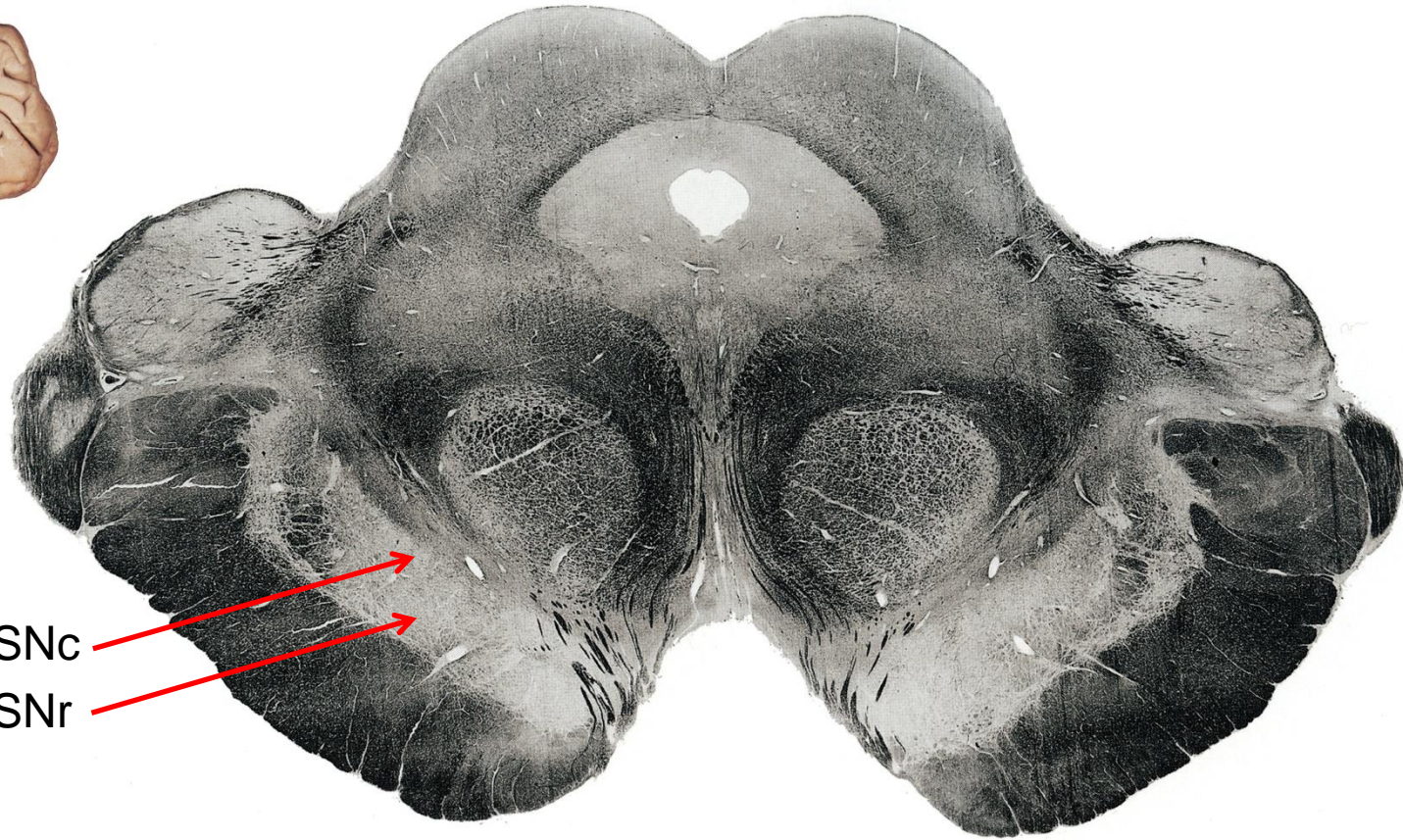
- The substantia nigra is part of the midbrain (mesencephalon).
- The substantia nigra is positioned just below the subthalamic nucleus, between the cerebral peduncle (anterior) and red nucleus (posterior).
- The substantia nigra has two parts:
  - Pars compacta (SNc) – part of the internal basal ganglia circuitry (pigmented & dopamenergic)
  - Pars reticulata (SNr) – part of the basal ganglia output system





