Disorders of the motor system

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Content

1. Motor system – physiological remarks

Movement = Complex activities unified to achieve the ultimate goal (visible movement)
Division of motor activity:

According to will, awareness:

- voluntary
- involuntary

According to purpose:

- support (attitude) - serves to maintain a certain position of the body
- targeted (motion)

According to origin:

- reflex
- given by the central motor program

Every movement (and reflex motor activity) should be seen as the result of a complex interaction of all motor structures!

Overview of mechanisms of movement control

Structures involved into motor system control:

1. Spinal cord
2. Brain stem
3. Cerebellum
4. Basal ganglia
5. Thalamus
6. Cerebral cortex

These are structures interacting with each other, not just a hierarchical arrangement (Fig.1)!

Support and targeted motor system

Support motor system

- the basis of movement is muscle tone
- on muscular tone is built up a system of attitude and upright reflexes = supporting motor system (depending on the activity of reticular formation, medulla oblongata, pons, midbrain and statokinetic sensor)

Targeted motor system

- the plan od voluntary movement is given by the activity of association cortex
- the program to perform voluntary movement is realized in the cerebellum (fast target movement) or in basal ganglia (slow and steady movements)
- the program goes through the thalamus into the motor cortex that controls the performance of movement

Spinal and brains stem centres of motor system

Spinal cord:

- is the lowest control centre of the motor system
- applied in spinal reflexes and reflexive motor system

- muscle tone is ensured by coordination of alpha and gamma neurons (combined feedback)
- muscle status information is permanently transferred to the appropriate spinal centre

Brain stem:

- medulla oblongata and pons Varoli are involved in mimics, phonation and speech
- mesencephalon is a centre of unconditioned visual and auditory reflexes - ensure movements of the head and body in response to light or sound stimulation
- brain stem participates in postural motor control
- reticular formation (spread over the entire length of the brain stem):
    - participates in the management of proprioceptive reflexes (gamma system), attitudinal reactions, upright reflexes, voluntary movements (descendent facilitation system)
    - the descendent inhibitory system, on the other hand, dampens the spinal reflexes
    - provides integration of proprioceptors, exteroceptors and statokinetic sensors with information from the cerebellum, brain stem, hypothalamus and cerebral cortex

For notes on physiology of other structures see below, chapters 3,4,5.

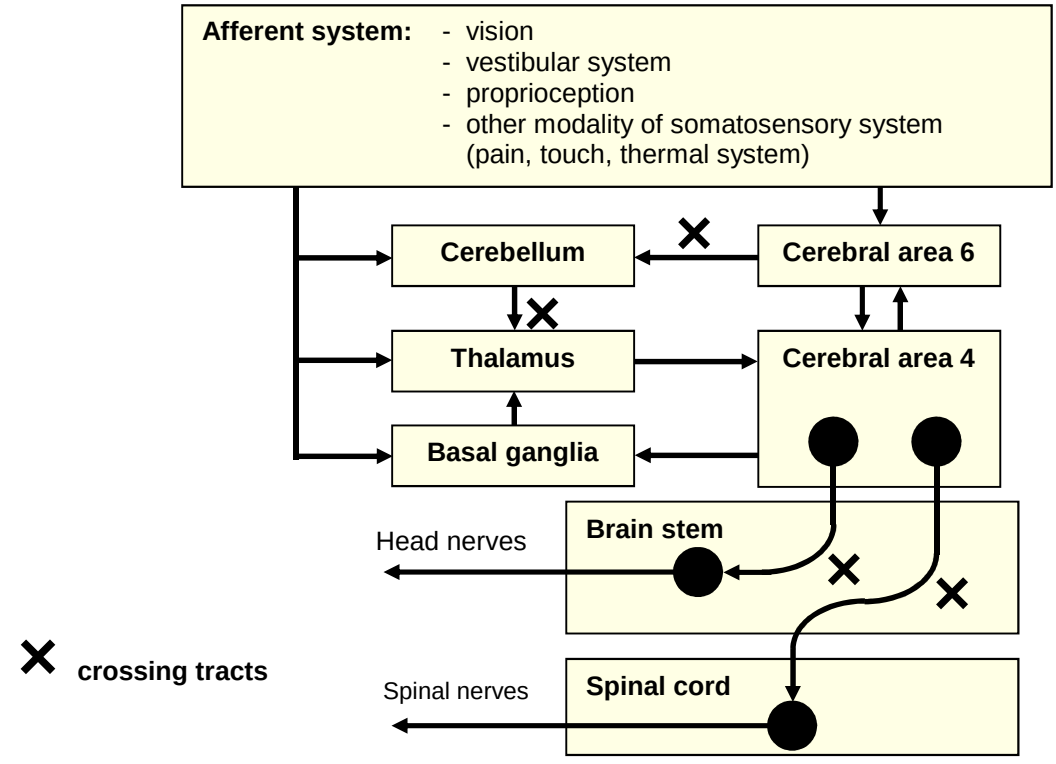

Fig. 1: Participation of individual structures in the management of targeted movement.

2. Disorders of motor function – general concepts

Impaired motor system activity concerns:
- muscle tone
- motor function

Both disorders often occur simultaneously but can be classified separately.

2.1 Disorders of muscle tone

Increased muscle tone:

a) Spasticity:
- occurs when corticospinal or corticonuclear tracts are damaged
- the muscle resists passive stretching, then the limb springy returns to its original position
- when the maximum resistance of the muscle is exceeded, a sudden relaxation of the muscle follows, another passive movement can then be done easily (the phenomenon of the clasp knife)

b) Rigidity:
- increase of plastic tone
- occurs when supraspinal regulatory circuits are damaged (e.g. damage of the dopaminergic substantia nigra in the case of the Parkinson's disease)
- passively stretched muscle puts the same resistance from the beginning to the end, but sometimes it passes through the passive movement several times by sudden decrease of the muscle tone (so-called gearwheel phenomenon)

Decreased muscle tone:

Hypotonia: arises from various reasons, from the damage of some parts of the spinal circuits, or some parts of the supraspinal control circuits of the muscle tone.

