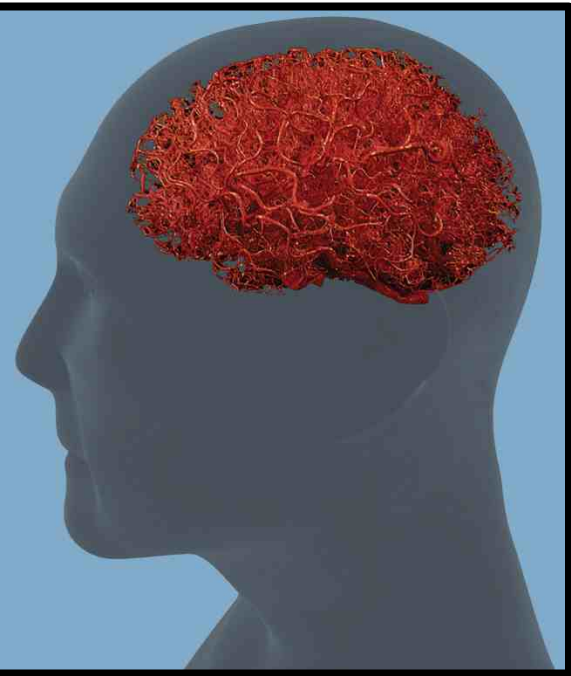


ALZHEIMER'S DISEASE AND DEMENTIA

ACUTE CARE 1

NURS 2830



Learning Objectives

- Definition of Alzheimer's disease progression
- Define and differentiate between dementia and Alzheimer's
- Define the 3 stages of AD?
- List at least 5 common symptoms of Alzheimer's
- Describe the changes that occur during the course of Alzheimer's
- Identify at least 3 risk factors associated with Alzheimer's
- Describe the role of caregivers
- Importance of person centered care and its implementation
- Importance of stress management with family and staff

DEMENTIA

An "umbrella" term used to describe a range of symptoms associated with cognitive impairment.

ALZHEIMER'S
50%-75%

VASCULAR
20%-30%

LEWY BODIES
10%-25%

FRONTOTEMPORAL
10%-15%

MIXED DEMENTIA = >1 NEUROPATHOLOGY - PREVALENCE UNKNOWN

Dementia

- Decline in mental ability severe enough to interfere with daily life
- Not a specific disease
- Not normal aging
- Caused by damage to brain cells from disease or trauma
- Many dementias are progressive

⁷ Alzheimer's Association. *What is Dementia?* Accessed June 8, 2015 from website: <http://www.alz.org/what-is-dementia.asp#causes>

Types of Dementia

- Alzheimer's disease
- Vascular dementia
- Dementia with Lewy Bodies (DLB)
- Mixed dementia
- Parkinson's disease
- Frontotemporal dementia
- Creutzfeldt-Jakob disease
- Normal pressure hydrocephalus
- Huntington's disease
- Wernicke-Korsakoff Syndrome



Vascular Dementia

- 2nd most common cause of dementia
- 20% - 30% of cases
- Caused by conditions that block or reduce blood flow to the brain
- Symptoms may occur suddenly following strokes or slowly as a result of cumulative damage

⁹ Alzheimer's Association. (2015) *Vascular Dementia*.

Mild Cognitive Impairment



Duration: 7 years

Disease begins in
Medial Temporal Lobe

Symptoms:
Short-term
memory loss

Mild Alzheimer's

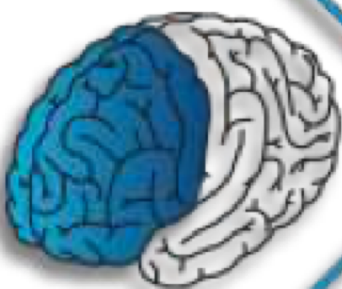


Duration: 2 years

Disease spreads to
Lateral Temporal &
Parietal Lobes

Symptoms include:
Reading problems
Poor object recognition
Poor direction sense

Moderate Alzheimer's

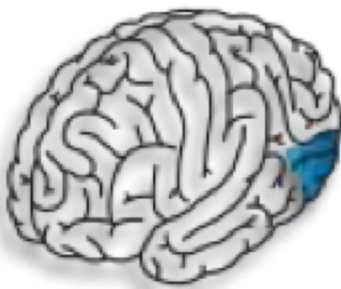


Duration: 2 years

Disease spreads to
Frontal Lobe

Symptoms include:
Poor judgment
Impulsivity
Short attention

Severe Alzheimer's



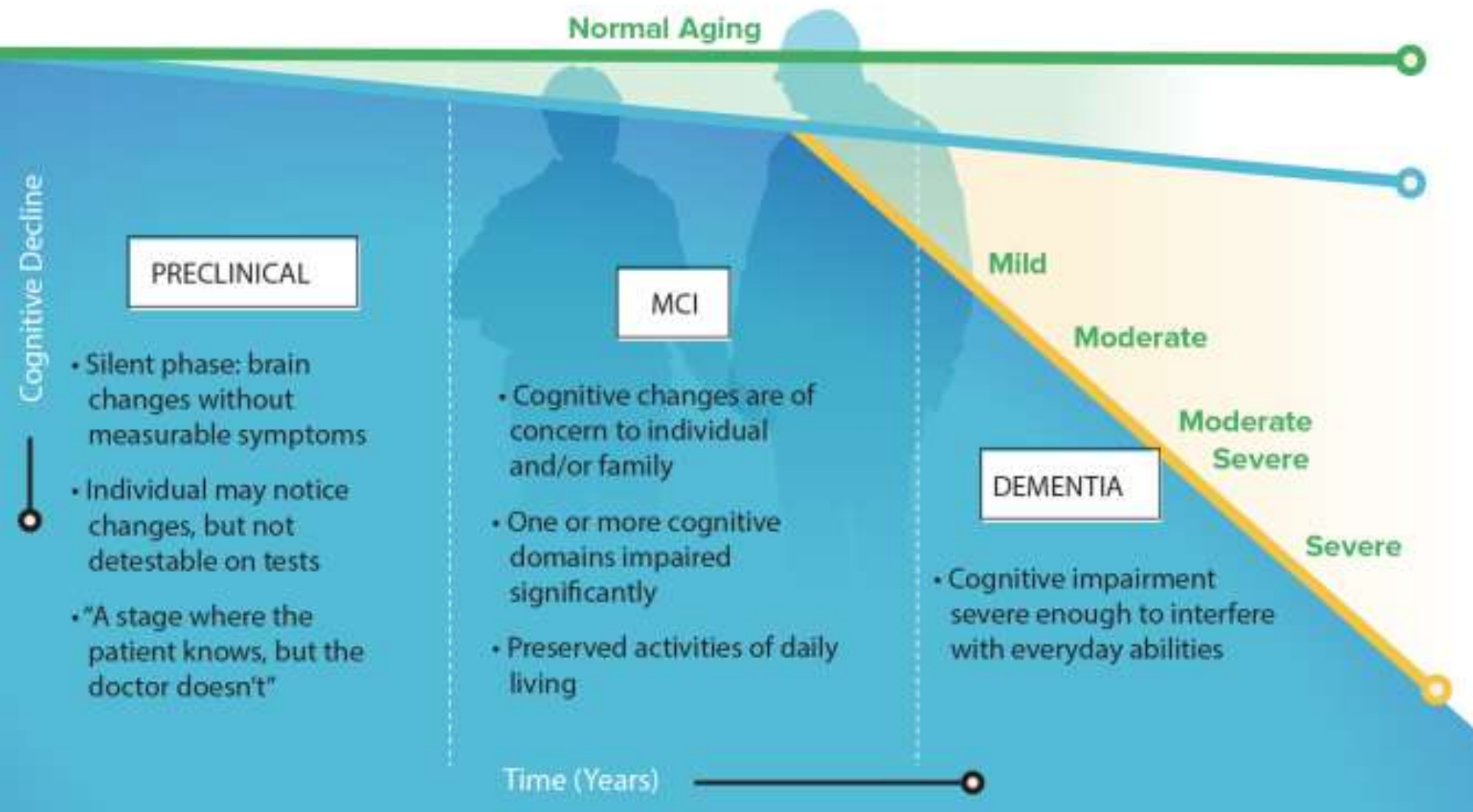
Duration: 3 years

Disease spreads to
Occipital Lobe

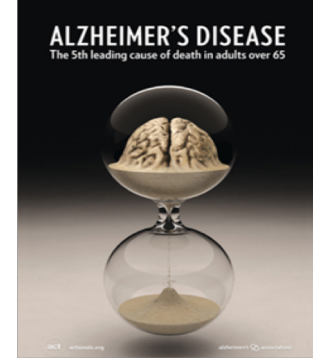
Symptoms include:
Visual problems

Progression from Normal Aging, through MCI and other stages of Dementia

Normal Aging Everyone experiences slight cognitive changes during aging

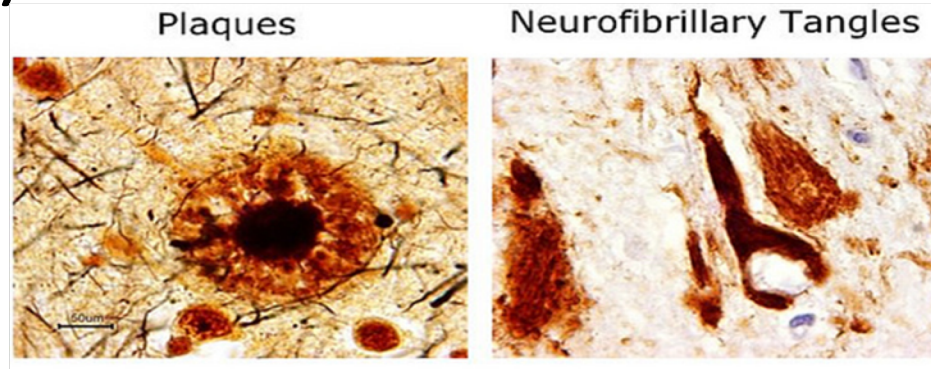


Alzheimer's Disease Theories



- Several theories proposed to explain the cause of AD but so far, no one theory can adequately explain all aspects of the disease
- Precise mechanisms for AD progression are also unclear
- 3 major theories (Cholinergic, Amyloid, Tau) currently regarded as the most likely explanation for AD
- being used as the basis for therapeutic development

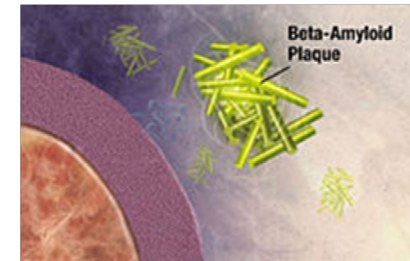
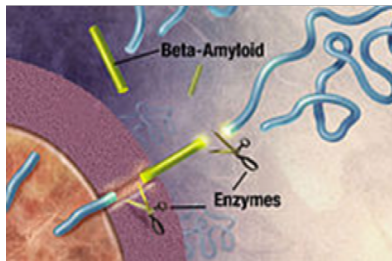
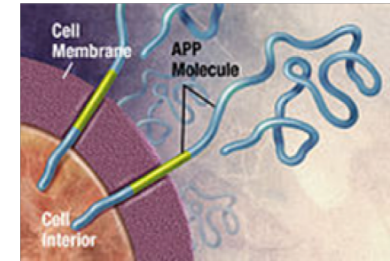
AD Pathology



- brain tissue under microscope
- 2 hallmarks of Alzheimer's disease are:
 - extracellular amyloid plaques
 - intra-neuronal neurofibrillary tangles (NFTs) composed of tau
- Described in 1907 by Alois Alzheimer they remain the major pathological abnormalities seen in AD

