IN THE NAME OF GOD

Dr.Leila Poorsaadat

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- symptoms include loss of memory ، judgment and reasoning ، and changes in mood and behaviour.
- ’s functioning at work ، in

.

Results: The overall crude prevalence of dementia among people aged ≥ 60 years was 7.9% (8.7% in women and 6.9% in men) and age standardized dementia prevalence rate in Iran based on WHO standard population was 8.1% (9.6% in women and 6.5% in men). The prevalence of dementia was observed as 3.7% among people aged 60–64 years, 6.2% in the age-group 65–69 years, 10.4% in the age-group 70–74 years, 14.4% in the age-group 75–79 years, and 13.0% in the age-group ≥ 80 years. West Azerbaijan had the lowest and North Khorasan had the highest age-sex adjusted prevalence rate of dementia. Our results indicated that only 21.2% of subjects with dementia were diagnosed. We observed that diabetes mellitus, depressed mood, illiteracy, and increased age were associated with dementia.

Prevalence of Dementia and Associated Factors among Older Adults in Iran: National Elderly Health Survey (NEHS)

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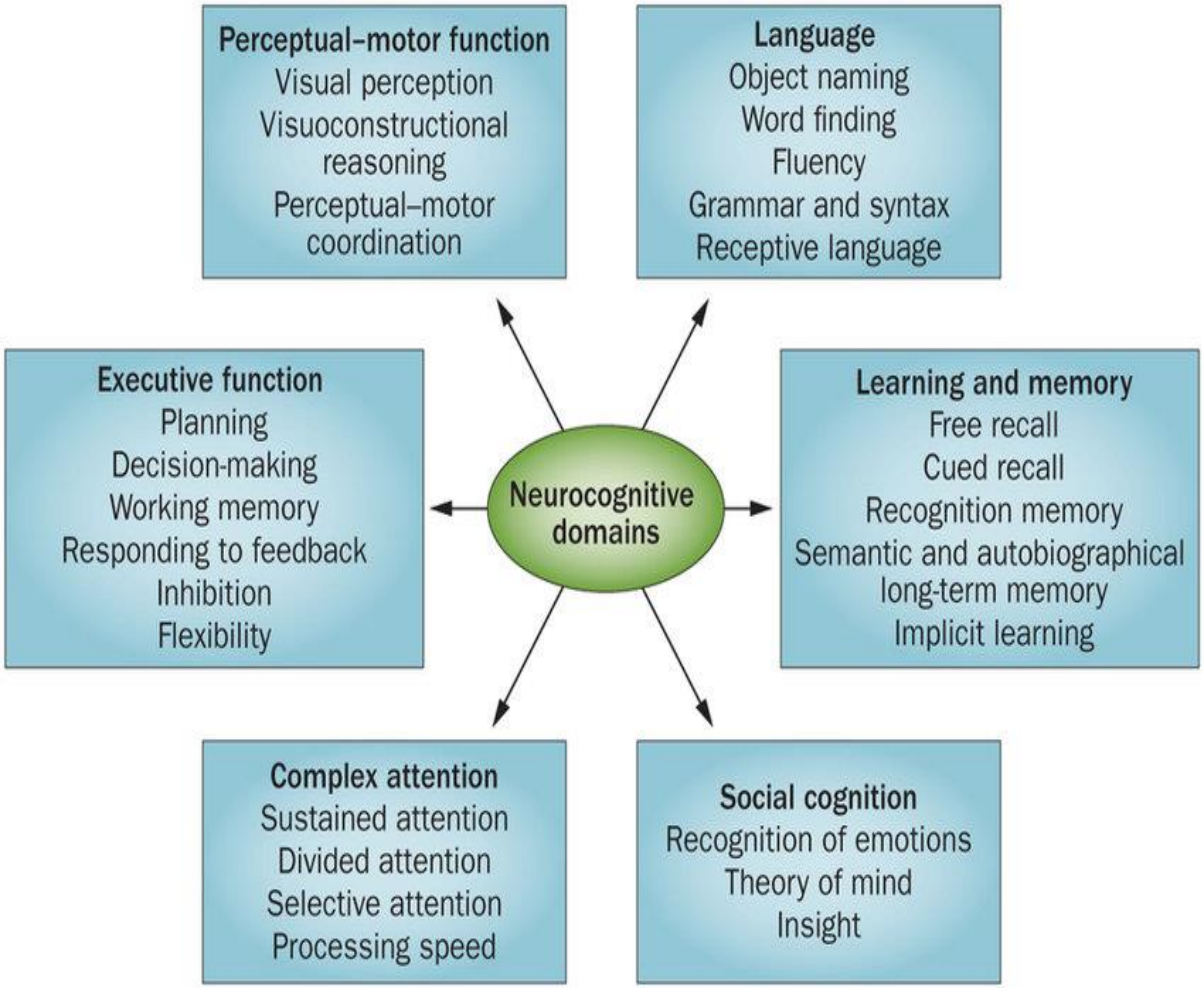
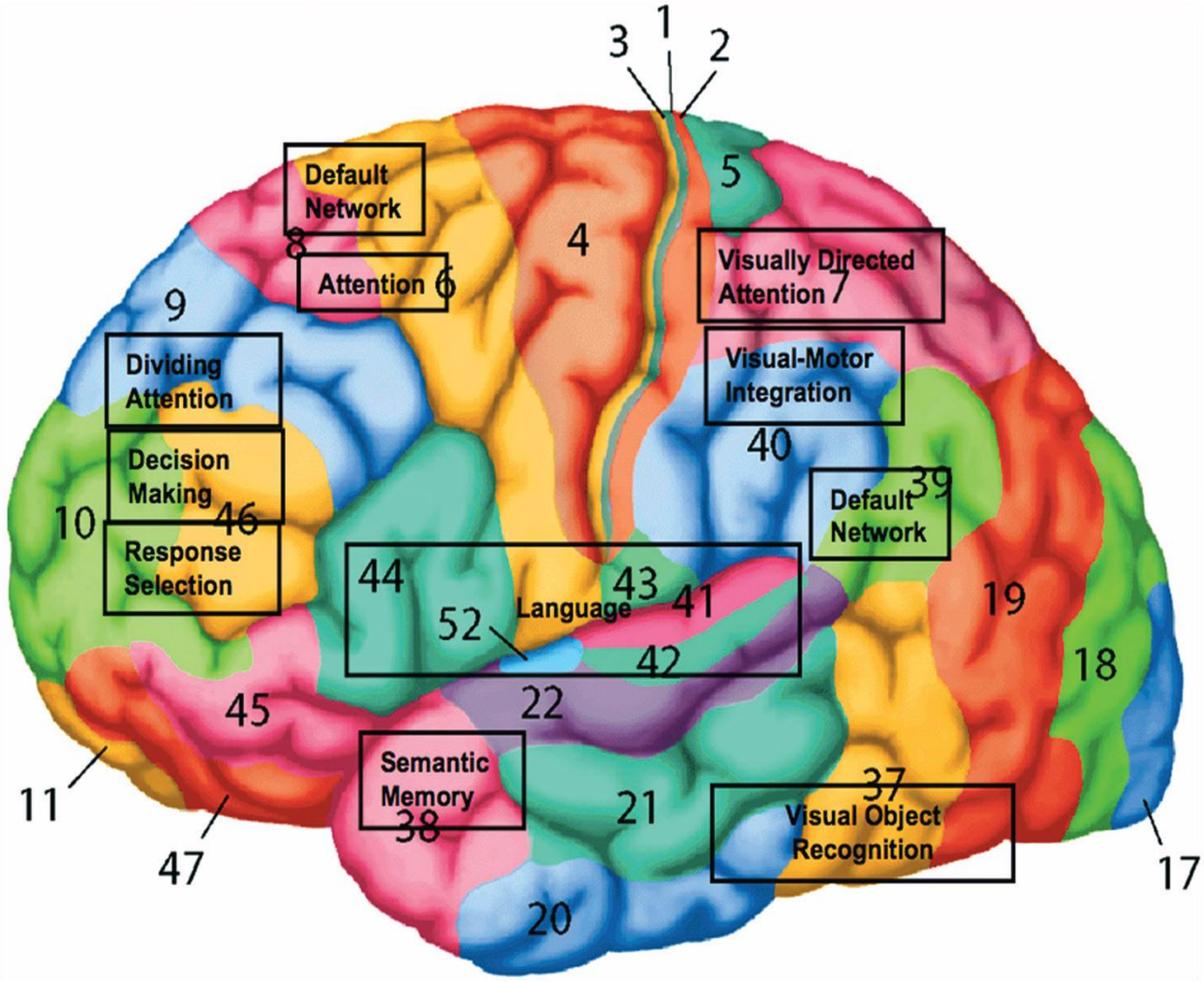

