1. **Neural circuits for movement control** (p.371-374)

(1) Lower motor neurons; send axons out of the brain stem and spinal cord to innervate the skeletal muscles of head and body.

(2) Upper motor neurons; cell bodies in the brain stem or cerebral cortex and axons descend to synapse with the local circuit neurons or with lower motor neuron.

(3) Cerebellum; motor control → detect motor error between an intended movement and the actual movement and reduce error through the projection to the upper motor neuron (p.441-443 Fig. 18.8, 18.9)
- Excitatory input from mossy fibers (execution) and climbing fiber (intend) to Purkinje cells
- Purkinje cell output to the deep cerebellar nuclear cells → error correction signal to modify movements

(4) Basal ganglia; control movement by regulating the activity of the upper motor neurons, suppress unwanted movements and prepare upper motor neuron circuits for the initiation of the movements → disorders: Huntington’s disease and Parkinson’s disease

![Overall structures involved in control of movement (Fig.15.1) Motor components of the human ganglia (Fig.17.1)](image)

2. **Basal ganglia**

(1) Mechanism – disinhibitory circuit; Inhibition of inhibition → activation (Fig.17.6)
(2) Organization of inputs to the basal ganglia and outputs from basal ganglia

3. Neurodegenerative disorders related to basal ganglia

- Huntington’s disease (HD) - hyperkinetic
  - a movement disorder consisting of rapid, jerky movements with no clear purpose
  - mutation of Huntingtin gene: unstable CAG triplet repeat (Glutamate) in coding region
  - Degeneration of striatum: projection from the caudate and putamen to the globus pallidus (external segment) is diminished

- Parkinson’s disease – hypokinetic
  - tremor at rest, slowness of movement (bradykinesia), rigidity of the extremities and neck, and minimal facial expression
  - genetic components: mutation of genes such as α-synuclein, Parkin, and DJ-1
  - treatment; enhancing release of dopamine in the caudate and putamen
  - Experimental evidence: studies from degeneration of the dopaminergic cells of substantia nigra induced by MPTP → similar symptom to Parkinsonian patients
  - progressive loss of dopaminergic neurons in the substantia nigra pars compacta projecting to and innervating neurons in the caudate and putamen
4. Hypokinetic and hyperkinetic disorders; balance of inhibitory signal is altered. (Fig. 17.8, 17.10)

(1) Direct pathway: Caudate/putamen inhibitory to GPi → release tonic inhibition of GPi to VA/VL complex of thalamus → frontal motor cortex

(2) Indirect pathway: Caudate/putamen inhibitory to GPe → release tonic inhibition of GPe to subthalamic nucleus → activation of GPi → increase tonic inhibition of GPi to thalamus

- Net effect:
  - Direct pathway activated → reduce tonic inhibition
  - Indirect pathway activated → increase inhibitory influences on the upper motor neurons (brake on the normal function of direct pathway)

Direct pathway: inputs from substantia nigra are diminished (D1 type) → globus pallidus (internal segment) more active → sustain the tonic inhibition from the GPi to the thalamus → less thalamic excitation of the motor cortex

Indirect pathway: inputs from substantia nigra are diminished (D2 type) → globus pallidus (external segment) less active → subthalamic nucleus activation increased → GPI more active

Projection from the caudate and putamen to the GPe is diminished → increase of the tonic inhibition from the GPe to the subthalamic nucleus → making the excitatory subthalamic nucleus less effective in opposing the action of the direct pathway → increase of thalamic excitation of the cortex; less tonic inhibition → leading to greater and often inappropriate motor activity