



The Neuroscience of Alzheimer's

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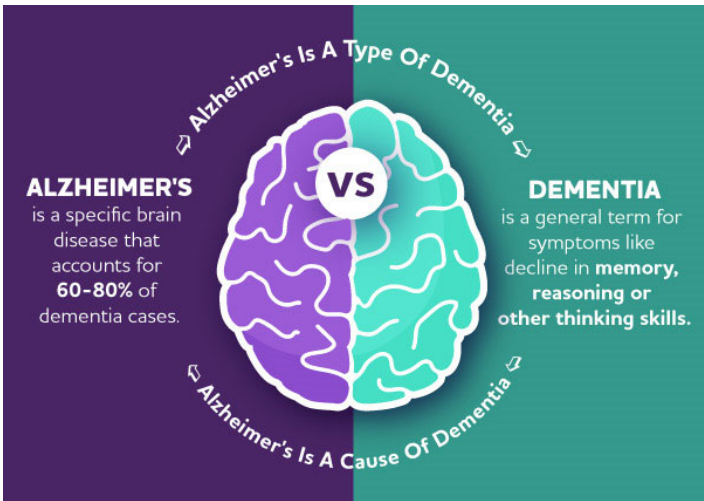
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 International Museum of Surgical Science
A Division of the International College of Surgeons

ASTC Association of Science and Technology Centers

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What is Alzheimer's Disease (AD)?



ALZHEIMER'S
is a specific brain disease that accounts for **60-80%** of dementia cases.

VS

DEMENTIA
is a general term for symptoms like decline in **memory, reasoning or other thinking skills.**

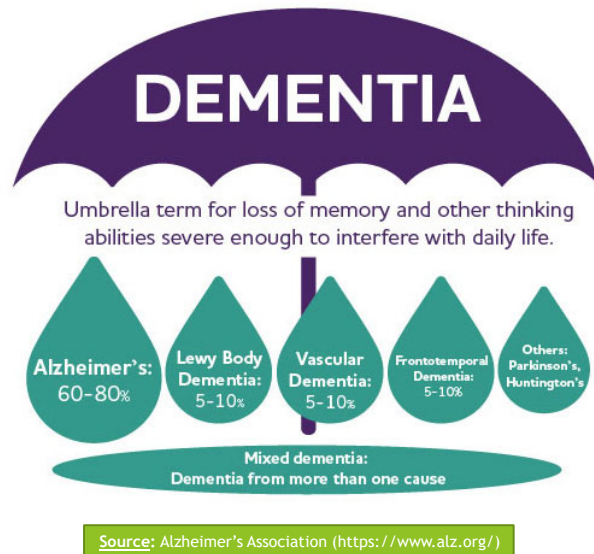
Alzheimer's Is A Type Of Dementia

Alzheimer's Is A Cause Of Dementia

Source: Alzheimer's Association (<https://www.alz.org/>)

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What is Alzheimer's Disease (AD)?

