MCB/Neuro 80 - Neurobiology of Behavior

Today's Topic:

MOTOR SYSTEMS - 3

Lecture 23

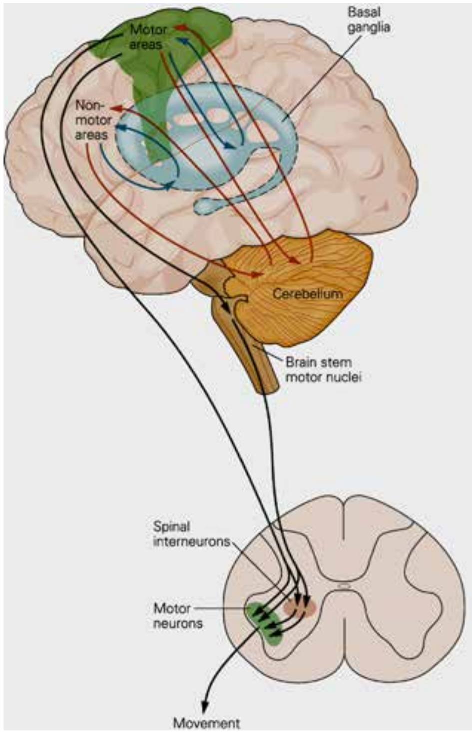
Optional reading: None

Lecture notes, review questions, office hour times available at:

https://canvas.harvard.edu/courses/59120


CLIMBING MT. POTENTIAL
(IN PRACTICE)
Response
Sensory/motor diseases
Upper Motor
Spinal Circuits
Neuronal processing
Cognition
Structural changes and aging
Long term synaptic plasticity
Memory systems
Stimulus (sensing information)
Information Coding
Other Senses
Visual system:
• Sensory transduction
• Visual circuits
• Cortical visual processing

Complex, hierarchical loops in motor system



Spinal cord, brain stem, and cortex contain motor control circuits

Each level receives sensory info

Each level can organize movements

Some are unconscious (balance, breathing)

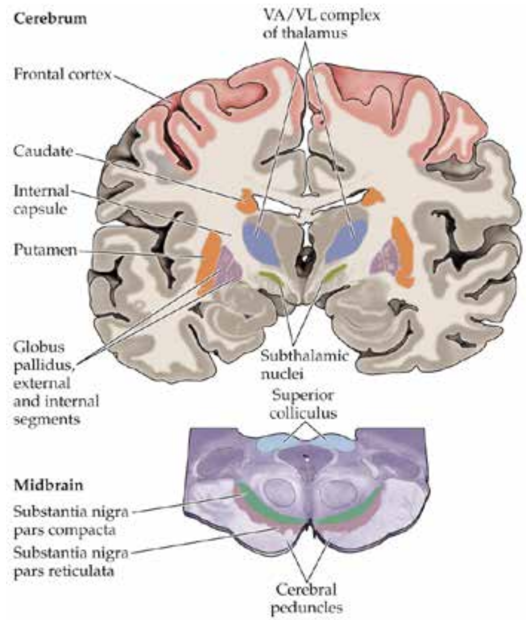
Lots of loops- still quite mysterious!

Also critical: Cerebellum and Basal Ganglia feedback during motor acts. Severe defects in movement in their absence (Basal ganglia: Parkinson’s and Huntington’s) and Cerebellar damage cause profound balance problems called “ataxias”)

Basal ganglia: key player in movement control/execution

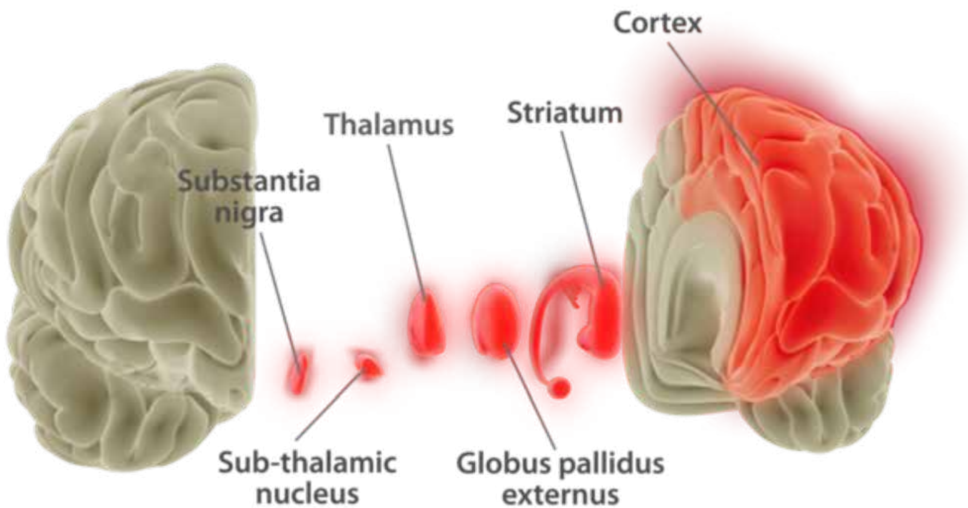
Basal ganglia are involved in action choice, motor learning and habit formation

Devastating diseases of the brain involve basal ganglia – Parkinson’s, Huntington’s, addictive behavior