- subthalamic nucleus
- substantia nigra

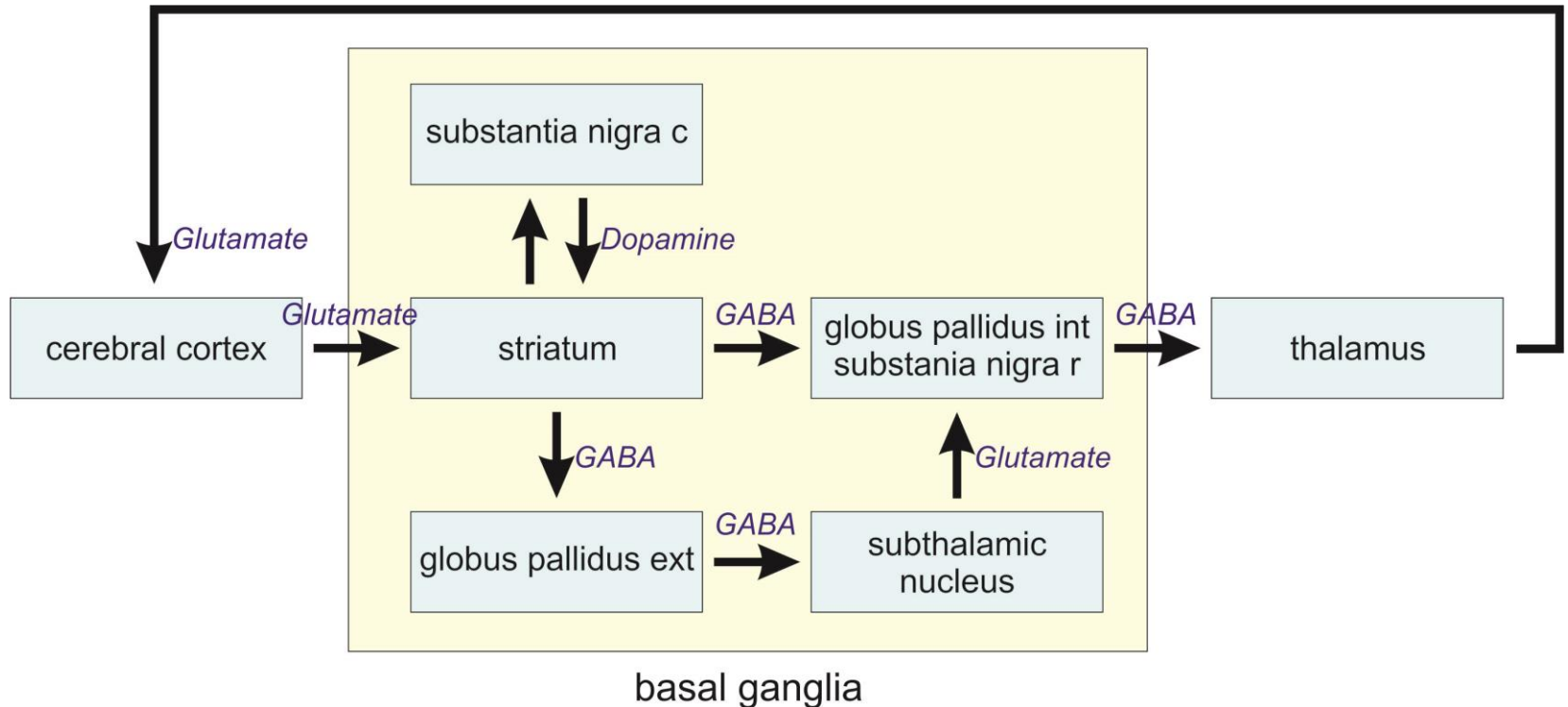




- SNc
- SNr

# Basal Ganglia Circuitry

- The main input to the basal ganglia is from cortex and is to the striatum.
- The input from cortex uses glutamate as the transmitter and is excitatory.



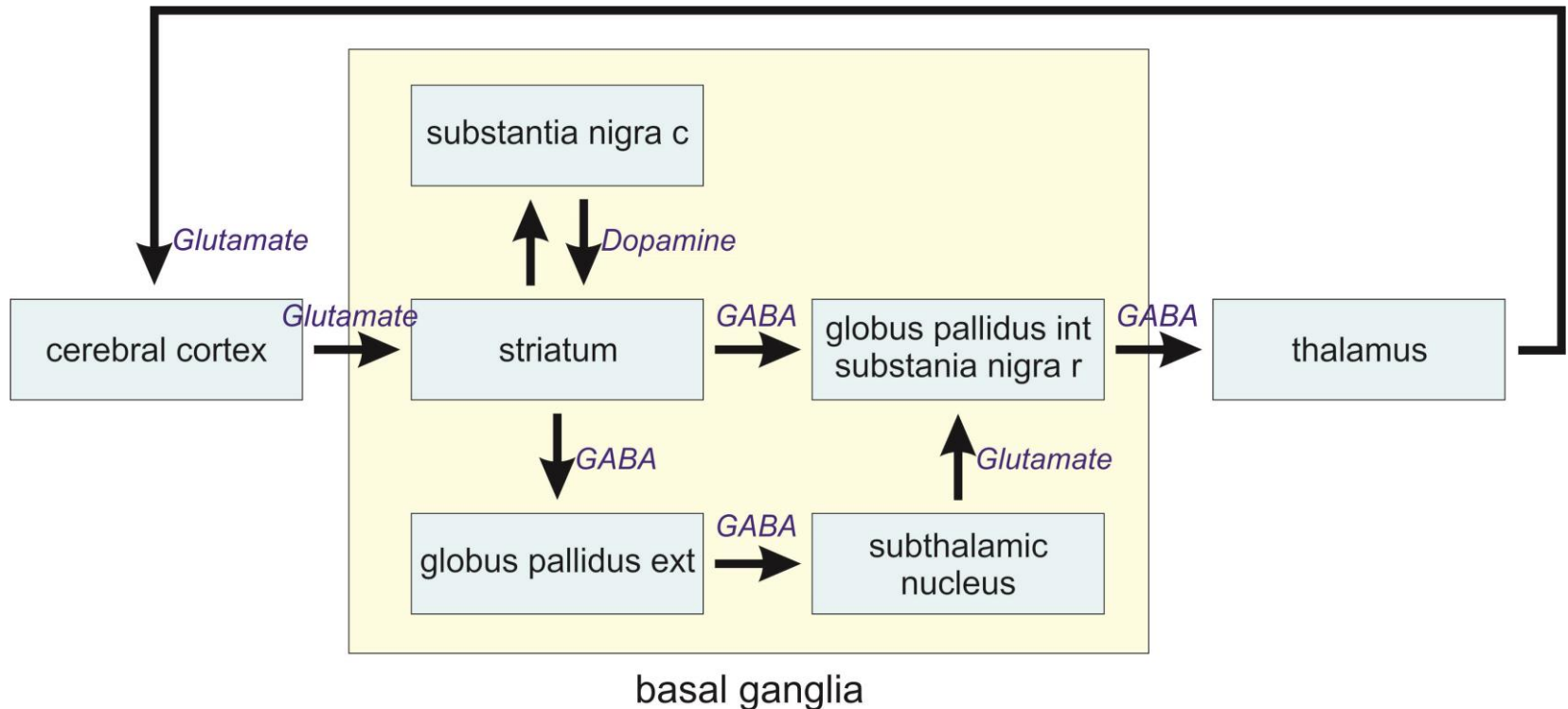
## Basal Ganglia Circuitry

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- Different parts of the striatum serve different functions:
  - caudate – eye movements & cognition
  - putamen – limb, trunk & facial movement
  - nuc. accumbens – emotion, drive & desire