Perceptual–motor function
Visual perception
Visuoconstructional reasoning
Perceptual–motor coordination
Language
Object naming
Word finding
Fluency
Grammar and syntax
Receptive language
Executive function
Planning
Decision-making
Working memory
Responding to feedback
Inhibition
Flexibility
Neurocognitive domains
Learning and memory
Free recall
Cued recall
Recognition memory
Semantic and autobiographical long-term memory
Implicit learning
Complex attention
Sustained attention
Divided attention
Selective attention
Processing speed
Social cognition
Recognition of emotions
Theory of mind
Insight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Default Network
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Attention
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Visually Directed Attention
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Dividing Attention
Visual-Motor Integration
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Decision Making
39
Default Network
10
46
Response Selection
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Language
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Semantic Memory
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37
21
Visual Object Recognition
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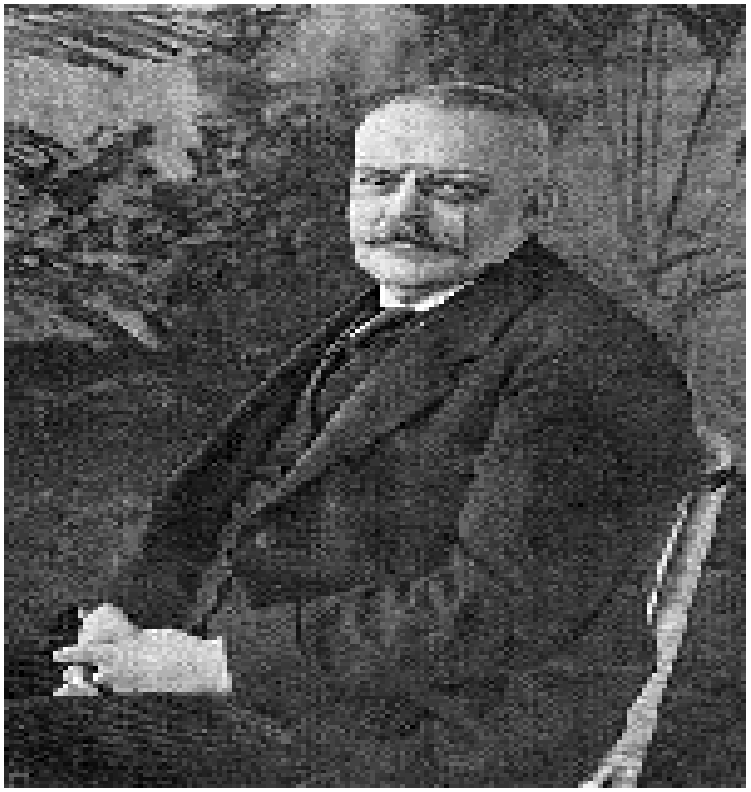
What is Alzheimer Disease?

