

Aging and Alzheimer 's disease

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Part 1



Espérance de vie

2006	Femmes	Hommes
France	86 ans	79 ans
Japon	88 ans	81 ans

- Education
- Alimentation
- Surveillance médicale....

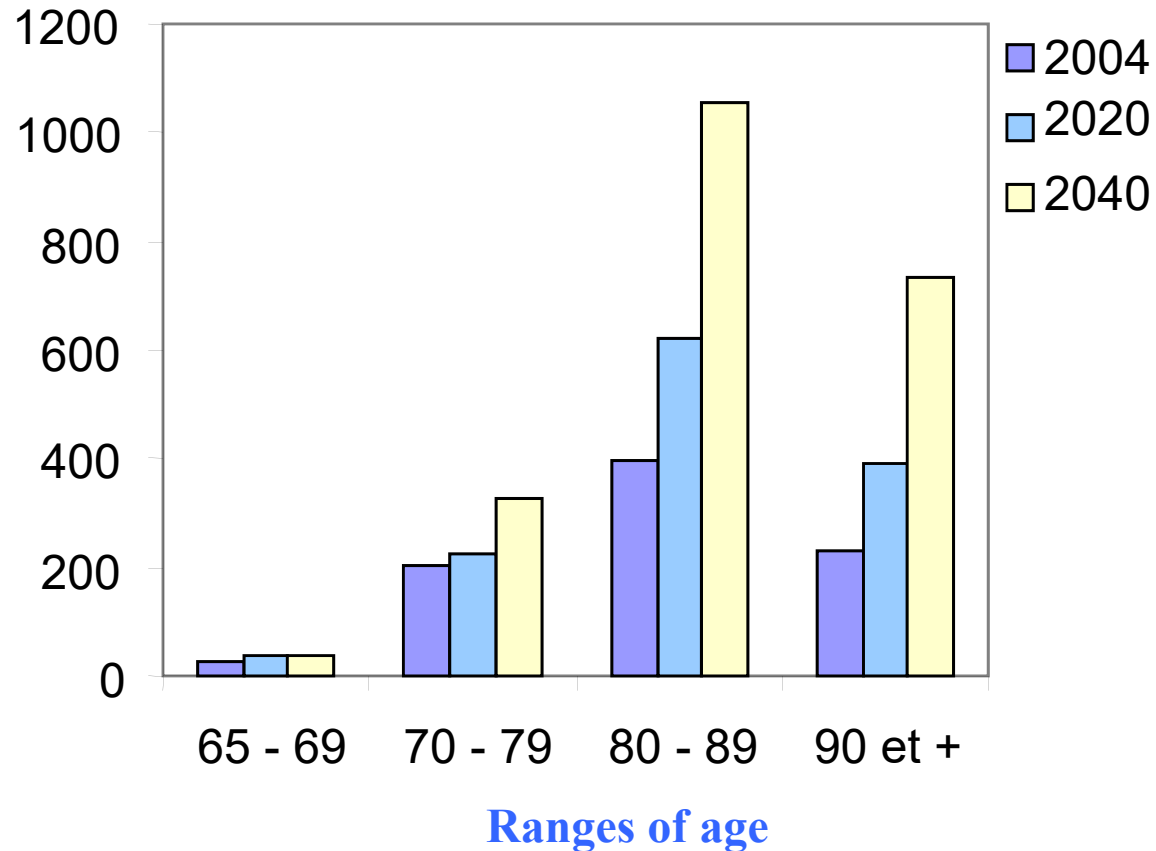
Augmentation du nombre de personnes atteints de pathologies associées à l'âge => 900 000 personnes atteintes de MA en France.