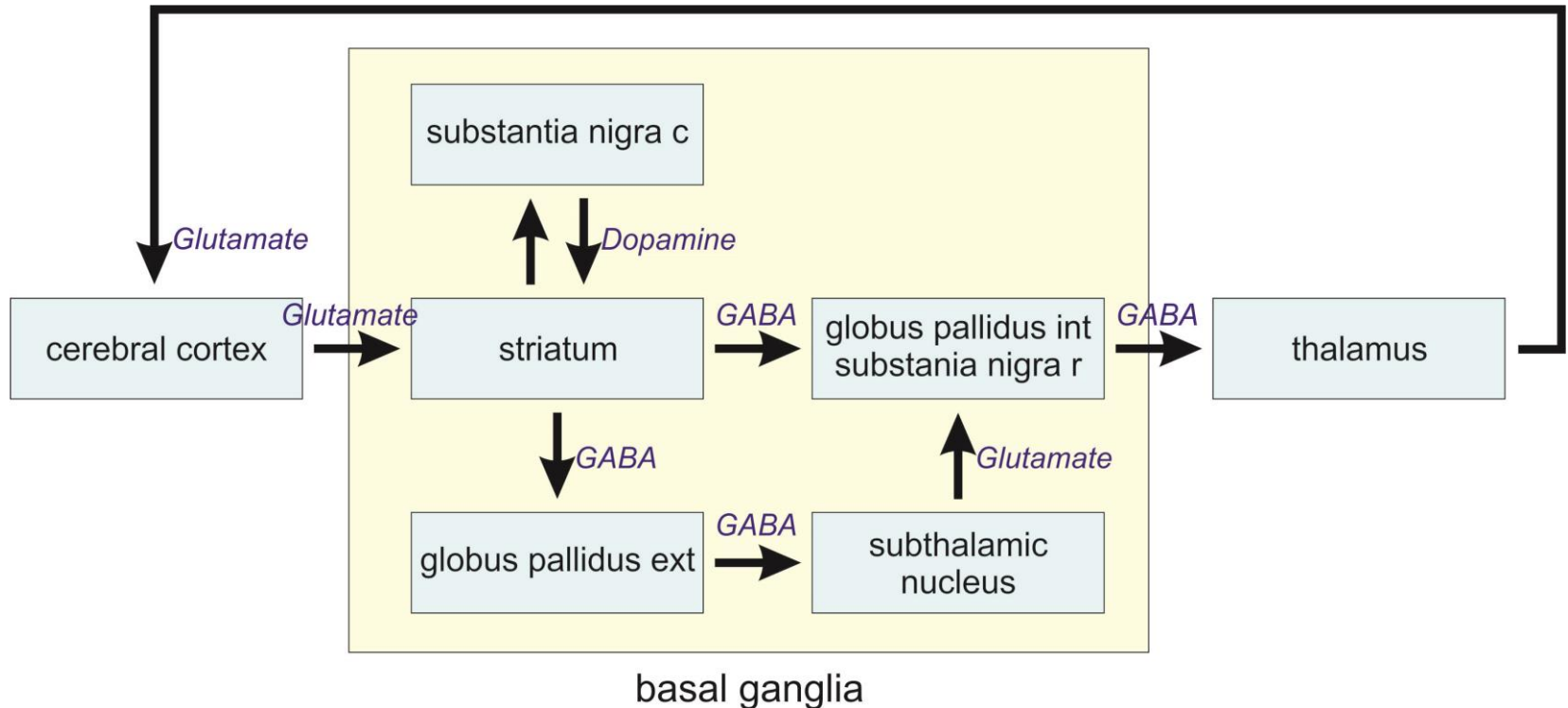
# Basal Ganglia Circuitry

- Medium spiny neurons in the striatum send axons to most basal ganglia nuclei.
- Medium spiny neurons use GABA as the transmitter, which is inhibitory.