- Alzheimer Disease is the most common form of dementia.

- gradual onset and continuing decline of memory, changes in judgment or reasoning, and inability to perform familiar tasks.

Who was Alzheimer?



- Alois Alzheimer 1864-1915
- Professor of Psychology in Breslau
- In 1907 described case of a 57 year old and subsequent pathological findings

AD IN IRAN

- The total sample size of the 4 selected studies was 2781. The prevalence of Alzheimer's disease in the current study was estimated to be 2.3% in the population of 67-78 years old. Age, genetics, depression and hy-pertension were determined as the risk factors for Alzheimer's disease, while daily listening to music, meeting weekly with friends and daily intake of vitamin E were considered as the factors with protective role in this dis-ease.

Alzheimer Disease

- no known cause or cure for the disease, but researchers around the world are working to find them.
- Two types:
  - sporadic AD can strike adults at any age, but usually occurs after age 65
  - familial autosomal dominant Alzheimer Disease (FAD), which runs in certain families

Sporadic Alzheimer Disease

- makes up 90 to 95 percent of cases of the disease.
- People with this form may or may not have a family history of the disease.
- Children of someone with Sporadic Alzheimer Disease have a somewhat higher risk of developing AD, when compared to people with no family history of the disease.

Familial Autosomal Dominant Alzheimer Disease (FAD)

- FAD is rare and makes up only 5 to 10 % of all cases of Alzheimer Disease
- FAD is passed from generation to generation due to a dominant inheritance pattern
- If a parent has the mutated gene, each child has a 50 per cent chance of inheriting it

Risk Factors for AD

- Advancing age
- Family history of Alzheimer Disease
- Low education levels
- Head injury
- Down Syndrome
- Environmental factors.

United States: 14% of people 71 years and older have dementia and AD accounts for 70% of them.

Main presentations of AD:

- Cognitive symptoms of AD most comm
- only include deficits in:
- - short-term memory
- - executive function
- - visuospatial function
- - praxis

Neuropsychiatric Symptoms

The earliest: :