2.2 Movement disorders

Paresis: partial inability of active voluntary movements (reduction of muscle power)

Plegia: total inability of active voluntary movement

Monoparesis, monoplegia: only one limb is affected
Hemiparesis, hemiplegia: only one half of the body is affected (right or left)
Paraparesis, paraplegia: simultaneous affection of both lower (less frequently both upper) limbs
Quadriparesis, quadriplegia: affection of all limbs

Contractures: fixed position of the limbs or other body parts in a fixed position
Hyperkinesia: pathological, abnormal, involuntary movements that interfere with voluntary or reflexive movements

Hyperkinesias include:

- tremor (shaking): is a rhythmic involuntary hyperkinesis of some parts of the body that is caused by contractions of both agonists and antagonists either at rest (resting tremor), static intimacy (static tremor) or movement (intentional tremor)
- cramps (convulsions, spasms): involuntary contractions of individual muscles or muscle groups of striated or smooth muscle (tonic: longer lasting muscle spasms, clonic: intermittent muscle cramps)
- fasciculation: spontaneous contractions of the muscle fibre groups (parts or whole motor units), visible as waves or twitching under the skin, but have no locomotor effect
- fibrillation: spontaneous contractions of individual muscle fibres, not visible, demonstrated electromyographically
- myoclonus: short-lasting clonic seizures affecting the individual muscles or parts of the limbs and the body; often affected mimic muscles
- tics: involuntary hyperkinesia resulting from damage of the non-pyramidal system; mostly affected small muscle groups
- ballism: violent involuntary movements with great excursions and intensity (as throwing something); when unilateral - hemiballism
- chorea: spontaneous, random, unpredictable movements of various parts of the body, especially on the limbs and face (sometimes resembling dancing)
- athetosis: slow rotating movements; when the neck muscles are affected, they are called torticollis

Bradykinesia: slowdown of the movement

Hypokinesia: reducing the amplitude of the movement

Akinesia: disorder of voluntary movement initiation

3. Disorders of the corticonuclear and corticospinal (pyramidal) tracts

The (pyramidal) motor system consists of (Figure 2):

- **upper motor neuron** (pyramidal cells in motor cortex), its axons form the corticonuclear and corticospinal tract
- **peripheral motor unit** (lower motor neuron, neuromuscular junction, striated muscle)

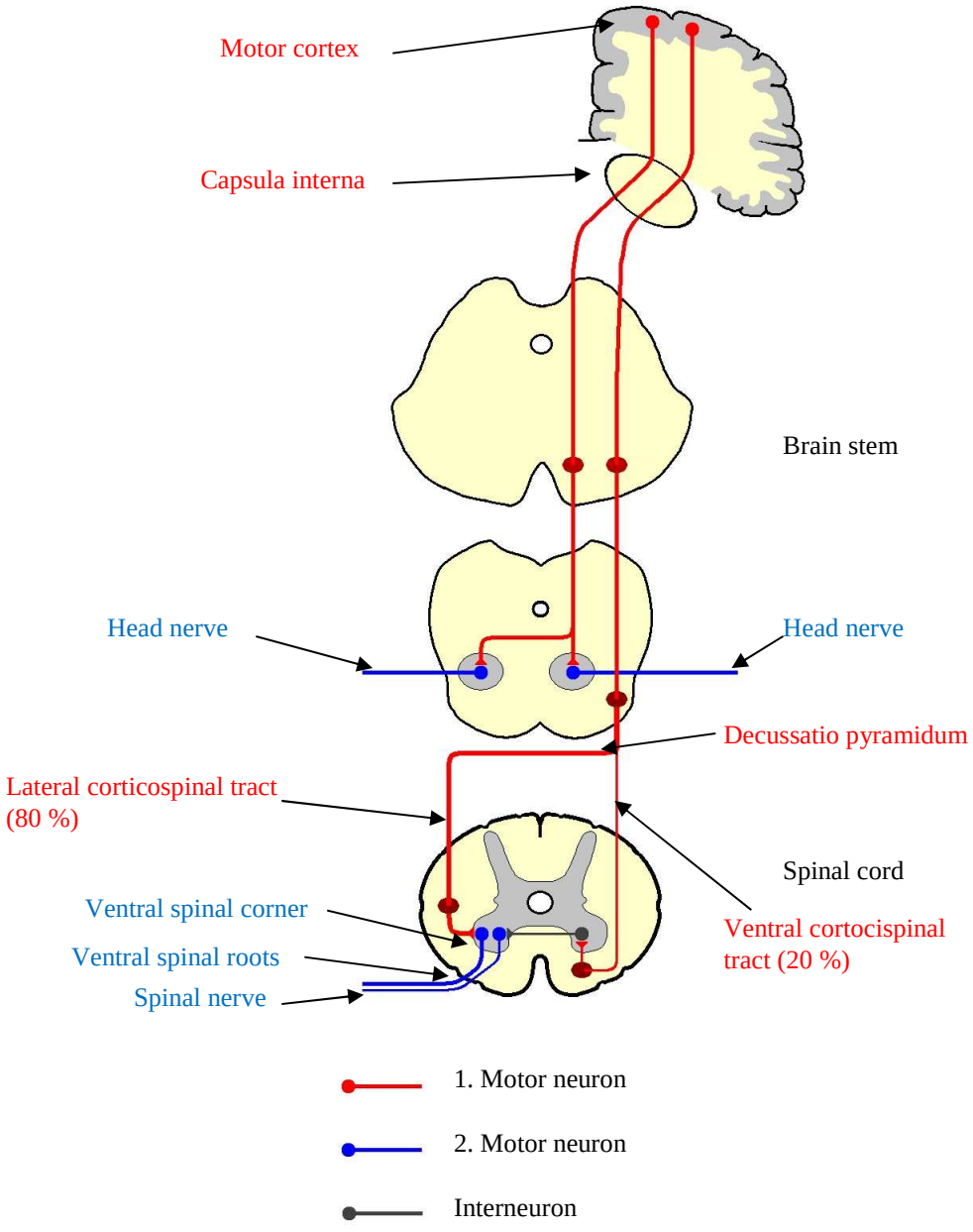

Fig. 2: Schema of motor tract.