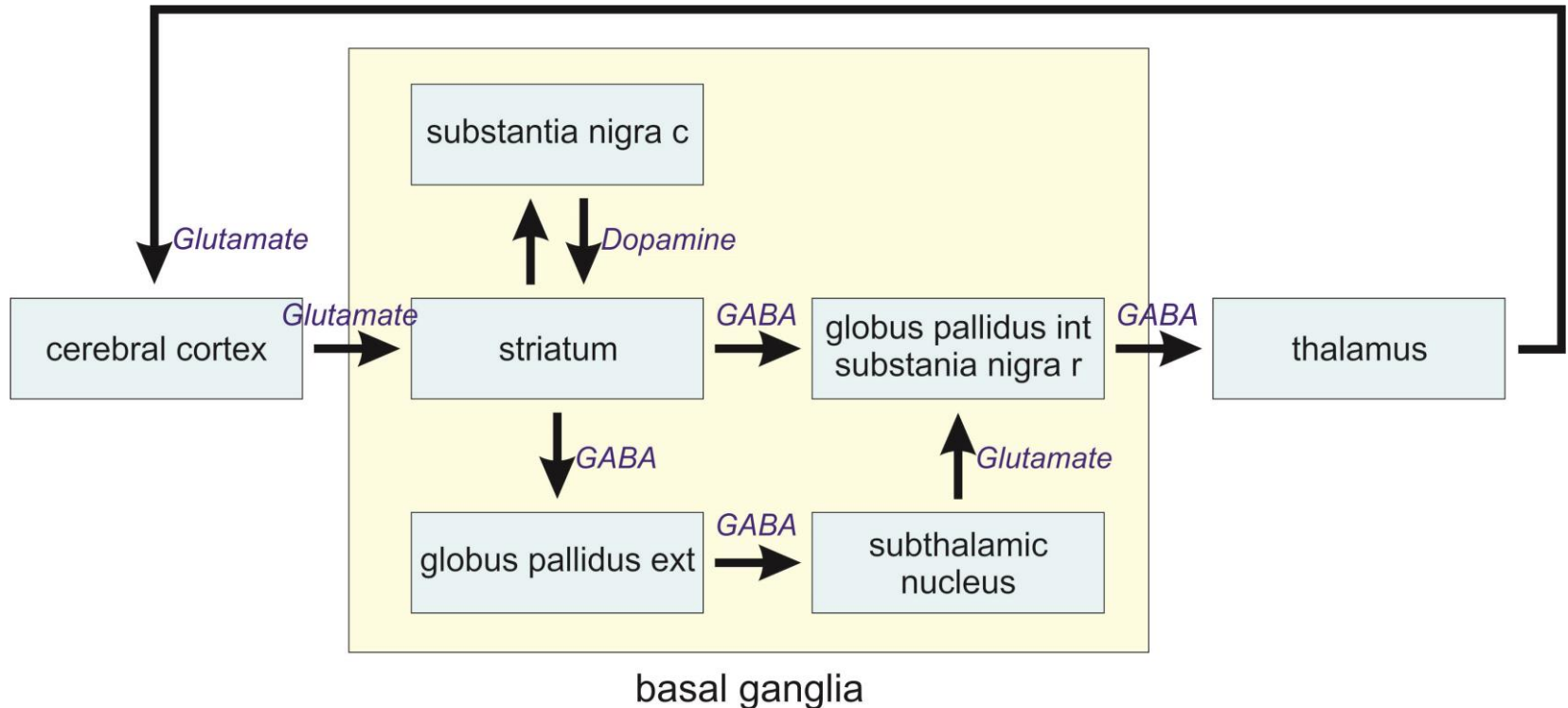
# Basal Ganglia Circuitry

- Intrinsic circuits process the information.
- Almost every known neurotransmitter is used in intrinsic basal ganglia circuitry.



# Basal Ganglia Circuitry

- The main basal ganglia output is from globus pallidus internal (Gpi) and substantia nigra pars reticulata (SNr).
- Basal ganglia connects to the ventral anterior and ventral lateral nuclei of thalamus.
- The output uses GABA and is inhibitory.



# Basal Ganglia Pathology

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- Degeneration of neurons in the basal ganglia can cause:
  - reduced body movements (hypokinesia)
  - increased body movements (hyperkinesia)
- Hypokinesia:
  - akinesia – impaired initiation of movements
  - bradykinesia– slower and reduced movements
  - rigidity – resistance when someone moves a resting limb
- Hyperkinesia include involuntary movements:
  - chorea – rapid movements
  - athetosis – slow writhing movements
  - ballisim – flailing limb movements



# Basal Ganglia Pathology

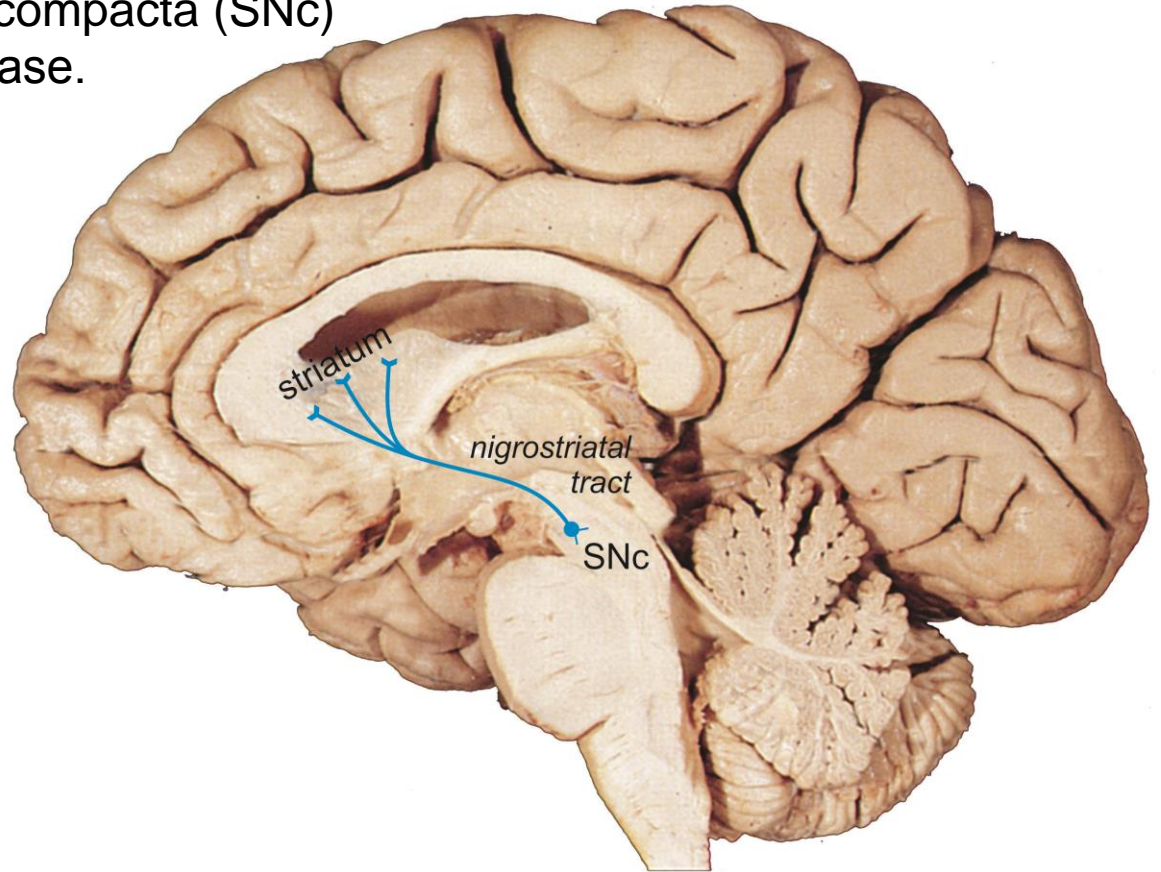
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- Basal ganglia pathologies also cause cognitive deficits and other neurological problems.