apathy,

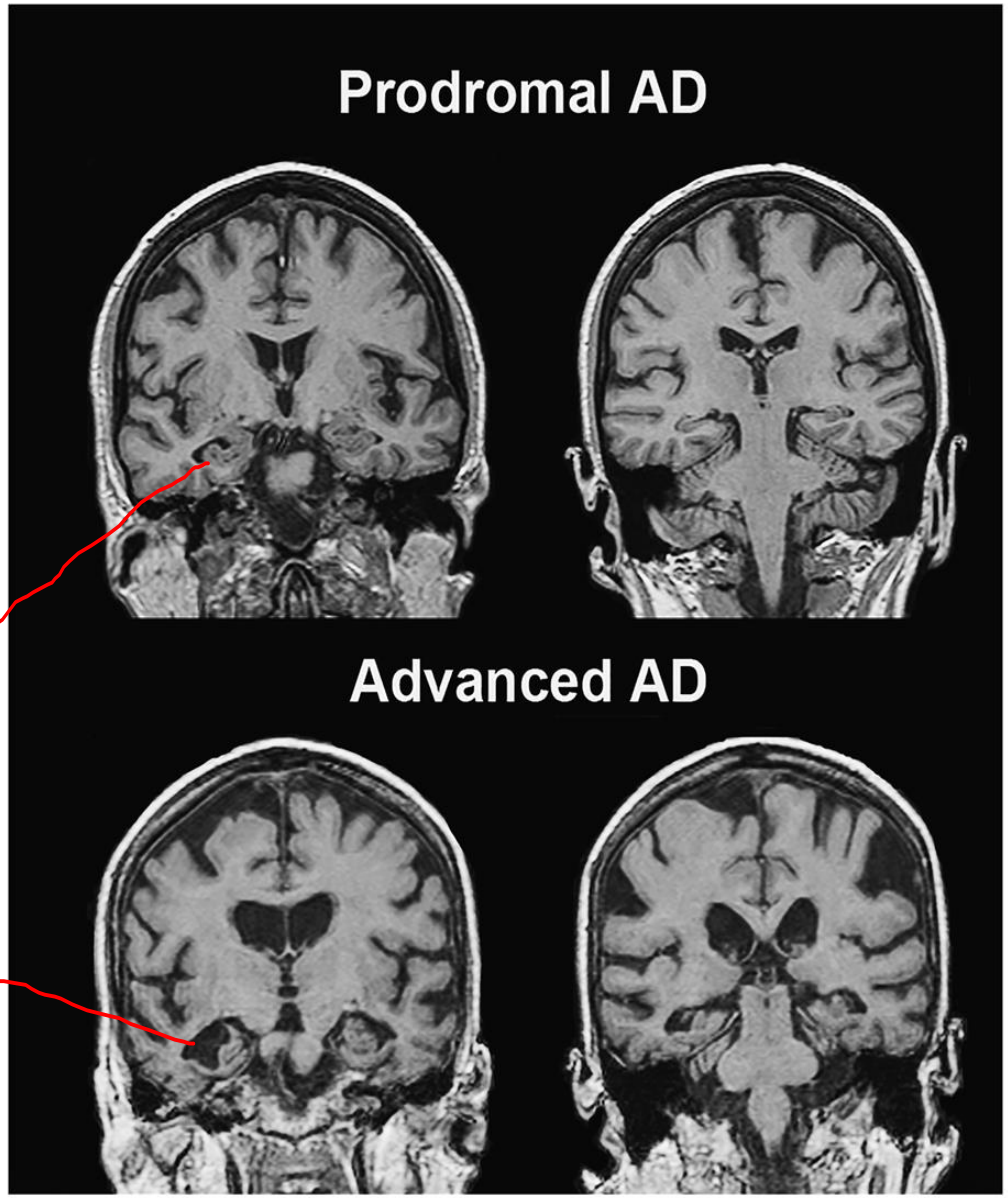
anxiety,

irritability.

Anxiety and irritability:

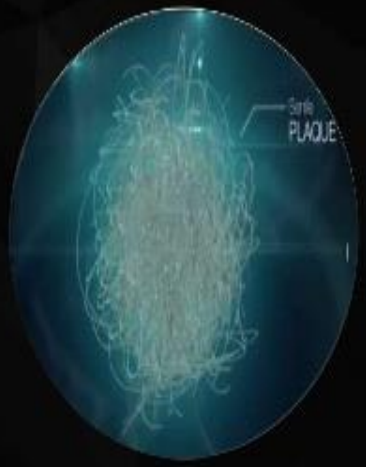
often provoked in situations that the patient finds challenging

Structural imaging: Mesial temporal atrophy



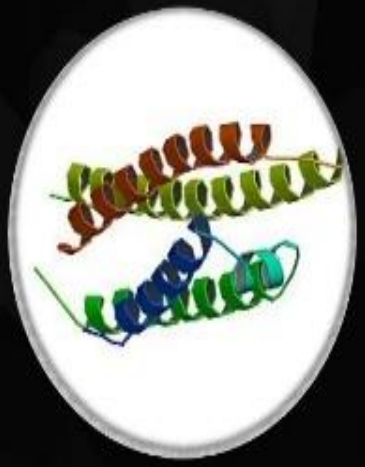
Biochemical Mechanism of AD

Biochemical Mechanism of AD can be studied under the following hypothesis

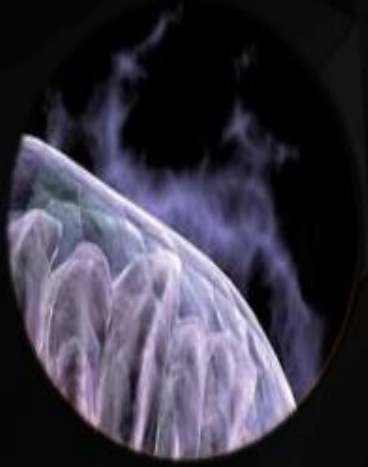


The amyloid cascade

The tau hypothesis



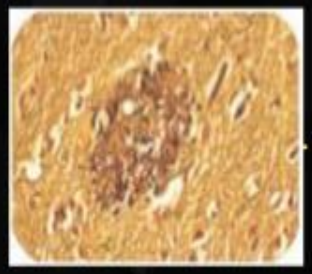
ApoE allel



Oxidative stress

AD AND BRAIN

*The biochemical hallmarks of Alzheimer's are the development of **protein plaques** composed of amyloid beta, and the development of **neurofibrillary tangles** that involve a protein called **tau**.*



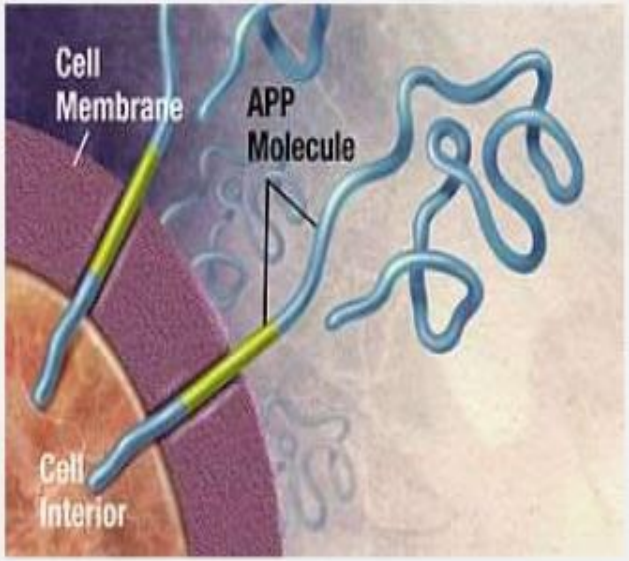
beta-amyloid plaques, which are dense deposits of protein & cellular material that accumulate outside and around nerve cells

- neurofibrillary tangles, which are twisted fibers that build up inside the nerve cell