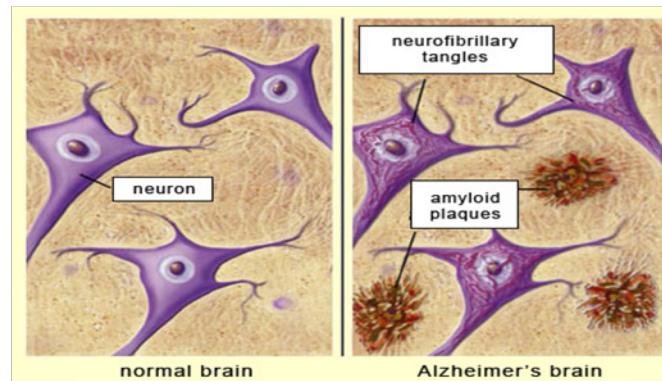
Amyloid Cascade Hypothesis

- Main focus of research to date
- Beta-amyloid ($A\beta$) is the main component of amyloid plaques (pathological hallmark of AD)
- Detailed understanding of how this protein fragment is clipped from its parent compound amyloid precursor protein (APP) by two enzymes – beta-secretase and gamma-secretase
- Researchers are developing medications aimed at every point in the amyloid processing pathway



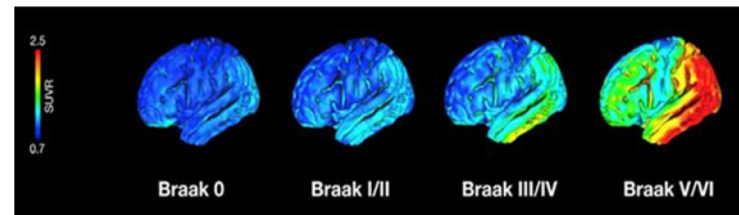
A β cascade hypothesis

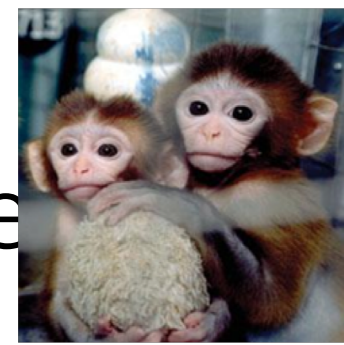
- Postulated that after amyloid plaques are deposited a cascade follows
- Causes inflammation and ultimately formation of neurofibrillary tangles (NFT's) (hallmark of AD)
- Problems with neurotransmitters and neuronal function in the brain and ultimately neurone death



New theories about AD Pathology

- We now know that tau accumulates in the medial temporal lobes of the brain during normal ageing
- Tau doesn't extend beyond the MTL until $A\beta$ is present in the cortex
- Tau PET scanning has allowed us to potentially stage AD in vivo
- Amount of tau in the brain correlates very closely with degree of cognitive impairment





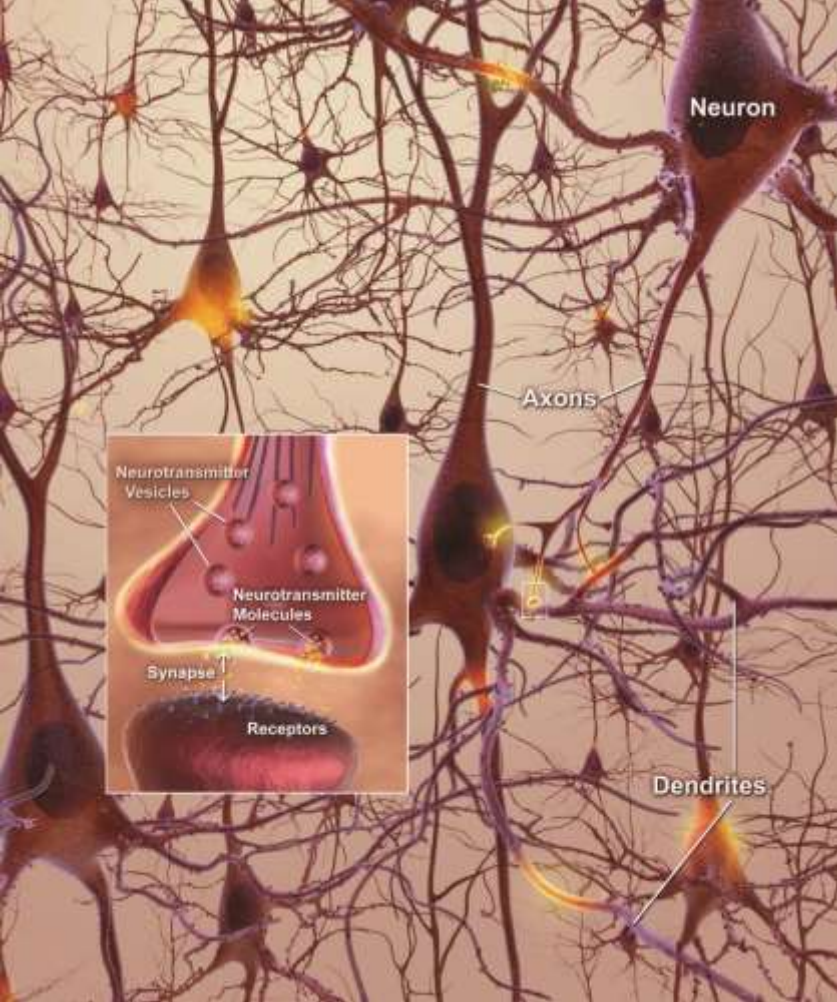
Anti-Amyloid strategies - Immunotherapy

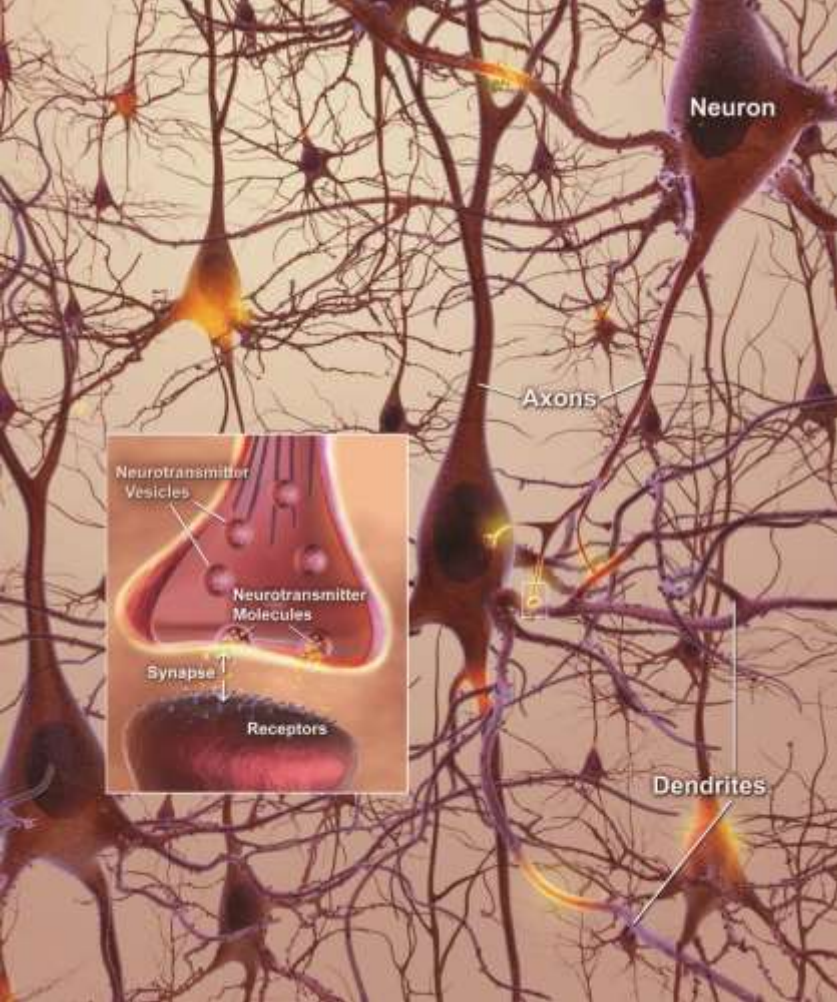
- Initial studies - injecting animals with $A\beta$ → good ab response → cleared amyloid plaques from brains
- Human studies prematurely ceased (2002) → development of brain inflammation (meningoencephalitis) in 6%
- BUT -evidence that treatment had removed amyloid plaque from the brain
- Idea of active immunisation not abandoned – several pharmaceutical companies early phases of developing new active vaccines

Tau



- Far fewer drug trials have focussed on tau
- No luck so far with anti- $A\beta$ treatments \rightarrow greater interest in tau
- Mouse and primate models of AD show amyloid plaques that respond to anti-amyloid therapy but no tau pathology like human AD
- Aged dogs develop AD-like disorder with $A\beta$ and NFT's
- Treatment of these animals with anti- $A\beta$ therapies reduces plaque load but no change in cognition or tau pathology
- There is a very robust correlation between tau pathology and clinical measures of dementia





Brain Mind Relation

Frontal Lobe

Planning
Reasoning
Problem solving
Morality
Personality
Social Skills
Recognising and
Regulating Emotions
Motor Functions
Motor speech area
of Broca

Parietal Lobe

Recognising sensation,
body position and objects
Sense of time and space
Reading and Comprehension area
Association between
functions of other
lobes

Temporal Lobe

Understanding
Language
Hearing
Speech
Memory
Learning
Sensory speech area
of Wernicke

Occipital Lobe

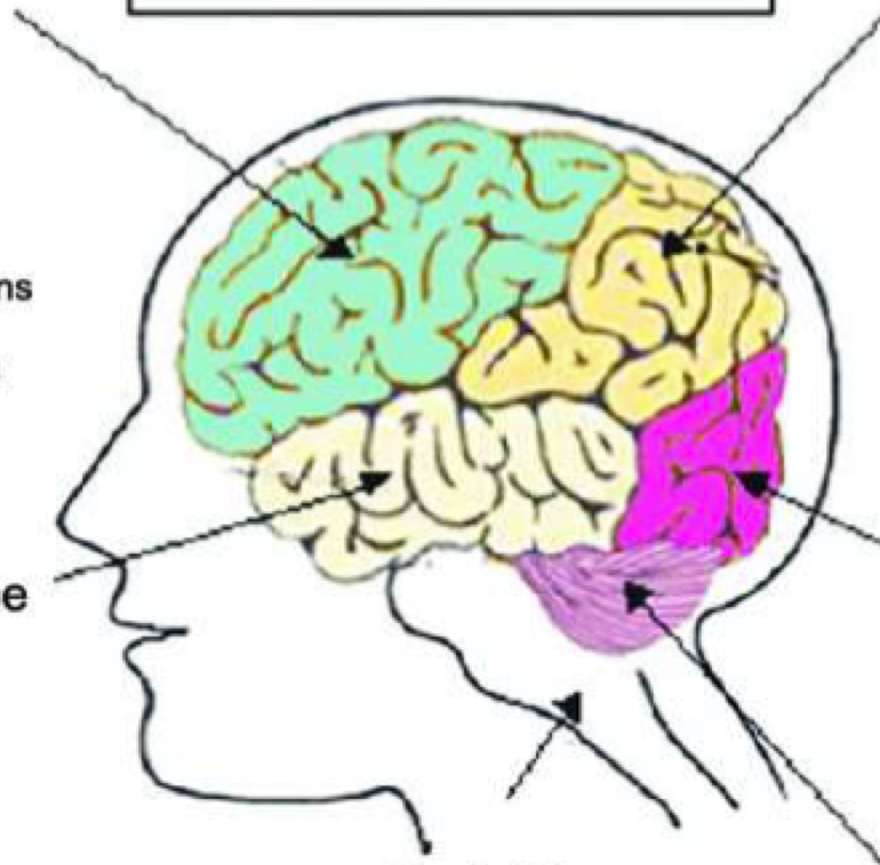
Vision and Integrating
visual information
(colour, shape and
distance)