3.1. Disorders of the upper motor neuron

- the nerve fibres of the pyramidal tract originate from motor cortical regions and terminate in the ventral horns of the spinal cord (corticospinal tract)
- part of the fibres comes from the parietal lobe and terminates in the dorsal horns of the spinal cord (allow for modulation of the movement)
- the corticospinal tract descends ipsilaterally through the internal capsule into the medulla oblongata, at the level of the junction of the medulla oblongata and the cervical spinal cord most of the fibres cross (forming the lateral corticospinal tract)
- about 20% of the fibres run without crossing (ventral corticospinal tract), the next crossing occurs at the level of the appropriate spinal segment, and a part (10%) remains uncrossed
- corticonuclear fibres originate from the lateral parts of the frontal and parietal lobes, then form synapses with the motoneurons in the nuclei of the motor cranial nerves, running both ipsilaterally and contralaterally to the nuclei of the cranial nerves (exception: n. facialis - in the lower half of the face only the fibres of the contralateral hemispheres)
- modulation of voluntary movement is ensured by following tracts: vestibulospinal, reticulospinal, tectospinal, rubrospinal

Central spastic palsy

= disorder of the upper motoneuron in any part of its course
Causes: most commonly circulatory disorders (ischemia, bleeding), injuries, autoimmune demyelinating processes, neuroinfections, tumours
Serious localization of lesions is the area of the capsula interna - the pyramidal tract is concentrated here into a small space, which is often affected by haemorrhage or ischemia, which damages all the fibres of the tract!
Symptoms:

- **palsy**: affected voluntary movement
- **spasticity** (spastic palsy), but not in the acute stage, there is hypotonia (spinal shock stage)
- **hyperreflexia**: increased reflex performance, reflexogenic zone expansion, reflex can be triggered even more distantly than usually (missing inhibitory influence of upper motor neuron)
- **the occurrence of so-called pathological reflexes** (normally not present in healthy individuals, physiologically only to the stabilization of the vertical position of the body, until about 12-18 months after birth), e.g. Babinski reflex - the extension of the thumb of the foot after irritation of its outer edge or mass reflexes (such as mass reflex, after a similar irritation, also flexion in the hip and knee joints and sometimes also defecation, urination and possibly perspiration and change in blood supply as a result of irradiation in the spinal cord below the lesion site occur)
- at the beginning, there is not primarily significant atrophy of the muscles because of the constant supply of hypertonic stimuli (or only mild atrophy due to inactivity)
- destruction of the corticonuclear and corticospinal tracts in the pons Varoli leads to complete loss of voluntary movement with fully preserved consciousness, the so-called **locked-in syndrome**, can imitate coma or vegetative state (the affected person is only capable of blinking and vertical eye movement)

3.2 Disorders of the lower motor neuron

- the lower motor neuron is a part of peripheral motor unit (with the neuromuscular junction and fibres of striated muscle innervated by the given neuron)
- the lower motor neuron bodies are located in the anterior spinal corners and in the nuclei of the head nerves
- the fibres of one motor neuron innervate a various number of muscle fibres (depending on the type of muscles and the softness of the movements) that are then contracted synchronously

Peripheral flaccid palsy

= damage of any parts of the spinal motor neuron or stem motor neuron (in the case of motor head nerves)

Causes: circulatory disorders, inflammation, tumours, traumas, degenerative diseases etc.

Symptoms:
- reduction to loss of active movement – **hypokinesis up to akinesia**
- reduction of muscle tone - **hypotonia up to atonia**
- reduction to loss of tendon reflexes – **hyporeflexia up to areflexia** (due to the motor-fibre disorder, the muscle is eliminated)
- **muscle atrophy**, reduction of muscle mass starts 2-3 weeks after nerve fibre disruption, so-called deafferentation neurogenic atrophy (muscle fibre cannot exist without neuron), there is an atrophy of the whole motor units
- **trophic skin changes** (trophic skin innervation disorder): skin is smooth, thin, pale or cyanotic, peels off, nails are frayed, hair loss is evident, later ulcers and decubitus are formed
- spontaneous **fibrillation and fasciculation** (after 3 weeks): due to the spontaneous activity of the neuromuscular junction (due to an excess of acetylcholine)
- denervated muscles undergo **fibrotic changes**

The character of motor disorder according to localization of lesion
The type of palsy and its distribution on the body depends on localisation and range of lesion of motor tract. In some localisations (brain stem, spinal cord) can the lesion damage the upper and lower motor neuron and central palsy of some part of the body is combined with peripheral palsy of some other part. The lesion of all fibres responsible for the innervation of a muscle leads to its plegia, the lesion of only a part of the fibres causes a paresis. Often, the lesion also affects the anatomically close structures of other functional systems; in addition to the motor tract and therefore the motor disorder can be combined, for example, with sensory and vegetative disorders.
Examples of localization of the lesion of the pyramidal system and its motor manifestations:

1. Cortical lesion of gyrus praecentralis
   - disturbance of the movement of the distal parts of contralateral limbs, especially the fragmentation of the movement of the acral parts
2. Complete lesion of capsula interna
   - contralateral central hemiplegia
3. Alternating brain stem syndromes (Fig. 3)
   = unilateral damage of the brain stem, a number of syndromes differing from those of particular cranial nerves

- contralateral central hemiplegia resulting from a damage of corticospinal tract and ipsilateral peripheral palsy of appropriate head nerve from the destruction of its nucleus

4. Transversal spinal cord lesion
   - bilateral central palsy below lesion level from a damage of corticospinal tract and peripheral palsy on the level of lesion from the destruction of motor neurones of frontal spinal corners
   - lesion in the cervical part of spinal cord → quadriplegia (over C4 also palsy of diaphragm), lesion of the thoracic part of spinal cord → paraplegia