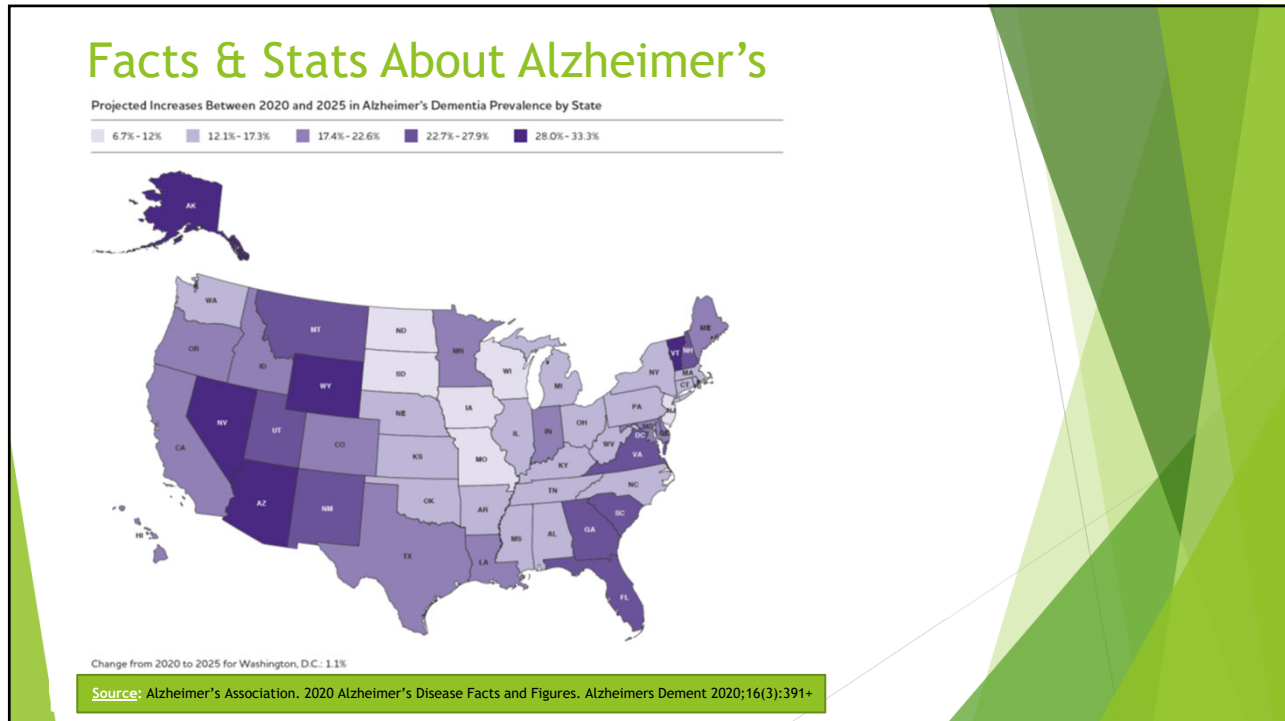


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Facts & Stats About Alzheimer's

- ▶ **5+ million Americans of all ages** have Alzheimer's
- ▶ **~5.8 million Americans age 65 and older** are living with Alzheimer's dementia in 2020
- ▶ **Almost two-thirds** of Americans with Alzheimer's are **women**
- ▶ **Older African-Americans are twice as likely** to have Alzheimer's or other dementias as older whites
- ▶ **Hispanics are about one and one-half times as likely** to have Alzheimer's or other dementias as older whites

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1 in 3

seniors dies with Alzheimer's or another dementia.

13.8 million

people age 65 and older are projected to have Alzheimer's dementia by 2050.

\$244 billion

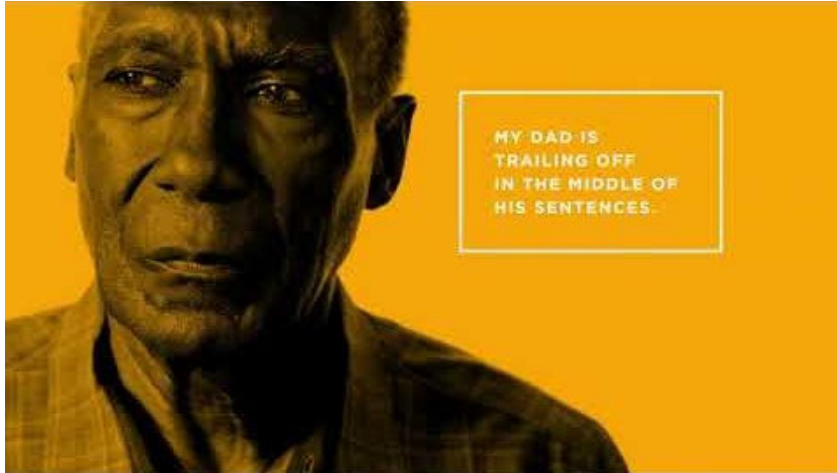
worth of care is provided by family members and other unpaid caregivers.

\$305 billion

is the projected national cost of caring for people with Alzheimer's and other dementias.

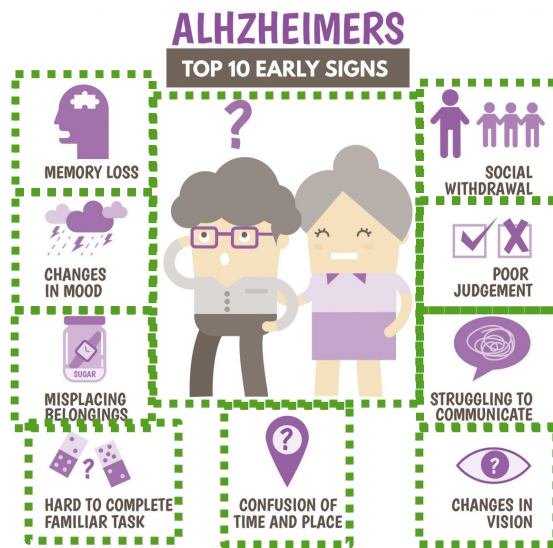
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Signs and Symptoms of Alzheimer's Disease