Brain Stem

Regulation of heart
beats, respiration,
body temperature
and other essential
body functions

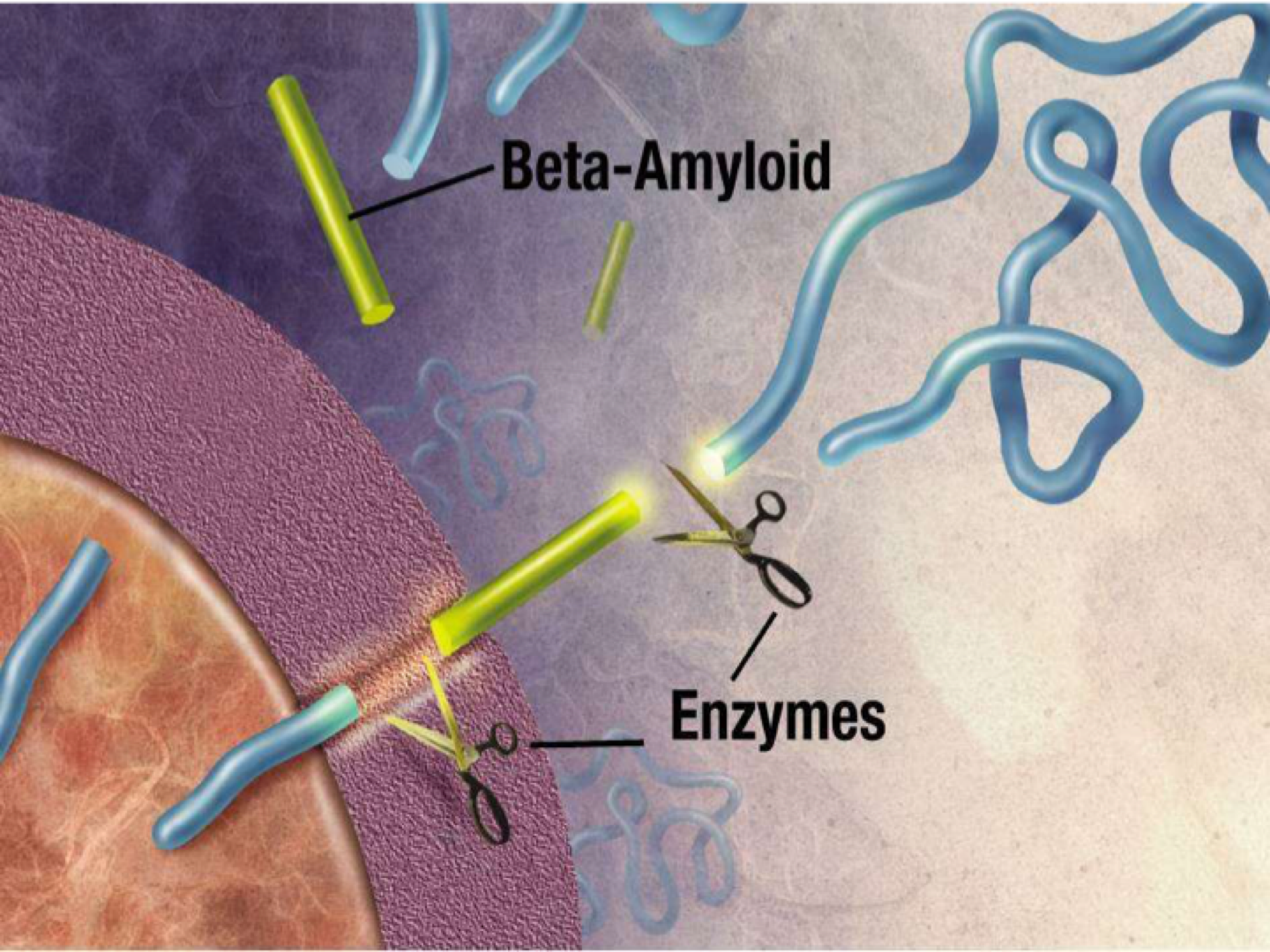
Cerebellum

Balance
Muscular co-ordination

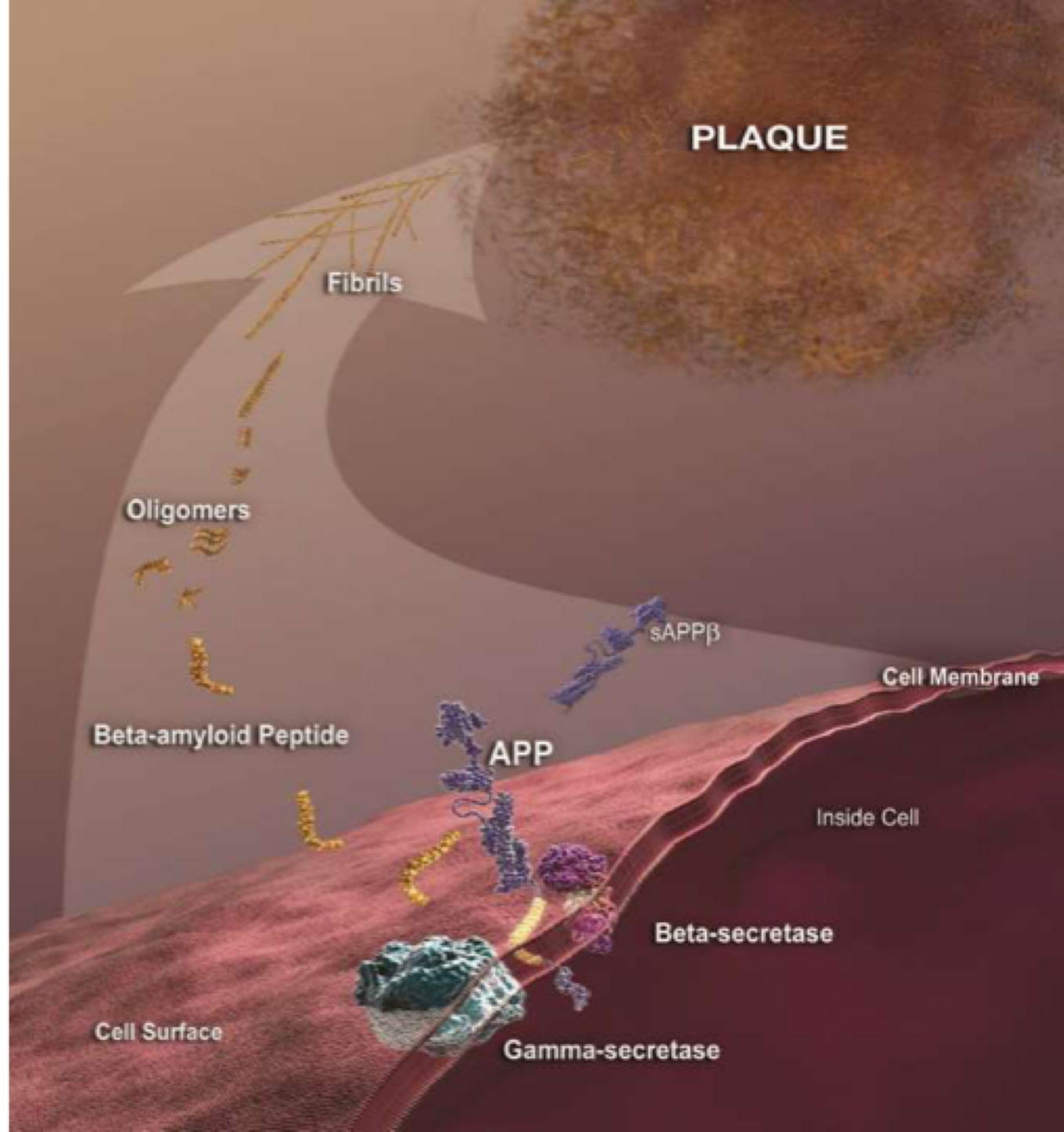


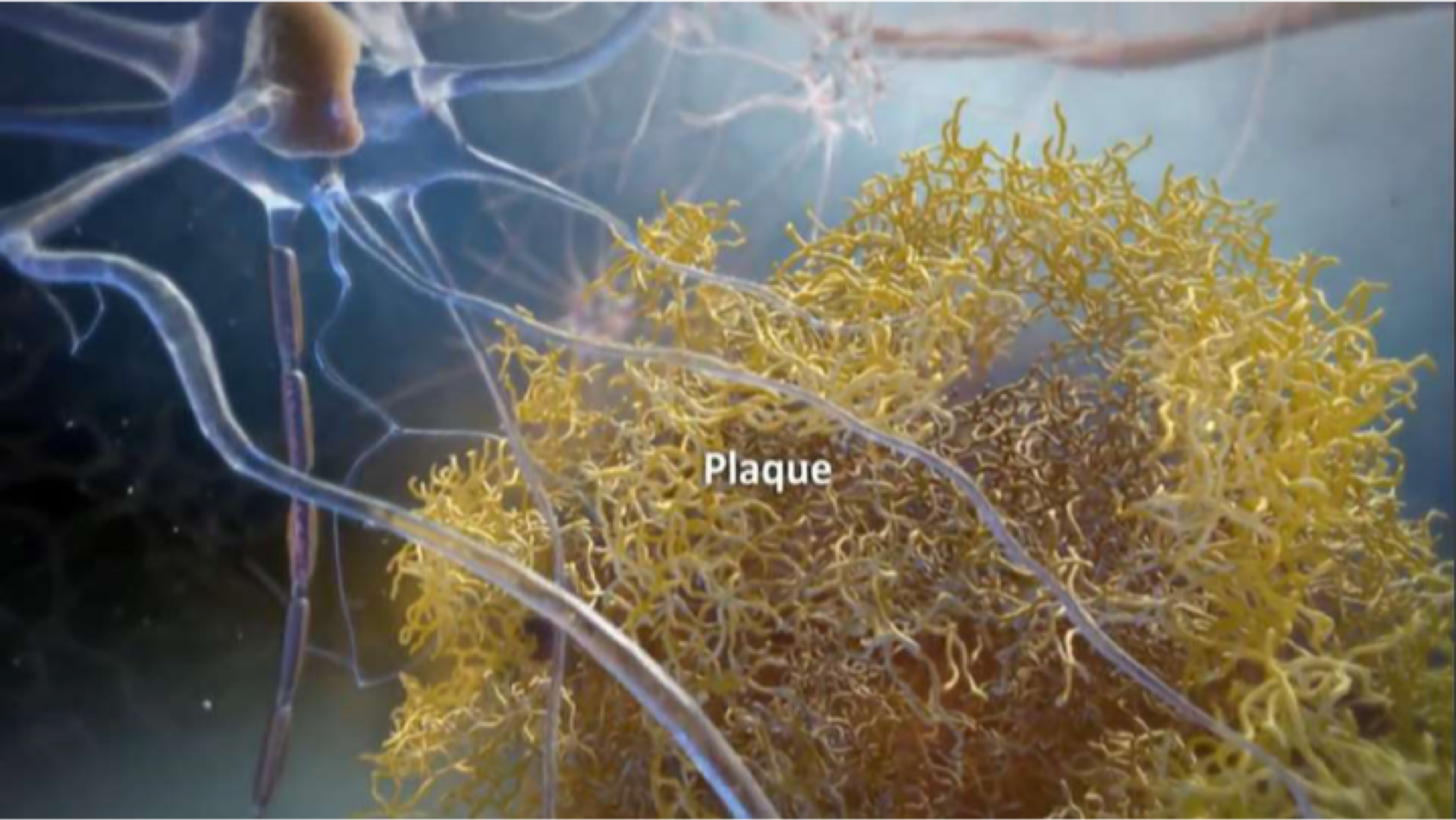


Peptide
Amyloid
Beta ($A\beta$)



