ALZEHIMER

[DEPTH OF BIOLOGY]

Neurodegenerative disease {degeneracy or loss of neuron in the brain particularly in the cortex}.

[DEPTH OF BIOLOGY]

Most common cause of dementia

Difficulty in learning new information

DEMENTIA- caused by damage in brain cells, technically a disease

Poor memory

CAUSES OF ALZEHIMER- not completely understood.

2 MAJOR REASONS

1.PLAQUES

2.TANGLES

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- A molecule called **AMYLOID PRECURSOR PROTEIN [APP]** is present in the cell membrane of neuron of brain
- **APP** is a protein like any other protein which gets used, broken down & recycled. [DEPTH OF BIOLOGY]
- It helps to grow & repair neuron itself after injury
- Normally it is chopped up by an enzyme called ALPHA SECRETASE & it`s buddy gamma-secretase
- This chopped up peptide is soluble & goes away.

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- Everything is all good.

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- But if another enzyme beta-secretase teams up with gamma-secretase then we get problem & now this left over fragment is not soluble & create a monomer called AMYLOID BETA.
- This monomer are chemically sticky & bound together just outside the neurons & form beta amyloid plaques

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- This plaques can potentially get b/w the neurons which can get in the way of neuron to neuron signalling.

[DEPTH OF BIOLOGY]

- If brain cells can`t relay & signal information.

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- The brain function like memory can be seriously impaired & this plaques can start immune response, may also cause inflammation which might damage surrounding neuron.

- Amyloid plaque can also deposit around blood vessels in the brain called AMYLOID ANGIOPATHY.
- It leads to weakens the wall of blood vessels & increase the risk of haemorrhage or rupture & blood loss.

TANGLES- another big part of Alzheimer disease found inside the cells as opposed by beta amyloid plaque.

- Just like other cell neurons are held together by their cytoskeleton which is partly made up of microtubules.
- [this are tract like] ⟹ shiftage of protein.

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- A special protein called as **TAU**- makes sure this track don't break apart.
- NOW,

Beta-amyloid plaque- initiate pathway inside the neuron

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- That head to activation of ***kinase enzyme***

- That transfer phosphate group to **TAU PROTEIN.**

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- Now, tau protein change it`s shape & stops supporting to micotubule & clumps up without tau protein.

- Forms other characteristics of alzhemier disease called neuron fibrillary tangles

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- Now, neurons with tangles & non- functioning microtubule can`t signal as well

- Sometime`s undergoing a poptosis or progressive cell death.

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- As neuron dies

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Large scale changes (in brain)

Brain atrophies or shrinks	Gyri get narrower

- As gyri gets narrower the sulci [grooves b/w gyri] get wider
- With atropy, ventricle fluid filled cavities in the brain

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CAUSES

- **Sporadic [90-95%]**
- Late onset.
- Combination of gene & environmental risk factor.
- **Here risk increase significantly with age**
- Age affect: 60-65 (1%)
- 50 % of people over 85years.

- Gene which cause

E gene ***APOE-e4***

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- **Familial [5-10%]**
- **Because** some dominant gene inherited.

It speed up the progression of disease
Early onset

- Caused by several gene mutation

- 1st mutation PSEN-I or PSEN-2

Chromosome- 14 1

- Linked to early onset Alzheimer

- This gene encodes for presenillin 1 or 2 both are protein subunit of gamma secretase

- Mutation in this gene can cause change in location where gamma secretase chops APP

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- & producing different length beta amyloid molecules; lead to forming plaque

- Another cause is trisomy 21 or down syndrome
- Involves extra copy of chromosome 21

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- & gene responsible for producing APP is located on chromosome 21; means people with down synd. Has extra APP gene that increase expression of APP.