5. Brown-Séquard spinal hemisyndrome (Fig. 4)
   = transversal interruption of one half of the spinal cord
   - ipsilateral central palsy below lesion level from a damage of corticospinal tract and ipsilateral peripheral palsy on the level of lesion from the destruction of motor neurones of frontal spinal corners (in addition ipsilateral loss of tactile and deep sensation due to interruption of the dorsal columns, and contralateral loss of thermic- and pain sensation due to a partial damage of the spinothalamic tract)

6. Interruption of the anterior spinal cord
   - ipsilateral peripheral palsy of muscles innervated from appropriate spinal segment

7. Interruption of the peripheral nerve
   - peripheral palsy of muscles innervated by the peripheral nerve

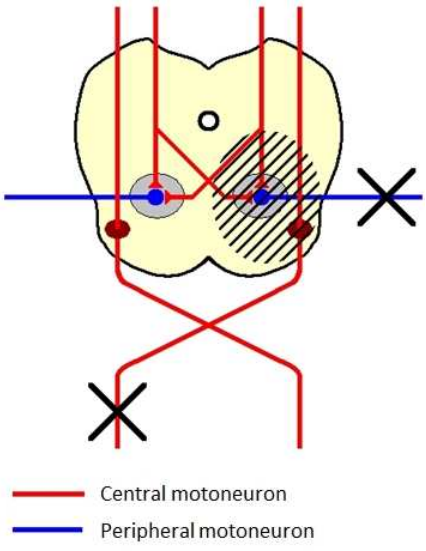

Fig. 3: The schema of a damage of motor tracts in alternating brain stem syndromes.

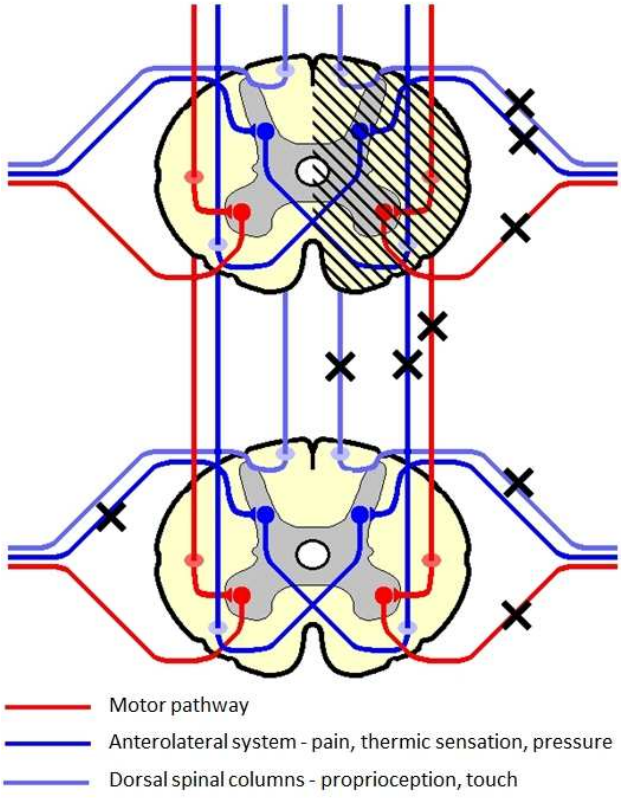

Fig. 4: The schema of a damage of motor tracts and sensitive tracts in Brown-Séquard spinal hemisyndrome.

3.3 Disorders of the neuromuscular junction

Neuromuscular junction = the space on which the motor nerve fibre is terminated on the skeletal muscle (Fig. 5)

- own transfer of the nerve impulse to the muscle fibre is accomplished with acetylcholine (the action potential reaches the terminal part of the nerve, followed by the release of the vesicle with acetylcholine into the synaptic cleft)
- follows the interaction of acetylcholine with nicotinic cholinergic receptors and depolarization of the postsynaptic membrane of the neuromuscular end plate
- the muscular action potential is induced (after exceeding the threshold potential of the excitable muscle cell membrane)
- acetylcholine on the neuromuscular junction is metabolised by acetylcholinesterase (the membrane of the plate may repolarize and respond to the further release of acetylcholine)

Disorders of transmission of the nerve impulse to the muscle:

1. Attenuation of acetylcholine synthesis or its reduced release:

Botulism (poisoning with botulinum toxin)

- botulinum toxin is irreversibly connected to cholinergic motor nerve endings
- it blocks synthesis and also release of acetylcholine
- the first symptoms of poisoning include vision impairment (diplopia), dizziness, dysarthria, dysphagia
- muscle paralysis develops rapidly and leads to respiratory failure

Myasthenic (Lambert-Eaton) syndrome

- failure of acetylcholine release from nerve endings
- the cause is not known
- affects the muscles of the armpit and pelvis, the body and the lower limbs
- sensory (paraesthesia) and vegetative disorders (dry mouth, constipation, micturition disorders, impotence)
- in a half of cases, the incidence of small cell lung carcinoma

2. Competitive cholinergic receptor blockade:

Tubocurarine a curariform substances

- derived from alkaloid curare (arrow poison)
- nowadays used in general anaesthesia such as myorelaxant
- suppression the effect of acetylcholine on the motor unit
- can be antagonized with acetylcholine (e.g. by increasing its concentration by blocking acetylcholinesterase)

3. Long-term depolarization of the neuromuscular junction:

Older type of myorelaxants like succinylcholine

- trigger initial muscle twitching: action similar to acetylcholine (depolarization, development of action potential)

- muscle paralysis is long-lasting (to the degradation of the substance)

4. Blockade of acetylcholinesterase:

- short-term (reversible) blockers: e.g., physostigmine, neostigmine - use for myasthenia gravis therapy, antagonism for the curariform myorelaxants
- long-term blockers: organophosphates (combat chemicals, insecticides)
- reducing the degradation of acetylcholine and increasing its concentration in the synaptic cleft