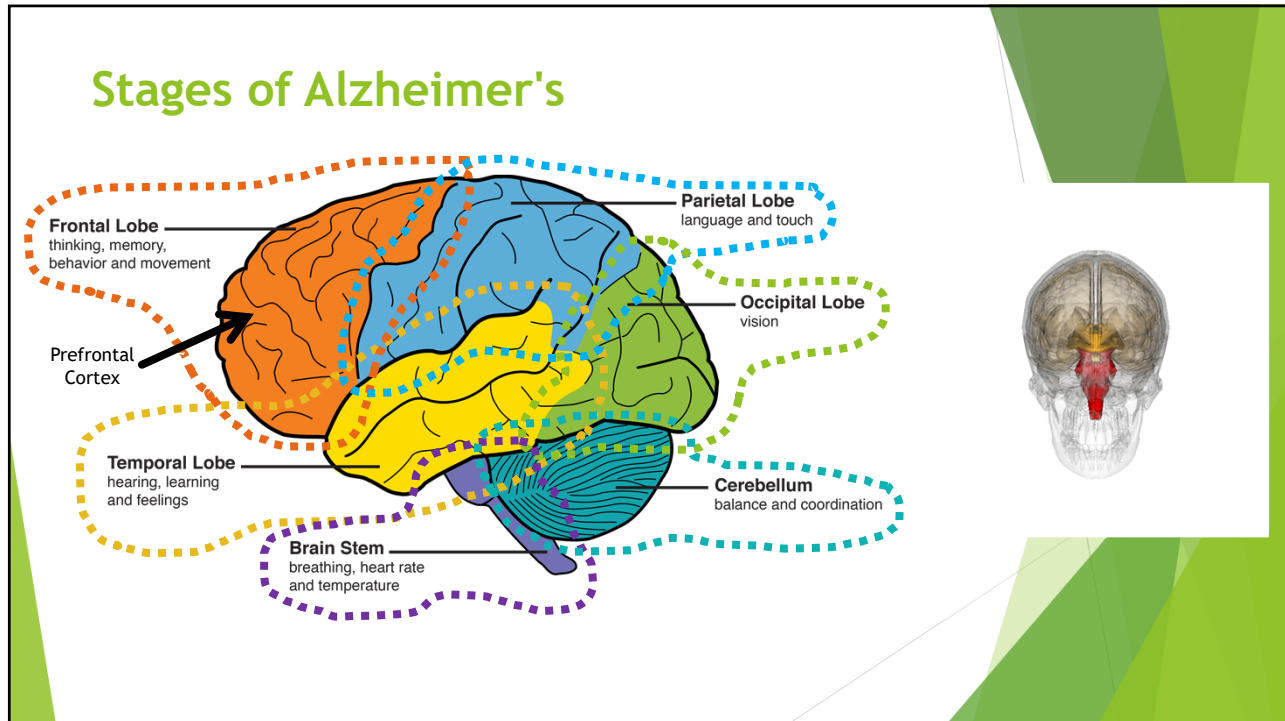


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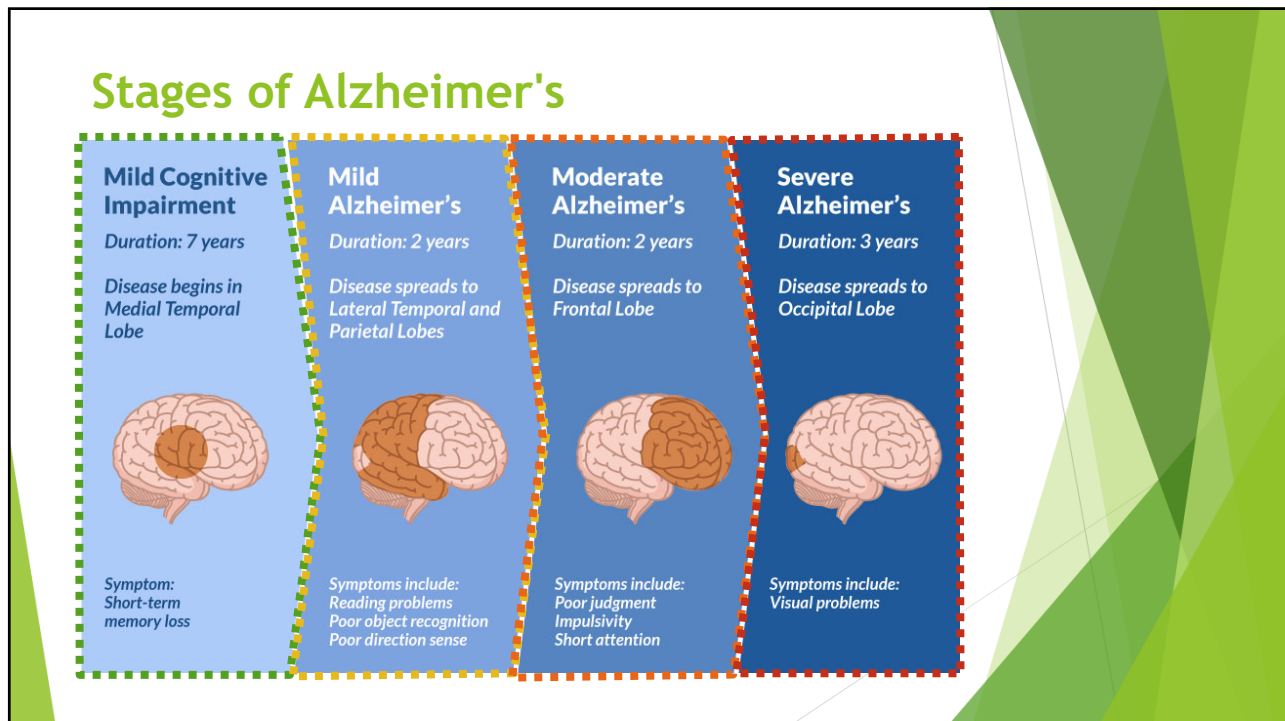
Signs and Symptoms of Alzheimer's Disease