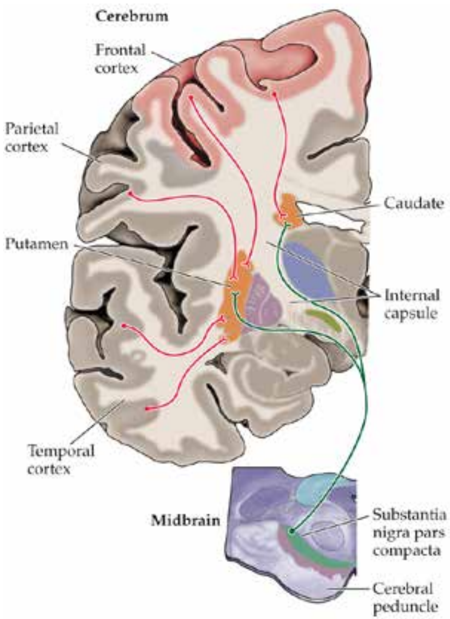
NEUROSCIENCE 6e, Figure 18.1

Basal ganglia: key player in movement control/execution



https://institute.progress.im/en/content/basal-ganglia

Basal ganglia – inputs



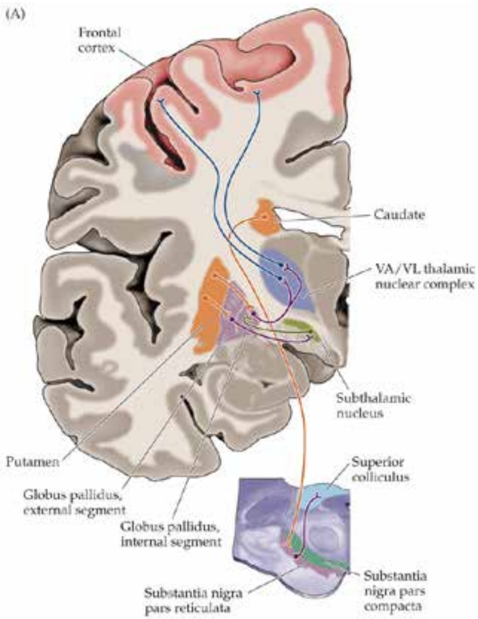
NEUROSCIENCE 6e, Figure 18.2

Caudate + putamen = striatum

Many cortical areas activate striatum

Substantia nigra sends dopamine input)

Basal ganglia – outputs



NEUROSCIENCE 6e, Figure 18.4 (Part 1)

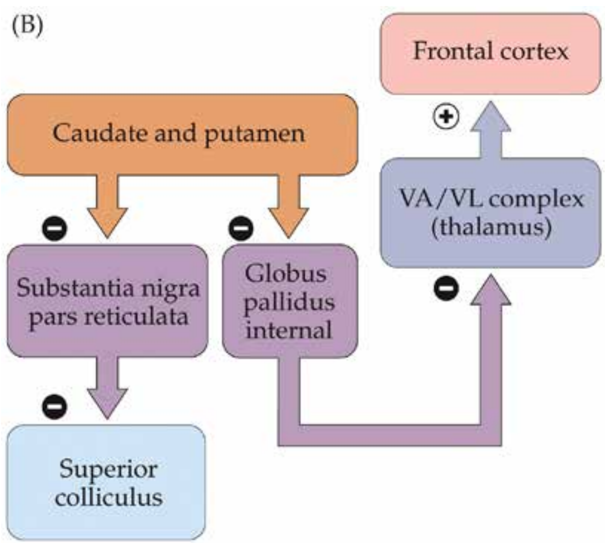
Putamen projects to Globus pallidus (inhibitory connections)

Globus pallidus has interesting intrinsic connectivity (mostly inhibitory connections)

GP projects to thalamus and subthalamic nucleus (a site of deep brain stimulation)

Caudate projects to substantia nigra pars reticulata (eye movements)

Basal ganglia – outputs



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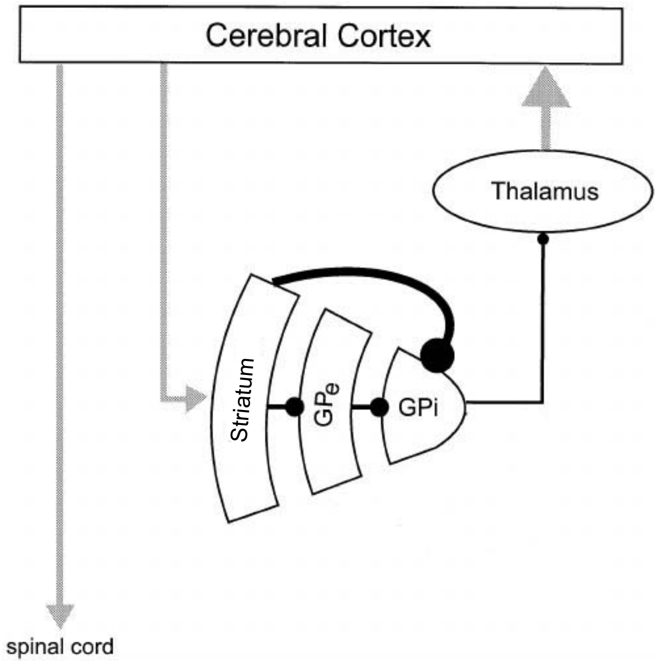
Basal ganglia – motor cortex loop



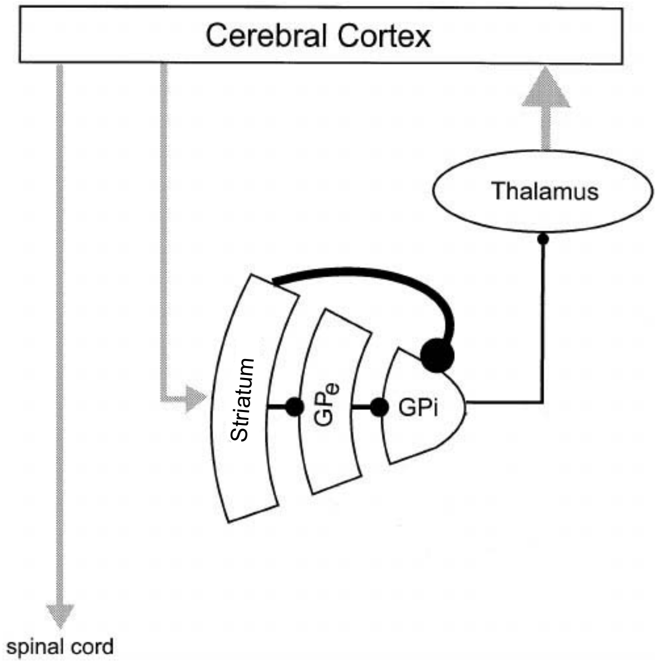
Cortex activates striatum (putamen + caudate)

Striatum inhibits globus pallidus internal (direct pathway)

Globus pallidus internal inhibits thalamus

(In the indirect pathway, globus pallidus has double-inhibition, which is sort of like excitation)