# Parkinson's Disease

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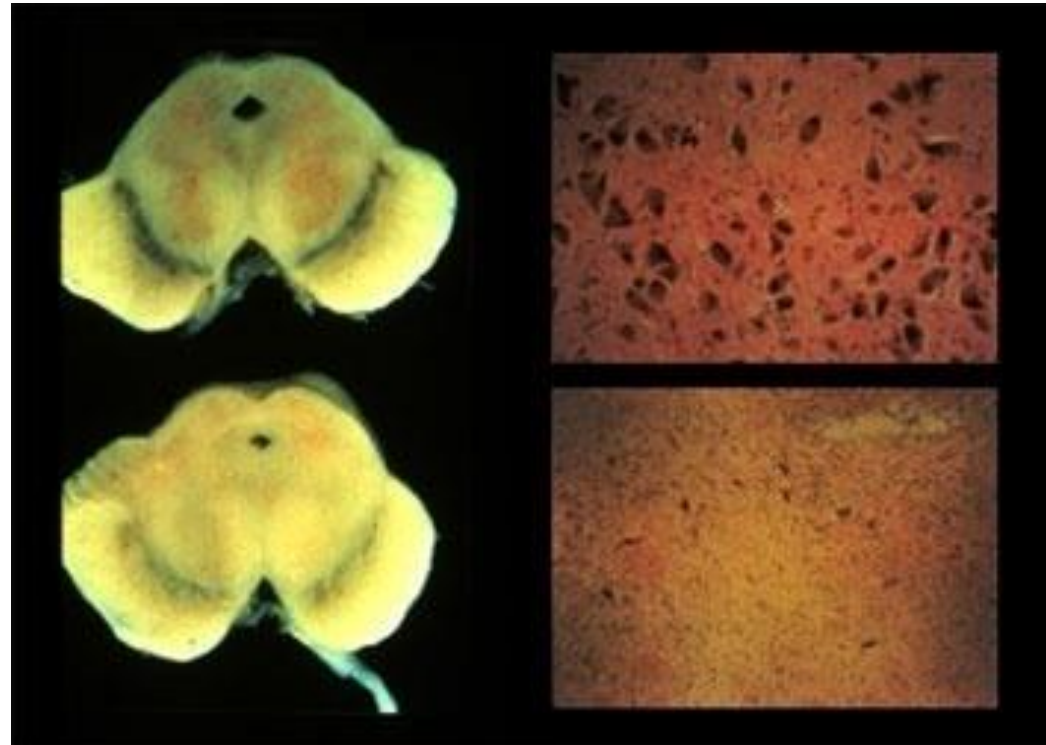
- Degeneration of the dopaminergic neurons in substantia nigra pars compacta (SNc) causes Parkinson's disease.



# Parkinson's Disease

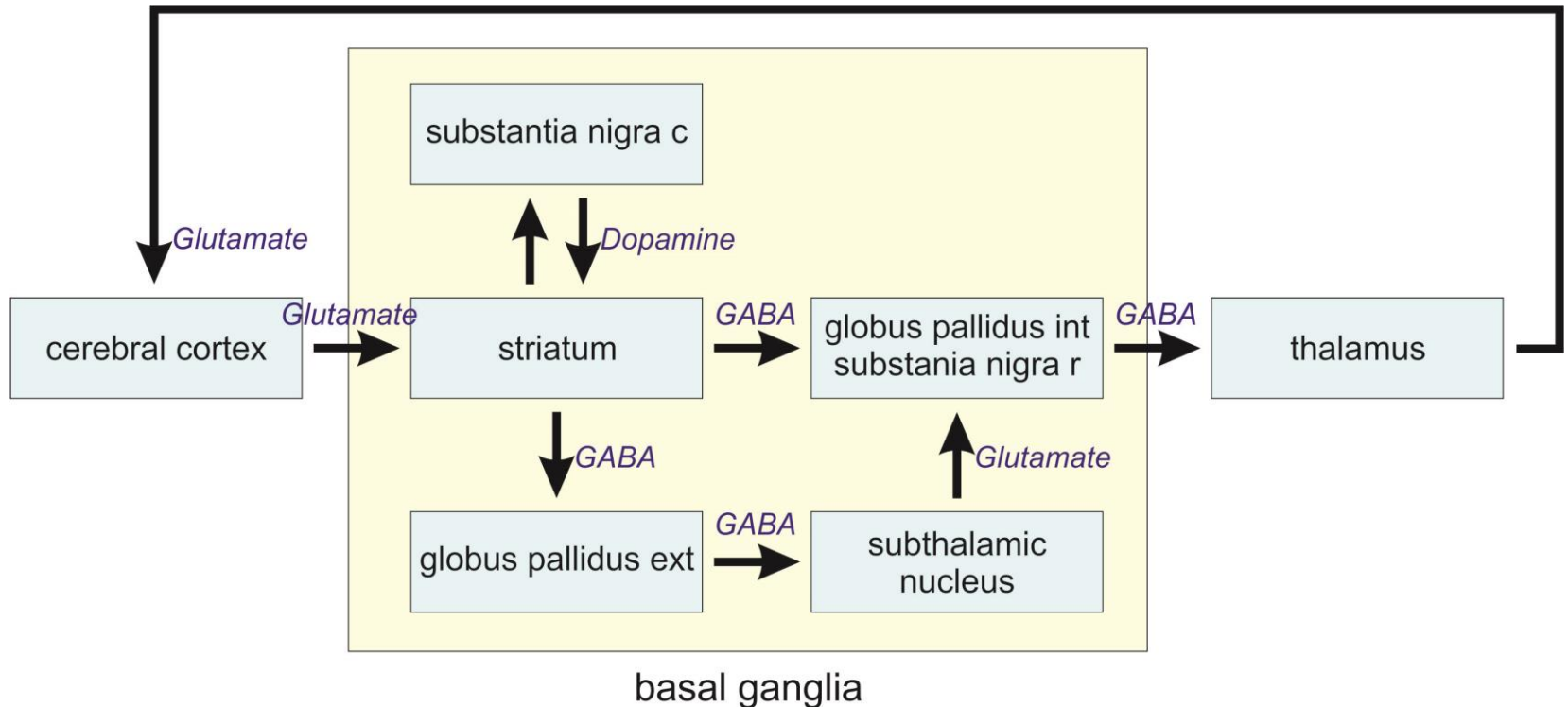
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- Degeneration of the dopaminergic neurons in substantia nigra pars compacta (SNc) causes Parkinson's disease.



# Parkinson's Disease

- Degeneration of the dopaminergic neurons in substantia nigra pars compacta (SNc) causes Parkinson's disease.



