BASAL GANGLIA

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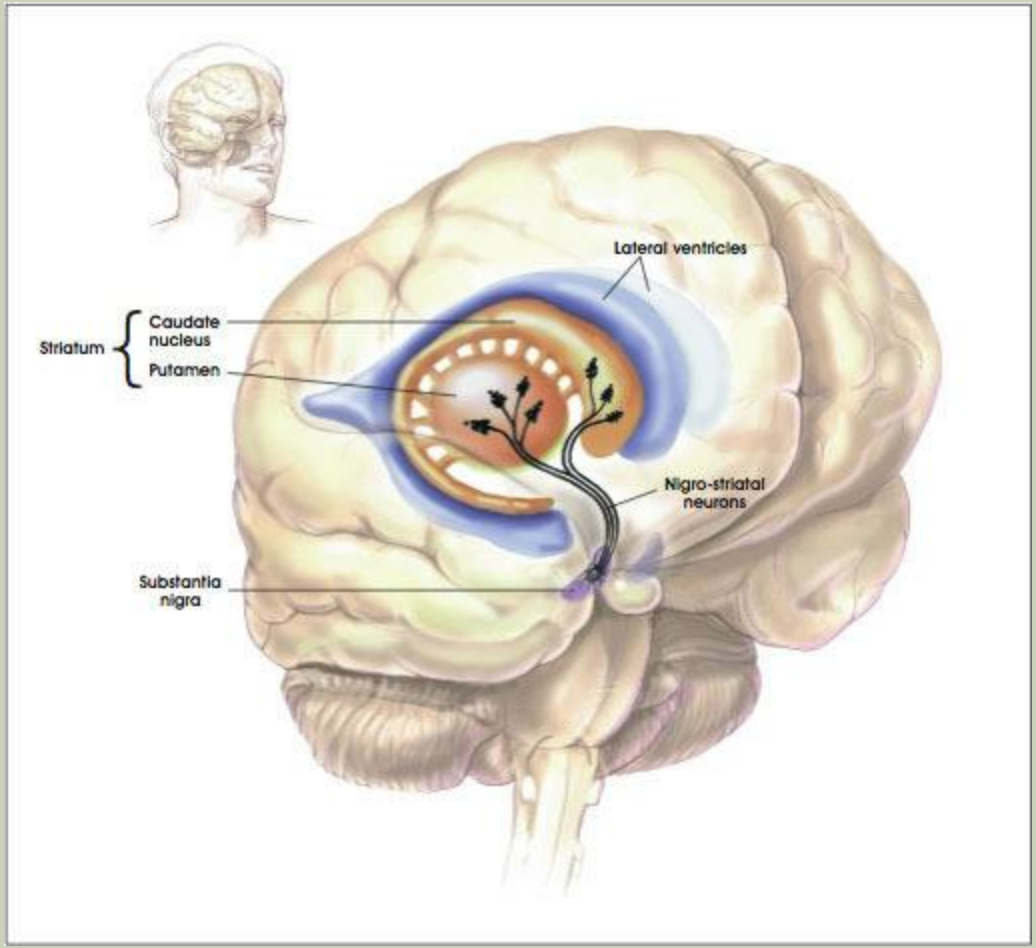
THE STRUCTURE INCLUDES:

- Striatum
- Pallidum
- Substantia Nigra
- Subthalamic Nucleus

STRIATUM

- The largest component of the basal ganglia.
- The structure has a striped appearance which is where it's name comes from.
- Two distinct masses of gray matter separated by white matter.
  - The two masses are called the caudate nucleus and putamen.