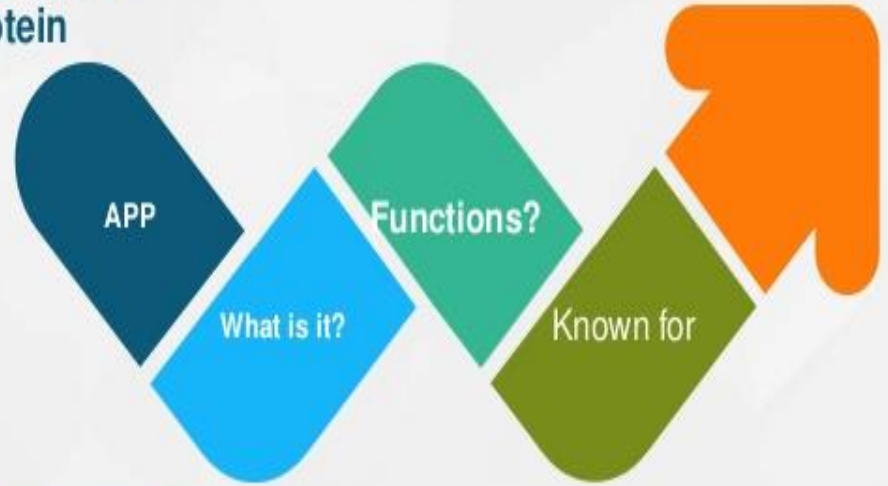
The amyloid cascade

Improper APP Processing

the primary component of amyloid plaques found in the brains of Alzheimer's disease



Amyloid precursor protein

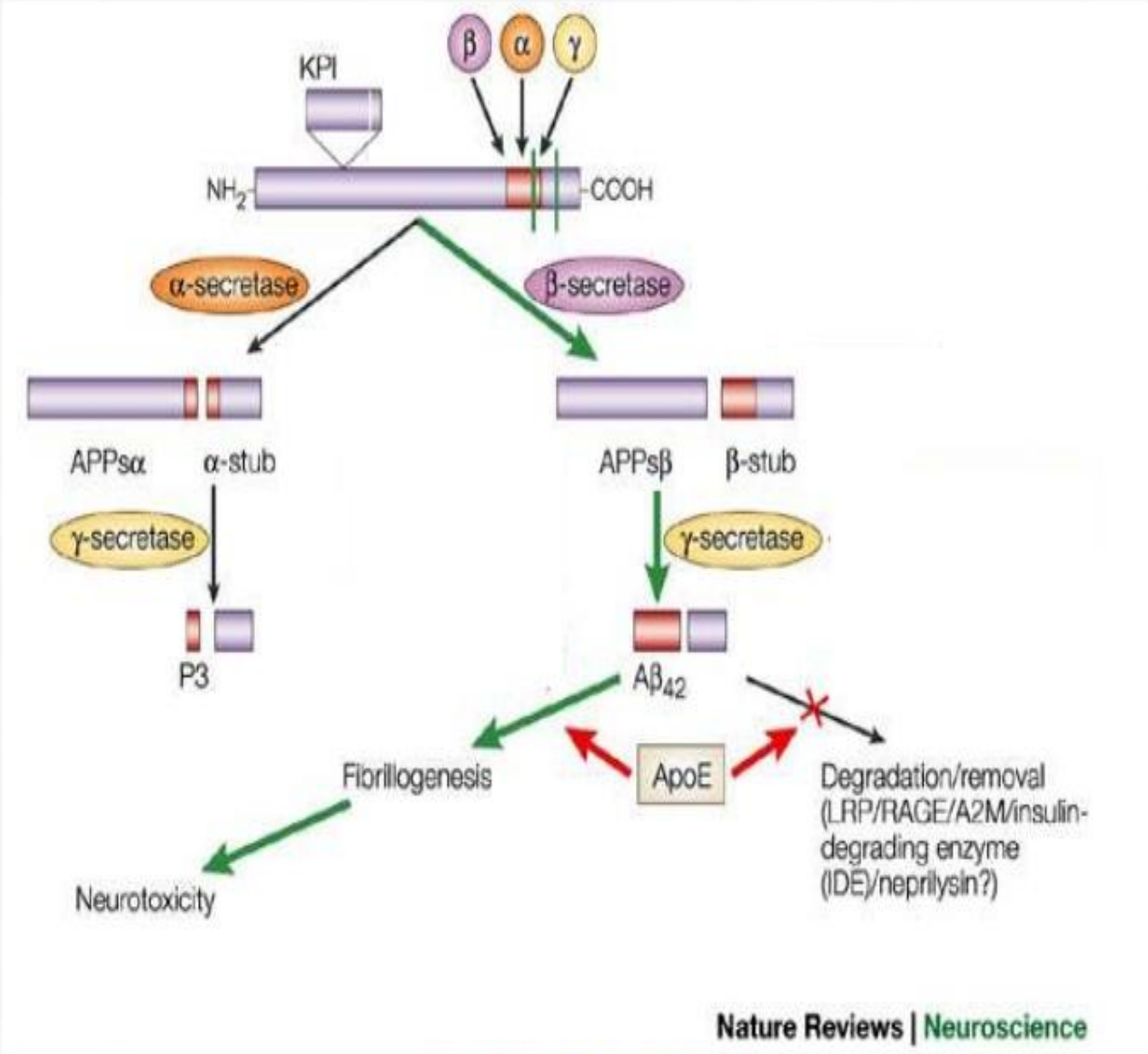


(APP) is an integral membrane protein expressed in many tissues and concentrated in the synapses of neurons.