2008 : 860 000 Cas diagnostiqués => 2020 : 900 000 cas diagnostiqués

Age: the major risk of the AD

Estimation of the evolution of the number of people affected by AD in France

People number (10^3)



200 000 new cases/year

A neurodegenerative disease: Alzheimer's disease



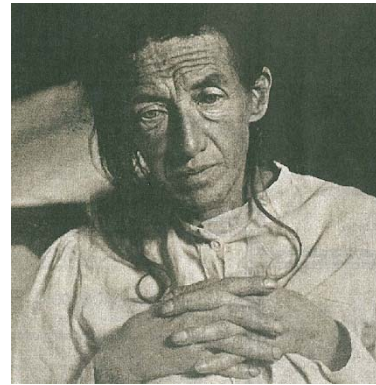
" La mémoire" René MAGRITTE 1936

Loss of memory
&
Spatial disorientation
&
Language disorders

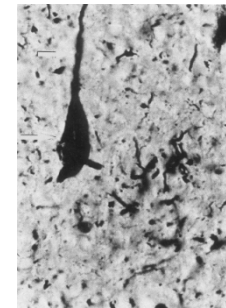
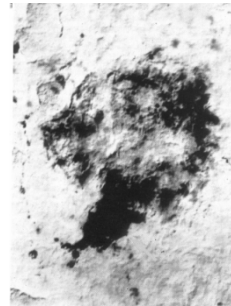


Behavioral modifications

Hallmarks of Alzheimer's disease



Alois Alzheimer (1906)
Psychiatric-neuropathologist
(1864-1915)

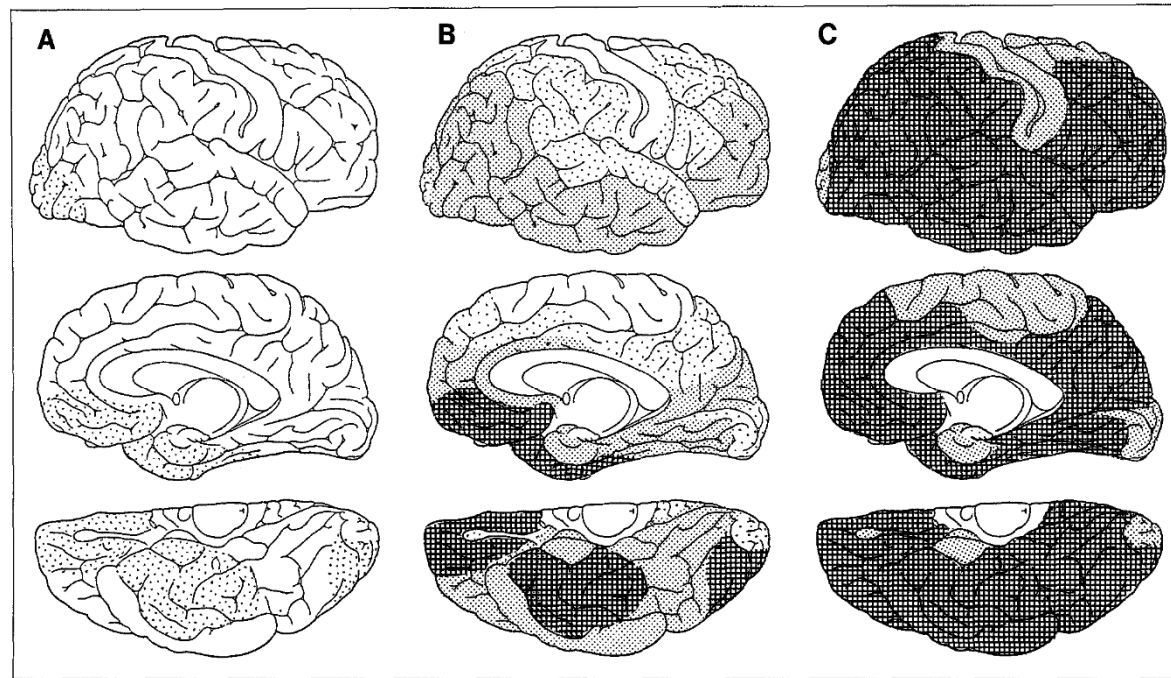


Senile plaques

Neurofibrillary tangles

Lesions of the neurodegenerescence observed in the cortex of the patient
in post-mortem autopsy