# Parkinson's Disease

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- Symptoms (hypokinesia):
  - difficulty initiating movements (akinesia) and slower movements (bradykinesia)
  - resting tremor, pronounced in the hands
  - all muscles resist being moved by another person (rigidity)

## Parkinson's Disease

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- The onset is typically after 50 years of age.
- ~1% of those 60 and older have Parkinson's.
- Consumption of caffeine reduces the risk of Parkinson's

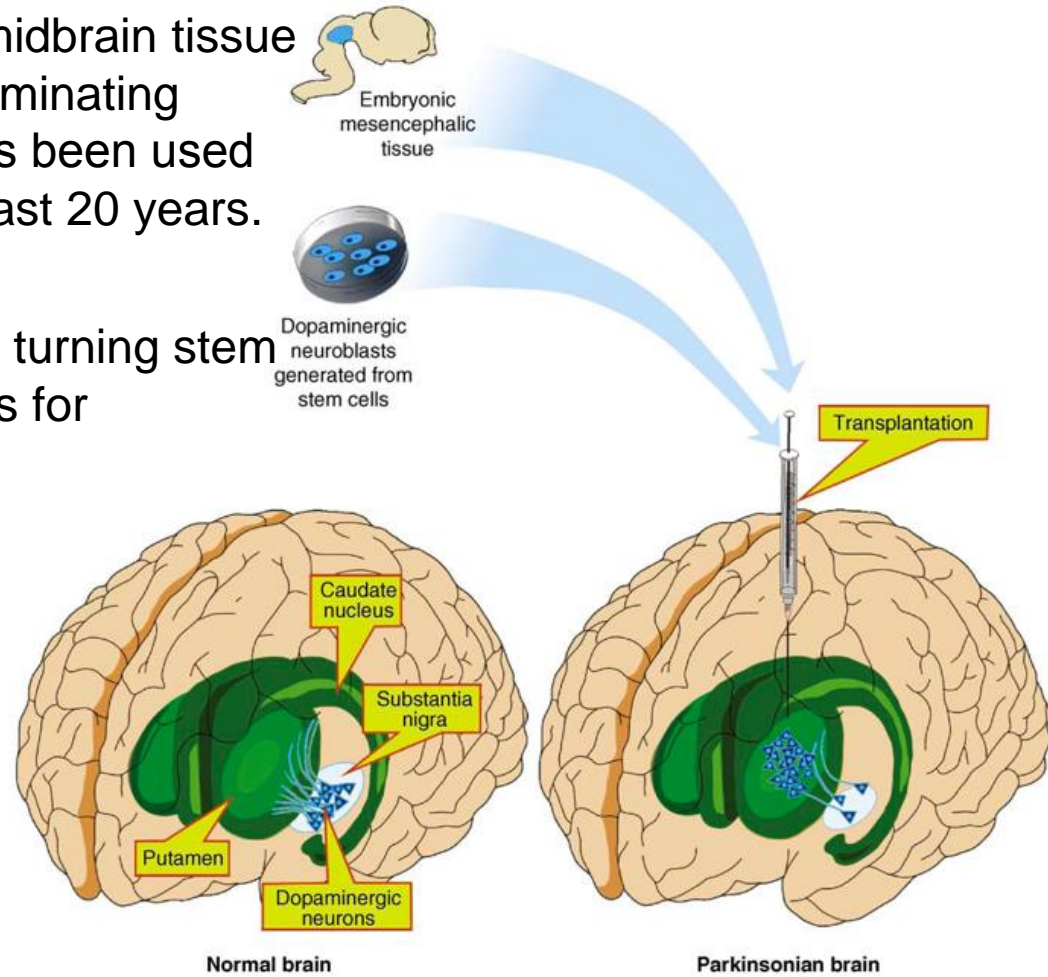
# Parkinson's Disease

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- Treatment is oral administration of L-DOPA; L-DOPA is a dopamine precursor that can cross the blood-brain barrier and is converted into dopamine within the striatum.

# Parkinson's Disease

- Transplantation of embryonic midbrain tissue to the striatum is effective in eliminating Parkinson's in animals, and has been used in over 400 patients over the past 20 years.
- Current research is focused on turning stem cells into dopaminergic neurons for therapeutic cell replacement.





## Parkinson's Disease

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- MPTP was originally synthesized by a chemistry graduate student. He was synthesizing a synthetic morphine for recreational purposes, and MPTP was a major impurity in his chemical reaction.
- He self administered his drug, and within a few days he had Parkinson's disease.
- He was successfully treated with L-DOPA but died a few months later from a cocaine overdose.
- Autopsy showed that his SNc dopaminergic neurons were lost.
- Unfortunately, this experiment was repeated later in the San Francisco drug community.
- MPTP is now used in the laboratory to induce Parkinson's disease in animals for research purposes.

# Huntington's Disease

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- Degeneration of medium spiny neurons in the striatum causes Huntington's disease or Huntington's chorea.
- The main symptom is hyperkinesia: involuntary rapid, random movements of the trunk and limbs; writhing of the hands is common.
- Symptoms typically appear midlife, 35-45 years of age.
- Huntington's disease is due to an inherited, dominant mutation.

