MOVEMENT DISORDERS

DISEASES OF THE EXTRAPYRAMIDAL SYSTEM
The extrapyramidal system ...

includes all that centers and pathways, which responsible for the organisation of movements with the exception of the pyramidal tract.
The function of the extrapyramidal system

- coordination of the movement behavior

- assurance of the order and „smooth” of movements
Parts of the extrapyramidal system

• cortical centers: there are centers in all the cortical lobes
• subcortical centers:
  • caudate nucleus
  • putamen
  • pallidum
  • subthalamical nucleus (Luys)
  • nucleus ruber
  • substantia nigra
  • reticular formation

striatum
nucleus lentiformis
There are two main clinically different groups caused by the disease of the extrapyramidal movement system:

- hypokinetic-hypertonic
  (rigid)
- hyperkinetic-hypotonic
hypokinetiс-hypertonic (rigid) syndrome

Parkinson’s disease, Parkinsonic syndromes
The etiology of the Parkinsonism

- primer, idiopathic form: Parkinson’s disease
  - the second most frequent progressive neurodegenerative disease
  - the prevalence is 1% in the 65 year old population and it increases to 4-5% in the 85 year old population
  - it is most frequently sporadic
  - approximately 10% of the cases are familiar (there are 10 indentified genes, which cause autosomal dominant, or recessive forms of Parkinson’s disease)
The etiology of the Parkinsonic syndromes

- symptomatic: Parkinson’s syndrome
  - trauma
  - tumor
  - inflammation (encephalitis)
  - stroke (ischemic, hemorrhagic)
  - toxic agents (CO, neuroleptic drugs)
The etiology of the Parkinsonic syndromes

- Diseases with Parkinsonic syndrome (Parkinson plus diseases)
  - Synucleopathies:
    - Multi System Atrophy (MSA)
  - Taupathies (abnormally phosphorylated Tau protein):
    - Progressive Supranuclear Palsy (PSP) = Steel-Richardson-Olszewski sy.
    - Corticobasal Degeneration
The neuropathologic basis of Parkinson’s disease

- degeneration of the substantia nigra and the striatum (Lewy bodies- citoplasmatic protein aggregations)
- disintegration of the dopamin-acetilcholin balance in the central nervous system
- decrease of the dopamin level and cholinergic dominance
the main symptoms of Parkinsonism

- rigidity
- tremor
- hypo-, and bradykinesia
- postural instability
rigidity

- The tone of the agonist és antagonist (flexor and extensor) muscles increases paralelly.
- The trunk and the extremities are in semiflected position.
- During passive movement of the extremities we can feel permanent resistance (cogwheel phenomenon).
- Very often assimetrical distribution.
tremor

- the agonistic and antagonistic (flexor és extensor) muscles contract with rhythmic, 6-8/sec. frequency
- the tremor is most prominent in resting position, the stress could provoke it
- the intended movements decrease the tremor and it is stopped during sleep
- very often assimetrical distribution
hypo-, and bradykinesia

- movements and walking become slow, sluggish and difficult
- shuffling gait with decreased excursion of legs
- difficulties in turning
- freezing: sudden stop in walking and movements
other signs

• on-off phenomenon
• retropulsion
• hypomimia, or blank face
• monotonous speech
• micrographia
• hypersalivation, hyperperspiration
• hyposmia, hypogeusia
• orthostatic hypotension
• constipation
• depression
• sleep disorders
Parkinson plus diseases
Multi System Atrophy (MSA) - Papp-Lantos disease

- the stages of the disease:
  - striato-nigral degeneration
  - olivo-ponto-cerebellar atrophy
  - Shy-Drager syndrome
- no, or mild asimmetricity in the parkinsonic signs
- early falls down
- autonomic dysfunctions (orthostatic hypotension, impotencia, incontinentia, respiratory stridor)
- „dropped head”
- pyramidal signs, cerebellar signs
- no, or just partial respons to levodopa therapy
Parkinson plus diseases
Progresive Supranuclear Palsy (PSP)-Steel-Richardson-Olszewski sy.

• postural instability, early falls down, axial rigidity, freezing
• supranuclear gaze paresis (predominantly vertical) downwards gaze!
• Frontal lobe signs (primitive reflexes, apathy, frontal demencia)
the Parkinsonic crisis could be life threatening !!