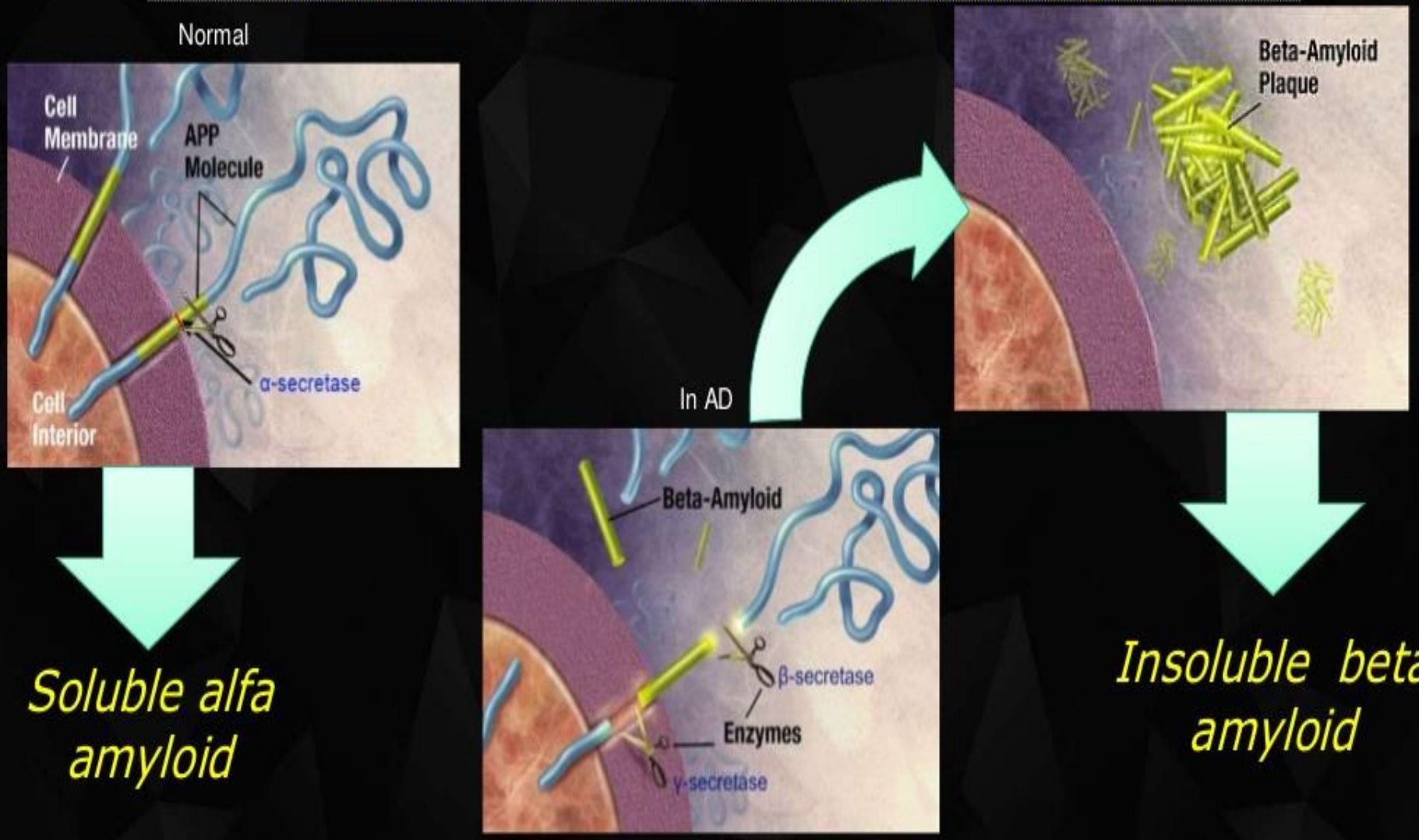
It has been implicated as a regulator of synapse formation, neural plasticity & iron export

APP is best known as the precursor molecule whose proteolysis generates beta amyloid (Aβ)

APP AND Secretases



Formation of beta-Amyloid Plaque



Enzymes act on the APP (amyloid precursor protein) and cut it into fragments. The beta-amyloid fragment is crucial in the formation of senile plaques in AD.