5. Other disorders of the neuromuscular junction:

Myasthenia gravis
- autoimmune disorder
- typical production of antibodies against the acetylcholine receptor on the neuromuscular junction
- circulating antibodies bind to receptors, there is a disorder of nerve-to-muscle transmission
- mainly affected muscles of the head, limbs, intercostal muscles and diaphragm
- the main symptom is muscle weakness and easy tiredness (typical primary symptoms: upper eyelid ptosis and diplopia)
- often associated with the persistent thymus in adulthood

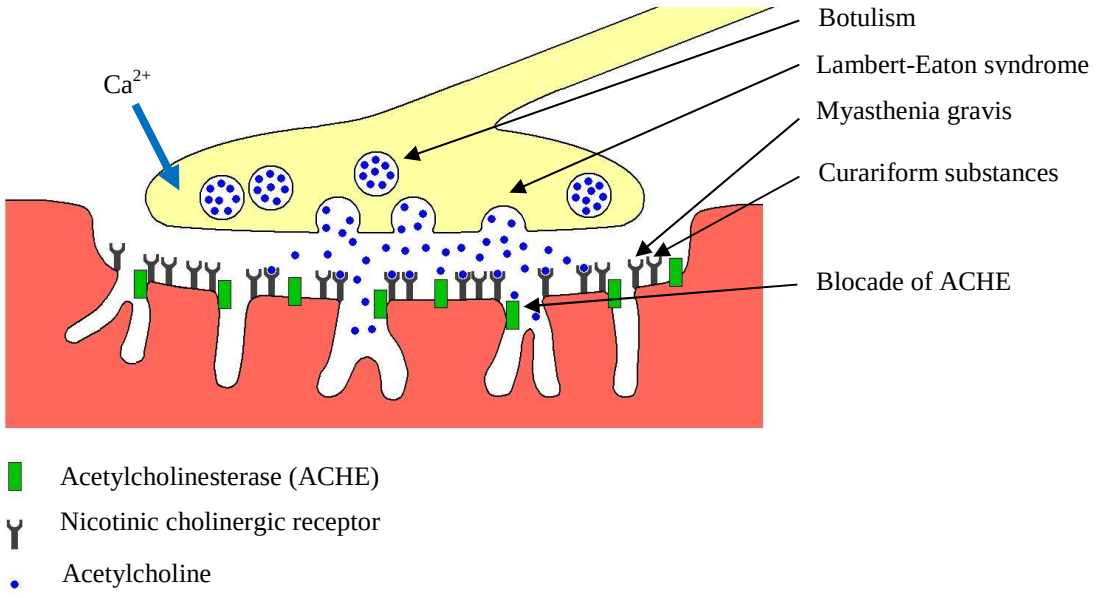

Fig. 5: The scheme of neuromuscular junction and possible disorders of its function.

Other clinical syndromes and nosological units associated with motor system disorder:

Spinal muscular atrophy:
- the basis is the degeneration of motor neurons of the ventral spinal corners, in some cases also of the brain stem motor neurons
- symptoms typical for peripheral palsy (onset such as muscle weakness and hypotonia)

- according to the age of the onset and progression, the individual forms (acute infantile, late juvenile, adult form)

Amyotrophic lateral sclerosis

- degeneration of central and peripheral motor neuron
- impaired also nuclei of cranial nerves (n. IX., X., XI., VII., V.)
- aetiology unknown, perhaps viral or autoimmune origin (a number of Cu-, Zn-superoxiddismutase-SOD mutations have been detected in familial cases)
- often starts as a bulbar form with dysphagia and dysarthria
- later symptoms of peripheral and central palsy (muscle weakness, atrophy, hyperreflexia, spasticity, pathological reflexes)
- the disease progresses and usually ends with death within 3 years (decrease in blood pressure, arrhythmia, arrest of breath)

Demyelination polyneuropathy

- congenital or acquired
- it is affection of myelin sheaths or Schwann cells (they produce myelin in the peripheral nervous system)
- manifested by motor weakness, mild loss of sensitivity, and generalized loss of tendon reflexes
- in severe cases also respiratory failure due to demyelination of intercostal nerves and n. phrenicus
- aetiology: genetic and autoimmune factors
- typical example: Guillain-Barré syndrome (inflammation polyneuropathy)

4. Disorders of the extrapyramidal system

Extrapyramidal motor system includes:

- basal ganglia
- motor nuclei in brain stem
- thalamic nuclei influencing motor system
- cerebellum

The main function of extrapyramidal system: coordination of initiation and course of voluntary and involuntary movements, maintenance and modulation of muscle tone, attitude and position (Fig. 6)

