Basal Ganglia & Cerebellum

Physiology Department

Assis. Prof. Sertaç Üstün

ustun.sertac@gmail.com

Basal Ganglia

- Area 6 of motor cortex is responsible for motor planning. It receive information from different regions to plan spesific movements
- Major subcortical input to area 6 is from thalamus; spesifically ventral lateral nucleus (VL) of thalamus and input to VL arises from basal ganglia.
- Basal ganglia receive information from cerebral cortex (frontal and parietal areas)

➢ *Cortex send information to basal ganglia; basal ganglia send this information to thalamus and thalamus send it to cortex (area 6).*

Basal Ganglia

- A loop where information cycles from the cortex through the basal ganglia and thalamus and then back to the cortex
- Function of this loop is the selection and initiation of willed movements.

Basal Ganglia

- Consist of
  - Caudate
  - Putamen

  } Striatum
  - Globus pallidus (Gpi, GPe)
  - Subthalamic nucleus
  - Substantia nigra

  - Loop:

    Cortex → Striatum → GPi → VL → Cortex (SMA)

Direct Pathway

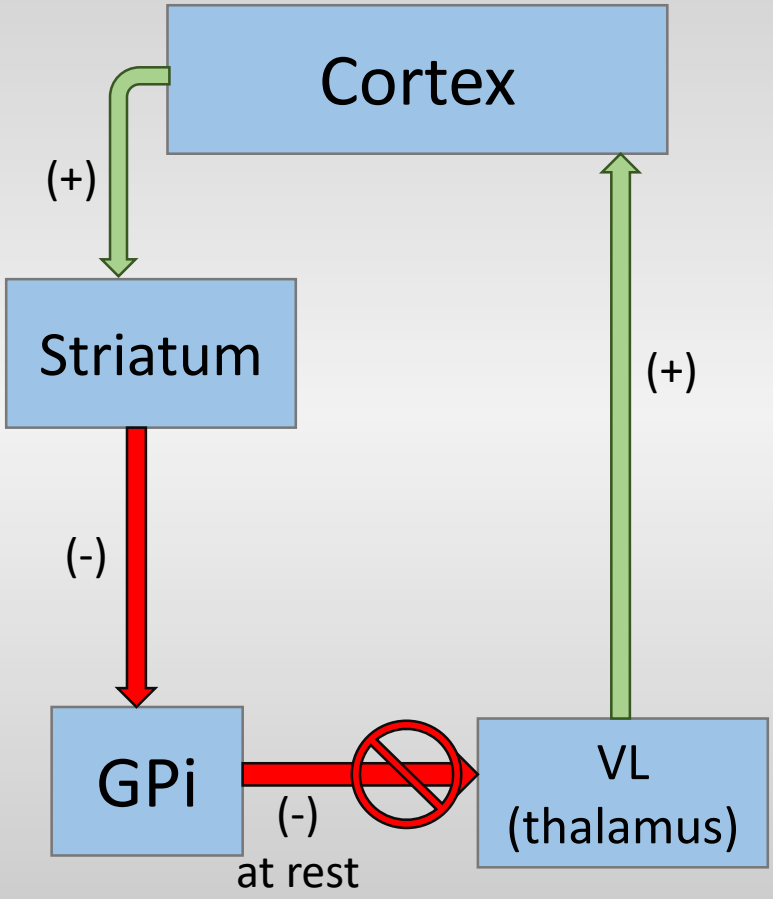
- Direct pathway allows the basal ganglia to enhance the initiation signal of desired movements.
- Loop originates with excitatory connections from the cortex and signal pass through basal ganglia and thalamus and activates the SMA.
- It serves as a funnel to focus signal.
  - ➢ Activation of widespread cortical areas focus onto SMA

Direct Pathway

Note: GPi are active at rest and constantly inhibit VL nucleus of thalamus

1. Cortical activation excites striatum
2. Active striatum inhibit GPİ
3. Inhibition of GPi, remove the inhibition signal of GPi to VL
4. VL become active and activate the cortex (SMA)

➢ Net effect of direct pathway is the activation of the thalamus which send signal to cortex to amplify the motor cortex activity



