

## The Action of Basal Ganglia in the Brain: from Basic Research to Neurological Diseases

### Outline

#### Basal ganglia circuits

##### Two major pathways running through the basal ganglia

##### 1) *Direct pathway (dopamine D1 receptor):*

Precentral motor fields (premotor, motor, supplemental Ctx) ↑ (glutamate, +)  
→ CP ↑ (GABA, -) → GPi & SNpr ↓ (GABA, -) → thalamus ↑ → premotor, supplemental cortices ↑

Function: activation of the direct pathway results in **facilitation** of movement

##### 2) *Indirect pathway (dopamine D2 receptor):*

Precentral motor fields (premotor, motor, supplemental Ctx) ↑ (glutamate, +)  
→ CP ↑ (GABA, -) → GPe ↓ (GABA, -) → subthalamic nucleus ↑ (glutamate, +)  
→ GPe & GPi ↑ (GABA, -) → thalamus ↓ → premotor, supplemental cortices ↓

Function: activation of the indirect pathway results in **inhibition** of movement

#### Dopaminergic modulation of the direct and indirect pathways:

- 1) Dopamine activates the direct pathway: movement ↑
- 2) Dopamine inactivates the indirect pathway: movement ↑
- 3) Therefore, the net effects of dopamine on the two pathways is to **facilitate** movements by acting on both pathways

#### Parkinson's disease:

**Symptoms:** Akinesia; bradykinesia, rigidity, tremor

**Aetiology:** Selective degeneration of dopaminergic neurons in SNpc with systematic disruption of mitochondria electron transport complex I activity including blood and muscle cells; Lewy bodies occur

**Mechanisms:** Lack of dopamine in the striatum → decreased activity of direct pathway (D1R) and increased activity of indirect pathway (D2R) → net effects: hyperactivity of Gpi neurons → thalamus activity ↓ → cortical activity ↓ → movement ↓

**Animal models:** drug-induced selective degeneration of dopamine neurons in SNpc

- 1) 6-OHDA lesion
- 2) MPTP: MPP<sup>+</sup> disrupts mitochondria electron transport complex I in dopamine neurons
- 3) Pesticide (rotenone): systematic disruption of mitochondria electron transport complex I activity; Lewy bodies occurs (α-synuclein)

**Drug therapy:** L-DOPA

#### Surgical intervention therapies:

**Strategy:** decrease the hyperactivity of Gpi neurons

- 1) Pallidotomy: selective lesion of the posterior (sensorimotor) part of Gpi
- 2) Deep brain stimulation (DBS): high frequency stimulation can block neural activity in Gpi.
- 3) Neural transplantation: iPS stem cells