Let’s go over the logic of the question in previous slide



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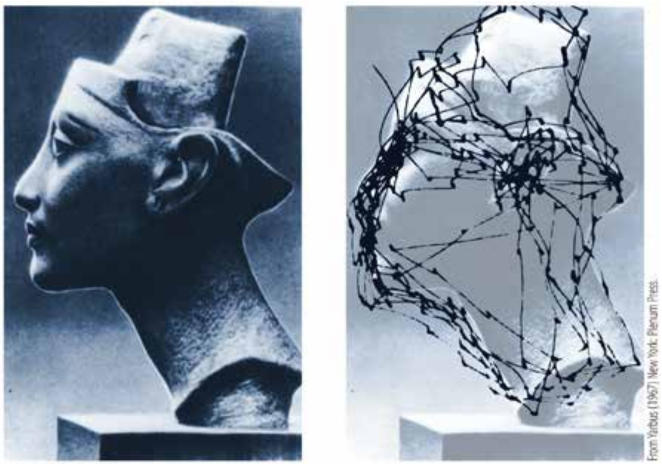
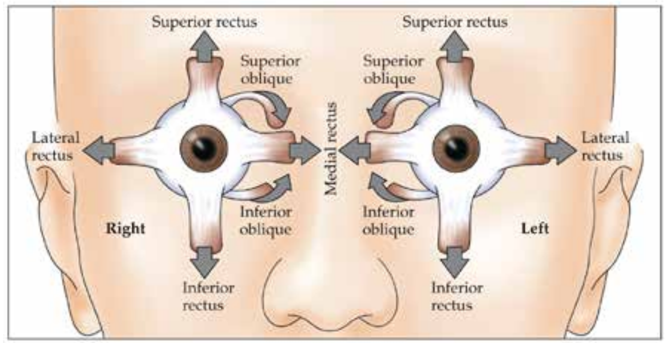
Example: controlling eye movements



NEUROSCIENCE 6e, Figure 20.1

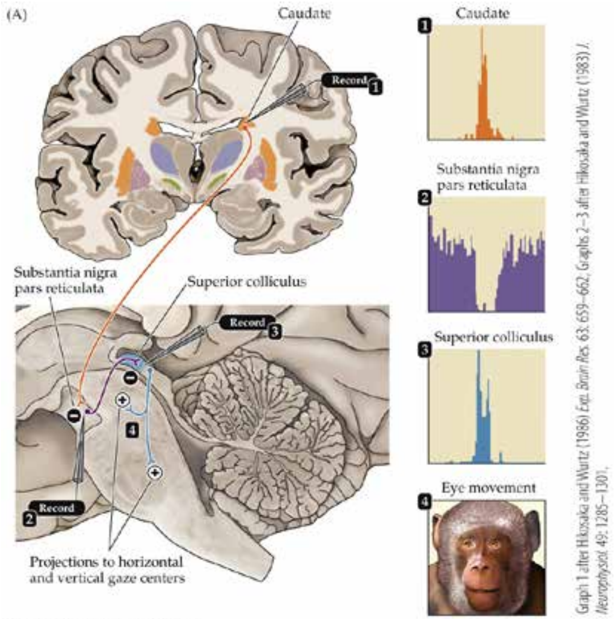


NEUROSCIENCE 6e, Figure 20.2

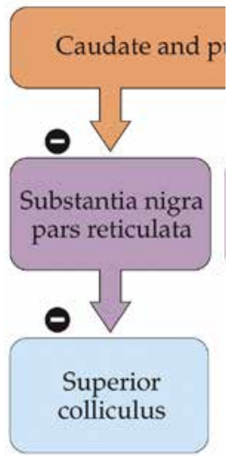
Our eyes are constantly scanning the visual scene. We make rapid movements called saccades, then fixate at one location.

Eye movements are controlled by a set of oculomotor muscles

Example: controlling eye movements



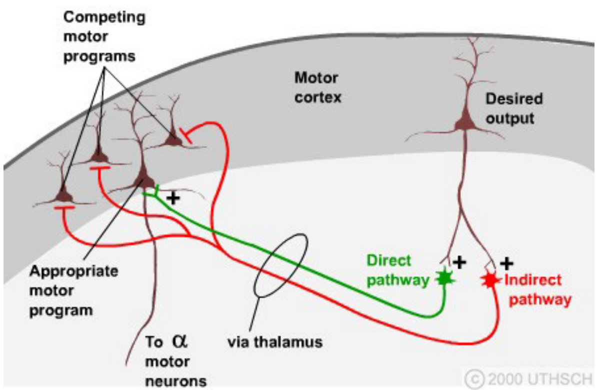
NEUROSCIENCE 6e, Figure 18.6 (Part 1)

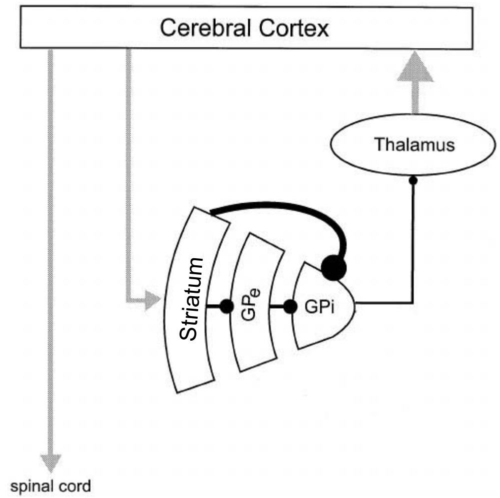


NEUROSCIENCE 6e, Figure 18.4 (Part 2)

- Cortex activates caudate
- Caudate neurons inhibit SNpr neurons (which are tonically active)
- SNpr neurons release inhibition on superior colliculus upper motor neurons, which then spike in a burst
- These bursting superior colliculus neurons then activate the appropriate eye muscles

Basal ganglia – action selection





Multiple motor programs (outputs) possible at any given time

Planning areas send information about the desired motor output to the direct pathway, which then help activate the appropriate upper motor neurons

Other competing motor programs are inhibited through the indirect pathway

Parkinson's disease

Approx 3-10 million worldwide affected.

2nd most common neurodegenerative disease. Which is the 1st ?