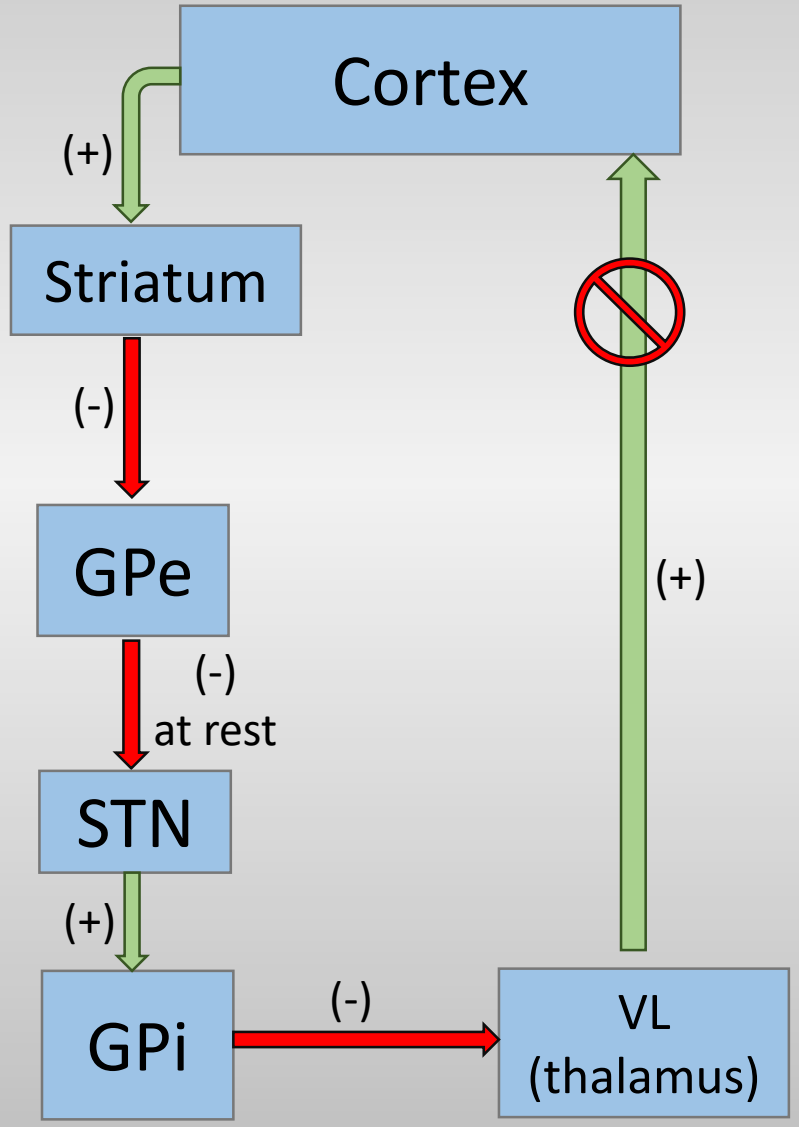
Indirect Pathway

- Indirect pathway antagonize the motor functions of the direct pathway
- It helps to prevent unwanted muscle contractions from competing with movements that we want.
- Activation of indirect pathway inhibit the thalamus which leads to a reduction of activity in motor cortex, and therefore muscular action.

Indirect Pathway

Note: GPe constantly inhibit Subthalamic nucleus (STN) at rest

1. Cortical activation excites striatum
2. Active striatum inhibit GPe
3. Inhibition of GPe, remove the inhibition signal of GPe to STN
4. STN become active and activate the GPi,
5. Active GPi send more inhibitory signal to VL and VL inhibits
6. Excitatory signal from VL to cortex reduces



Direct/Indirect Pathway

- Information from the cortex flows through the direct and indirect pathways in parallel and regulate thalamus
- Direct pathway facilitate the thalamus // Indirect pathway inhibit the thalamus

- ➢ Direct pathway helps to select certain motor actions that we want
- ➢ Indirect pathway simultaneously suppresses competing unwanted motor actions.

Direct/Indirect Pathway

Basal ganglia increase signal/noise ratio:

- *Direct pathway strengthen the signal (wanted movement); while indirect pathway weaken the noise (unwanted movements)*

In summary, basal ganglia;

- facilitate movement by focusing activity from widespread regions of cortex onto the SMA (direct pathway)
- serve as a filter that keeps inappropriate movements from being expressed (indirect pathway)

Basal Ganglia Disorders

- Inhibition of thalamus by basal ganglia increase

  → Hypokinesia: Paucity of movements
- Inhibition of thalamus by basal ganglia decrease

  → Hyperkinesia: Excessive movements

- While Parkinson's Disease could be an example for the first condition; Huntington's Disease could be an example for the second