Can possibly increase amt of amyloid plaque

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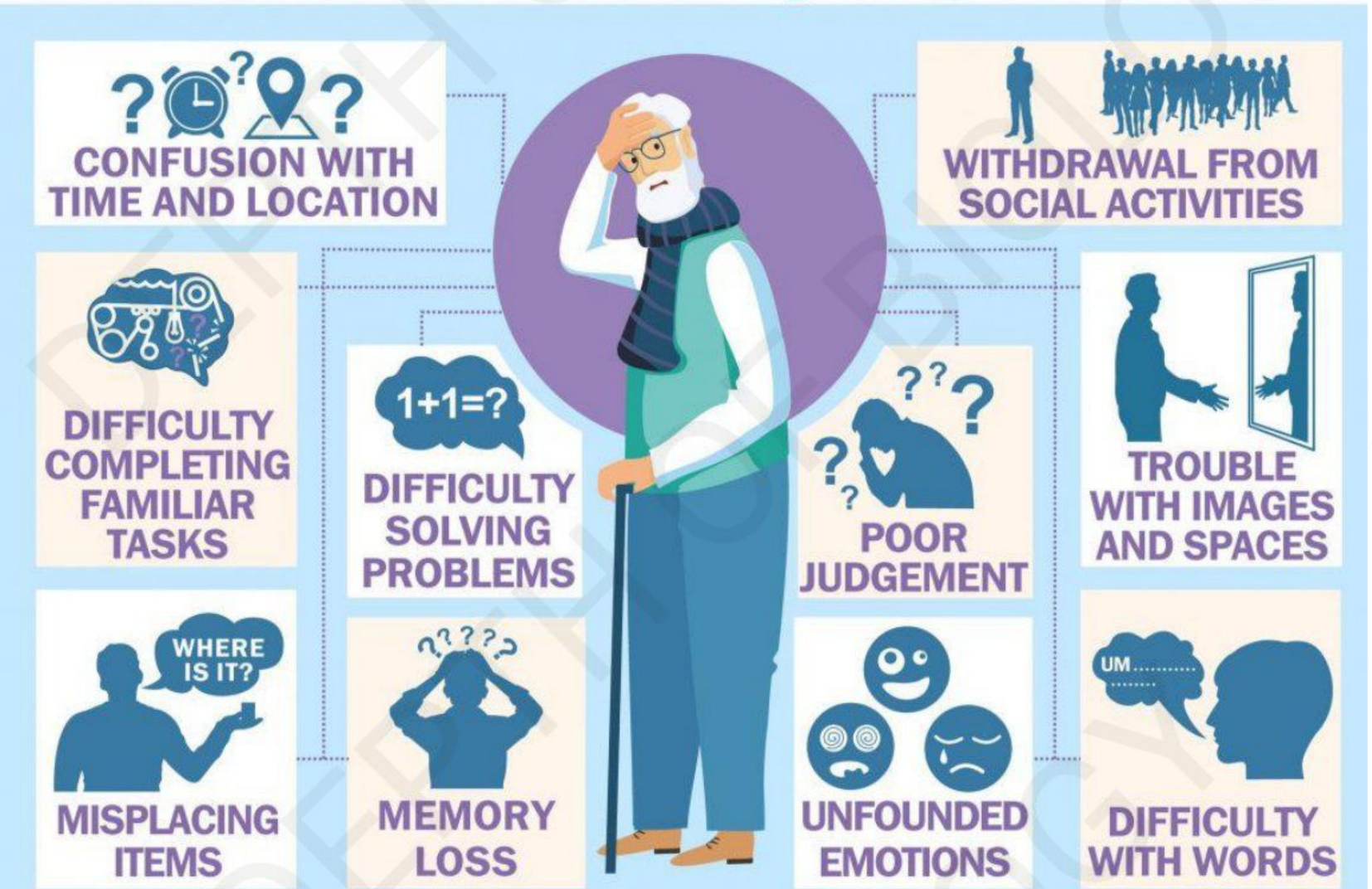
SYMPTOMS



1. Plaques & tangles build up
2. Neuronal damage accumulates

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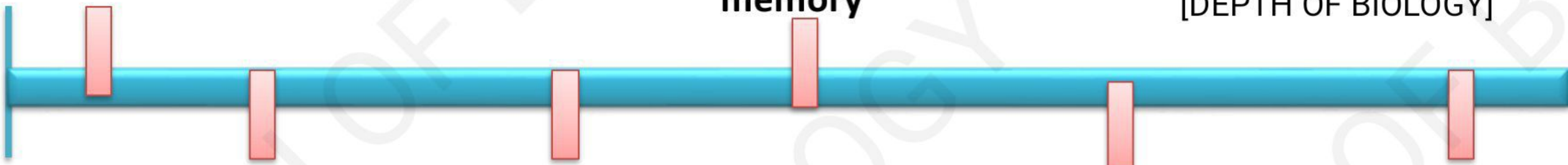
early stage-

Undetectable symptoms



At progression – Patient loses short term memory

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Progression continue-

Loss of motor skill & language also affected

DIAGNOSIS – difficult ; brain biopsy [after autopsy]

- Exclude other causes of dementia

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TREATMENT

- no cure [DEPTH OF BIOLOGY]
- Some medications exist but very small benefit