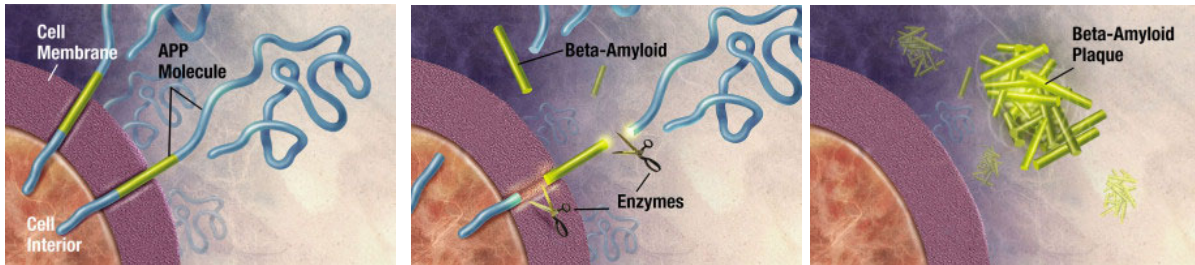
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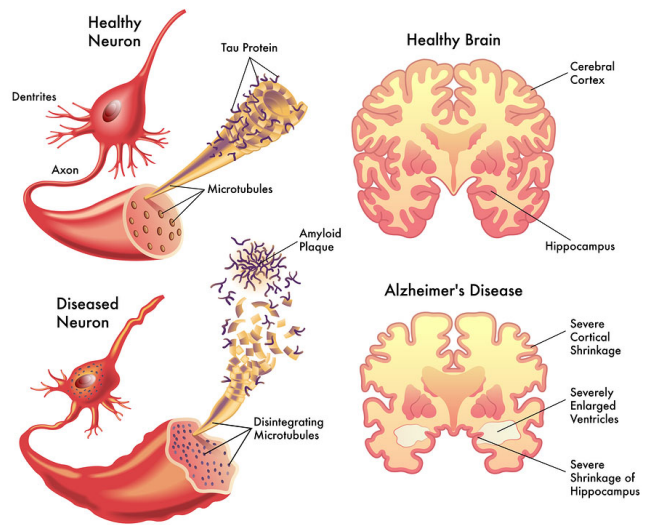
Pathological Causes of Alzheimer's Disease

- ▶ Plaques are deposits of a protein fragment called beta-amyloid (BAY-tuh AM-uh-loyd) that build up in the spaces between nerve cells



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Pathological Causes of Alzheimer's Disease

- ▶ Tangles are twisted fibers of another protein called tau (rhymes with “wow”) that build up inside cells



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Healthy	Alzheimer's Disease
 <p>Neurons</p>	 <ul style="list-style-type: none"> - Aβ plaque buildup - Neurofibrillary tau tangles - Synapse loss - Excitotoxicity - Axonal/dendritic injury - Degeneration/cell death - Release of pro-inflammatory molecules - Oxidative stress
 <p>Astrocytes</p>	 <ul style="list-style-type: none"> - Proliferation - Activated morphology - Tight-junction dysfunction - Inflammatory cytokine release - Altered trafficking and degradation pathways
 <p>Microglia</p>	 <ul style="list-style-type: none"> - Proliferation - Activated morphology - Inflammatory cytokine release - Dysregulated immune response - Altered trafficking and degradation pathways
 <p>Oligodendrocytes</p>	 <ul style="list-style-type: none"> - Demyelination - Degeneration/cell death - Oxidative stress
 <p>Pericytes</p>	 <ul style="list-style-type: none"> - Tight-junction disruption - Blood-brain barrier breakdown - Degeneration/cell death
 <p>Vascular endothelial cells</p>	 <ul style="list-style-type: none"> - Tight-junction disruption - Blood-brain barrier breakdown - Degeneration/cell death