Lateral ventricles
Striatum
Caudate nucleus
Putamen
Nigro-striatal neurons
Substantia nigra

PALLIDUM

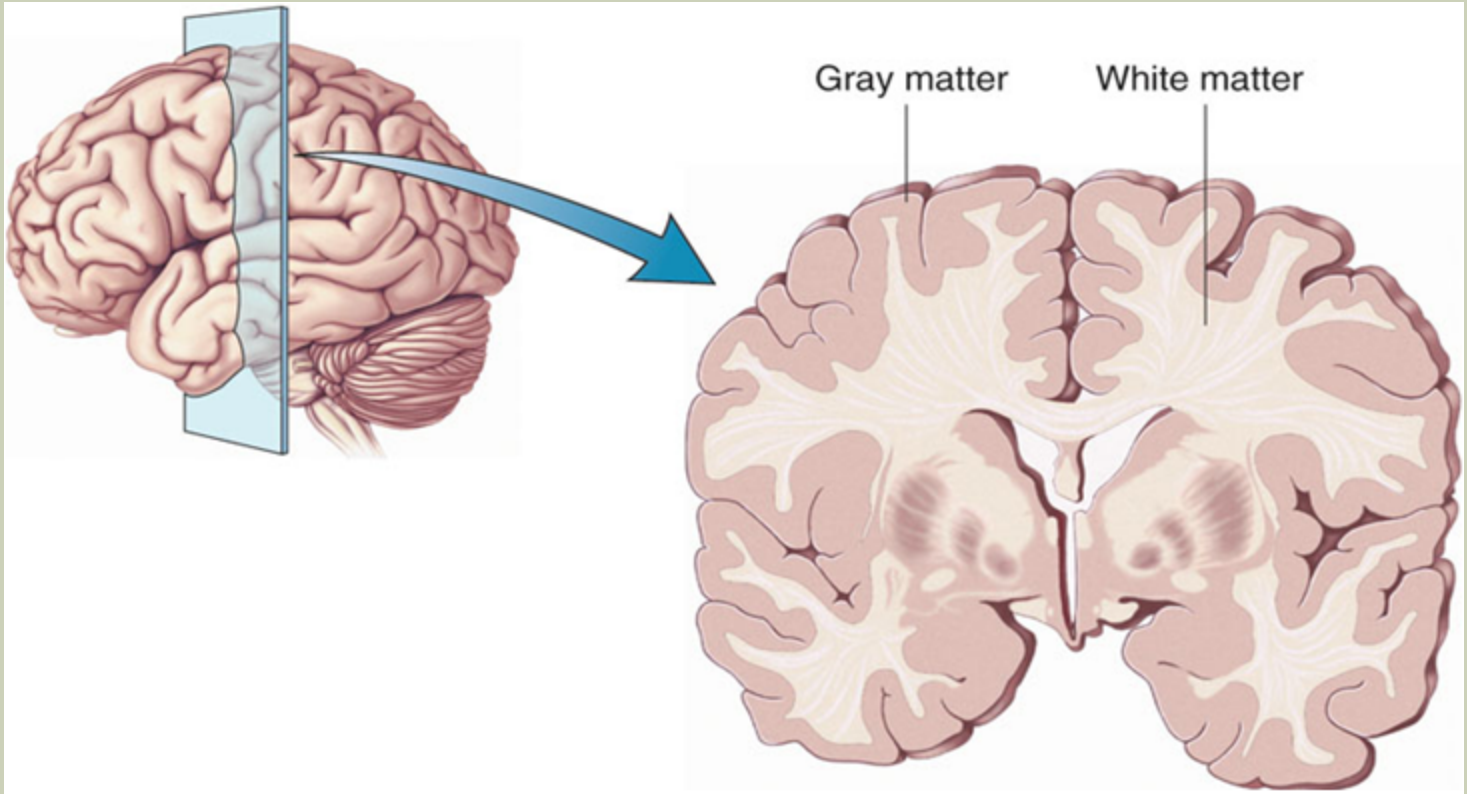
- Consists of a large structure called the globus pallidus and a smaller ventral extension called the ventral pallidum.
- The globus pallidus can be divided into two functionally distinct parts: the medial (internal) and lateral (external) segments.

GLOBUS PALLIDUS

- Both the medial and lateral segments contain primarily GABAergic neurons, which makes them have inhibitory effects on their targets
- The external segment or GPe receives most of its input from the striatum via the direct and indirect pathways
- The internal segment or GPi receives signals from the striatum via the direct and indirect pathways.
- Pallidal neurons operate using a disinhibition principle.