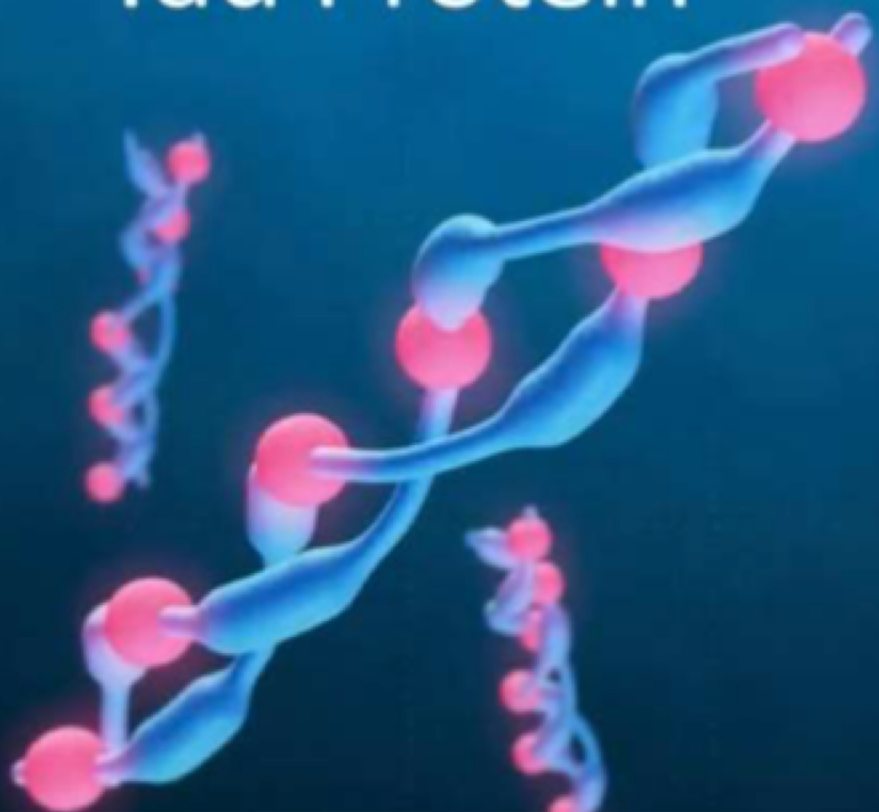






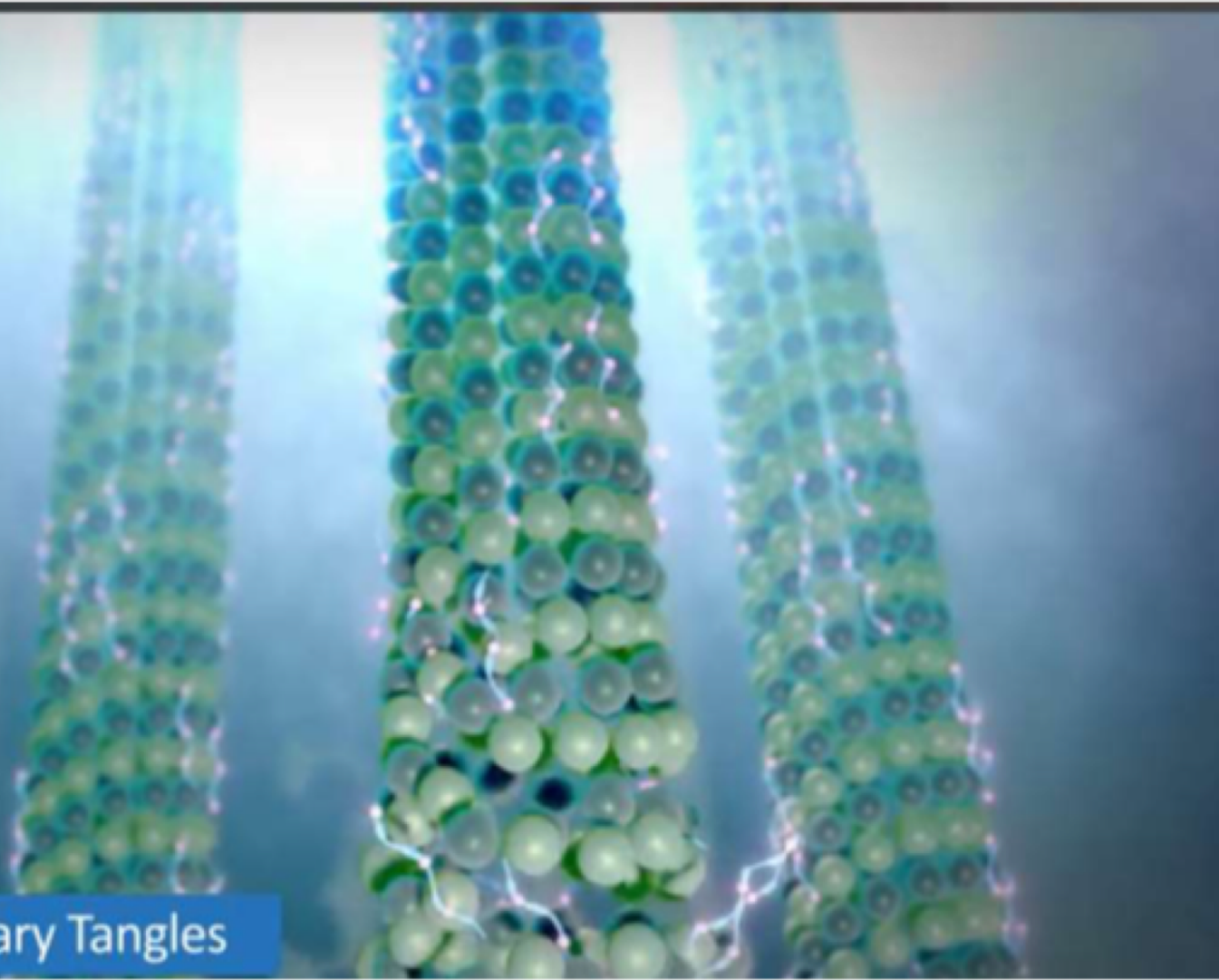
Plaque

Tau Protein

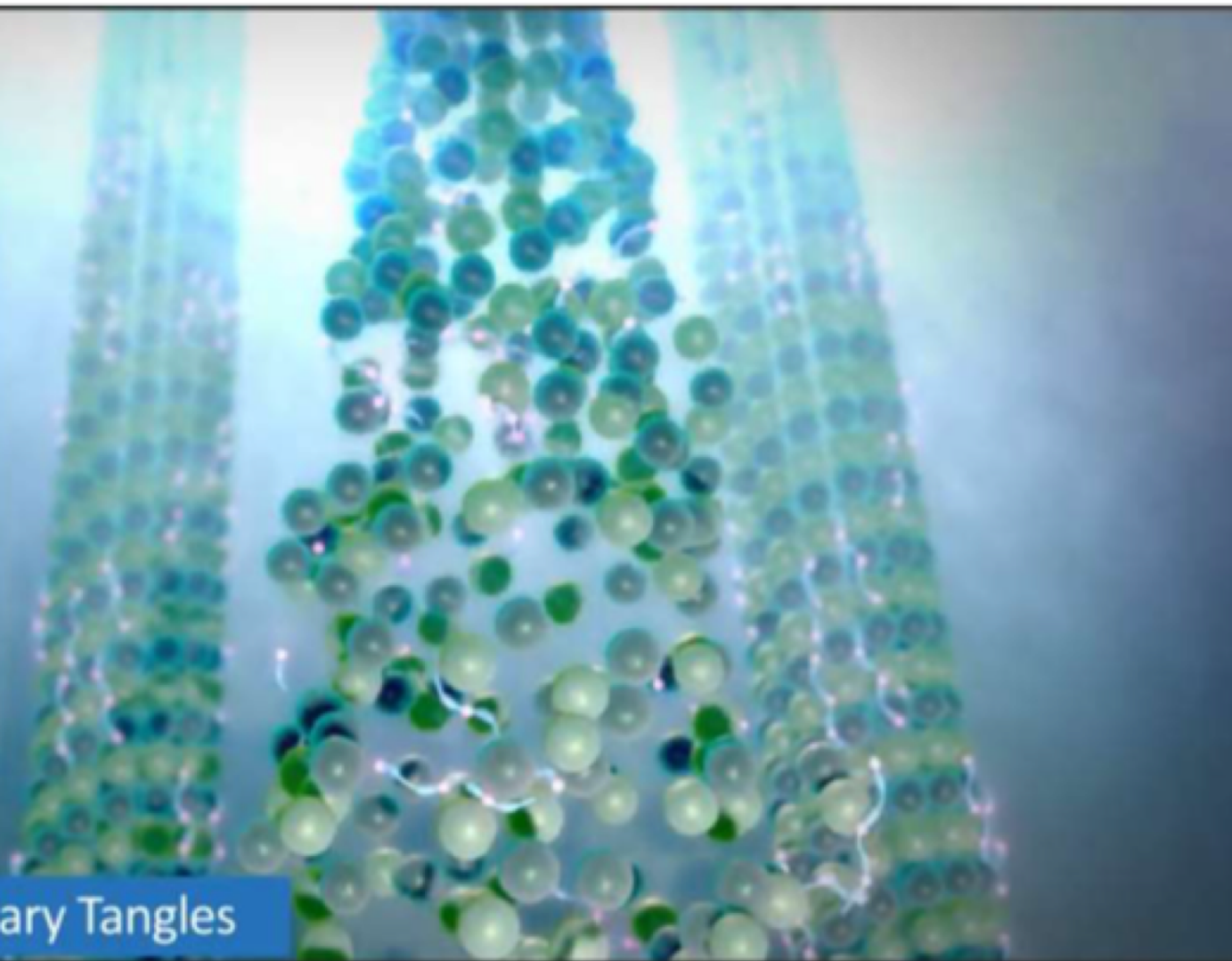


Peptide
Amyloid
Beta ($A\beta$)