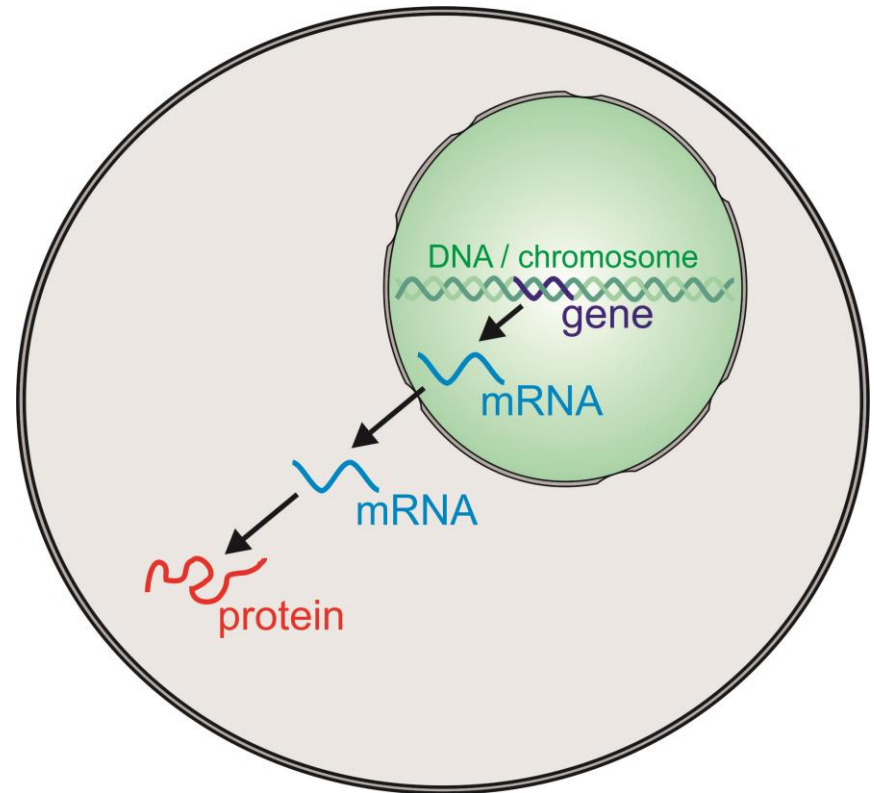
# Genes & Protein Synthesis

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Protein synthesis:

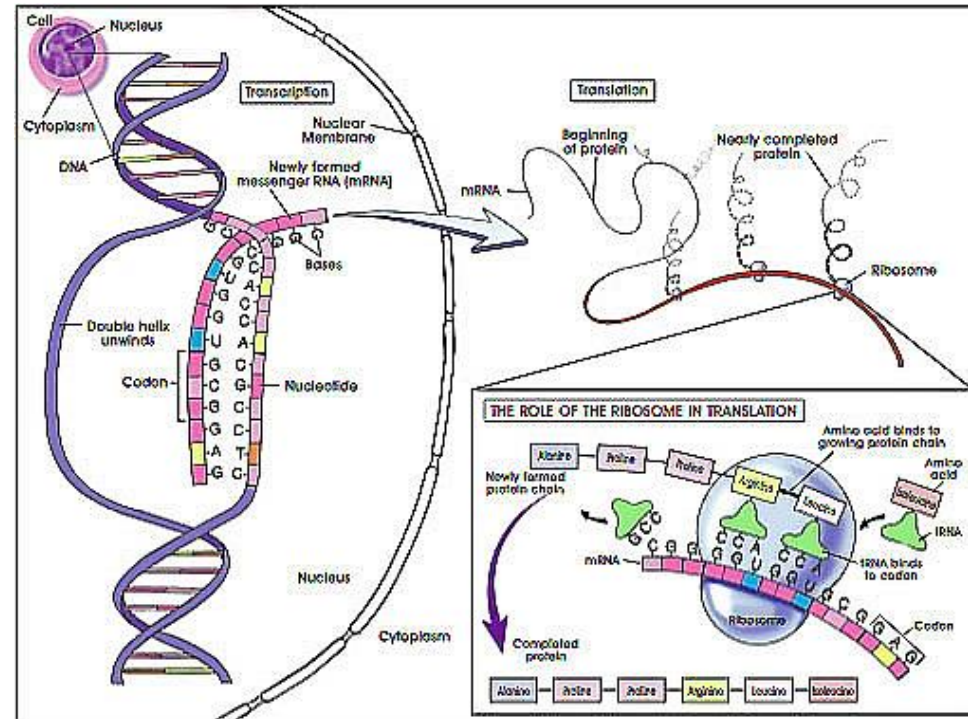
- The sequence of nucleotides in DNA (a gene) is used as a template for synthesis of messenger RNA (mRNA) in the nucleus
- mRNA is used as a template for synthesis of a protein in the cytoplasm.

DNA (gene) > mRNA > protein



# Genes & Protein Synthesis

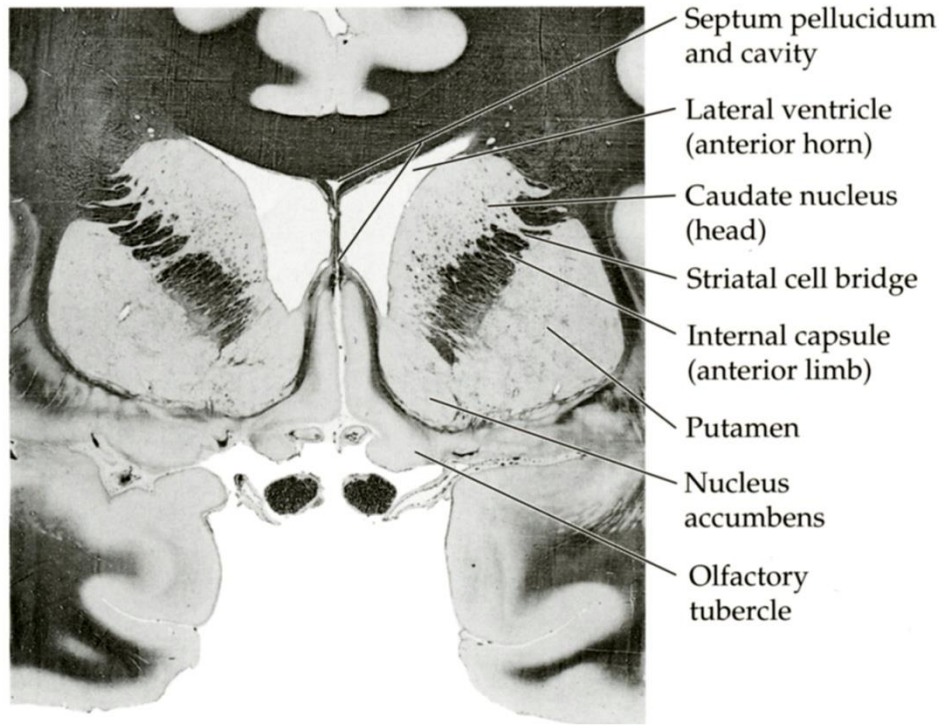
- DNA is a chain of four nucleotides.
- mRNA is a chain of four slightly different nucleotides.
- Protein is a chain of amino acids.
- The sequence of three nucleotides in the mRNA, a codon, specifies the amino acid to assemble into the protein being synthesized.
- Thus, the sequence of nucleotides in a gene (DNA) ultimately determines the sequence of amino acids in a protein.