Pathological Causes of Alzheimer's Disease

Penney, J., Ralvenius, W.T. & Tsai, L. Modeling Alzheimer's disease with iPSC-derived brain cells. *Mol Psychiatry* 25, 148-167 (2020). <https://doi.org/10.1038/s41380-019-0468-3>

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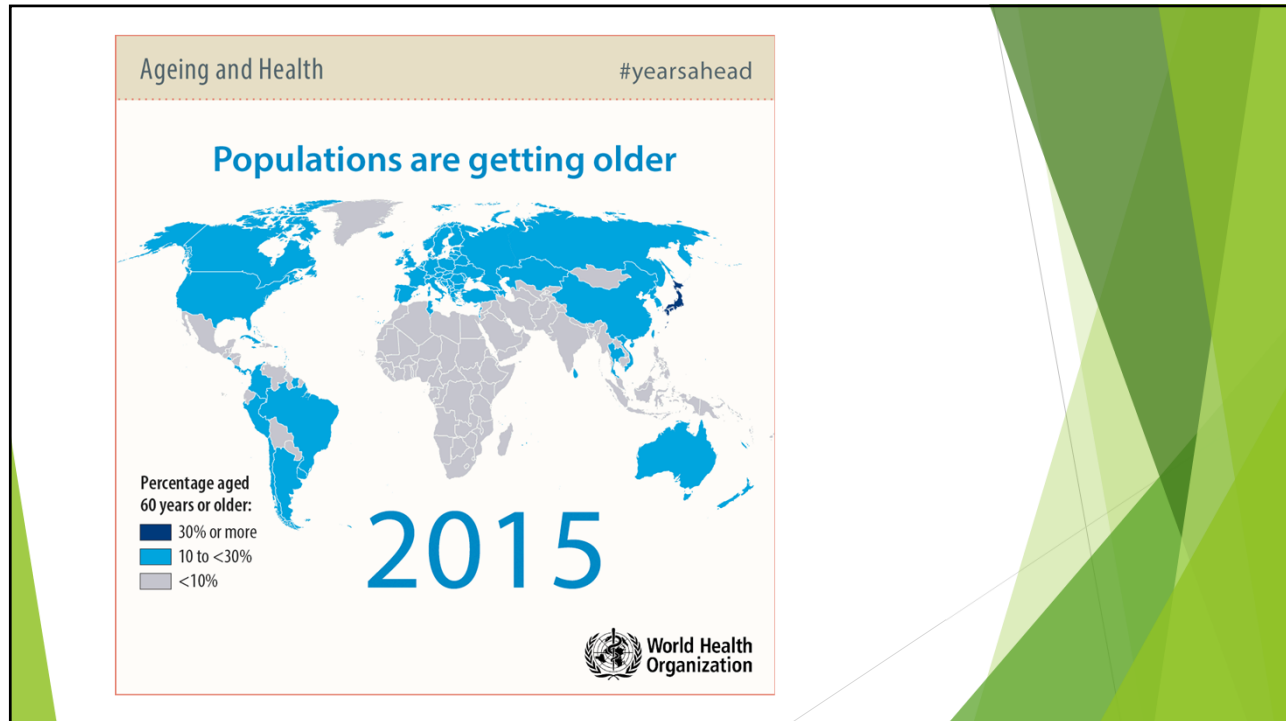
Pathological Causes of Alzheimer's Disease