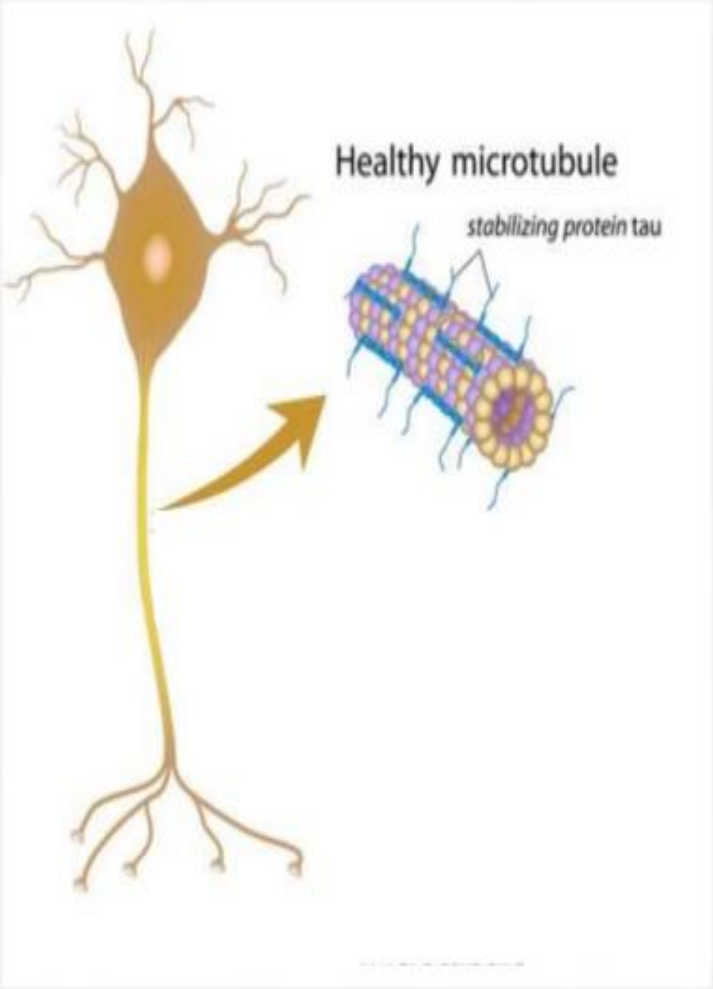
Formation of beta-Amyloid Plaque

The tau hypothesis

Formation of neurofibrillary tangles (Nfts)

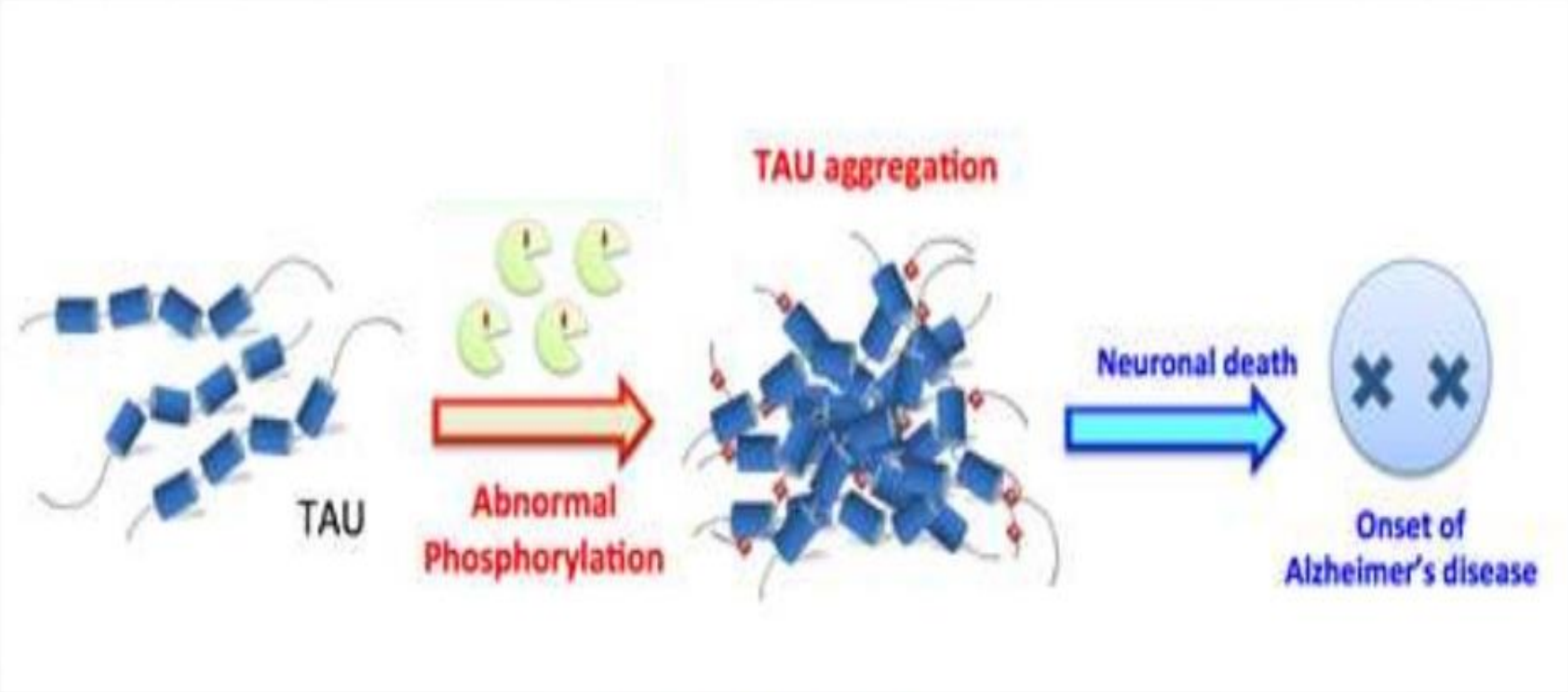
- AD is also considered a **tauopathy** due to **abnormal aggregation of the tau protein.**

- A protein called tau stabilizes the microtubules when phosphorylated, and is therefore called a **microtubule-associated protein.**

