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) \( \uparrow \) (glutamate, +)
\( \rightarrow \) CP \( \uparrow \) (GABA, -) \( \rightarrow \) GPi & SNpr \( \downarrow \) (GABA, -) \( \rightarrow \) thalamus \( \uparrow \rightarrow \) premotor, supplemental cortices \( \uparrow \)
Function: activation of the direct pathway results in facilitation of movement

2) Indirect pathway (dopamine D2 receptor):
Precentral motor fields (premotor, motor, supplemental Ctx) \( \uparrow \) (glutamate, +)
\( \rightarrow \) CP \( \uparrow \) (GABA, -) \( \rightarrow \) GPe \( \downarrow \) (GABA, -) \( \rightarrow \) subthalamic nucleus \( \uparrow \) (glutamate, +)
\( \rightarrow \) GPe & GPi \( \uparrow \) (GABA, -) \( \rightarrow \) thalamus \( \downarrow \rightarrow \) premotor, supplemental cortices \( \downarrow \)
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 \( \uparrow \)
2) Dopamine inactivates the indirect pathway: movement \( \uparrow \)
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 \( \rightarrow \) decreased activity of direct pathway (D1R) and increased activity of indirect pathway (D2R) \( \rightarrow \) net effects: hyperactivity of Gpi neurons \( \rightarrow \) thalamus activity \( \downarrow \rightarrow \) cortical activity \( \downarrow \rightarrow \) movement \( \downarrow \)
Animal models: drug-induced selective degeneration of dopamine neurons in SNpc
1) 6-OHDA lesion
2) MPTP: MPP+ disrupts mitochondria electron transport complex I in dopamine neurons
3) Pesticide (rotenone): systematic disruption of mitochondria electron transport complex I activity; Lewy bodies occur (\( \alpha \)-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