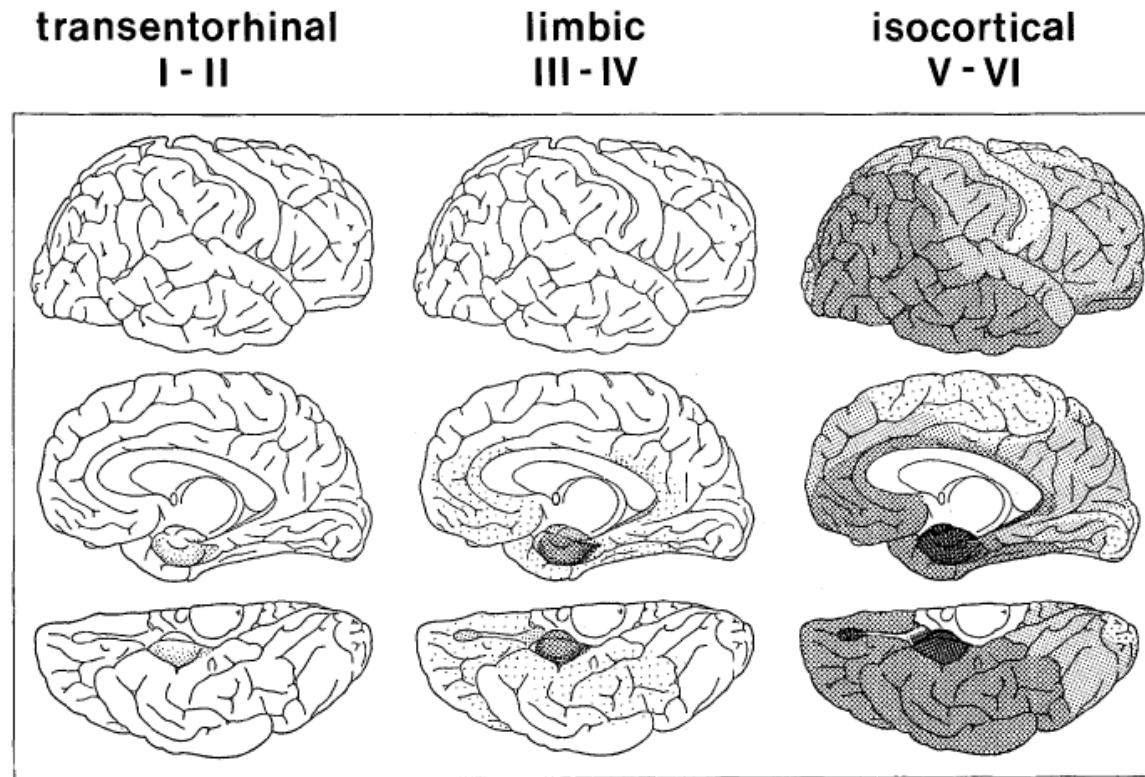
The evolution of amyloid plaques



Amyloid

Braak et al., 1991

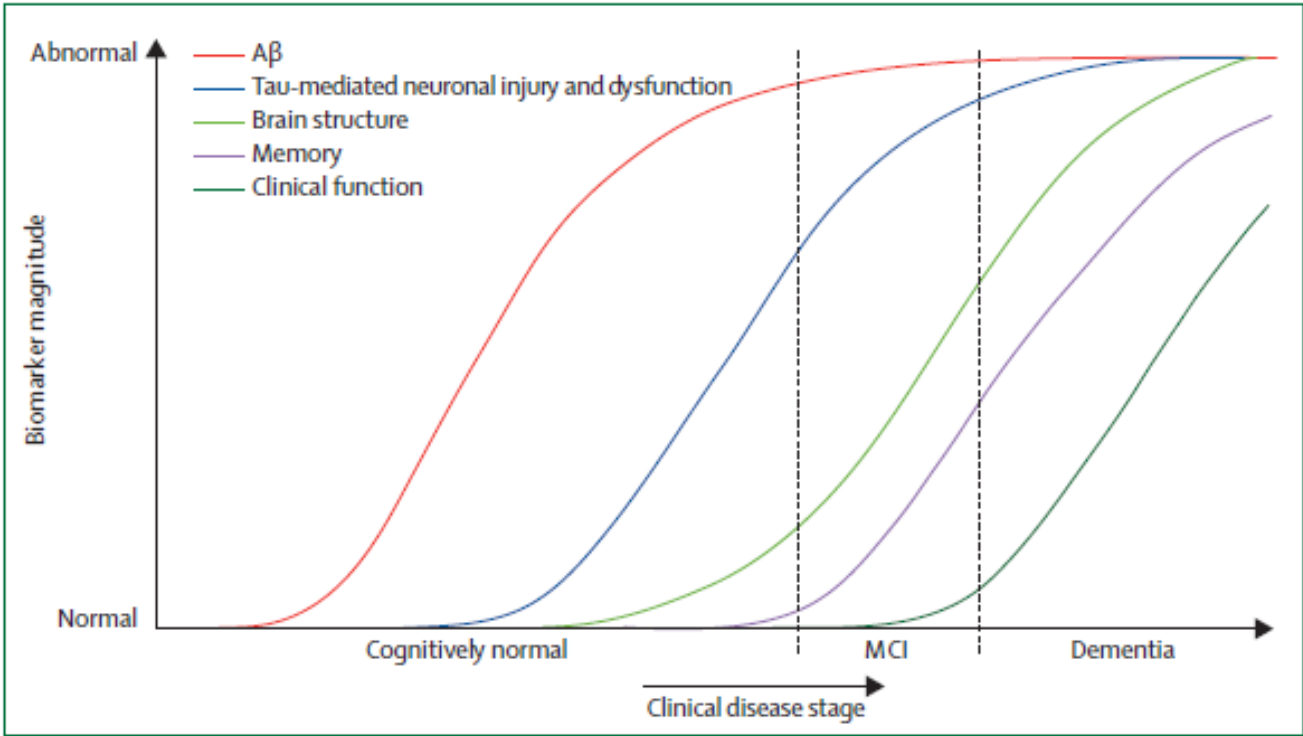
The evolution of neurofibrillary tangles



Neurofibrillary changes

Braak et al., 1991

Evolution of Alzheimer's disease over the time



Jack et al., 2013

The different stages of the Alzheimer's disease

-
 - Preclinical early stage (prodromal stage)
 - Moderate stage
 - late stage, dementia

- Genetic inheritance