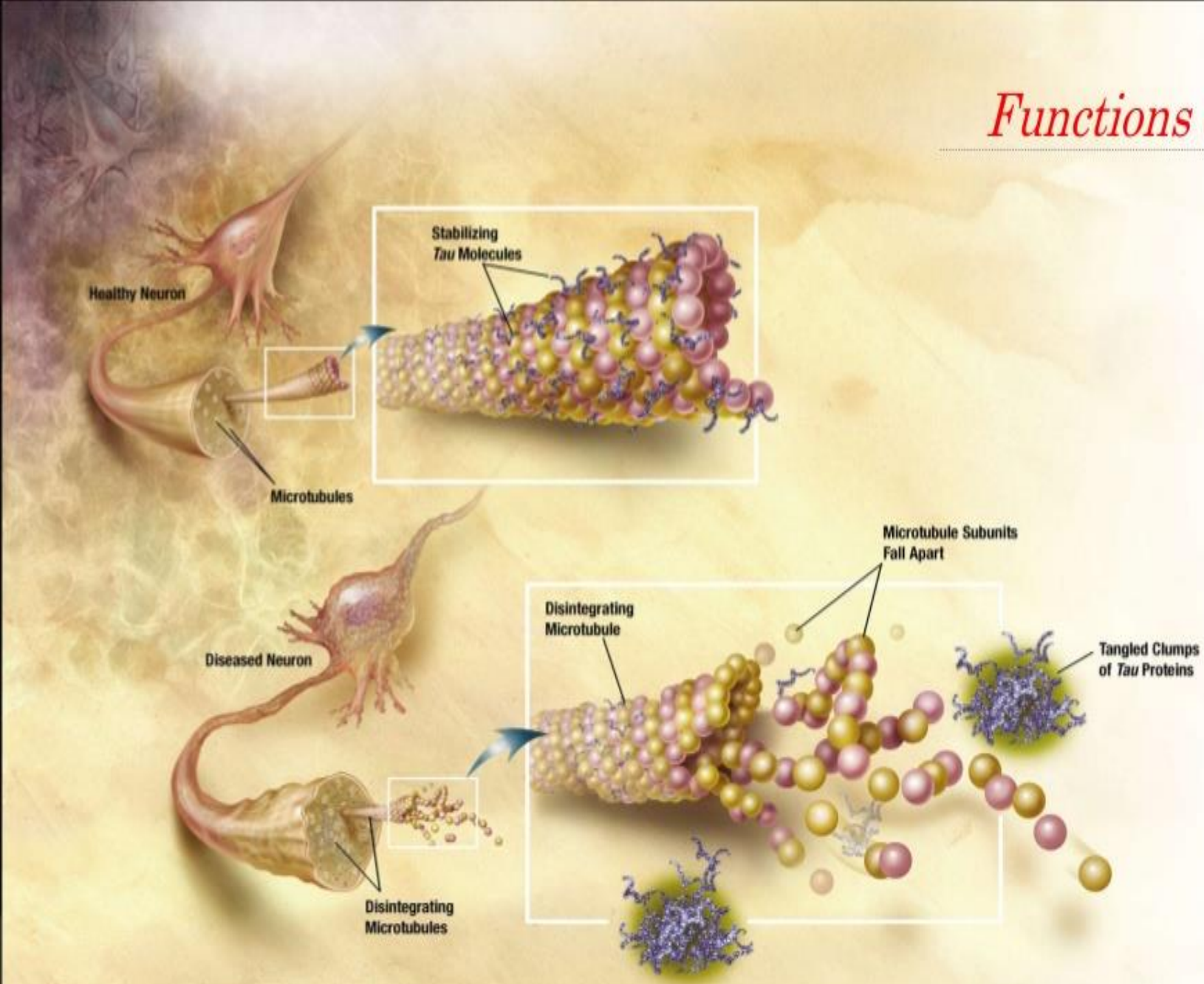


Breakdown of Cellular Structure

- In AD, tau undergoes chemical changes, becoming hyperphosphorylated; it then begins to pair with other threads, **creating neurofibrillary tangles (NFTs)** and disintegrating the neuron's transport system.



Functions of tau



Formation of neurofibrillary tangles (Nfts)

Effects of Beta amyloid plaque & NFTs

- The formation of NFTs within a cell, and beta-Amyloid Plaque outside the cell, can affect neighboring cells and lead to more cell death.
- Without medication to slow the progression of Alzheimer's the cycle will continue and lead to massive cell death within the brain.

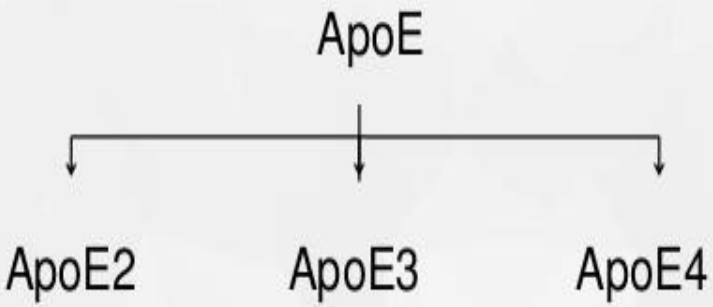
AD

- Though most people develop some plaques and tangles as they age, those with Alzheimer's tend to develop far more. They also tend to develop them in a predictable pattern, beginning in areas important for memory before spreading to other regions.

- It's the destruction and death of nerve cells that causes memory failure, personality changes, problems carrying out daily activities and other symptoms of Alzheimer's disease.

ApoE allele & AD

- ApoE is an arginine-rich protein.
- Present in chylomicrons, LDL & VLDL. Astrocytes also make apo-E;
- It is involved in cellular transport of lipids in CNS.
- Gene for Apolipoprotein E → on 19th chromosome.
- In humans, there are three alleles of this gene encoding Apolipoprotein E.



- People with ApoE4 allele show larger content of Amyloid β in their brain.

Oxidative stress

- Oxidative stress in the brain is likely to occur as the brain uses up to 20% of the body's inspired oxygen. The brain also houses large concentrations of poly unsaturated fatty acids, which may undergo lipid peroxidation.

- Deposition of amorphous proteins like beta amyloid & tau proteins acts as free radicals and increase further damage.

THANK YOU