Alzheimer’s Disease

06.11.22

Alzheimer’s Disease

- The most common type of Dementia
- A general term for the **impared ability** to remember, think, or make decisions that interferes with doing everyday activities.
- Dementia is **not a general part of aging**, but a group of disorders caused by **abnormal brain changes.**

Common types of dementia

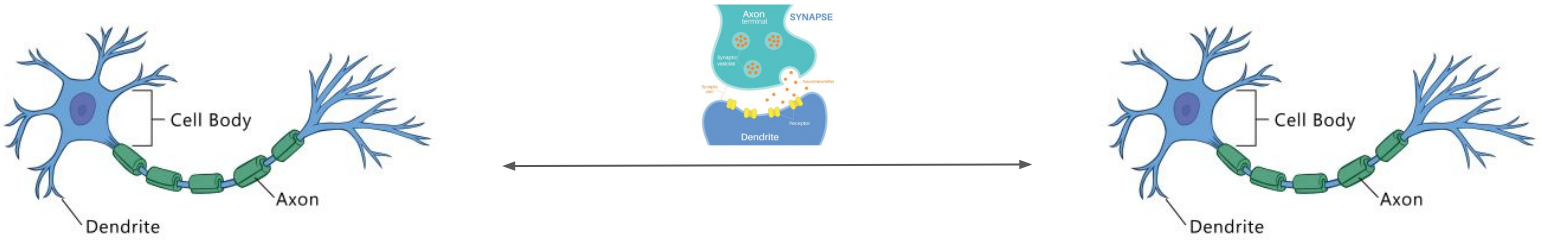
Types	***Description***
Alzheimer's disease	Account for 60-80% of cases caused by specific changes in the brain. First-degree relative with AD increases the risk of developing it by 10-30%
Vascular dementia:	10% of cases are linked to strokes or other issues with blood flow to the brain e.g. diabetes, high blood pressure and high cholesterol
Lewy body dementia:	Apart from memory loss, patients also encounter movement problems, alertness and trouble sleeping
Fronto-temporal dementia	Changes in behaviors and personalities.
Mixed dementia:	More than 1 type, hence the progression is much faster
Reversible causes	Reversible underlying cause such as side effect of medication, increased pressure in the brain, vitamin deficiency and thyroid hormone imbalance.

Stages

Stages	***Description***
1: No cognitive decline	Healthy
2: Age-associated memory impairment	Difficulty remembering where they put their glasses, or the names of acquaintances, but can easily pass a clinical interview.
3: Mild cognitive impairment	Difficulty finding common destinations, poor work performance, and inability to recall words or names are signs of mild cognitive decline.
4: Mild dementia	Struggle to remember personal history, as well as current events. Maintaining finances or travel may also become difficult
5: Moderate dementia	A patient may be unable to recall major aspects of their current lives, like a home address or grandchild's name. They may experience disorientation with dates and times.
6: Moderately severe dementia	Can't remember the names of close ones and have little awareness of recent personal history.
7: Severe dementia	Verbal abilities and basic motor skills are lost. Brain becomes unable to tell the body what to do.

What is happening inside the brain?

Most neurons have 3 basic parts:

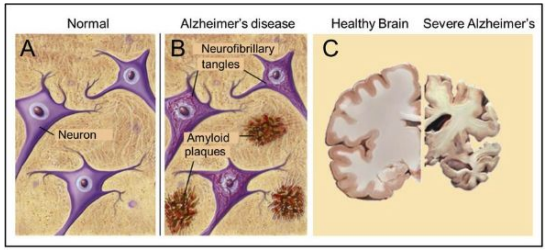


Key biological processes in the brain

1. **Communication**: Between neurons via synapse
2. **Metabolism**: Breaking down of chemicals and nutrients within a cells. This required energy in the form of **oxygen and glucose**
3. **Repair, remodeling and regeneration**: **Long-lived**, they must constantly maintain and repair themselves. Important for learning, memory and possibly brain repair.

Characteristic of an AD's brain

Characteristics	***Description***	***Result***
Amyloid Plaques	Beta-**Amyloid protein** that are collected between neurons clump together to form **plaques**	Disrupt cell functions
Neurofibrillary tangles	Abnormal chemical changes causes **tau protein** to detach from microtubules and binds to each other to forms tangles.	Disrupt transport and communication
Loss of neuronal connection and cell death	Brain shrinkage	Disrupt functions and communication
Vascular contributions	Vascular issues e.g. Beta-Amyloid deposits in the arteries	Reduced blood flow and oxygen to the brain and reduced break down of the blood-brain barriers



Causes:

- Diseases that **damage brain cells** cause dementia.
- This damage interferes with the **cell's abilities to communicate effectively.**
- When brain cells in a particular region become damaged, it **disrupts the communication among neurons**, resulting in **loss of function and cell death**

Diagnosis

Defining vs Staging

- Biomarkers to define the disease:
  - Amyloid
  - Tau
- Biomarkers to stage the disease:
  - MRI atrophy measure
  - FDG PET
  - CSF total Tau
- Clinical syndromes to stage the disease

Tests

- Tests on attention, memory, problem solving and other cognitive abilities to see if there are cause for concern

  e.g. spell simple words backward, Add and subtract basic equations, repeat words, then remember them later in the appointment, name objects properly, understand visual and spatial cues like the distance and location of objects, draw a clock with evenly spaced number

- Physical exams, blood, genetic tests and brain scans

ATN Framework

A: Amyloid

- Cerebrospinal fluid bio-makers: to measure beta-amyloid 42 (amyloid plaque)
- Amyloid PET

T: Tau

- CSF: to measure tau and phospho-tau (tau tangles)
- Tau PET

N: Neuro-degeneration

- Structural MRI
- FDG PET (metabolism)
- CSF/ plasma total tau
- Neurofilament light chains (blood test)

ATN profiles	Biomarker category	
A-T-N-	Normal AD biomarkers	
A+T-N-	Alzheimers pathophysiology	Alzheimer's pathophysiological continuum*
A+T-N+	Alzheimers pathophysiology	
A+T+N-	Alzheimers disease	
A+T+N+	Alzheimers disease	
A-T+N-	Non- AD pathophysiology	
A-T-N+	Non- AD pathophysiology	
A-T+N+	Non- AD pathophysiology	