Causes: Idiopathic (basically means unknown!), genetic/environmental factors may play a role

Parkinson's gait:
https://www.youtube.com/watch?v=yhj1PktNA1c

No cure (yet)

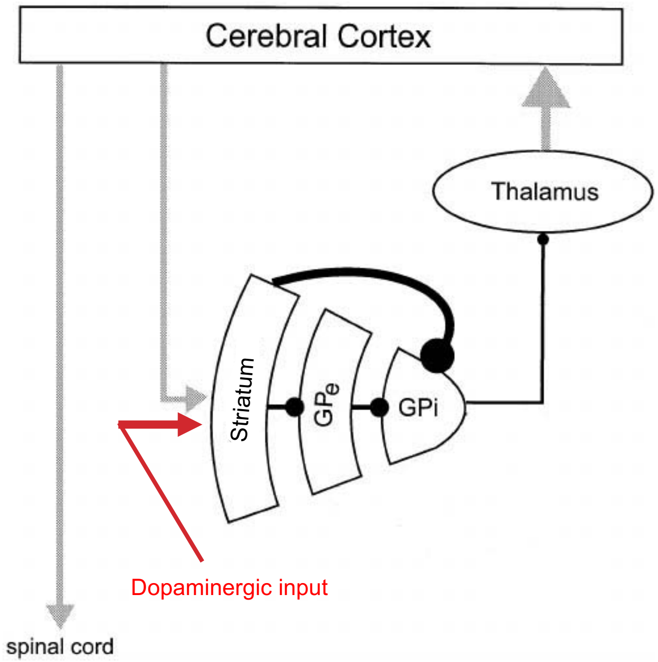
Therapy: L-DOPA (dopamine precursor) + DOPA decarboxylase inhibitor to prevent peripheral side effects of excess dopamine

Monoamine oxidase inhibitors (inhibit MAO, which breaks down dopamine)

Dopamine agonists

Deep brain stimulation

Basal ganglia – affected in Parkinson's



Striatum is not excited as efficiently in Parkinson's because a certain type of dopaminergic neurons degenerate.

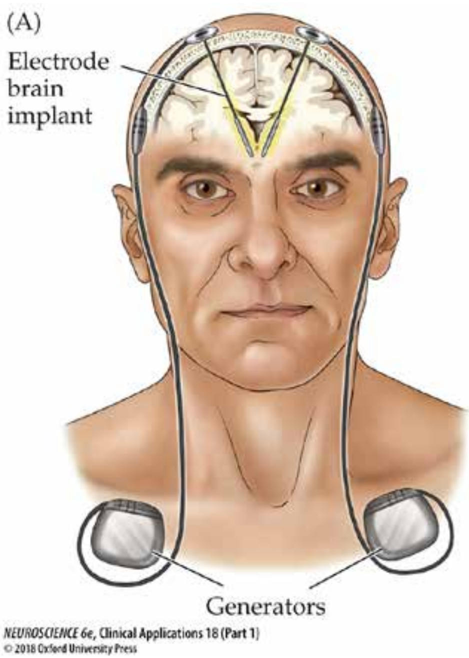
Striatum then poorly inhibits globus pallidus

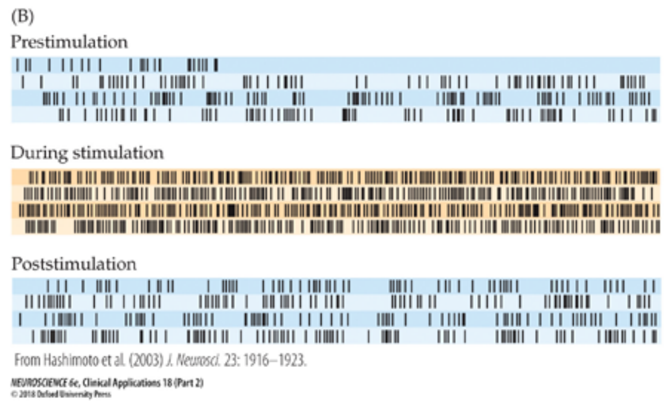
Globus pallidus is more active and inhibits thalamus

Thalamus then provides less input to cortex to initiate movement

One treatment: provide exogenous dopamine to activate striatum more

Deep brain stimulation





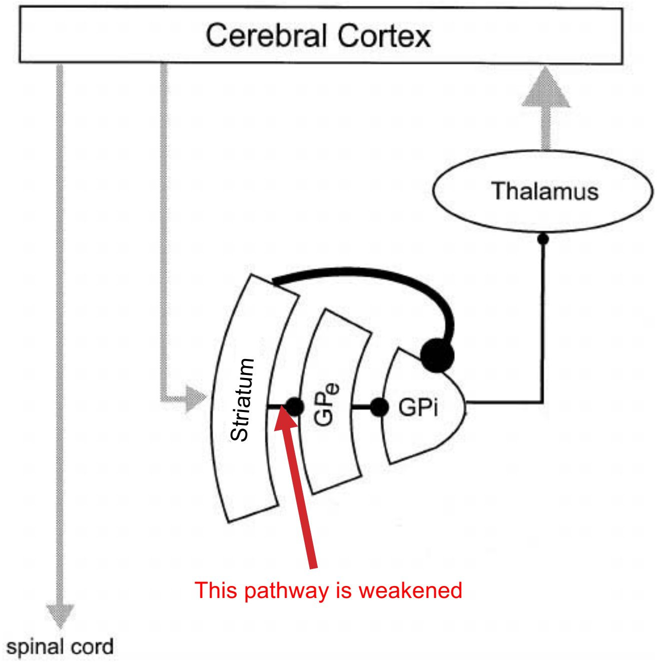
- Deep brain stimulation is used for some movement disorders
- Electrodes are placed in sites in basal ganglia or thalamus
- Experiments in monkeys point to altered basal ganglia activity during stimulation

Huntington's disease (chorea)

Video of hemi-ballismus: https://www.youtube.com/watch?v=oaxIkjNI_T4

Video of patient with Hungtingtons chorea:
https://www.youtube.com/watch?v=BnBpTsWiIhg

Basal ganglia – affected in Huntington's



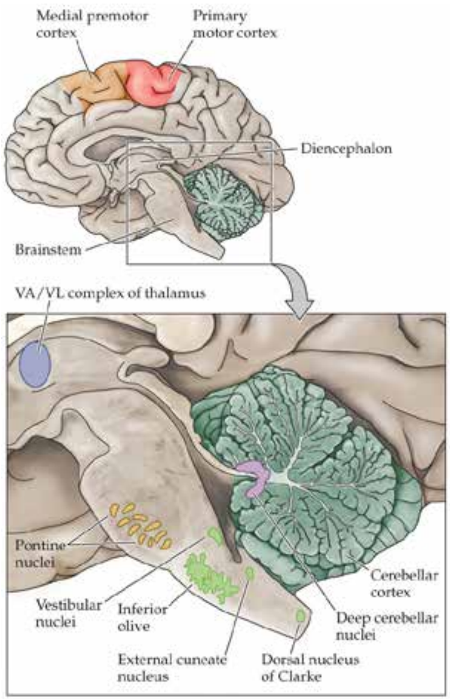
Striatum input to globus pallidus via the indirect pathway is reduced (red arrow)

