Cerebellum

(Learning objective: 117)

Cortex
Basal ganglia
Thalamus
Cerebellum
Brainstem
Spinal cord

Sensory events

MOVEMENTS
Two major recurrent loops of the motor cortex:
1. cerebellar loop
2. basal ganglia loop

A. cerebellar loop
a. Cortical input runs to cerebellum from MI, SMA, PM, SI, 5 and 7 areas through pontine nuclei
b. all sensory modalities provide input to cerebellum
Feedback through motor nuclei of the thalamus

B. basal ganglia loop from the cortex through basal ganglia and motor nuclei of the thalamus to the cortex

Anatomy of the cerebellum

- 10% of the whole amount of the brain
- 2 hemispheres + vermis
- 10 lobes
- Cortex (gray matter)
- White matter (200 million input)
- Deep nuclei
  - Dentate nucleus
  - globosus + emboliformis nucleus (interpositus)
  - Fastigial nucleus
  - (Deiters nucleus)
Cerebellar functions:
1. postural function
2. Coordination of intention and actual movement. Comparison of afferent copy and efferent copy.
3. Coordination of muscles during movement (agonists, synergists, antagonists). Continuous, precise and coordinated activity of muscles.
Voluntary movements and postural functions
Somatotopy in the cerebellum: multiple mapping

Cerebellum

Vermis
Anterior Lobe
Posterior Lobe
Floccular Lobe (balance)

Somatotopy, homunculus

Somatotopy in the cerebellum: multiple mapping
Cellular organization of the cerebellum

1. Molecular layer
2. Purkinje cell (ganglion) layer
3. Granule cell layer

Inhibitory elements of the cerebellum:
- purkinje cells
- basket cells
- stellate cells
- Golgi cells
- Lugaro cells

Excitatory elements of the cerebellum:
- mossy fibers
- climbing fibers
- granule cells
- parallel fibres
1. Mossy fibers terminate at excitatory granule cells
2. Granule cells give parallel fibers that form synapses with many Purkinje cells
3. Parallel fibers also form synapses with inhibitory basket cells
4. Basket cells then form synapses with inhibitory Purkinje cells: inhibition of inhibition = release
5. Climbing fibers go to a single Purkinje cell - induction of complex spikes (multi-phase action potential)

Golgi cell: inhibition of granule cells

Lugaro cell: feedback modulation of Golgi cells (Purkinje cells), serotonin sensitive

Inhibition: GABA (gamma-aminobutyric acid)
Functional organisation of the cerebellum:

1. archi(vestibulo) cerebellum
   - **Output nuclei**
     - Nucleus Deiters
     - fastigial nucleus

2. paleo(spino)cerebellum
   - interpositus nucleus
     - fastigial nucleus

3. neo(cerebro)cerebellum
   - dentate nucleus

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**1. Vestibulocerebellum (archicerebellum)**

**Structure**: flocculonodular lobe, vermis

**Afferent**: vestibular, vision

**Efferent**: Deiters nucleus, fastigial nucleus *(formatio reticularis)*

**Function**: eye and head movement, gait and balance, postural functions

**2. Spinocerebellum (paleocerebellum)**

**Structure**: paravermis

**Afferent**:
- spinocerebellar tract, vision, vestibular *(consequence of motion)*
- cortex *(motor program)*

**Efferent**: interpositus nucleus → brainstem (red nucleus), spinal cord, thalamus - cortex

**Function**: correction of movement patterns based on feedback (correction of muscle tone, power, coordination of flexors and extensors)
3. Cerebrocerebellum (neocerebellum, pontocerebellum)

**Structure:** lateral hemispheres

**Afferent:** sensory-motor cortex (BA 4,3,1,2,5,7), prefrontal cortex (via pons)

**Efferent:** dentate nucleus

1. → thalamus → cortex
2. → red nucleus → oliva inferior → cerebellum

**Function:** planning, initiation and termination of movements (timing), motor learning
**vestibulocerebellum**  
(archicerebellum)