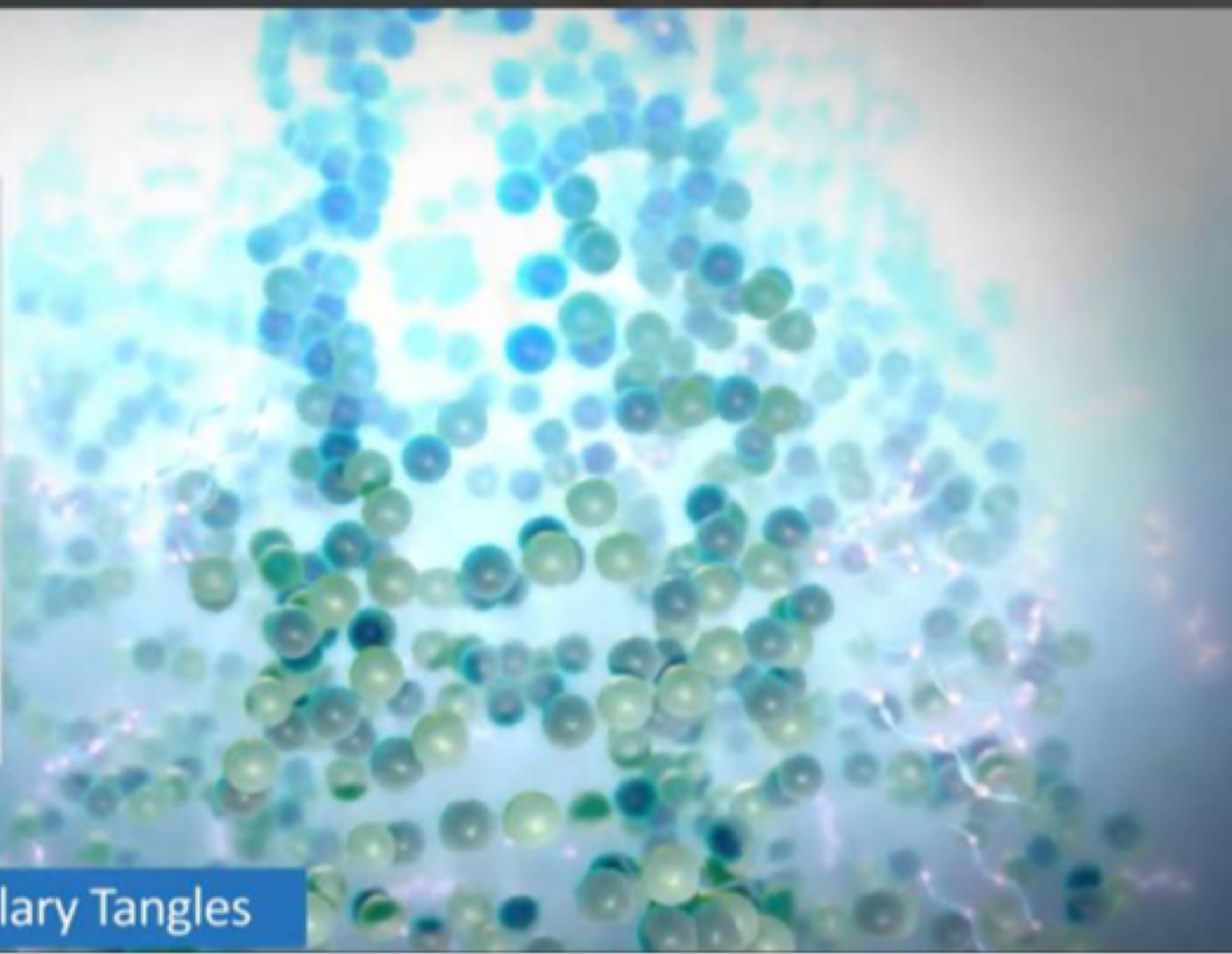




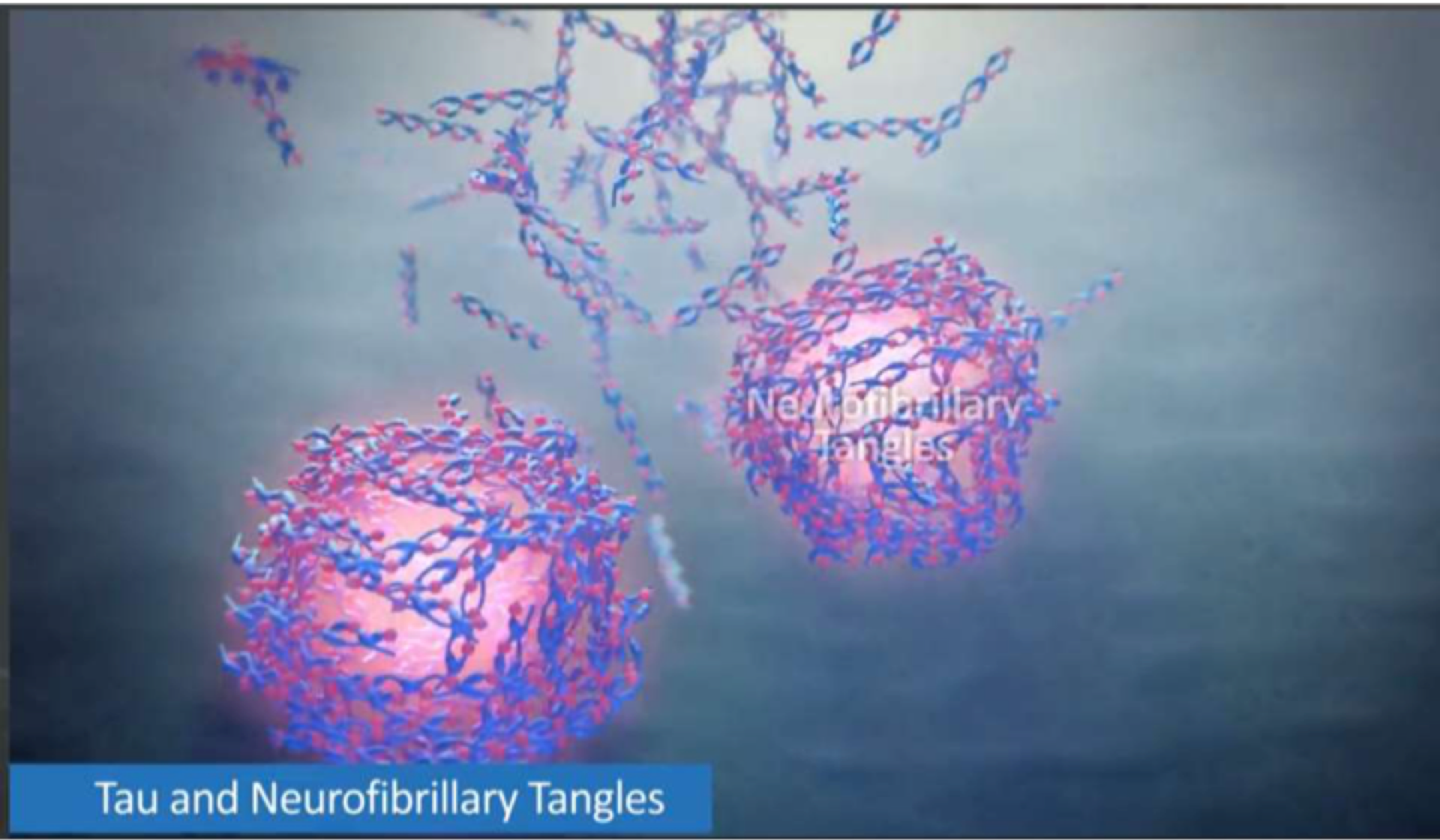
Tau and Neurofibrillary Tangles



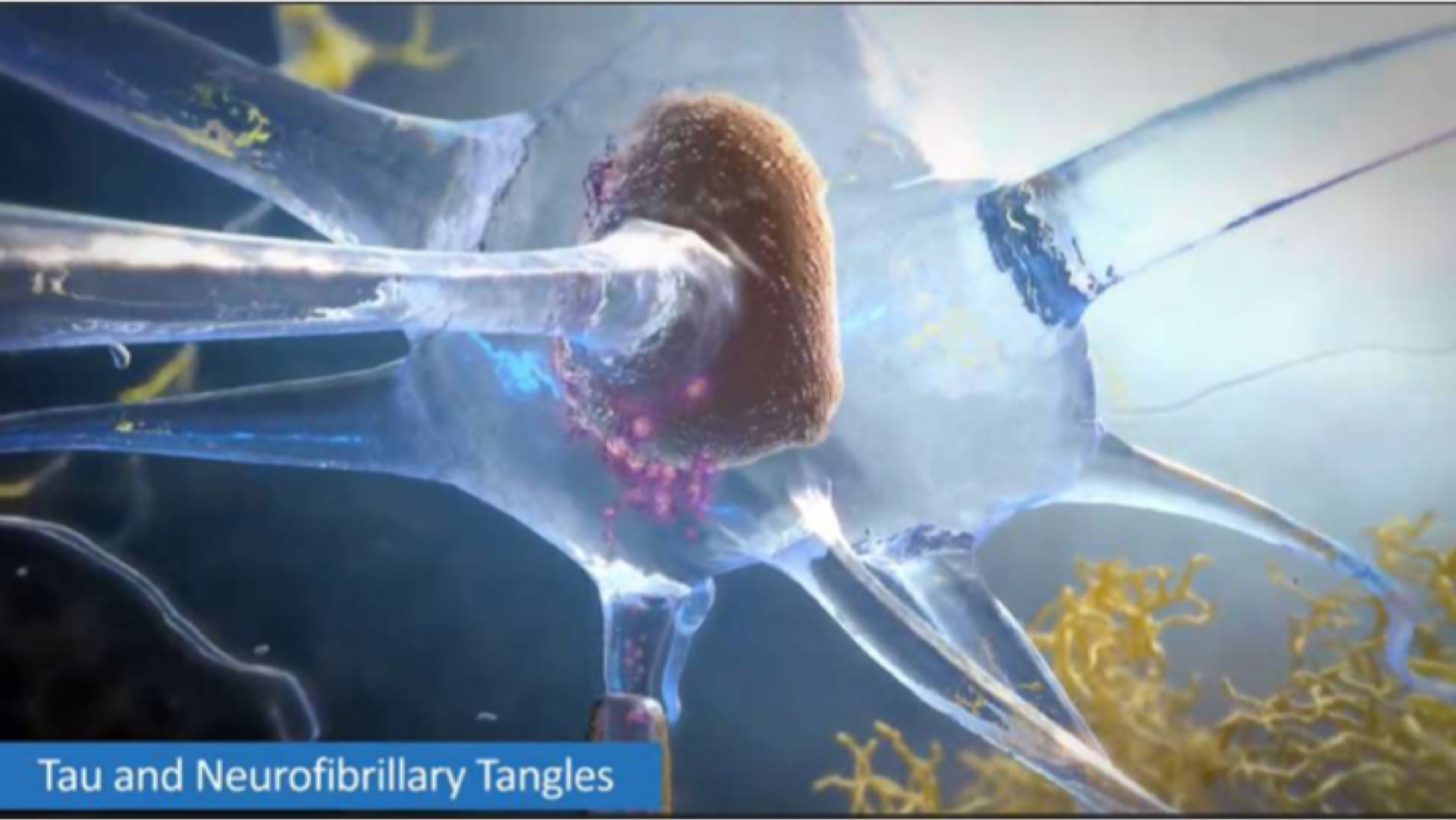
Tau and Neurofibrillary Tangles



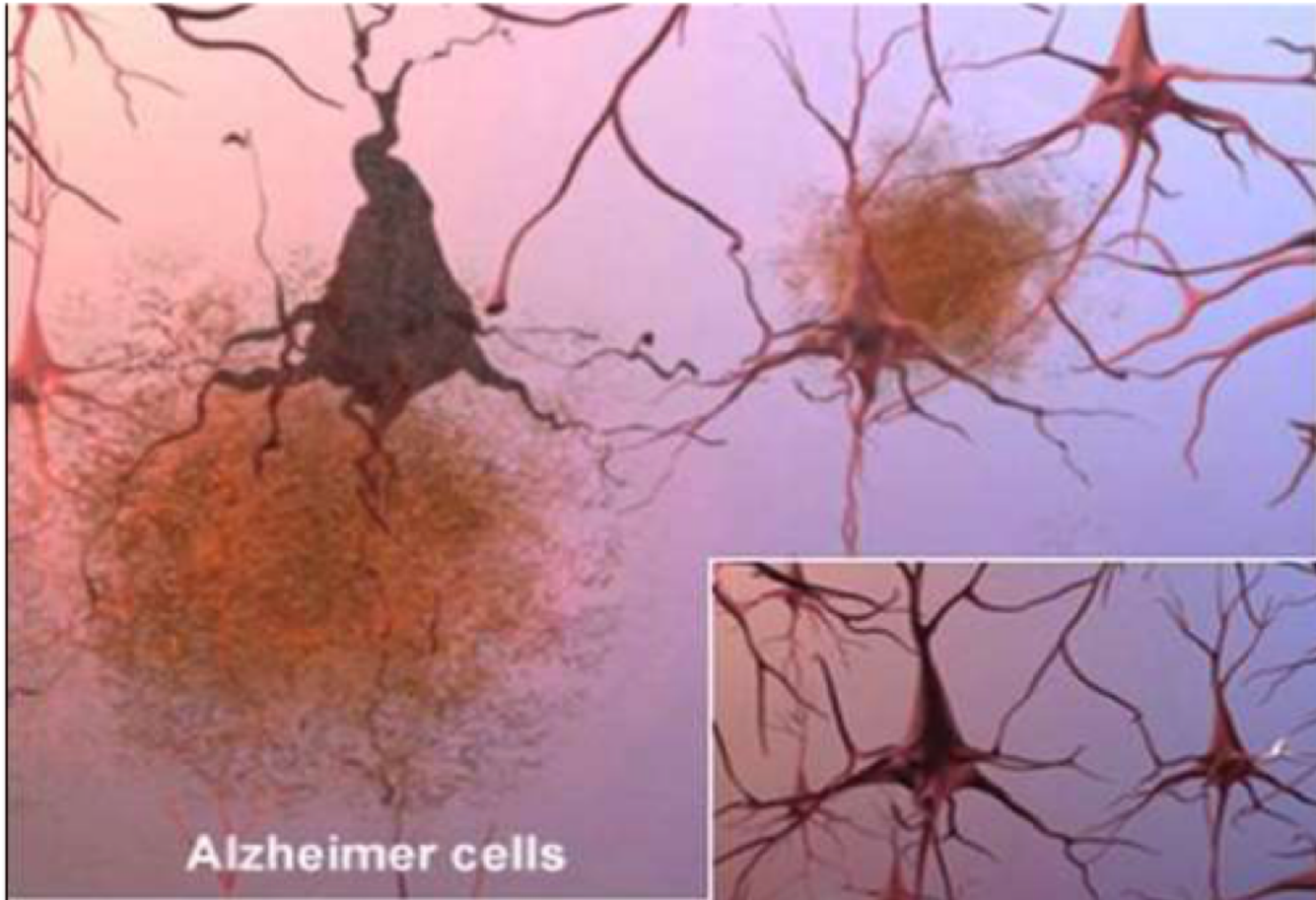
Tau and Neurofibrillary Tangles



Tau and Neurofibrillary Tangles



Tau and Neurofibrillary Tangles



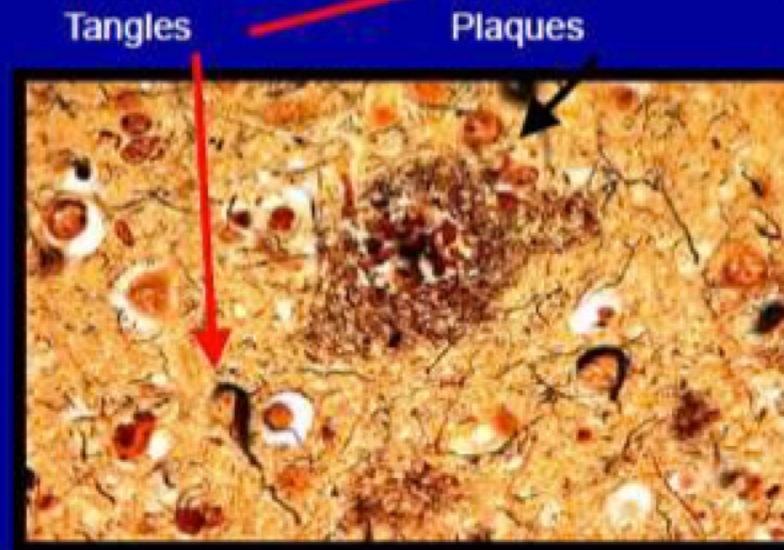