The indirect pathway cannot oppose the direct pathway very well, making the globus pallidus much less active

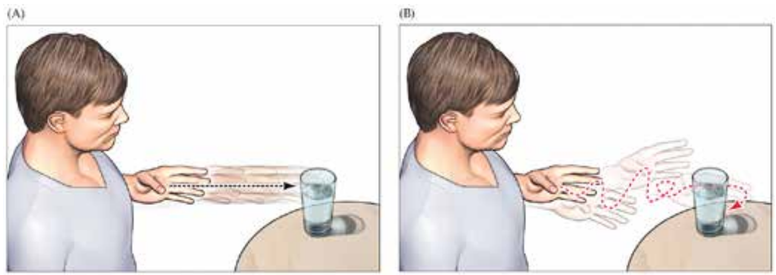
Thalamus is not inhibited effectively and keeps transmitting "unwanted" movement to cortex

Patients have lots of unwanted movements.

A quick note about cerebellum



NEUROSCIENCE 6e, Figure 19.2

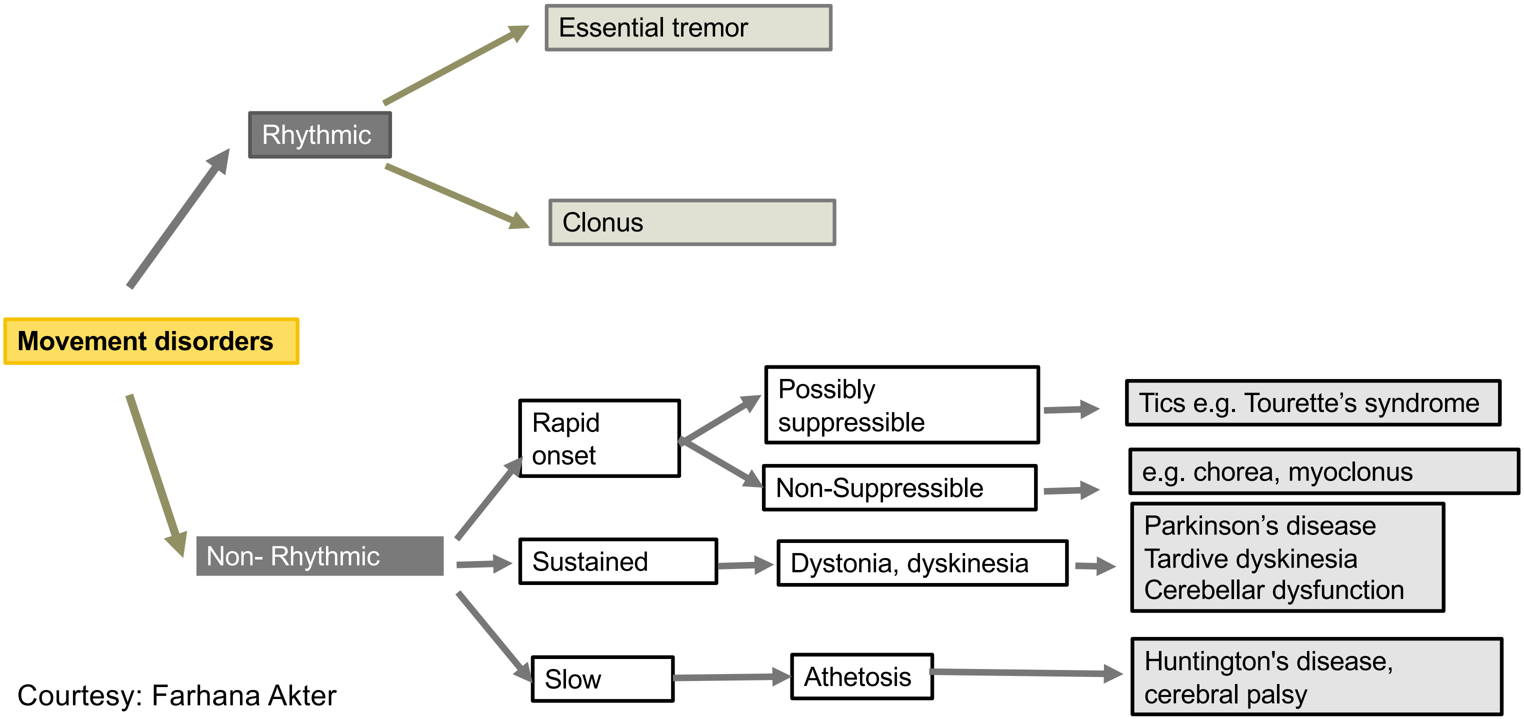


NEUROSCIENCE 6e, Figure 19.16

Roles in motor control:

- Motor adaptation
- Smooth, purposeful movements

Movement Disorders

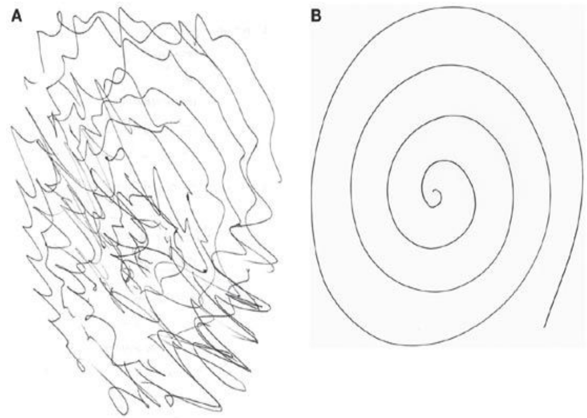


Courtesy: Farhana Akter

Essential Tremor

- The most common type of tremor
- Uncontrollable shaking
- Usually affects hands, but can affect other parts of the body e.g. the head, voice
- Worse during motion (Parkinson's tremor is resting type)