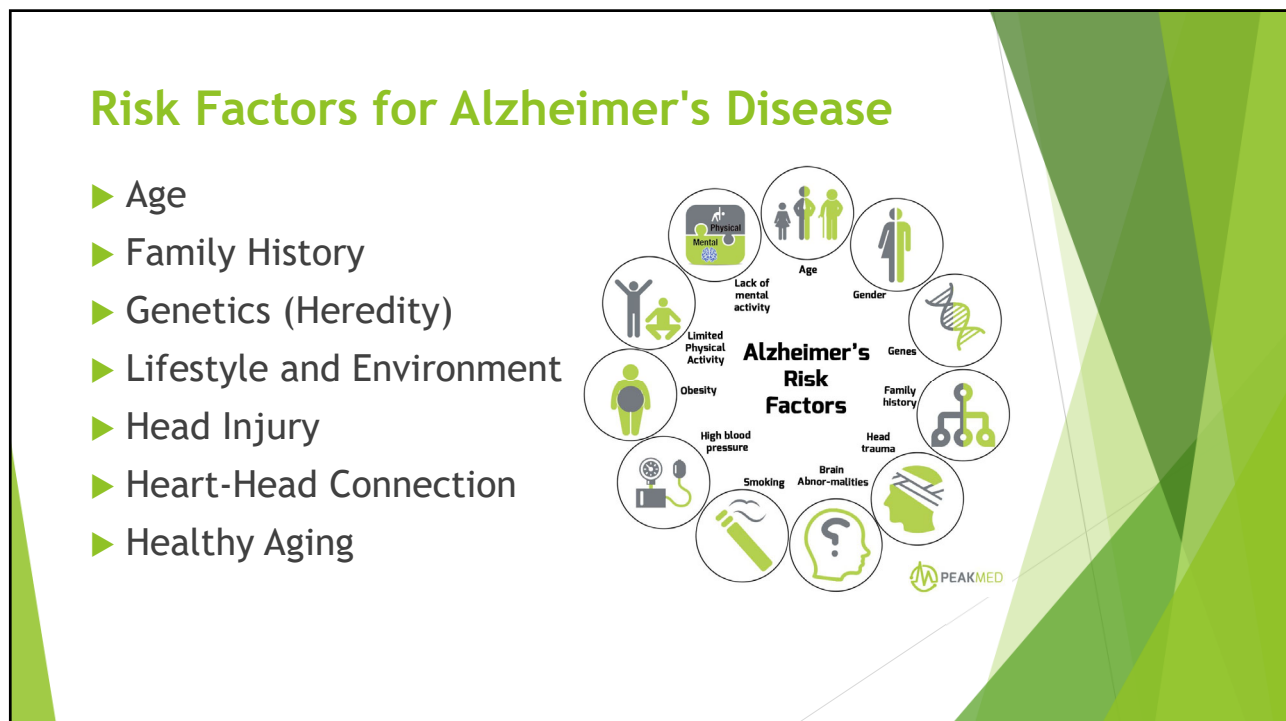
Alzheimer's & the Brain

<https://youtu.be/0GXv3mHs9AU>

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How Is Alzheimer's Disease Diagnosed?

- ▶ Medical history
- ▶ Mental status tests
- ▶ Physical exams
- ▶ Neurological exams
- ▶ Diagnostic or genetic tests
- ▶ Brain imaging

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Technological Advances in AD Research

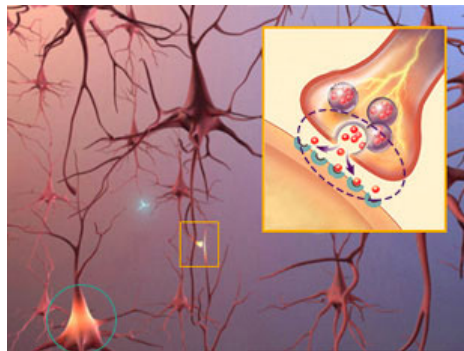
▶ Brain Imaging

The diagram illustrates various brain imaging technologies used in AD research, categorized by their function and molecular focus:

- MRI (Magnetic Resonance Imaging):** Labeled as **SFM** (Structural, Functional, Molecular). It shows a patient in the scanner and brain scans comparing a **Healthy Control** and **Alzheimer's Disease** patient.
- CT (Computed Tomography):** Labeled as **S** (Structural). It shows a patient in the scanner and a brain scan image.
- PET (Positron Emission Tomography):** Labeled as **FM** (Functional, Molecular). It shows a patient in the scanner and brain scan images for **Healthy Control**, **Mild Cognitive Impairment**, and **Alzheimer's Disease**.

Legend:
S = Structural
F = Functional
M = Molecular

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Source: Alzheimer's Association (<https://www.alz.org/>)

How Is Alzheimer's Disease Treated?

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GENERIC	BRAND	APPROVED FOR	SIDE EFFECTS
Donepezil	Aricept	All stages	Nausea, vomiting, loss of appetite, muscle cramps and increased frequency of bowel movements.
Galantamine	Razadyne	Mild to moderate	Nausea, vomiting, loss of appetite and increased frequency of bowel movements.
Memantine	Namenda	Moderate to severe	Headache, constipation, confusion and dizziness.
Rivastigmine	Exelon	Mild to moderate	Nausea, vomiting, loss of appetite and increased frequency of bowel movements.
Memantine + Donepezil	Namzaric	Moderate to severe	Nausea, vomiting, loss of appetite, increased frequency of bowel movements, headache, constipation, confusion and dizziness.

