Neurodegenerative Disease	Clinical Presentation	Disease Gene	Lesion	Aggregate
Alzheimer Disease (AD) ↓ACh	Early Stages: • Memory deficits (rapid forgetting) • Anomia (word loss) Middle Stages: • Further memory & language define • Visuospatial deficits • Agnosias (loss of knowledge) • Mood & Personality changes Late Stages: • Global aphasia • Motor dysfunction	*APP* (21) Amyloid precursor protein *PSEN1* (14) & *PSEN2* (1) Presenilin *APO-E* (19) APO-E4 → ↑Aβ amyloid → ↑risk APO-E2 →↓Aβ amyloid → ↓risk	Senile plaques extracellular	Aβ Amyloid
			Neurofibrillary tangles Intracellular	Hyper-phosphorylated Tau
Pick Disease Frontotemporal Lobar Dementia (FTLD)	Behavioral disinhibition Personality change Aphasia Dementia		Cortical Pick Bodies	Round Tau TDP-43
Parkinson Disease (PD) ↑ACh, ↓DA, ↓Serotonin "Lewy Parks Taurist's cars"	**Hypo-kinetic Disorder** - "**TRAP**" Substantia Nigra Degeneration **T**remor - pill rolling tremor that disappears w/ movement **R**igidity - cogwheel rigidity **A**kinesia or Bradykinesia **P**ostural instability & Shuffling gait	*α-synuclein* *Parkin* *UCHL1*	**Lewy** Bodies Intracellular	*α-synuclein* **Tau**
Lewy body Dementia	Dementia Hallucinations Parkinsonian features		Cortical Lewy Bodies Intracellular	*α-synuclein*
Huntington Disease (HD) ↓ACh, ↑DA, ↓GABA "Dominant Hunters CAGe their pray"	**Hyper-kinetic Disorder** - "**AC/DC**" **A**utosomal **dominant** **C**horeiform movement **D**ementia, Depression, mental Disturbances **C**audate & Putamen (Striatum) atrophy	**CAG** trinucleotide repeats (4) Expansion of repeats during spermatogenesis → anticipation		Mutant huntingtin
Amyotrophic Lateral Sclerosis (ALS) "Lou Gehrig Disease"	Upper & lower motor neuron signs **UMN:** spasticity, hyperreflexia, dysarthria, dysphagia **LMN:** atrophy, fasciculations, hyporeflexia, weakness	*SOD1* C9 *ORF* 72 Chromosome 9 hexanucleotide repeat		Mutant SOD1 TDP-43