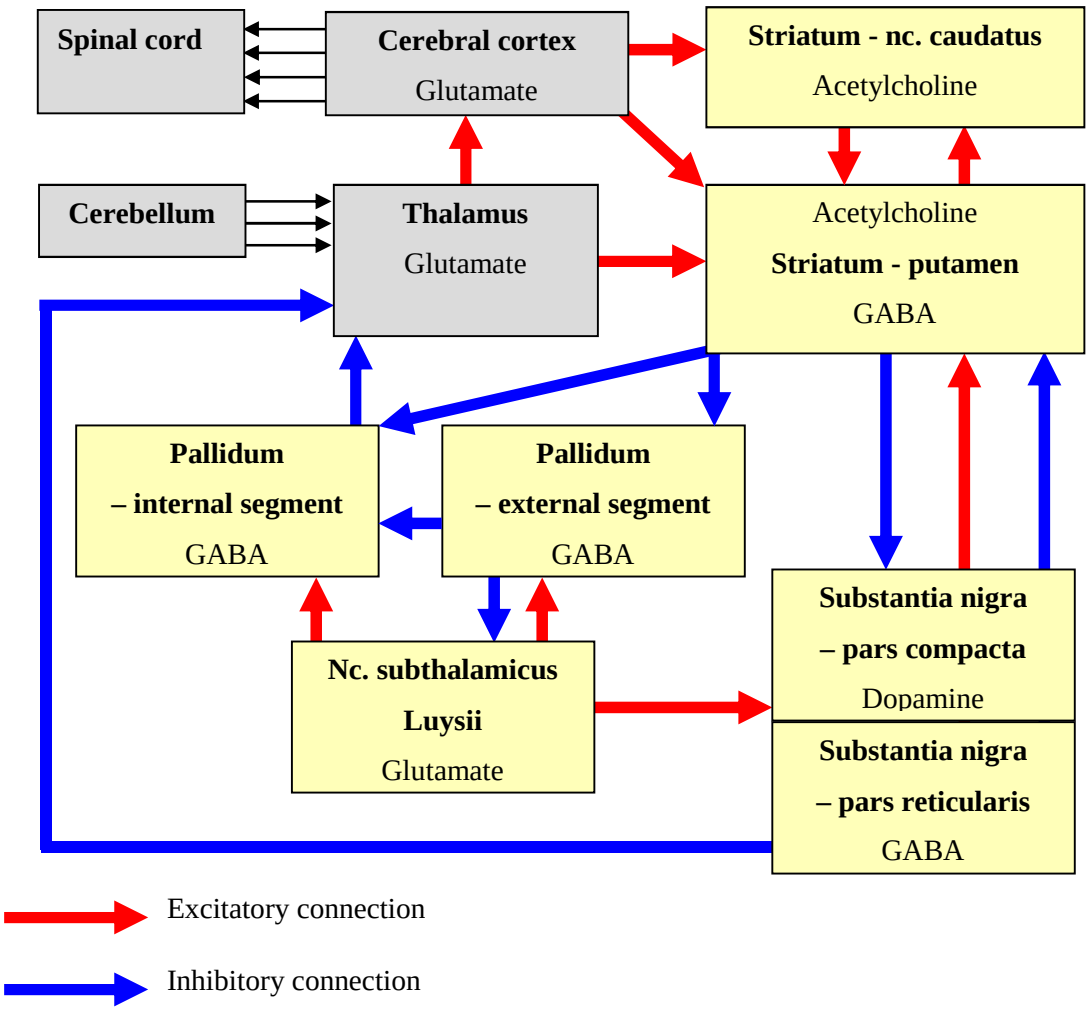

Fig. 6: Involvement of basal ganglia.

Basal ganglia include:

- nucleus caudatus and putamen (together form a functional unit striatum)
- globus pallidus (pallidum)
- substantia nigra
- nucleus subthalamicus Luysii

Sometimes there are assigned:

- nucleus basalis Meynerti
- nucleus accumbens
- nucleus ruber
- nuclei of amygdala

Function of basal ganglia: elaboration of involuntary movement programs, control of direction, amplitude, speed and force of involuntary and voluntary movements
The main manifestations of their disorders:

- disorders of muscle tone
- disorders of position
- decreased movement activity
- involuntary pathological movements

4.1 Hypokinetic syndromes – Parkinsonism

= clinical syndrome includes these symptoms: hypomimia, flexion of the hull, slowdown of voluntary movement, disturbances of gait, restraint from rest to movement, muscle rigidity, resting tremor

Common sign of this syndrome: **disorder of nigrostriatal dopaminergic system**

4.1.1 Parkinson's disease

- Neurodegenerative disorder of the substantia nigra
Aetiology: unknown, perhaps the influence of exogenous toxins (herbicides), about 20% of the patients influence the inheritance (genetic disposition increases sensitivity of nigrostriatal system to toxic effects)
Pathophysiological background: Progressive loss (apoptosis) of pigment dopaminergic neurons providing connection of the substantia nigra and striatum, followed by dopamine deficiency in the nigrostriatal system (compared to cholinergic activity)
Symptoms:

- resting tremor, increases by emotions, disappears in sleep, tremor of fingers is described as so-called counting of money
- muscle rigidity
- slowdown of movements (bradykinesia)
- instability of posture
- disorders of gait, especially difficulty in starting, short steps, difficulty in stopping or changing the direction of gait
- decrease of volume of speech
- fatigue up to apathy
- later rigidity affecting especially flexors
- hypomimia (face does not express emotional expressions)
- also affection of the autonomic system: increased sweating, systemic hypotension, peripheral vasomotor instability, constipation, disorders of bladder emptying
- paradoxical kinesis - sudden, time-limited ability of almost normal targeted movement (dance, precise shooting) due to enormous emotional experience (joy, anger)

4.1.2 Other examples of hypokinetic syndrome:

Progressive supranuclear degeneration
= loss of neurons in the globus pallidus, nucleus subthalamicus, substantia nigra, in periventricular grey matter, in nucleus dentatus of cerebellum

Corticobasal degeneration
= atrophy of the cortex in the gyrus praecentralis, frontal lobe, upper part of occipital lobe, loss of pigment neurons in the substantia nigra and locus coeruleus

Nigrostriatal degeneration
= loss of neurons in the striatum

Olivopontocerebellar atrophy
= atrophy of nuclei in the pons Varoli, inferior olive and cortex of cerebellum

Parkinsonism from other causes
- from disorder of blood supply of the basal ganglia
- from hypoxia and manganese or CO poisoning

4.2 Hyperkinetic syndromes

= are due to a reduction in motor suppression affecting the (motor) thalamic nuclei on the cortical motor region

4.2.1 Huntington's disease (Huntington's chorea)

Aetiology: congenital, autosomal dominant disease (mutation of the huntingtin gene localized on the chromosome 4, increased CAG triplet repeat leading to the extension of the polyglutamine tract in the huntingtin protein)
Pathophysiological background: degeneration of the striatal neurons, disorder of modulation of the motor output from basal ganglia
Clinically, it usually begins to manifest in the adulthood (around 30 years of age).

