# Neurodegenerative disease

**Neurodegenerative diseases** are characterized

- **progressive destruction of neurons**
- **by reactive proliferation of glia**
- **by storing protein deposits**

The clinical manifestation is diverse depending on the affected structures.

## Pathogenesis

The basic pathogenetic mechanism is a "change in the secondary structure" of the affected protein, when the proportion of "β-sheet" increases (see also the article Causes of pathological conformation of proteins) - the protein thus acquires other properties (it is resistant to chemical and physical influences). The cell cannot process it, so it accumulates, can be toxic or induce apoptosis. On the other hand, there is a lack of functional protein.

## Diagnostics

A clinical diagnosis is made on the basis of clinical, paraclinical and genetic examinations. However, only a neuropathological diagnosis using macroscopy, microscopy, protein analysis (immunohistochemistry, western blot) and nucleic acids is definitive

## Alzheimer's disease

🔎 *For more information see Alzheimer's Disease.*

Alzheimer's disease is characterized by the presence of amyloid plaques and neurofibrillary tangles.

**Amyloid plaques**are *extracellular deposits* of *amyloid-β-peptide*. Pathological amyloid-β-peptide (A-β-42) arises from amyloid precursor protein (APP) by cleavage by γ-secretase. The normal product (A-β-40), which is two amino acids shorter, is formed by α-secretase. Pathological amyloid-β-peptide induces neuronal apoptosis and stimulates glia.

**Neurofibrillary tangles** *are intracellular* aggregates of hyperphosphorylated τ-protein *(see Tauopathy).*

Early Alzheimer's disease tends to be familial – associated with genetic mutations (mutations of APP, γ-secretase components; the presence of the apoprotein E *ApoE4* allele is also a risk), the late form tends to have a more complex etiology.

## Tauopathy

Tauopathies are rare diseases associated with τ-protein mutation.

**τ-protein** (tubulin-associated unit) strengthens the microtubule structure. Its hyperphosphorylated form does not fulfill this role, but aggregates to form amyloid.

- Progressive supranuclear palsy (Steele-Richardson-Olszewsky)
- Corticobasal degeneration
- Pick's disease - frontotemporal atrophy (Pick's bodies intracellularly)
- Dementia with argyrophilic grains

## Synucleinopathy

**α-synuclein** is abundantly present in the CNS, but its role is not entirely clear. The pathological form creates Lewy bodies inside the cells and induces apoptosis.

- Parkinson's disease
- Dementia with Lewy bodies
- Multiple system atrophy

## Triplet diseases

The pathological protein is the product of a mutated gene in which there is expansion of trinucleotide repeats.

- Huntington's disease
- Spinocerebellar ataxia

# Motor neuron disease

It is a group of diseases affecting upper (in the cortex) and lower (in the spinal cord or in the trunk) motoneurons.

- Amyotrophic lateral sclerosis (ALS) - most cases are sporadic, 5-10% are caused by a mutation in superoxide dismutase 1, which produces excessive free radicals.

# Prion diseases

🔎 *For more information see Prions.*

# Source

## Links

MATĚJ, Radoslav. Seminář Neurodegenerativní onemocnění. 3. LF UK 2010