Parkinson's Disease

- 1% of all people over 60 is affected
- Symptoms: Slowness of movements (bradykinesia), difficulty in initiating willed movements (akinesia), increased muscle tone (rigidity), tremors (especially at rest) and cognitive deficits
- Cause: Degeneration of substantia nigra neurons.
  - Substantia nigra use dopamine and dopamin facilitates the direct pathway by activating cells in stiratum.
  - Reduction of dopamin weaken the direct pathway and closses the funnel that feeds activity to the SMA

Parkinson's Disease

- Central goal for therapy: increase the level of dopamin
  - Most used method: L-dopa (precursor to dopamine)
- Other medhods:
  - DA agonists
  - Brain surgery: motor cortex, GP, STN etc.
  - Deep brain stimulation: Surgically implanted bilateral electrodes in STN work as a pacemaker (There are theories about how deep brain stimulation works)

Huntington's Disease

- Rare, hereditary, progressive and inevitably fatal syndrome
- Charactherized by hyperkinesia, abnormal movements (dyskineisa), dementia
- Symptoms: Spontaneous, uncontrollable, rapid movements of a various parts of the body

- Cause:
  - Loss of neurons in striatum, GP, cerebral cortex
  - Loss of inhibitory output to the thalamus

Cerebellum

- Making a movement required sequence of muscle contractions.
- Even for a simple movement lots of muscles are contract and each contraction should have exactly right amount of force and precise timing.
- Cerebellum responsible for precise execution of movements.
- Cerebellum also stores memories of these movements.

Cerebellum

Cerebellar Lesions

- Uncoordinated and inaccurate movements: ataxia
- For touching your nose you should move your shoulder, elbow and wrist simultaneously but in cerebellar lesion;
  - people move each joint sequentially: dyssynergia (decomposition of synergistic multijoint movement)
  - Also they will either come up short for nose or poking themselves in the face: dysmetric

Cerebellum

Cerebellar Lesions

- Patients show no abnormal tremor while at rest but show dramatic tremor when they try to move.
- Cerebellar tremor is caused by uncoordinated contracions of muscles which used in particular movement
- Cerebellar lesions symptoms are similar to ethanol intoxication

Cerebellum

- Cerebellum is a thin sheet of cortex which is repeatedly folded into folias to increase the surface area.
- Deep cerebellar nuclei relay most of the cerebellar output to various brain stem structures

Cerebellum

- Midline region is called vermis
- Vermis seperates two cerebellar hemispheres
- Vermis; send output to brain stem and contributes *ventromedial descending pathways* that controls axial muscles
- Hemispheres; are related to other brain structure that contribute to *lateral pathways* that control distal muscles

Motor Loop of Cerebellum

- From frontal areas 4 and 6, somatosensory areas, posterior parieatal cortex pyramidal neurons send their axons and form a big projection to pons (20 times bigger than pyramidal tract)
- Pons send this information to cerebellum
- Cerebellum projects back to the thalamus and then motor cortex

Motor Loop of Cerebellum

- Motor loop of cerebellum is critical for proper execution of planned, voluntary, multijoint movements.
- Cerebellum receive the signal for intention of movement and send the information about movement direction, timing, force to primary motor cortex.
- This regulations based on sensory information in motor loops.
- Also it is based on past experiences (Cerebellum also involved motor learning).

Motor Loop of Cerebellum

- Cerebellum also provides signal for refining the motor program during the course of the movement.
- It compares information about «what muscles should be doing» and «what they actually are doing».
- If this comparison fails between intended movement and the actual one, cerebellum made compensatory modifications for ongoing motor program.

Motor Learning

- During learning new skills, movements are slow and uncoordinated and required constant concentration.
- Practice makes perfect: With practice movement become smooth and eventually it can be performed unconsciously.
- Motor memory is different than other type of memories.
- Relatively permanent: Hard to gain; hard to forget.

References

- **Bear**, Mark F., Barry W., Connors and Michael A., Paradiso, **Neuroscience**: **Exploring the Brain**. Philadelphia: Wolters Kluwer, 2015

- Widmaier, Eric P., Raff, Hershel,Strang, Kevin T. **Vander's Human Physiology**: The Mechanisms of Body Function. Boston: McGraw-Hill, 2016.

- **Purves**, D., Augustine, G. J., Fitzpatrick, D., Hall, W. C., LaMantia, A.-S., McNamara, J. O., & Williams, S. M. **Neuroscience**. Sunderland, MA, 2011

- Hall, John E., Arthur C. **Guyton**. **Guyton and Hall textbook of medical physiology**. Philadelphia, PA: Saunders Elsevier, 2016