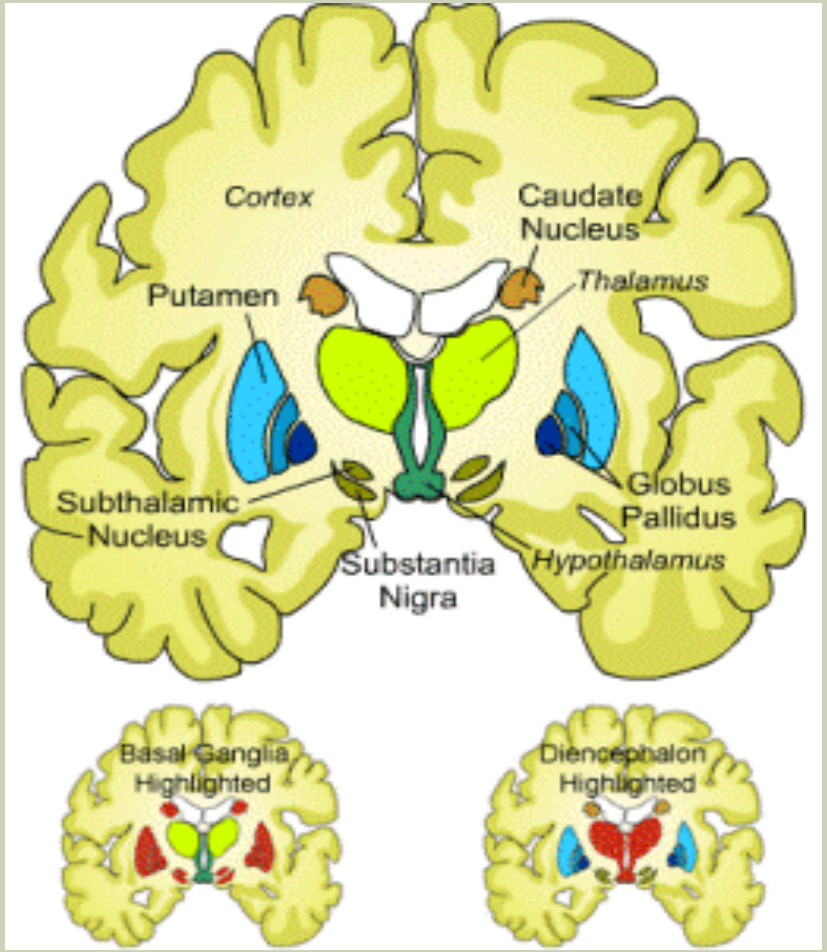
SUBSTANTIA NIGRA

- The substantia nigra is a gray matter portion of the basal ganglia that is divided into SNr (reticulata) and SNc (compacta).
- SNr often works in unison with GPi, and the SNr-GPi complex inhibits the thalamus.
- SNc produces the neurotransmitter dopamine, which is very significant in maintaining balance in the striatal pathway.


Gray matter
White matter

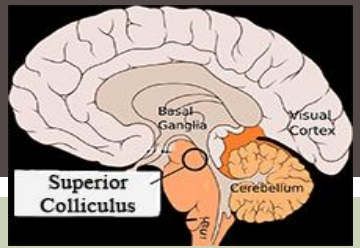
SUBTHALAMIC NUCLEUS

- The subthalamic nucleus (STN) is a gray matter portion of the basal ganglia, and the only portion of the ganglia that produces an excitatory neurotransmitter, glutamate.
- The role of the subthalamic nucleus is to stimulate the SNr-GPi and it is part of the indirect pathway.
- The subthalamic nucleus receives inhibitory input from the external part of the globus pallidus and sends excitatory input to the GPi.


Cortex
Caudate Nucleus
Thalamus
Putamen
Globus Pallidus
Subthalamic Nucleus
Substantia Nigra
Hypothalamus
Basal Ganglia Highlighted
Diencephalon Highlighted

Function(s) Overview:

- Functions associated with the basal ganglia include control of voluntary motor movements, procedural learning, routine behaviors/habits, eye movements, and cognition/emotion
  - basal ganglia uses GABA as major neurotransmitter
- experimental studies provided results that the basal ganglia exerts an inhibitory influence on a number of motor systems which releases an inhibition which causes motor systems to then become active.