- Treatment: Nothing or drugs, avoid triggers, physical therapy, deep brain stimulation,

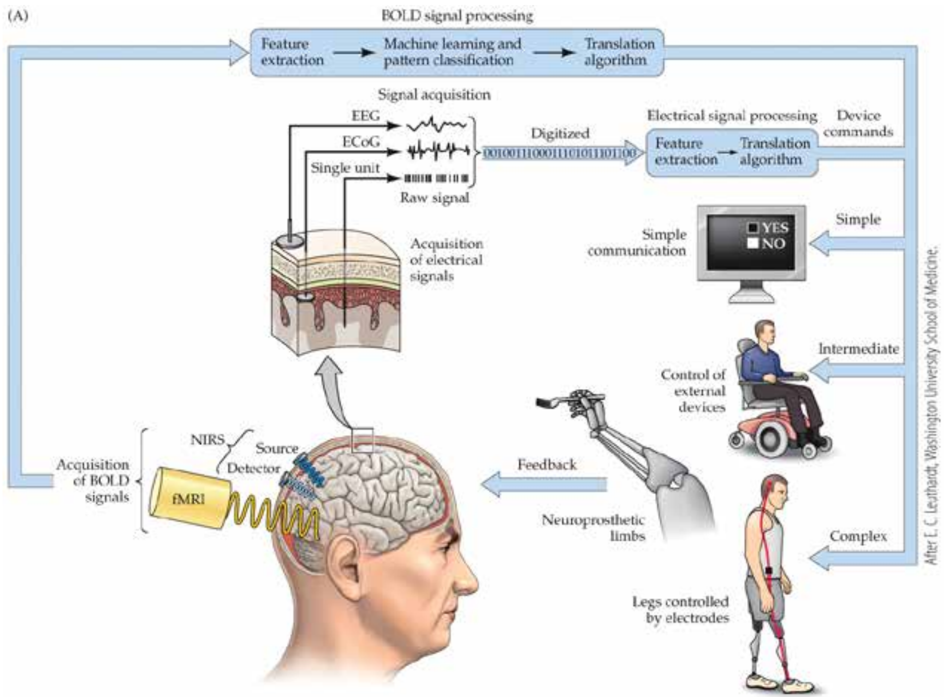


Ask a patient to draw a spiraling circle.

A: Patient with essential tremor
B: Normal

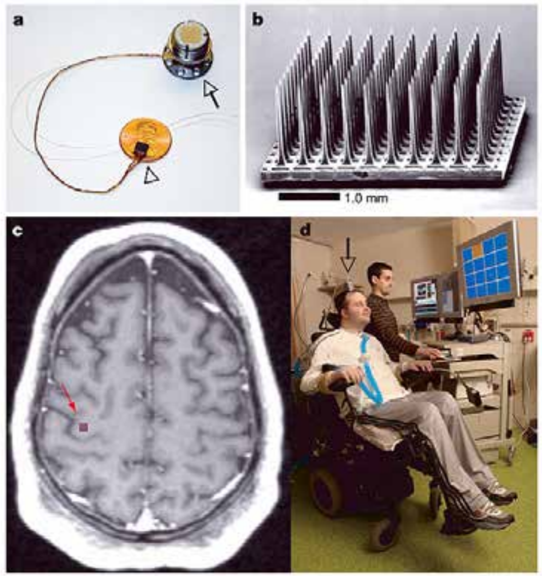
Courtesy: Farhana Akter

Brain-computer interface



NEUROSCIENCE 6e, Box 17B (Part 1)

Brain-computer interface



Hochberg LR et al. Neuronal ensemble control of prosthetic devices by a human with tetraplegia. *Nature.* 2006. 442: 164-171

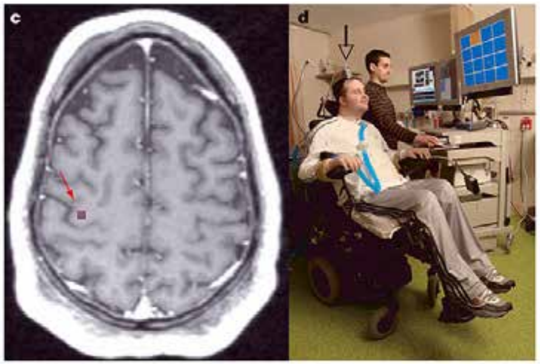
Problems:

Implanting sensors in appropriate location

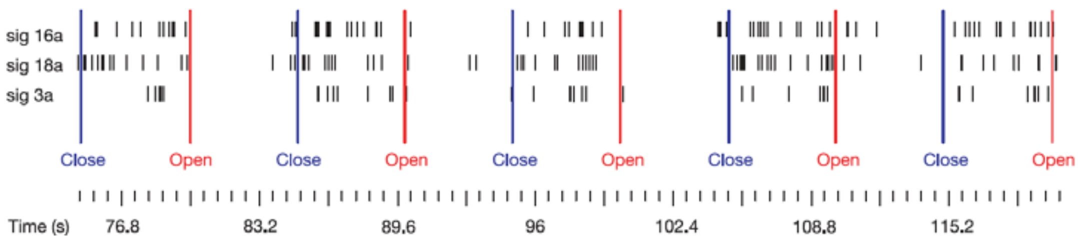
Ensuring biocompatibility

Powering these sensors for long periods of time

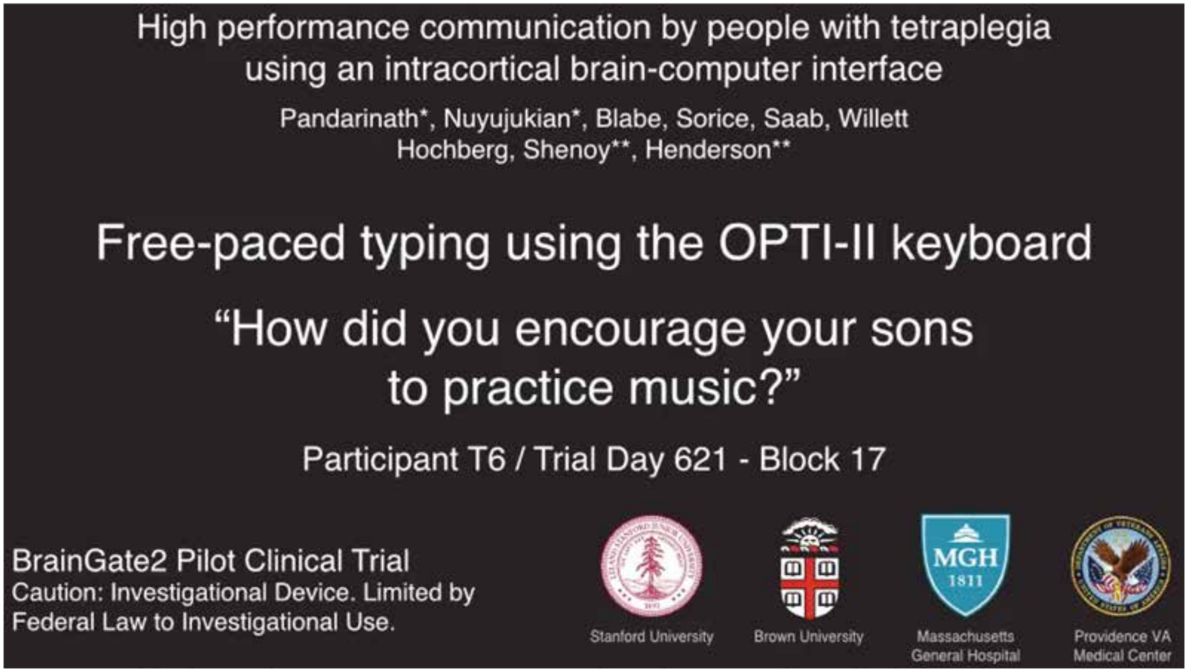
Motor cortex activity during “imagined” movement



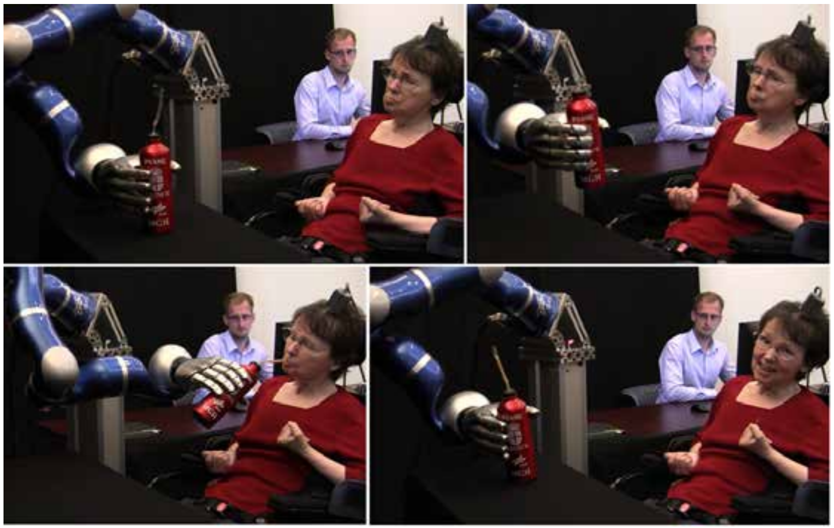
Even years after the spinal cord injury, the motor cortex becomes activated in the way expected when imagining hand/arm movements!



Typing with Brain Computer Interface



Brain-computer interface



https://youtu.be/ogBX18maUiM

Nature. 2012 May 17; 485(7398): 372–375.

Learning Objectives

Voluntary movements involve feedback loops and complex circuits among motor cortex, thalamus, basal ganglia, cerebellum and brainstem

Basal ganglia direct and indirect pathways

How dopamine systems impact basal ganglia, and their relation to Parkinson’s and Huntington’s diseases

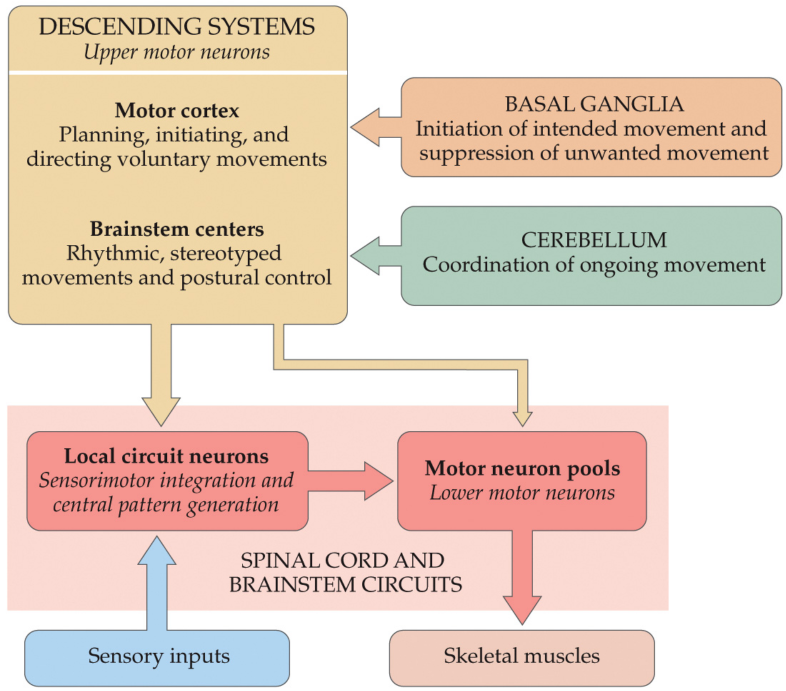
Brain-computer interface

Lecture 22 & 23 -Motor Systems 2

Pre-class notes for November 20 and 25, 2019
Reading: *Neuroscience ed. 6* by Purves et al., pages 392-397, 407-413, 427

Primary motor cortex - Contains upper motor neurons, which control contralateral body parts. Stimulation of specific sites in motor cortex usually leads to coordinated movements across multiple joints. Large neurons in layer 5 send their axons down the spine to synapse onto lower motor neurons and interneurons in the spinal cord.

Provides commands to initiate voluntary movement and control complex movement. Primary motor cortex is topographically organized. The motor cortex, in coordination with other areas of the brain integrates information from multiple sensory systems and sends depending axons to the motor control regions of the brainstem, to spinal cord interneurons, and to lower motor neurons themselves.



