

Neurodegenerative forms of parkinsonism

- Neurodegenerative forms of parkinsonism can be broadly classified as synucleinopathies or tauopathies.
- Synucleinopathies
 - Characterized by the presence of stable unfolded oligomers or multimers of α -syn
 - Main protein component of Lewy bodies and Lewy neurites that represent the defining hallmark of Parkinson disease
- Taupathies
 - Disorders associated with intracellular deposition of abnormally phosphorylated tau (p-tau), found as neurofibrillary tangles (NFT), neuropile threads, or abnormal tau filaments.
 - Progressive Supranuclear Palsy (PSP) is a taopathy, and the most common form of atypical parkinsonism

Synucleinopathies

- Subgroup of neurodegenerative diseases, characterized by impairment of **alpha-synuclein metabolism**, resulting in abnormal intracellular deposits and can further be divided into those with and those without the formation of Lewy bodies
- Diseases with Lewy bodies
 - Parkinson disease / Parkinson disease dementia
 - Lewy body disease
- Multiple systemic atrophy (MSA)
- Pure autonomic failure
- Rapid eye movement (REM) sleep behavior disorder

- Parkinson's disease (PD)
- Dementia with Lewy bodies (DLB)
- Multiple system atrophy (MSA)
- Pure autonomic failure (PAF)
- Isolated rapid eye movement
- sleep behavior disorder (iRBD)

		α -syn strains	leading α -syn inclusion pathology	main areas of neuronal loss
classical α -synucleinopathies	PD			 - substantia nigra pars compacta
	DLB			 - neocortex - substantia nigra pars compacta
	MSA			 - SND - OPCA - brainstem nuclei - autonomic nuclei in the spinal cord
prodromal α -synucleinopathies	iRBD		 GCI	 - brainstem nuclei - other areas within the CNS ?
	PAF		 GCI	 - sympathetic ganglia - postganglionic fibers - CNS ?

α -syn monomers