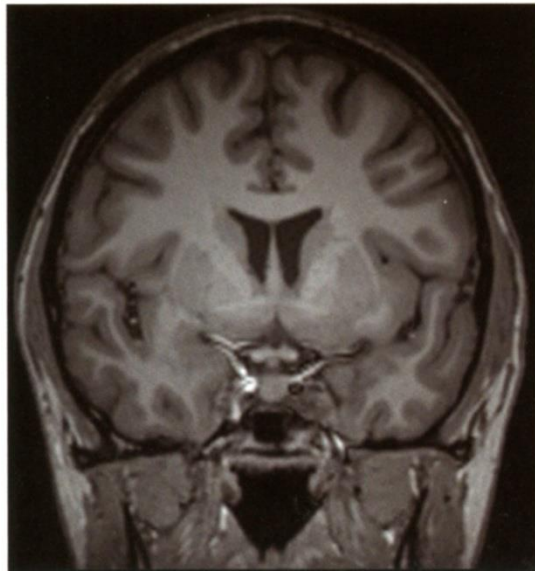
# Huntington's Disease

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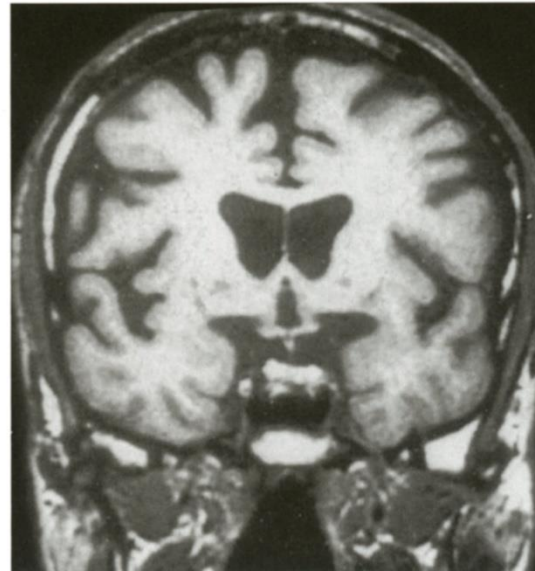
- Huntington's disease is due to an inherited, dominant mutation:
  - Due to an abnormal repeat of the CAG nucleotides in the *huntington* gene.
  - CAG encodes for the amino acid glutamine.
  - The CAG repeats in the gene result in a polyglutamine sequence in the huntington protein.
  - The huntington protein is expressed by medium spiny neurons in the striatum.
  - The mutant protein kills medium spiny neurons over time.



**normal MRI**



**Huntington disease MRI**



# Huntington's Disease

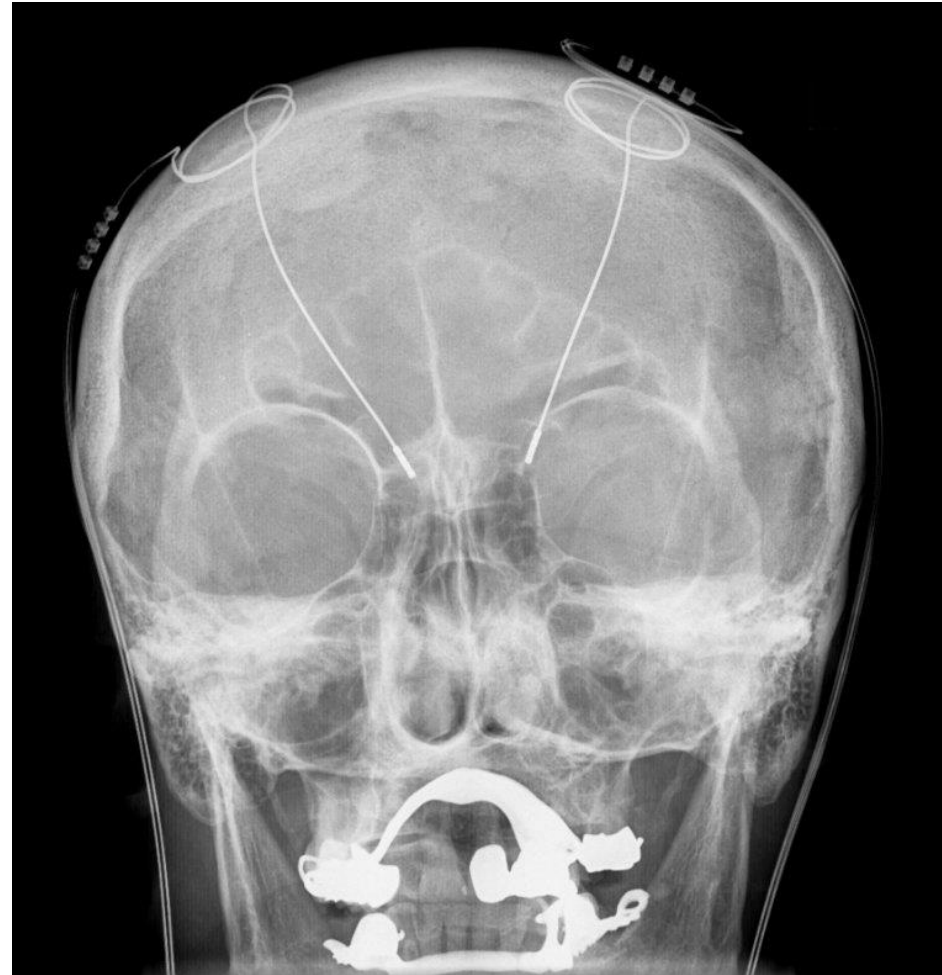
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<https://www.youtube.com/watch?v=JzAPh2v-SCQ>

## Deep Brain Stimulation (DBS)

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- DBS is used to treat numerous motor diseases.
- Electrodes are implanted in the globus pallidus internus or subthalamic nucleus.
- The frequency and strength of the stimulus is determined empirically.
- The effect can be dramatic, particularly with Parkinson disease.





# Deep Brain Stimulation (DBS)

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<https://www.youtube.com/watch?v=uBh2LxTW0s0>