**Spinocerebellum**  
(paleocerebellum)
Consequences of cerebellar damage: Cerebellar signs

- **Charcot’s triad**: nystagmus, intention tremor, telegraphic speech
  - Balance disorders (Romberg’s test)
  - Dizziness
  - Nystagmus
- Ataxia (awkward movements)
- Hypotonia
- Co-ordination problems
- Dysmetria (Dimension problem between the goal and muscle performance, finger-to-nose test; heel-knee test)
- Dysdiadochokinesia (Supination and pronation of the hand is problematic)
- Star-like gait
- Rhythmic, monotonous speech
- Intention tremor (Closer to the target bigger the movement of the fingers)
- Rebound
- Disorder of weight approximation

*Signs are ipsilateral and NOT contralateral as in the pyramid tract!*
The Basal Ganglia

(Learning objective: 116)
1. N. caudatus,
2. Putamen
3. Globus pallidus
4. Substantia nigra,
5. N. subthalamicus,
Inputs of the basal ganglia:

1) cortico-striatal
2) Nigro-striatal
3) Thalamo-striatal
Output of the basal ganglia

1) Globus pallidus pars interna to the thalamus
   - ventral-lateral nucleus
   - ventral-anterior nucleus
   - centro-median nucleus

2) Substantia nigra pars reticulata to the thalamus
   - ventral-lateral nucleus
   - ventral-anterior nucleus

   to the superior colliculus

   to the Pedunculopontine tegmental nucleus of the pons

Main cell types of neostriatum:

Medium spiny neurons
- receiving cortical tracts
  a. GABA + substance P/dynorphin
  D1 dopamine receptor
  b. GABA + encephalin
  D2 dopamine receptor

Cholinergic interneurons (~10%, no spines)

1. Direct ("go") path (D1): ctx → STR → GPint → thal → ctx
2. Indirect ("no-go") path (D2): ctx → STR → GPext → SN → GPint → thal → +ctx
3. Hyperdirect path: ctx → SN → GPint → thal → ctx

p.c. = pars compacta – dopamine – nigrostriatal pathway
p.r. = pars reticularis, ext. = external, int. = internal

p.c. = pars compacta – dopamine – nigrostriatal pathway
p.r. = pars reticularis, ext. = external, int. = internal

- p.r. silence releases colliculus leading to eye movement
- excitatory (glutamate)
- inhibitory (GABA)
From the thalamus to the cortex:

1) - skeletomotor loop (area 6)
2) - oculomotor loop (FEF)
3) - associative loop (prefrontal cortex)
Parkinson’s disease

1. Reduced and slow movements (hypo- and bradykinesia)
2. Muscle tone↑ (cogwheel rigidity)
3. Resting tremor with low frequency
4. Disturbances of gait and posture
5. Blunted affect (mask-like face)
6. Disorder of planning and problem solving, slow thinking

Pathogenesis: dopaminergic cell loss in substantia nigra pars compacta
Alpha-synuclein: regulation of transmitter release in dopaminergic synapses + neuronal survival (aggregation in Parkinson’s - Lewy-bodies)

Treatment:
- L-DOPA (dopamine’s progenitor)
- Dopamine receptor agonists
- Deep brain stimulation

Lewy-body: aggregated alpha-synuclein and other proteins

Normal substantia nigra Parkinson’s
Neuromelanine containing dopaminergic cells Reduced number of dopaminergic cells
Disorder of dopaminergic transmission: positron emission tomography (PET)

Neuromelanin-sensitive magnetic resonance imaging (MRI)

Decreased intensity in Parkinson’s substantia nigra

Deep brain stimulation (DBS) in Parkinson’s disease
Disorders of the basal ganglia
(formerly together with Parkinson’s: extrapyramidal symptoms)

**Chorea:** large amplitude „dancing“ movements of extremities

**Huntington’s disease:** 4. chromosome, CAG-triplet expansion

- *huntingtin* protein (glutamine↑), aggregation
- GABA-ergic spiny neurons↓
- severe cognitive disorder: disorganized thinking
- extreme swings of mood

**Ballism:** involuntary flinging, swinging, and jerking movements of proximal extremities (n. subthalamicus lesion)

**Athetosis:** slow, sinuous, writhing movements (putamen lesion)

**Tic:** repetitive, nonrhythmic, stereotyped, circumscribed movement or vocalization (e.g. eye blinking, throat clearing)

**Tourette’s disease**

**Dystonia:** tone↑ in circumscribed muscles (e.g. torticollis):

- hereditary (*torsin* gene) or drug-induced (dopamine antagonists that also induce *tardive dyskinesia* [e.g. grimacing, tongue protrusion, lip smacking])