Week 7 CNS: Sensory and Motor Disorders

Neurodegenerative Disorders (ALS, Alzheimer's, Parkinson)

Neurodegenerative Disorders Affecting Motor Function: progressive degeneration of the structure and function of the nervous system. Incurable, debilitating, leading to a gradual decline in cognitive, motor, or functional abilities. Inherited.

- Common pathological mechanisms: protein misfolding, neuroinflammation, oxidative stress, neuronal loss.
- Parkinson's: loss of dopaminergic neurons affecting substantia nigra in the basal ganglia. Tremors, rigidity, bradykinesia. Mostly for >600 yo
- Amyotrophic Lateral Sclerosis (ALS): diagnosed when patients are in their 40s or 50s. ALS targets motor neurons in the spinal cord and brain, leading to muscle weakness and atrophy. A progressive condition affecting the control of muscle movement. There is a genetic predisposition to this condition.
- Huntington's: degeneration of nerve cells in basal ganglia. Uncontrolled movements, emotional disturbances, cognitive decline, starting in 40s-50s yo.
- Multiple Sclerosis (MS): autoimmune that damages myelin sheath in the CNS. Wide range of neurological symptoms. Typically shows up when patients are in their 20s to 40s, may be caused by both environmental and genetics.
- Myasthenia Gravis (MG): autoimmune affecting the communication between nerves and muscles, leading to muscle weakness and fatigue. MG fluctuates in the nature and severity of symptoms, often affecting muscles controlling eye movements, facial expressions, and swallowing.

Neurodegenerative Disorders Affecting Cognitive Function: types of dementia. Decline in memory, thinking, behavior, and reduced function.

- Alzheimer's: the most common. AD is marked by the accumulation of amyloid plaques and tau tangles in the brain, leading to neuronal death (memory and cognition areas). Progressive memory loss, confusion, and changes in behavior and personality.
- Vascular dementia: results from conditions that block or reduce blood flow to the brain. It often follows a stroke or series of mini-strikes. Symptoms vary depending on the affected brain region: impaired judgment, inability to plan, and loss of motivation.
- Lewy Body dementia: characterized by the presence of Lewy bodies, commonly seen in those with Parkingson's. Cognitive decline, fluctuating alertness, visual hallucinations, and Parkinsonian motor symptoms. Cognitive decline is more variable.
- Frontotemporal dementia: cell degeneration in those areas affects behavior, personality, and language (NOT memory). Socially inappropriate behavior, impulsivity, and language difficulties. Aphasia may occur.

Patho of Alzheimer's:

- Neuronal damage and loss in the hippocampus and cortex, areas crucial for memory and cognitive functions.
- The disruption of neuronal communication, cell death, and brain atrophy contribute to the clinical manifestations of AD. Neuroinflammatory response, dysfunctional mitochondria, activated microglia, and oxidative stress are also involved in preventing the breakdown of beta-amyloid and the formation of plaque.
- Ultimately, the loss of synaptic plasticity and neural transmission leads to cholinergic dysfunction and the loss of neuronal repair and remodeling.

Alzheimer's: Clinical Application

- IMPORTANT: AD may cause or coexist with MDD or bipolar. The cognitive decline in AD can exacerbate or trigger all types of emotional and behavioral symptoms.
- A neurobehavioral specialist can assist with care. Late in the process, AD patients need to be in specialized units.
- The tx of AD is as much about family support (respite care) as it is about the patient.

Alzheimer's: Risk Factors

- 10% occur in early related to a genetic autosomal dominance in 3 genes
- 90% occur in late AD related to 2 gene mutations in the PAOE gene, which is instrumental in creating a protein. Pts with altered APOE genes are more likely to have increased serum lipids, contributing to vascular and AD.
- Other factors: age (>65), family history, modifiable (CV health status, HTN, DN, obesity, smoking), and lifestyle (physical activity, low-fat diet, and increased cognitive engagement)

Alzheimer's: Clinical Manifestations

- Mini-Mental Status Exam (MMSE): most used neuropsychological test for AD screening and other dementia.
- Preclinical (No Symptoms)
  - Changes in the brain associated with Alzheimer's start occurring, but no symptoms are visible.
  - May last for years or even decades.
- Early Cognitive Impairment
  - Small decline in cognitive abilities, including memory and thinking skills.
  - Still able to perform activities of daily living.
- Mild Cognitive and Functional Impairment
  - Memory loss becomes noticeable.
  - Difficulties with language, like finding the right words.
  - Difficulty organizing thoughts and planning.
  - Challenges in performing tasks that require multiple steps.
  - Personality changes, such as becoming withdrawn or depressed.
- Moderate Cognitive and Functional Impairment
  - Significant memory loss and confusion.
  - Difficulty recognizing friends and family members.
  - Problems with expressive and receptive language.
  - Requires assistance with daily activities and personal care.
  - Changes in sleep patterns with increased risk of wandering and becoming lost.
  - Behavior changes, including suspiciousness and agitation.
- Severe Cognitive and Functional Impairment
  - Loss of ability to communicate coherently.
  - Requires full-time assistance with personal care.
  - Loss of physical function, such as walking, sitting, and eventually swallowing.

Alzheimer's: Dx

- Comprehensive assessment: hx, physicals, neurologic tests, cognitive tests, neuroimaging (CT or MRI)
- Genetic testing may help identify a genetic predisposition
- CRUCIAL to eliminate other causes of dementia that present with similar symptoms to AD, including:

A definitive diagnosis of Alzheimer's disease is only possible at autopsy upon examination of brain tissue.

Condition	Examples
Infection	Meningitis, Creutzfeldt-Jakob disease
Nutritional deficiencies	Vitamin B1 or B-12 deficiency, Wernicke's encephalopathy
Medication side effects	Antipsychotics, anticonvulsants, anticholinergics
Drug or alcohol use	Acute intoxication, opiate or amphetamine overuse
Metabolic disorders	Hypoglycemia, heavy metal exposure, hypothyroidism
Vascular disease	Multiple small strokes, aphasia

Alzheimer's: Tx

- Symptoms management and quality of life. No cure.
- Cholinesterase inhibitors (donepezil) for mild and moderate cases. NMDA receptor antagonists block glutamate.