Symptoms:
- progressive hyperkinesis, choreatic movements of the whole body
- dementia of subcortical type: memory loss, slowing of mental processes, apathy, emotional lability, lack of care for personal hygiene, disintegration of personality
- the disease lasts usually 10-30 years, it is not fatal itself, the cause of death is usually a fall, the pneumonia from immobility or other complications

4.2.2 Wilson's disease (hepatolenicular degeneration)

Aetiology: autosomal recessive inheritance, mutation of a gene encoding transmembrane ATPase carrying copper
Pathophysiological background: ineffective binding of copper to ceruloplasmin (binding of copper to ceruloplasmin decreases the formation of free radicals), copper is deposited in tissues, e.g. in the cerebral cortex, basal ganglia (dominated by putamen atrophy), liver, pancreas, kidneys, bones, joints, cornea etc.

Symptoms of basal ganglia and cerebral cortex disorder:

- dystonia
- muscle rigidity
- swung movements
- mental retardation (due to storage of copper in the cerebral cortex)
- if the disease is not treated, chronic copper intoxication leads to hepatic failure

4.2.3 Sydenham chorea (St. Vitus Dance)

Aetiology: streptococcal infection
Pathophysiology: disorder of the striatum, corpus Luysii and nucleus subthalamicus (decrease of production of GABA in these structures)
Symptoms: acute chorea, symptoms disappear after 3-4 months, it mostly affects school age children

5. Cerebellar disorders

The cerebellum consists of 3 anatomically, phylogenetically and functionally defined parts:
Archicerebellum (vestibulocerebellum)
- Consists of the lobus flocculonodularis and the nucleus fastigii.
- Controls vertical posture and equilibrium.
- Receives information from the vestibular sensor, proprioceptors and information about eyeball movements.
- Efferent signaling goes to the vestibular nuclei, thalamus and reticular formation.

Paleocerebellum (spinocerebellum)
- Most of the vermis, medial parts of the hemispheres, nucleus globosus, nucleus emboliformis)
- Controls coordination of postural muscles and muscle tone, ensures adequate posture and muscle tone during movements.
- Receives afferent information from the proprioceptors.
- Efferent signaling goes to the thalamus, primary motor cortex in the frontal lobe and to spinal motoneurons

Neocerebellum (cerebrocerebellum)
- Lateral parts of the cerebellar hemispheres, nucleus dentatus
- Includes programs for voluntary movements, hypothetic internal models of movements, coordinates voluntary movements of acral parts of the extremities - the cortex-pons-cerebellum-dentate nucleus-thalamus-cortex circuit.

The cerebellum cooperates with the contralateral brain hemisphere that controls contralateral body side movements. Therefore, each cerebellar hemisphere influences movements on the ipsilateral body side.

The cerebellum is involved also in cognitive and affective functions, speech, sensory processing!

Causes of cerebellar damages
- Developmental disorders (often combined with brain stem malformations) – e.g. cerebellar agenesis or hypoplasia, Dandy-Walker syndrome, Arnold-Chiari malformation
- Intoxication: The most frequent cause of the transient cerebellar dysfunction is acute ethanol intoxication. Chronic ethanol abuse may lead to permanent disorder.
- Mechanical trauma (Mechanical destruction of the cerebellum by injury or surgery, e.g. due to a tumour, is called posterior fossa syndrome.)
- Vascular causes: ischemia, haemorrhage
- Cerebellar tumours: Compression and destruction of cerebellar tissue, often cerebrospinal fluid circulation disorders (even hydrocephalus). The cerebellum is a frequent location of the medulloblastoma in children.
- Demyelinating diseases disorders: sclerosis multiplex, acute disseminated encephalomyelitis after varicella virus infection, post-irradiation demyelination
- Hereditary cerebellar ataxias = heterogeneous group of hereditary diseases affecting the cerebellum and, in many cases, also other neural (brain stem, spinal cord, peripheral nerves) as well as extraneural organs.
  - ❖ <u>Friedreich's ataxia</u>
    - Autosomal recessive, mutation in the gene encoding mitochondrial frataxin protein (related to iron metabolism)

- Manifestation already in the first decade: development of ataxia, dysarthria, hyporeflexia, loss of pain and thermic sensation
- Cardiomyopathy
- Premature death mostly due to cardiac failure.

❖ Ataxia teleangiectasia
- Autosomal recessive
- Ataxia is accompanied by teleangiectasia in the skin, conjunctiva, lung circulation, - liver
- Often also immunodeficiency and increased incidence of tumours

❖ Autosomal recessive spastic ataxia (ARSAC)

❖ Autosomal recessive cerebellar ataxia (ARCA-1, ARCA-2)

❖ Ataxia with oculomotor apraxia (AOA-1, AOA-2)
- Autosomal recessive, ataxia combined with oculomotor deficits

❖ Spinocerebellar ataxia (SCA)
- Group of more than 40 autosomal dominant diseases with different mutations
- They are manifested with cerebellar ataxia and variable complex of neurological and non-neurological symptoms.
- In some of the SCAs (e.g. SCA 1, SCA2, SCA3, SCA6, SCA7 etc.) are so called CAG repeats – the gene contains higher number of CAG repetitions causing expansion of polyglutamine tract in the protein. The protein acquires pathological features including resistance to proteolytic enzymes. Therefore, pathological protein molecules accumulate in the cell that express the gene. Protein aggregates interfere with function of the cells and finally lead to its degeneration.
- The most frequent type is SCA1. In the Czech Republic, the most frequent is SCA2.
- SCA2 is caused by extension of CAG repeat in the ataxin-2 encoding gene on the chromosome 12. It is manifested by progressive cerebellar ataxia, weak tendon reflexes, amyotrophy, dementia.