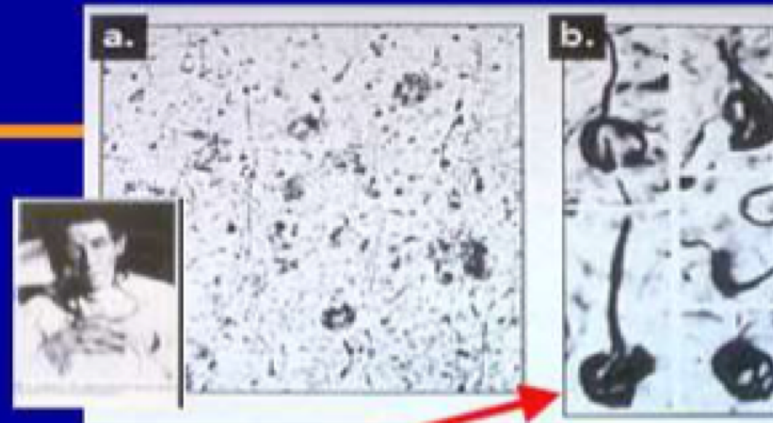
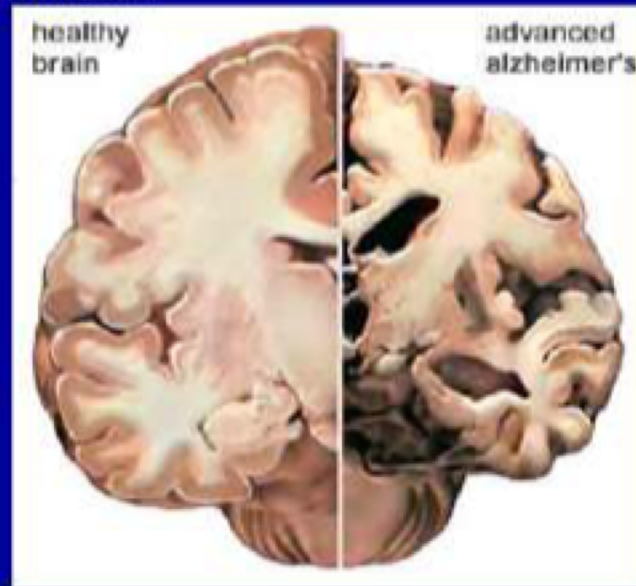
Alzheimer cells



healthy cells

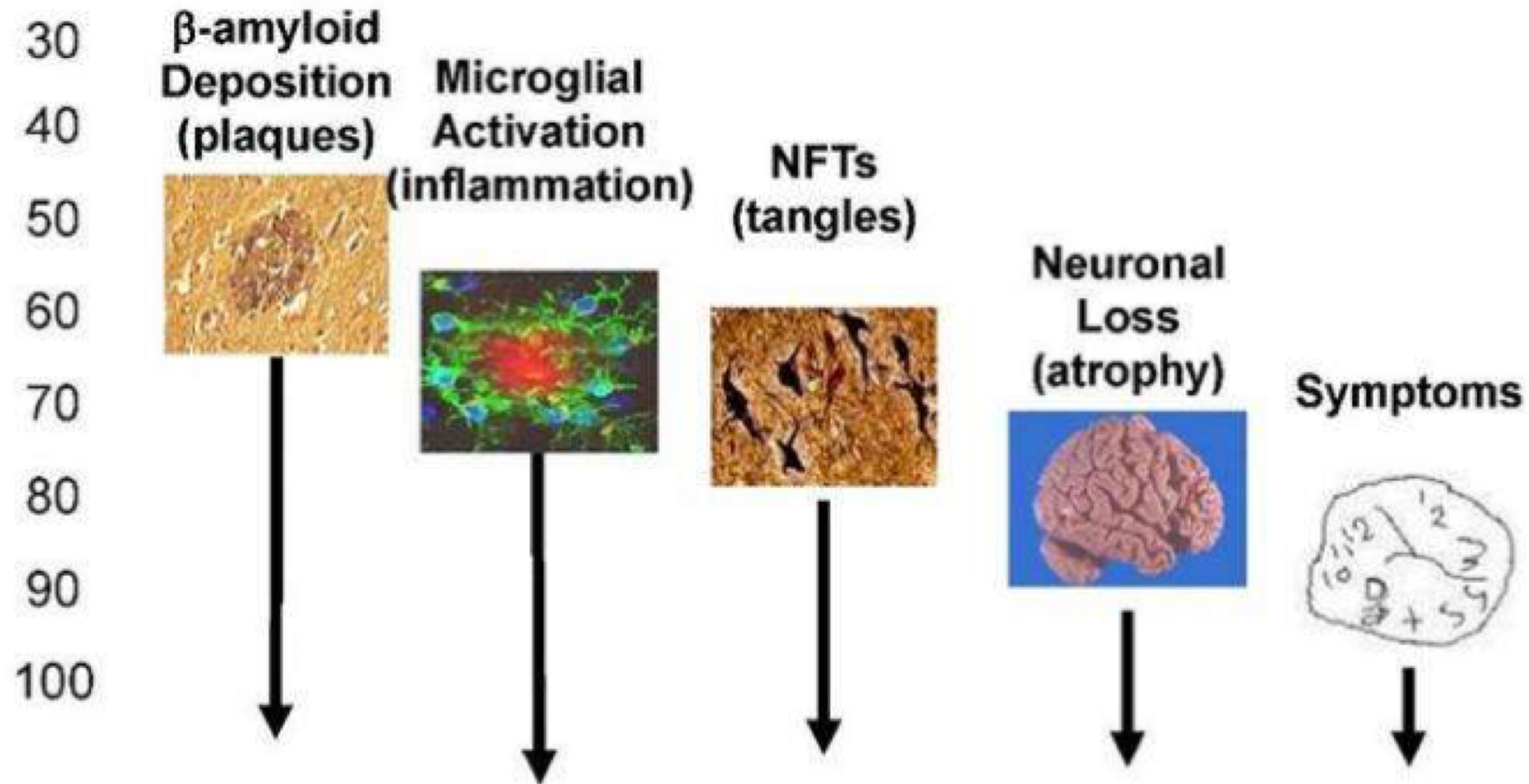
Neuropathology of AD

- Plaques (Amyloid- β)
- Neurofibrillary tangles (NFT) (tau)
- Nerve cell and synapse dysfunction, loss of connections, cell death, brain shrinkage
- Inflammation