Function: Eye Movement

- Different brain regions and networks within the brain influences eye movements as they converge on a midbrain area, which is called the superior colliculus (SC).
- The way in which the superior colliculus drives an eye movement toward a directed corresponding point is due to a “bump” of neural activity in the deep layers of the SC
- This process begins by the Superior colliculus receiving a strong inhibitory projection from the basal ganglia, which comes from the substantia nigra (SNr)
- Any movement within the eye is due to some type of “pausing” in the SNr. After activation in the caudate nucleus, GABAergic projections inhibits the SNr which then leads to the superior colliculus being inhibited

Function: Behavior

- The basal ganglia has the ability to be trained and choose behaviors to carry out based on rewards in the past which is why the temporal sequencing of movements is another function of the basal ganglia.
- The basal ganglia is involved and focuses in on the level of motivation depicted within an individual.
- An example is when a person who is immobile responds to an emergency or various types of auditory and cues being used to stimulate them. However, after the response and the stimuli has passed the individual falls back into the same immobility prior, this is called kinesia paradoxica.

https://www.youtube.com/watch?v=jOuw35-7uPw

Function: Neurotransmitters

- This role of motivation stems from the limbic part of the basal ganglia involving the nucleus accumbens (NA), ventral pallidum, and ventral tegmental area (VTA).
- In order to understand the central role in the brains reward systems experimental studies have been performed.
- These studies demonstrate the dopaminergic projection from the VTA to the NA.
- For example, an animal will bar-press very energetically if a brief pulse of electrical current follows each press. Many things that humans find rewarding such as additive drugs, good tasting food, music, and sex cause activation of the VTA dopamine system.

Parkinson's Disease:
Video

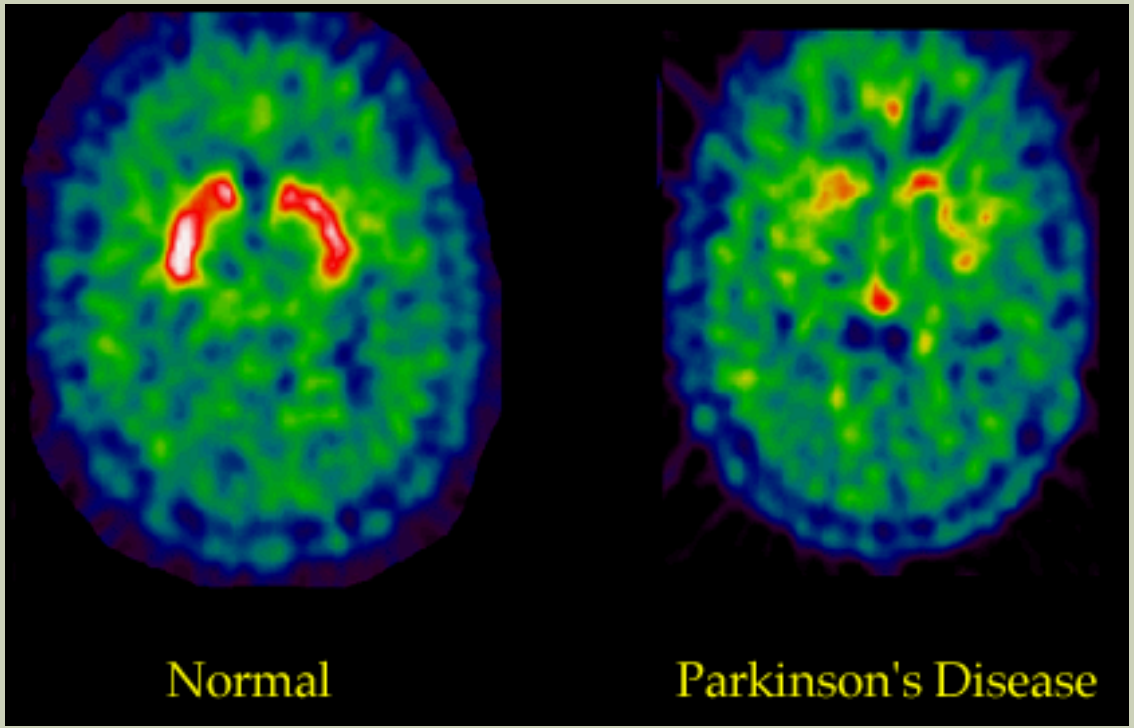
https://www.youtube.com/watch?v=CqEwPqUO1Bw