- complete immobility
- aphagia and anarthria
- extreme rigidity
- fever
- cardiovascular insufficiency
- bedsores, pneumonia, deep vein thrombosis, lung embolism
treatment

DRUGS

• MAO B inhibitors (Selegilin, Rasagiline)
• Amantadin (PK Merz)
• Dopamin agonists (ergotamine type: Bromocriptin, non ergotamin type: ropinirole, pramipexole, apomorphine)
• L-DOPA substitution (L-DOPA+DOPA decarboxilase inhibitor)
• COMT inhibitors (entacapone)
• L-DOPA+DOPA decarboxilase inhibitor+ COMT inhibitor (Stalevo)
• anticholinergic drugs (metixene, procyclidine)
treatment

SURGICAL (just in very severe cases, when the antiparkinson drugs are uneffective)

- deep brain stimulation – DBS (uni-, or bilateral)
- target zones: STN, pallidum, thalamus VIM nucleus
- thalamotomy, pallidotomy (uni-, or bilateral)
- neurotransplantation (inplantation of fetal mesencephalic cells into the caudat nucleus and putamen region)
treatment

• physiotherapy (training, special exercises)

• psychotherapy
diseases characterized with hyperkinesis and hypotonia

- chorea
- ballism
- athetosis
- Dystonias (focal, or generalised)
- myoclonus
- tic
Chorea

• features: irregular, sudden onset, fast movements which involve first of all the distal part of extremities, but could appear in the truncal, facial and tongue muscles as well

• the emotional effects, stress could provoke it

• the anatomical basis is the degeneration of the putamen and the caudat nucleus
Chorea

- **forms:**
  - inherited (Huntington chorea, autosomal dominant)
  - symptomatic (chorea minor, chorea gravidarum, caused by traumas, tumors, inflammation, stroke in the above mentioned brain regions)
ballism

- features: violent, big movements in the proximal muscles of the extremities with sudden onset. Because of these movements the patient can fall down.
- anatomical basis: the degeneration of the subthalamical nucleus (Luys)
- forms:
  - idiopathic
  - symptomatic (caused by traumas, tumors, inflammation, stroke in the above mentioned brain regions)
athetosis

- **features:** slow, „vermin-like” movements in the distal muscles of the limbs, but the facial muscles could be involved as well
- **anatomical basis:** the degeneration of the striatum and the pallidum
- **forms:**
  - idiopathic
  - symptomatic (caused by traumas, tumors, inflammation, stroke in the above mentioned brain regions)
treatment

- dopamin antagonist: tiaprid (Tiapridal)
- chlorpromazin (Hibernal)
- Haloperidol
- clonazepam (Rivotril)
- amantadin
Dystonias - generalised forms

• primer, idiopathic
  - dystonia musculorum deformans (Oppenheim dystonia)
  - DOPA-responsive dystonia

• secunder
  - Wilson’s disease (hepatolenticular degeneration) - problem with the copper metabolism
  - Hallervorden Spatz’s disease – problem with the iron metabolism
  - ischaemic, or toxic brain injury
  - tardive dyskinesia, or dystonia – could be the side effect of the neuroleptic drugs
Dystonias- focal forms

- blepharospasm
- hemifacial spasm
- oromandibular dystonia (Meige syndrome)
- spastic dysphonia
- cervical dystonias (torticollis, antero-, latero-, ill. retrocollis)
- writer’s cramp, „musican’s cramp”

- the focal dystonia could be the side effect of antiemetic drugs: thietylperazine (Torecan), metoclopramide (Cerucal), domperidone (Motilium)
treatment

- L-Dopa (in L-Dopa responsive forms)
- Anticholinergic/antihistaminic agents: trihexyphenidyl (Artane), Procyclidine (Kemadrin), ethopropazine (Parsidol)
- Baclofen
- Clonazepam (Rivotril)
- Antiepileptic drugs: Carbamazepine (Tegretol, Neurotop), Gabapentin (Neurontin, Gordius)
- Dopamine-depleting agents: Tetrabenazine, Reserpine
- Dopamin antagonists: Tiapridal
- Local infiltration of the involved muscles with botulinum toxin
- DBS
myoclonus

- features: fast, irregular movement of a muscle group, or a muscle region of the body. It involves first of all the distal part of the body and axial muscles, or the palatal muscles
- The anatomical basis could be cerebral (cortical, subcortical), and spinalis lesions, or the degeneration of the so called „myoclonic triangle”: nucl. ruber, nucl. dentatus, oliva inferior
- forms:
  - idiopathic
  - associated with epilepsy
  - symptomatic
treatment

- clonazepam (Rivotril)
- carbamazepine (Tegretol, Neurotop)
- levetiracetam (Keppra)
- valproic acid (Convulex, Depakine)
- piracetam (Nootropil)
tic

• features: irregular, stereotyped, fast movement of a muscle group with sudden onset, or could be

• stereotyped repetition of words, which most frequently obscene words (Gilles de la Tourette syndrome: both multiple motor and vocal tics, for at least 1 year, tics changing over time, the onset of tics before the age of 21 years)
treatment

- dopamine receptor antagonists: Haloperidol, Risperidon (Risperdal), Ziprasidone (Ziprexa)
- \( \alpha_2 \) agonists: Clonidine
- monoamin depletors: Tetrabenazine
- clonazepam (Rivotril)
- SSRI-s: Paroxetine, Citalopram, Venlafaxine...