PATHOLOGIES ASSOCIATED WITH AD

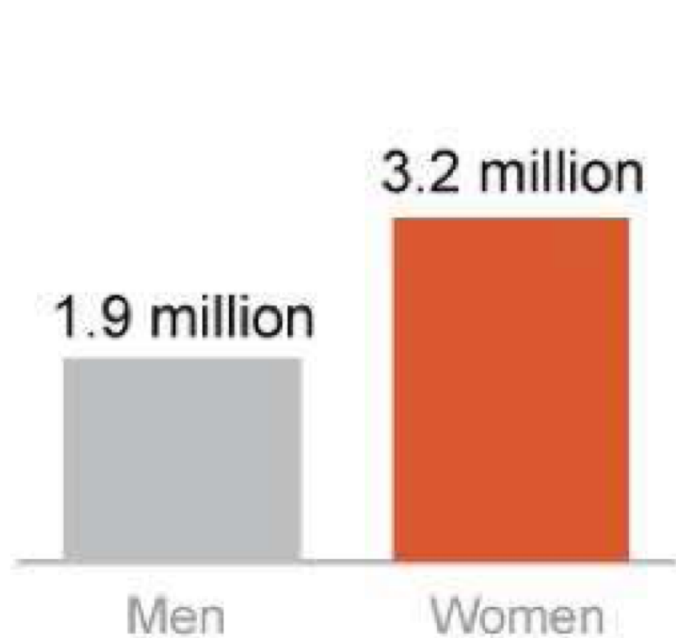
AGE



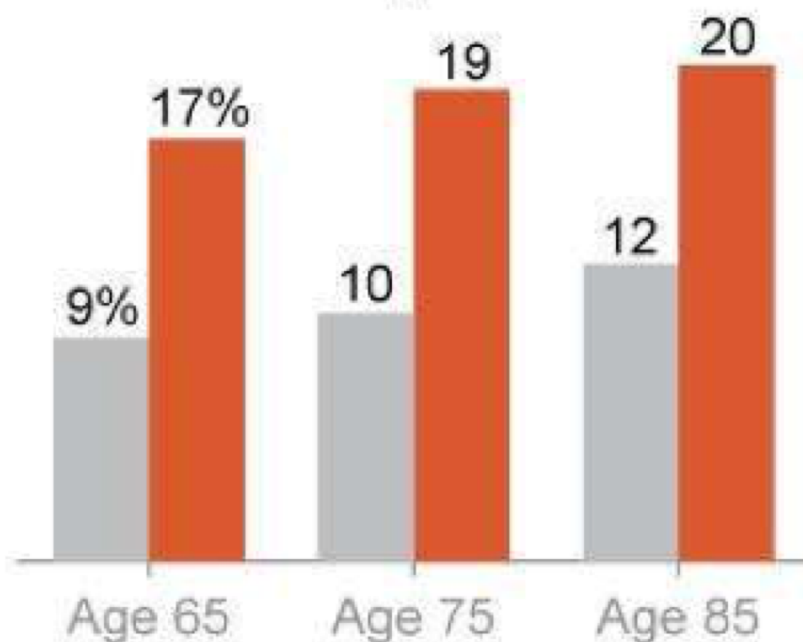
Gender and Alzheimer's disease

Women make up a larger share of Alzheimer's patients than men and have a greater risk of developing the disease as they age.

Number of people ages 65 and older in the U.S. with Alzheimer's:



Percent chance a person will develop Alzheimer's during his or her remaining lifetime:



HOW IT WORKS

1 Clumps of amyloid protein clog up brain and poison cells

2 Patient given jab packed with antibodies that find and latch on to the clumps

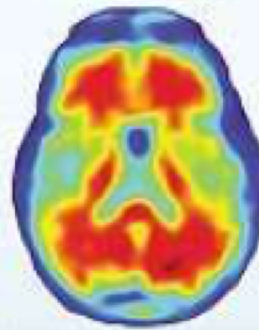
3 This alerts the immune system, which sends in cells able to break up the toxic amyloid and flush it out of the brain.

THE RESULTS

(Danger protein is shown in red)

High dose treatment

Initial scan



One year later

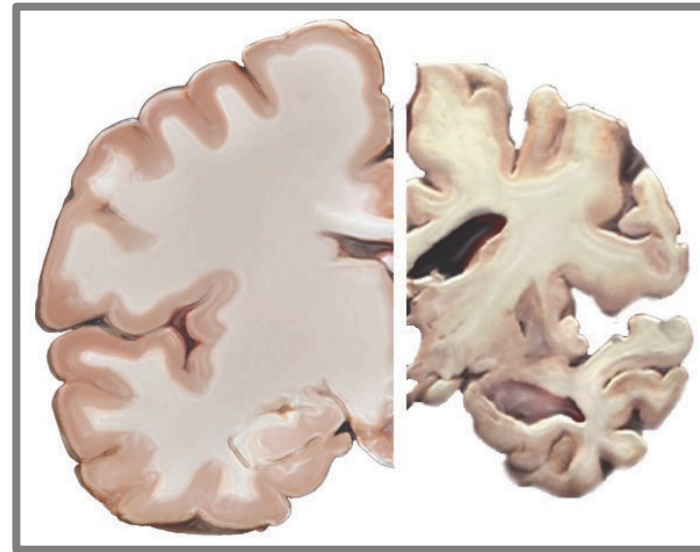


Placebo treatment



Alzheimer's Disease: Overview

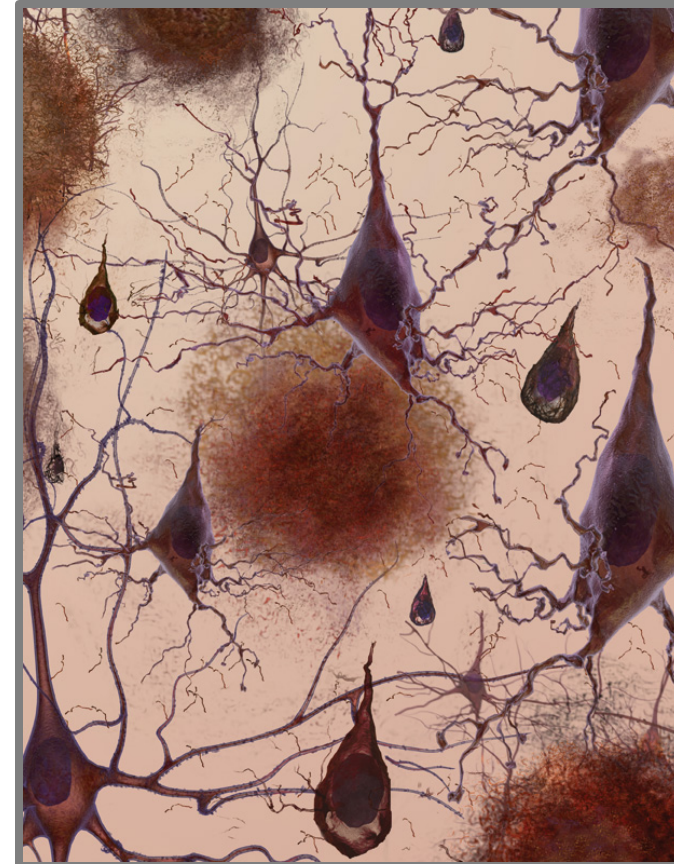
- Most common type of dementia
- 60% - 80% of cases
- Progressive – symptoms gradually worsen over number of years
- Identified in 1906 by Dr. Alois Alzheimer



¹⁰ Alzheimer's Association. *What is Alzheimer's?* Accessed June 8, 2015 from website: http://www.alz.org/alzheimers_disease_what_is_alzheimers.asp

Alzheimer's Disease: Physical Changes

- Brain shrinks dramatically
 - Nerve cell death
 - Tissue loss
- Plaques: abnormal clusters of protein fragments
- Tangles: twisted strands of another protein



Alzheimer's Disease: Causes

- Precise changes in brain largely unknown
- Probably develops as a result of complex interactions among:
 - Age
 - Genetics
 - Environment
 - Lifestyle
 - Coexisting medical conditions

¹³ Alzheimer's Association. Risk Factors. Accessed June 8, 2015 from website: http://www.alz.org/alzheimers_disease_causes_risk_factors.asp

10 Warning Signs of Alzheimer's

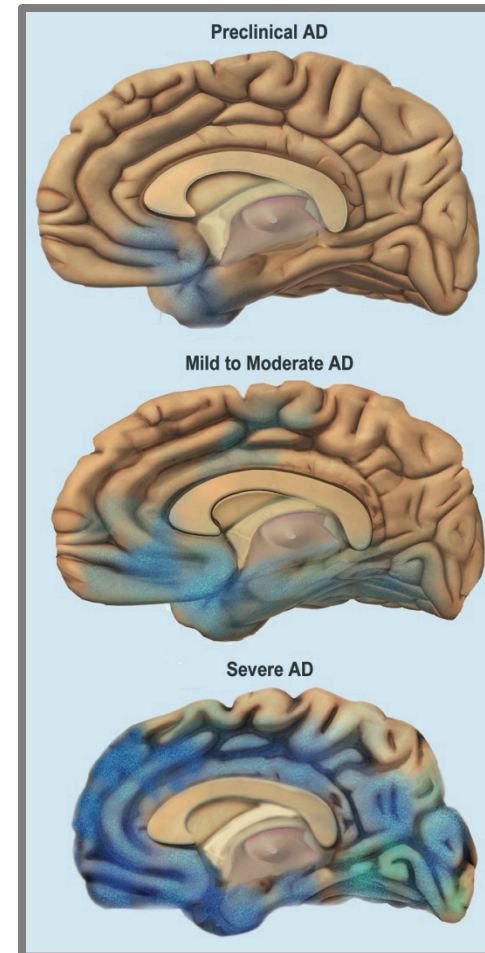
1. Memory loss that disrupts daily life
2. Challenges in planning or solving problems
3. Difficulty completing familiar tasks
4. Confusion with time or place
5. Trouble understanding visual images and spatial relationships
6. New problems with words in speaking or writing
7. Misplacing things and losing the ability to retrace steps
8. Decreased or poor judgment
9. Withdrawal from work or social activities
10. Changes in mood and personality

¹⁵Alzheimer's Association. (2009) *Know the 10 Signs*.

Stages of Alzheimer's Disease

- Average lifespan 4-8 years after diagnosis; as long as 20 years
- Progresses slowly in 3 stages:
 - Mild (early-stage)
 - Moderate (middle-stage)
 - Severe (late-stage)

¹⁷ Alzheimer's Association. *Stages of Alzheimer's*. Accessed June 8, 2015 from website: http://www.alz.org/alzheimers_disease_stages_of_alzheimers.asp



Mild Alzheimer's (Early-Stage)

- Able to function independently
- Common difficulties:
 - Forgetting familiar words
 - Losing everyday objects
 - Trouble remembering names
 - Greater difficulty performing tasks
 - Forgetting material just read
 - Increasing trouble with planning, organizing

¹⁸ Alzheimer's Association. *Stages of Alzheimer's*. Accessed June 8, 2015 from website: http://www.alz.org/alzheimers_disease_stages_of_alzheimers.asp

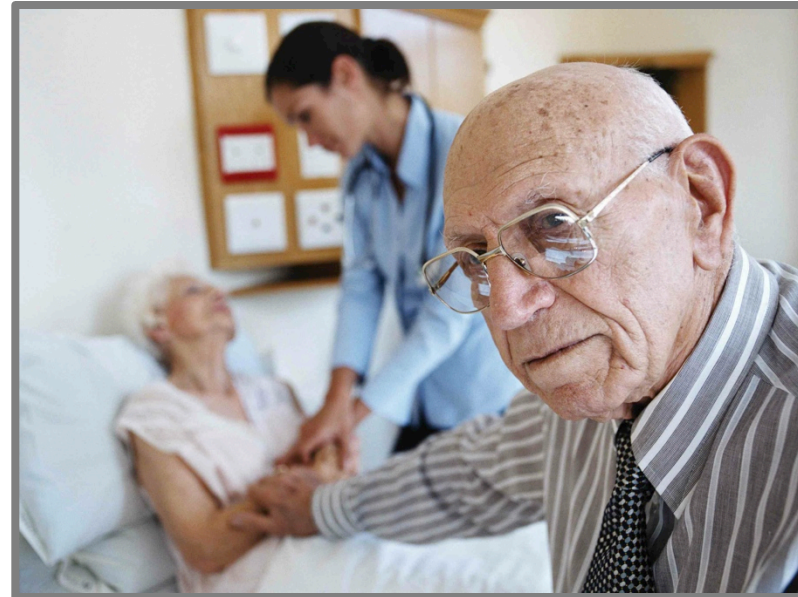
Moderate Alzheimer's (Middle-Stage)