Play until 1:50

Parkinson's Disease:
Causes

- Also known as idiopathic/primary parkinsonism, hypokinetic rigid syndrome, or paralysis agitans
- Progressive neurodegenerative disorder of central nervous system
- Associated with dysfunction in basal ganglia
- Caused by death of dopamine generating cells in substantia nigra
- Also involves damage to striatum
- Often called disorder of the basal ganglia

Parkinson’s Disease



https://www.atrainceu.com/course-module/2441019-143_parkinsons-module-04

Parkinson's Disease:
Function

- Basal ganglia gets input from many cortical areas then projects to motor cortex via Thalamus
- Substantia nigra connected with nuclei of basal ganglia
- When dopamine input from substantia nigra lost, output from basal ganglia to motor cortex changes
- Excitation/inhibition of motion affected

Parkinson's Disease:
Behavior

- "Paralysis of the Will"
- Limbic part of basal ganglia controls movement and motivation
- Basal ganglia deterioration can cause "kinesia paradoxia"
- Damage to basal ganglia cause issues with appetitive behaviors

Parkinson's Disease:
Symptoms

- **Movement symptoms: shaking, rigidity, slowness of movement, difficulty walking**
- **Cognitive-behavioral symptoms: dementia, depression and sensory/sleep/emotional problems**
- **Symptoms worsen over course of disease**

Parkinson's Disease:
Treatments

- No known treatments currently
- Pharmacologic and surgical therapies used to restore/increase lost dopamine in basal ganglia
- Decrease symptoms by using L-DOPA and dopamine antagonists
- Try to change diet and rehabilitation
- Last resort is surgical therapies- lesion in thalamus or overactive basal ganglia area
- Most effective is deep brain stimulation

Huntington's Disease

- Hyperkinetic disorder
- Autosomal dominant disorder
- Disease that causes defects in behavior, cognition, and uncontrolled rapid, jerky movements
- Leads to mental decline and behavioral symptoms

Huntington's Disease: Causes

- The faulty gene is found on chromosome number 4.
- A normal copy of the gene produces *huntingtin*, a protein. The faulty gene is larger than it should be and produces a larger form of *huntingtin*.
- Cells in the basal ganglia are very sensitive to the effects of the abnormal huntingtin. This makes them function poorly and eventually die.
- The brain normally sends messages through the basal ganglia to control movement and thinking, as well as motivation. Since this part of the brain is damaged, it causes problems with control of movement, behaviour and thinking.

Huntington's Disease: Function

- Two pathways of neural connections between the motor cortex and the basal ganglia control the coordination of movements.
  - Direct and Indirect pathways

- As nerve cells in the striatum of basal ganglia die under the influence of HD, both of these pathways are eventually damaged.