How Is Alzheimer's Disease Treated?

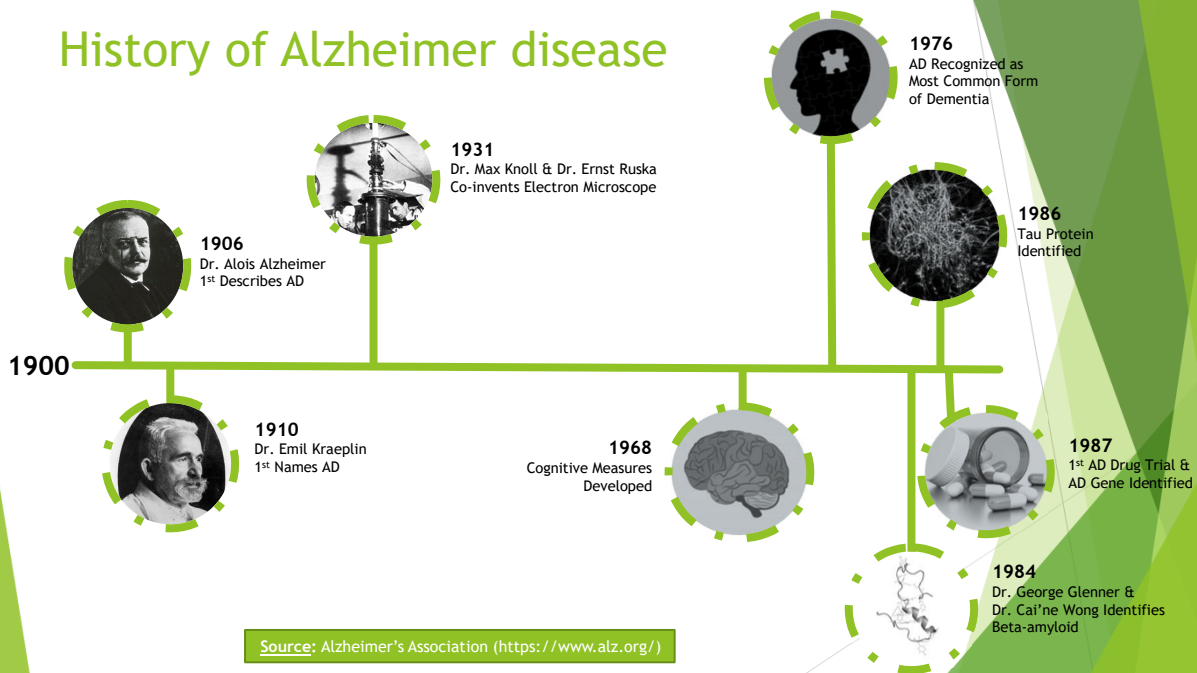
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How Is Alzheimer's Disease Treated?


- ▶ Treatments for Behavior Changes
 - ▶ Wandering, agitation, anxiety, depression, aggression, anger, etc.
- ▶ Treatments for Sleep Changes
- ▶ Alternative Treatments
 - ▶ Caprylic acid (Axona®)
 - ▶ Coenzyme Q10 or ubiquinone
 - ▶ "Coral" calcium supplements
 - ▶ Ginkgo biloba
 - ▶ Huperzine A
 - ▶ Omega-3 fatty acids
 - ▶ Phosphatidylserine
 - ▶ Tramiprosate

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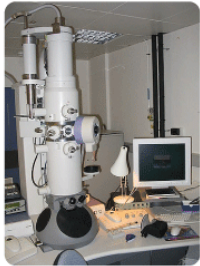
History of Alzheimer disease



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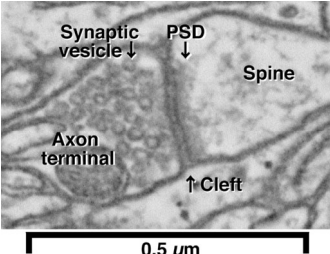
LIGHT MICROSCOPE



ELECTRON MICROSCOPE

Technological Advances in AD Research

Microscopy



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History of Alzheimer disease

- 1990** - Timeline start
- 1993** 1st AD Risk Factor Gene (APOE-e4) Identified & Drug Approved by FDA (Tacrine/Cognex)
- 1995** 1st Transgenic Mouse for AD Developed
- 1999** AD Vaccine Successful in Mice
- 2003** National AD Genetics Study Begins
- 2004** 1st Report on Imaging Agent (Pittsburgh Compound B) & AD Neuro-imaging Initiative
- 2008** AA & CDC Launch Road Map to Prevent Cognitive Impairment
- 2009** QC Program for CSF Biomarkers Launched
- 2010** AD Clinical Trial Database Established, TrialMatch[®] Launched, & Biomarker Changes in AD Discovered
- 2013** New Genetic Risk Factors for AD Identified
- 2018** Dementia Care Practice Recommendations Published
- 2019** International Research Network Established