NEUROSCIENCE 6e, Figure 16.1

Neurons in motor cortex are tuned to different parameters of movement, including direction, velocity, joint angle etc. There is some evidence that stimulation of specific sites in motor cortex can lead to coordinated movements across multiple joints

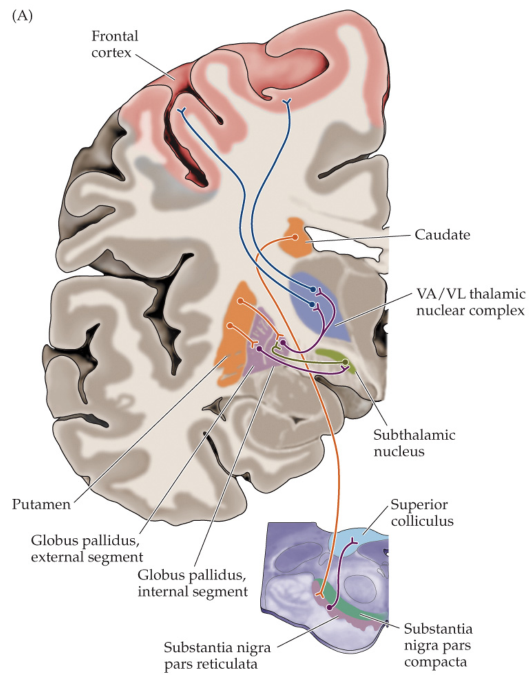
Premotor cortex - Contains neurons that help plan more complicated actions. Also contains *mirror neurons,* which are active not only when planning/performing complicated actions, but also when watching the same types of actions.

Basal ganglia - A group of nuclei lying deep in the subcortical white matter of the frontal lobes that organize motor behavior. The major components are the striatum (caudate and putamen), substantial nigra, globus pallidus external segment (GPe) and globus pallidus internal segment (GPi) which connects to nuclei in the thalamus and brain stem. The basal ganglia is essential for motor initiation and control, habit formation and reward-based learning. Contains 2 different pathways the *direct* and *indirect pathway*.

Direct pathway - a subset of projection neurons (medium spiny neurons) link the striatum directly to the basal ganglia output: GPi and the substantia nigra. Since both the striatum and globus pallidus are GABAergic, activating this pathway, provides less inhibition to the thalamus and brain stem.

Indirect pathway - a subset of medium spiny neurons in the striatum project to the GPe, which in turn projects to the GPi. Because there is a chain of inhibitory connections (disinhibition), activating this pathway provides more inhibition to the thalamus and brainstem.

Parkinson's disease - A neurodegenerative disease with symptoms that include shaking, rigidity, slowness and difficulty walking. Dopaminergic neurons which help activate the direct pathway degenerate, this leads to an increase in the GPi activity and causing more *inhibition* to the thalamus.



NEUROSCIENCE 6e, Figure 18.4 (Part 1)
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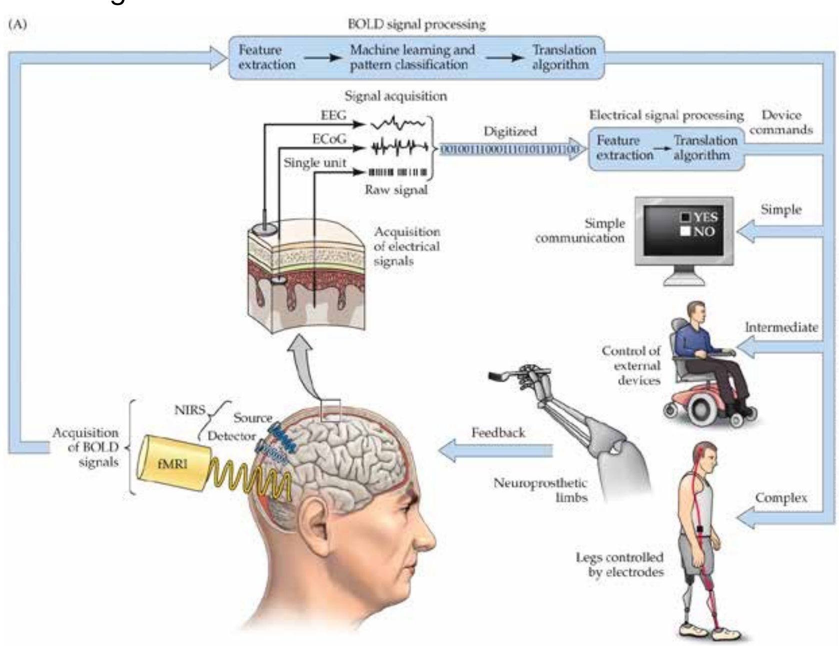
Huntington's disease - A genetic disease that is characterized by abnormal, hyperkinetic movements. Caused by the degeneration of medium spiny neurons in the striatum that specifically project to the GPe, resulting in the inactivation of the indirect pathway and decreased inhibition to the thalamus.

Cerebellum - structure located dorsal to the pons and medulla that plays an important role in motor coordination, motor learning and other cognitive functions. The cerebellum influences movements primarily by modifying the activity patterns of upper motor neurons. A primary function of the cerebellum is to detect the difference or "motor error" between an intended movement and the actual movement and thus modulate the upper motor neurons to reduce the error. These corrections can be made both during the movement and as a form of motor learning.

Brain computer interface - uses brain signals to control either devices or muscles using bidirectional communication between the nervous system and a computer.



NEUROSCIENCE 6e, Box 17B (Part 1)

Learning Objectives: (By the <u>end</u> of Lecture 22 you should be able answer questions about the following)

1. Explain how all observable behavior is the result of the coordinated activity of muscles.
2. Differentiate the behavioral output of activating a lower motor neuron versus an upper motor neuron in primary motor cortex and other "higher" areas.
3. Describe the motor cortex organization – loose topography.
4. How neurons in cortical areas code for movement parameters – population coding.
5. Brainstem nuclei controlling movement – postural adjustment.

By the end of **Lecture 23** you should be able answer questions about the following

1. Voluntary movements involve feedback loops and complex circuits among motor cortex, thalamus, basal ganglia, cerebellum and brainstem
2. Basal ganglia direct and indirect pathways
3. How dopamine systems impact basal ganglia, and their relation to Parkinson's and Huntington's diseases
4. Brain-computer interface