Huntington's Disease: Function

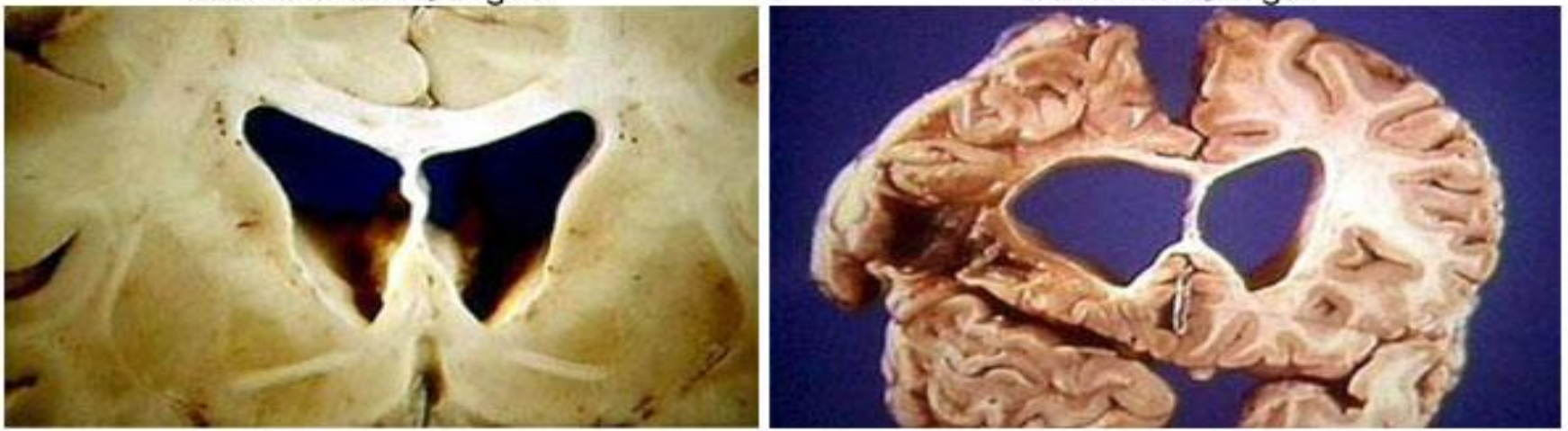
- The neurons of the indirect pathway are generally affected first, which explains why involuntary movement is often seen during the start of adult forms of HD.

- As the disease progresses, both types of striatal neurons die off, disrupting both the indirect and direct pathways and producing an overall decrease in movement and memory.

Huntington's Disease

Figure D-4: Effect of HD on the Basal Ganglia

Normal Basal Ganglia vs. HD Basal Ganglia



The basal ganglia of the human brain, showing the impact of HD on brain structure in this region. Note especially that the brain of a person with HD has bigger openings due to the death of nerve cells in that region.

Source: Singer, Jonathan. Huntington's Disease. Online. Available at: http://ist-socrates.berkeley.edu/~jmp/HD.html

Huntington's Disease: Symptoms

- Symptoms usually develop between ages 30 and 50, but they can appear as early as age 2 or as late as 80.

- Uncontrolled movement of the arms, legs, head, face and upper body.

Huntington's Disease: Symptoms

- Decline in thinking and reasoning skills, including memory, concentration, judgment and ability to plan and organize.
- Alterations in mood, especially depression, anxiety, and uncharacteristic anger and irritability.
- Obsessive-compulsive behavior, leading a person to repeat the same question or activity over and over.

Huntington's Disease: Treatment

- There is currently no cure for Huntington's disease and no way to slow or stop the brain changes it causes.
- Treatments focus on managing symptoms so patients can live a manageable lifestyle.

Huntington's Disease: Treatment

- Antipsychotic drugs
- Tetrabenazine
- Antidepressants

- Psychotherapy
  - provide talk therapy to help a person manage behavioral problems, develop coping strategies, manage expectations during progression of the disease.

- Speech therapy
- Occupational therapy

RESEARCH

Clues to How an Electric Treatment for Parkinson's Works

by Carl Zimmer

- **Drugs are not enough for some Parkinson's patients**
- **Deep Brain Stimulation (D.B.S)**
- **"We have people who, when they're not taking their meds, can be frozen," said Dr. Starr. "When we turn on the stimulator, they start walking."**

- Scientists originally thought that the electrical signals shut down the neurons that were malfunctioning in their production of dopamine
- Found that beta rhythm is important the D.B.S
- Synchronized like an orchestra - keep regions of the brain on the same time table
- You can have a too strong or too weak signal and both are detrimental.
- People with Parkinson’s have extremely strong beta rhythms in the their motor cortex.

- During the surgical placement of electrodes the motor cortex is monitored while patients reach out to touch dots on a screen. Their motor cortex becomes less synchronized as their movements improve.
- Scientists know that this is a treatment but not a cure. It only treats electric brain signals, not the biological bases of the disorder.
- Shows how DSB can be a potential treatment for those with depression and obsessive compulsive disorder

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