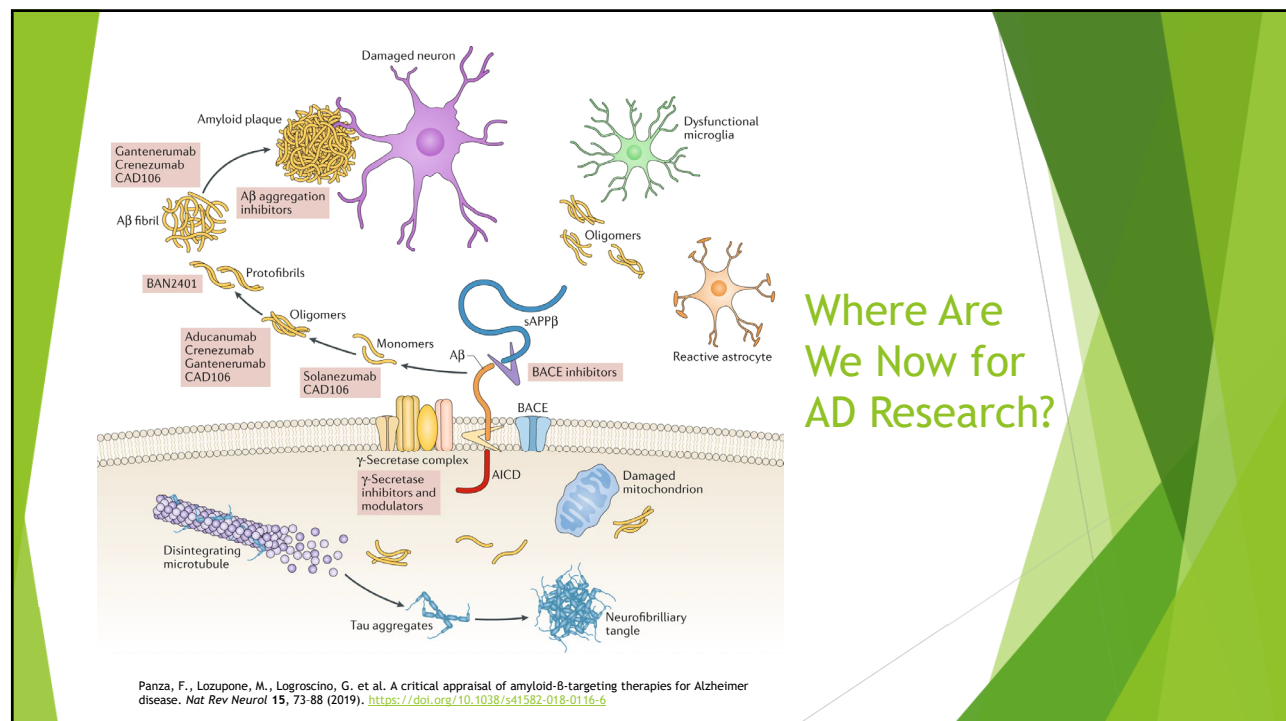
Source: Alzheimer's Association (<https://www.alz.org/>)

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AD Milestones in Infrastructure, Policy, & Law

- ▶ **1974** - Congress established the National Institute of Aging
- ▶ **1980** - Alzheimer's Association founded
- ▶ **1983** - November declared National AD Month
- ▶ **2008** - International Society to Advance Alzheimer's Research and Treatment formed
- ▶ **2011** - President Obama signs National Alzheimer's Project Act
- ▶ **2015** - Alzheimer's Accountability Act signed into law

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Where Are We Now for AD Research?

- ▶ Tau protein
 - ▶ AADvac1 (*a vaccine*)
- ▶ Inflammation
- ▶ 5-HT2A Receptor
- ▶ Alzheimer's prevention trials
 - ▶ Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (A4) Study
 - ▶ Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU)
 - ▶ The Alzheimer's Prevention Initiative (API)

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Technological Advances in AD Research

- ▶ Home Monitoring and Other Electronic Devices
 - ▶ Clocks
 - ▶ Communication Aids
 - ▶ Electrical Appliance Use Monitoring
 - ▶ GPS Location and Tracking Devices
 - ▶ Home Care Robots
 - ▶ In-Home Cameras
 - ▶ Medication Management
 - ▶ Picture Phones
 - ▶ Reminder Messages

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