5.1 Manifestations of cerebellar diseases – cerebellar extinction motor syndrome

Cerebellar extinction syndrome has 3 basic motor components:

1) **Cerebellar ataxia** (see below) – It consists of:
   - asynergy = disorder of movement coordination, lack of coordination of activity of individual muscles or muscle groups (limb asynergy = small asynergy, trunk asynergy = great asynergy)
   - dysmetria (mostly hypermetria) = incorrect extent of the movements. Delayed and insufficient activation of antagonistic muscles leads to delayed termination of movements, overshooting. It is due to lacking prediction ability that is necessary for timely correction signals to adjust the movements.
   - adiadochokinesia = inability to perform fast alternating movements (e.g. pronation – supination)
2) **Intention tremor** – occurs during targeted movements, disappears in rest
3) **Passivity** (cerebellar hypotonia) – decreased muscle tone, increased extent of joint movements and decreased resistance to passive movements with the extremities

These three basic disorders give rise to particular symptoms of cerebellar lesions:

– Posture disorders (posture ataxia): titubations, falls preferentially backwards, independent on head position, wide base

- Gait disorders (gait ataxia): staggering, backwards directed deviations (retropulsion) and forwards (propulsion)
- Speech disorders: non-fluent, incoherent, slurred, saccaded speech due to asynergy and adiadochokinesia of the orofacial and respiratory muscles
- Muscle tone disorders: hypertonia of the trunk extensors and hypotonia of the limb muscles
- Oculomotor disorders – sight nystagmus, inability of fluent following of an moving object by eyes due asynergy and hypermetria of the oculomotor muscles
- Macrography – due to hypermetria

Except for motor disorders, cerebellar diseases are manifested also by the cognitive-affective syndrome (Schmahmann's syndrome).
Individual symptoms of cerebellar diseases can be expressed with variable intensity depending on extent and localization of the cerebellar lesion (whole cerebellum affection, restricted lesions):

Paleocerebellar syndrome:
- Caused by medial cerebellar lesions affecting both the achicerebellum and paleocerebellum
- The symptoms are usually bilateral because the medial lesion affects both sides of the paleocerebellum with high probability.
- It is manifested by gait and posture ataxia. Isolated flocculonodular lesion (rare) causes symptoms similar to vestibular disorders.
- Falls and deviations are to various directions, but most often backwards.

Neocerebellar syndrome
- Caused by lateral cerebellar lesions affecting lateral part of one of the cerebellar hemispheres.
- The symptoms are mostly unilateral (ipsilateral relative to the lesioned side) because a bilateral lesion that does not affect central structures is less probable.
- Neocerebellar ataxia: asynergy, dysmetria, adiadochokinesia and intention tremor of the extremities

Combined (global) cerebellar syndrome
- The most frequent because most of the cerebellar diseases (degenerations, intoxications...) affect all its parts.

5.2 Manifestations of cerebellar diseases – cerebellar irritation motor syndrome

- Opposite to the extinction syndrome, resembles the parkinsonian syndrome
- Increased plastic tone of the flexor muscles
- Flection position of the trunk and limbs
- Resting tremor
- Hypokinesia or akinesia

6. Ataxia

= disorder of movement coordination

- Voluntary movements are in principle possible and muscle power is not reduced (in contrast to palsy)
- Coordination and cooperation between individual muscles and muscle groups are deteriorated.
- Lack of continuity and inappropriate phasing, sequencing and length of the movement adjustment
- Decreases fluency and effectivity of movements.
- In severe cases, locomotion and self-service are disabled (complete invalidity of the patient)

Types of ataxia:

- Cerebellar
- Spinal
- Vestibular

6.1 Cerebellar ataxia

- One of the manifestations of the extinction cerebellar syndrome (see above)
- Consists of following disorders:

1) Asynergy (see above)
2) Dysmetria (see above)
3) Adiadochokinesia (see above)

These basic components of ataxia lead to particular disorders (for details see Chapter 5.1):

- Disorders of posture (posture ataxia)
- Disorders of gait (gait ataxia)
- Speech disorders
- Oculomotor disorders
- Macrography

Cerebellar ataxia is accompanied by other symptoms of cerebellar damage (see above).

Cerebellar ataxia does not markedly worsen after closing of the eyes (processing of information in the diseased cerebellum is deteriorated, the mechanism of ataxia is central disorder of movement coordination, it is not due to lack of information)!
Contrary to vestibular ataxia, gait deviations and deviations of the arms stretched forward are to various directions.

6.2 Spinal ataxia

- Syndrome of the dorsal spinal columns
- Loss of proprioception (receptors in the joints, tendons, cartilages, fascias and muscles) and partially also tactile sensation. thermic sensation and nociception are preserved = tabic dissociation of sensation

Causes
- Tabes dorsalis – component of the 3rd stage of syphilis (neurolues)
- Vitamin B12 deficit, demyelinating processes, HIV infection, mechanic injury of the dorsal part of the spinal cord

Symptoms:
- Dysmetria – the muscles are activated inappropriately, difficulties with maintenance of movement direction and targeting the goal of the movement
- Fast, irregular deviations, jerks, titubations
- Excessive elevation and stomping with the lower limbs (so called "Prussian soldier gait")
- Titubations, deviations and falls to all directions

Spinal ataxia worsens significantly after eye closing (lack of proprioception can be partially compensated with visual control of body position and movement)!

6.3 Vestibular ataxia

Arises from a lesion of the peripheral part of the vestibular system (the labyrinth and n. VIII)

Causes:
- Complication of otitis media
- Skull trauma
- Menier's syndrome
- Tumours in the pontocerebellar angle, n. VIII neurinoma
- Herpes zoster oticus
- N. VIII inflammation
- Ischemia of the vestibular sensor

Symptoms:
- Vertigo
- Spontaneous nystagmus with direction toward the healthy side (the eyeballs move from one side to another and back, the slow component is due to predominance of the healthy labyrinth, the fast component is a compensation return of the eyeball; the direction of nystagmus is determined according to the fast component)
- Titubations and falls always to the affected side
- Tonic deviations of the extremities to the affected side
- Often also perception hearing disorder with tinitus

Vestibular ataxia worsens after eye closing (lack of information from the vestibular system is partially compensated by vision)!

7. Literature

McPhee, S. F., Hammer, G. D.: Pathophysiology of Disease: An Introduction to Clinical Medicine, Sixth Edition, 2010, The McGraw-Hill Companies, Inc.