- Requires increasing care
- Symptoms include:
 - Forgetfulness of personal history
 - Confusion about place or time
 - Need for help with bathing, toileting, dressing
 - Changes in sleep patterns
 - Increased risk of wandering
 - Personality and behavioral changes

¹⁹ Alzheimer's Association. *Stages of Alzheimer's*. Accessed June 8, 2015 from website: http://www.alz.org/alzheimers_disease_stages_of_alzheimers.asp

Severe Alzheimer's (Late-Stage)

- Typically longest stage
- Requires full-time care
- Loss of awareness of recent experiences and surroundings
- Changes in physical abilities (walking, sitting, swallowing)
- Vulnerable to infections



²⁰ Alzheimer's Association. *Stages of Alzheimer's*. Accessed June 8, 2015 from website: http://www.alz.org/alzheimers_disease_stages_of_alzheimers.asp

Risk Factors: Age

- #1 risk factor is advancing age
- Approximately doubles every 5 years after age 65
- 1 in 3 people age ≥ 85

²¹ Alzheimer's Association. *Risk Factors*. Accessed June 8, 2015 from website:

http://www.alz.org/alzheimers_disease_causes_risk_factors.asp

²² Alzheimer's Association, *2015 Alzheimer's Disease Facts and Figures*, March 2015



Risk Factors: Family History, Education

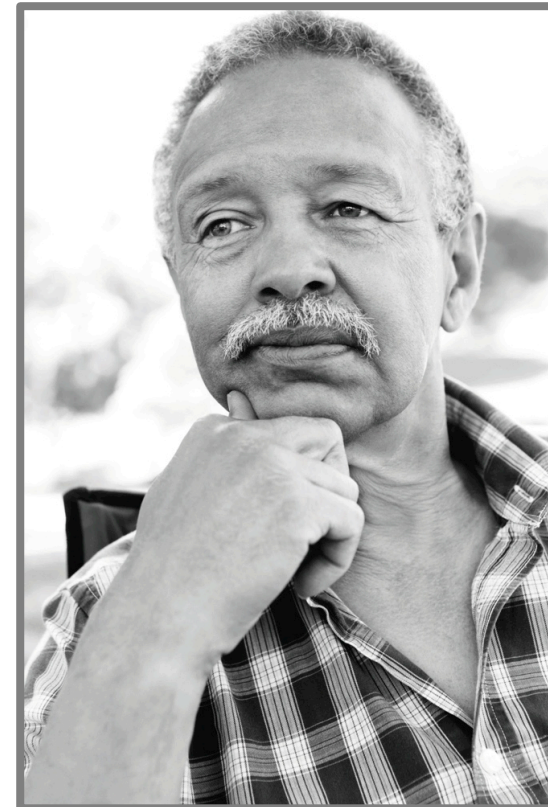
- Family history
- Hereditary/Genetics
- Education, cognitive engagement



²³ Alzheimer's Association. *Risk Factors*. Accessed from website:
http://www.alz.org/alzheimers_disease_causes_risk_factors.asp

Risk Factors: Race & Ethnicity

- African-Americans: 2 times greater risk
- Hispanics: 1.5 times greater risk
- Cardiovascular risk factors more common
- Lower levels of education, socioeconomic status



Risk Factors: Women

- 2/3 of affected population
- 16% of women age ≥ 71 (11% of men)
- At age 65 have more than 1 in 6 chance (1 in 11 for men)
- Age ≥ 60 , are twice as likely to develop Alzheimer's than breast cancer

²⁵ Alzheimer's Association, *AAIC Press Release*, July 21, 2015
²⁶ Alzheimer's Association, *Public Health E-News*, July 22, 2015



Modifiable Risk Factors: Head Trauma

- Moderate and severe traumatic brain injury
 - Moderate injury: 2.3 times greater risk
 - Severe injury: 4.5 times greater risk
- Risk remains for years after injury



²⁷ Alzheimer's Association. (2015) *Traumatic Brain Injury*.

Modifiable Risk Factors: Lifestyle

- Increases risk
 - Current smoking
 - Midlife obesity
- Decreases risk
 - Physical activity
 - Heart-healthy diets: DASH, Mediterranean diet
 - Mental and social activity

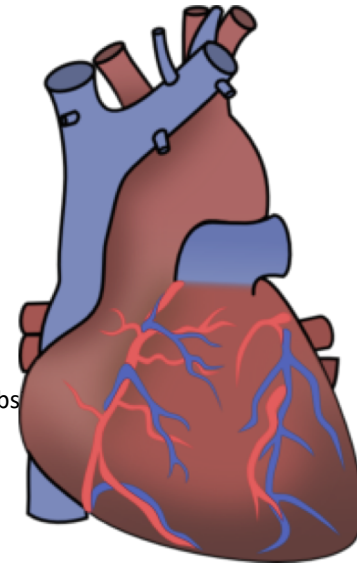
²⁸ Alzheimer's Association. (2014) *Alzheimer's and Public Health Spotlight: Heart Health and Brain Health*.

²⁹ Alzheimer's Association. *Prevention and Risk of Alzheimer's & Dementia*. Accessed July 16, 2015 from website: http://www.alz.org/research/science/alzheimers_prevention_and_risk.asp

Modifiable Risk Factors: Cardiovascular

- Heart-head connection
- Cardiovascular risk factors:
 - High blood pressure in midlife
 - Heart disease
 - Stroke
 - Diabetes

³⁰ Alzheimer's Association. *Prevention and Risk of Alzheimer's & Dementia*. Accessed July 16, 2015 from http://www.alz.org/research/science/alzheimers_prevention_and_risk.asp



Diagnosing Alzheimer's Disease

- No single test
- Medical evaluation
 - Medical history
 - Mental status testing
 - Information from family and friends
 - Physical and neurological exams
 - Rule out other causes



³¹ Alzheimer's Association. *Diagnosis of Alzheimer's Disease and Dementia*. Accessed June 8, 2015 from website: http://www.alz.org/alzheimers_disease_diagnosis.asp

Treating & Managing Alzheimer's

- No cure
- Drug and non-drug treatments
- Primary goals of treatment:
 - Maintain quality of life
 - Maximize function in daily activities
 - Enhance cognition, mood, behavior
 - Foster safe environment
 - Promote social engagement



³² Alzheimer's Association. *Health Care Professionals and Alzheimer's*. Accessed June 8, 2015 from website: <http://www.alz.org/health-care-professionals/medical-management-patient-care.asp>

Alzheimer's: Co-Morbidities

- Additional chronic conditions (e.g., heart disease, diabetes, depression)
- Difficult to manage
- Higher rates of hospitalizations and costs
 - 3 times as many hospital stays
 - 3 times average Medicare costs
- Preventable hospitalizations

³³ Alzheimer's Association. (2013) *Combating Alzheimer's Disease: A Public Health Agenda*.



Alzheimer's: Unique Aspects

- Financial hardship
 - May lose income and savings
 - Increased reliance on public programs
- Stigma
- Vulnerability to abuse

³⁴ Alzheimer's Association. *Abuse*. Accessed July 16, 2015 from website: <https://www.alz.org/care/alzheimers-dementia-elder-abuse.asp>

Alzheimer's: Caregivers

- Responsibilities:
 - Dressing, bathing, toileting, feeding
 - Shopping, meal preparation, transportation
 - Medication
 - Financial management
 - Emotional support
- Increasing levels of care
- Results in complete dependence



³⁵ Alzheimer's Association. (2015) *Alzheimer's Disease Caregivers*.

New Insights into Women and AD Risk

- Almost 2/3 of Americans with Alzheimer's disease are women
- Why are women at higher risk?
- Belief: Women live longer than men
- and older age is biggest AD risk
- New research suggests higher risk could be due to biological or genetic factors, different life experiences, (e.g., education, occupation), rates of heart disease, or even sex-based standards for cognitive tests
- New Alzheimer's Association Supported Studies

Four Key Studies

- **Reproductive History** (Gilsanz et al., AAIC, 2018)
 - Three or more children, fewer miscarriages, menstrual periods at a younger age, later age of menopause all related to lower dementia risk
- **Pregnancy** (FOX ET AL., AAIC, 2018)
 - More months in pregnancy = lower dementia risk
 - Not simply estrogen exposure, but better nutrition, reducing or stopping smoking and drinking, also may be that having more kids increases cognitive reserve through cognitive challenge
- **Hormone Therapy** (Gleason et al., AAIC, 2018)
 - No negative effect on cognition in women who initiated hormone therapy between ages 50-54, but those who initiated ages 65-79 had lower global cognition
- **Better Verbal Memory**
 - Advantage in verbal memory mask early AD, so we may need sex-specific test “cut points” to improve early detection in women
 - Results may guide women’s healthcare during and after the menopausal transition and help women make personalized and informed decisions

Special Populations: LGBT Seniors (Fazio et al., AAIC, 2018)

- 2.7 million LGBT people over age 50, with that number doubling over next 15 years
- 200,000 LGBT individuals with dementia in the US, but almost nothing was known about the prevalence of dementia among people without HIV/AIDS dementia
- LGBT community faces similar health concerns as the general public, but LGBT with dementia face uniquely challenges
 - Even with recent advances in LGBT rights, LGBT older adults often marginalized and face discrimination
 - 2X as likely to age without a spouse or partner, 2X as likely to live alone, and 3-4X times less likely to have children –limiting their support
 - 40% of LGBT older people in their 60s and 70s say their healthcare providers don't know their sexual orientation
 - • Pressing health issues for LGBT people:
 - Lower rates of accessing care (up to 30%)
 - Increased rates of depression
 - Higher rates of obesity in the lesbian population
 - Higher rates of alcohol and tobacco use for LGBT persons
 - Higher risk factors of cardiovascular disease for lesbians

Special Populations: Oldest Old (Leung et al., AAIC, 2018)

- Studied 4,100 persons aged 95-110 in 11 countries
- Prevalence increased with age in all countries
- Risk of dementia and cognitive/functional decline varied significantly between countries (i.e., cultural and lifestyle factors play a role in remaining physically and cognitively healthy)
- Persons with higher levels of education had lower prevalence of dementia and cognitive impairment
- Women in this age group had a higher risk of dementia and cognitive impairment

Special Populations: Younger Onset AD (Rhodius-Meester et al., AAIC, 2018)

- Studies of survival times in persons with dementia have varied considerably (3 - 12 years)
- • 4,495 early-onset dementia patients in a memory clinic with any type of dementia, MCI, or subjective cognitive decline
- The median survival time across all groups was **6 years**, but varied by dementia type:
 - • 6.4 years in FTD • 6.2 years in AD • 5.7 years in VAD • 5.1 years LBD
 - • 3.6 years for rarer causes of dementia
- Survival time hardly differed when comparing younger patients (age 65 or younger) to those older than 65 • Despite being younger and perhaps physically 'healthier

Conclusion: Key Points

- Disease likely develops as result of multiple factors
- Symptoms worsen over time; average lifespan 4-8 years (up to 20)
- Risk factors include: age, family history, head trauma, education, lifestyle, cardiovascular conditions
- African-Americans, Hispanics, women more likely to develop
- 3 key public health intervention tools:
 - Surveillance/monitoring
 - Primary prevention (risk reduction)
 - Early detection and diagnosis