Familial mutations of APP, PSEN1 and PSEN2

- Susceptibility genes, APOE4

- Late onset sporadic AD with complex and unknown origin

Detection of the pathologie

Early screening

Mild Cognitive impairment (MCI)

- Memory tests

 - Mini Mental Score Examination

- Cerebral MRI

 - Control of the cerebral cortex and hippocampus atrophy

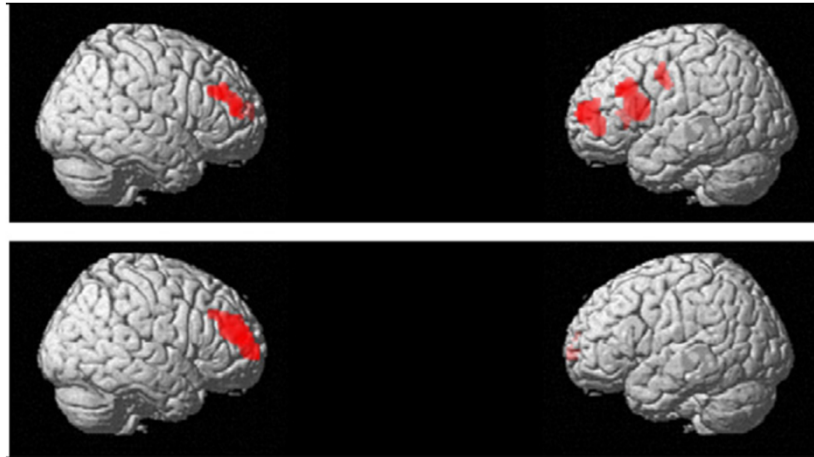
 - Detection of plaques by the Pittsburg compound-B (PIB)

- Detection by markers in the CSF and in blood

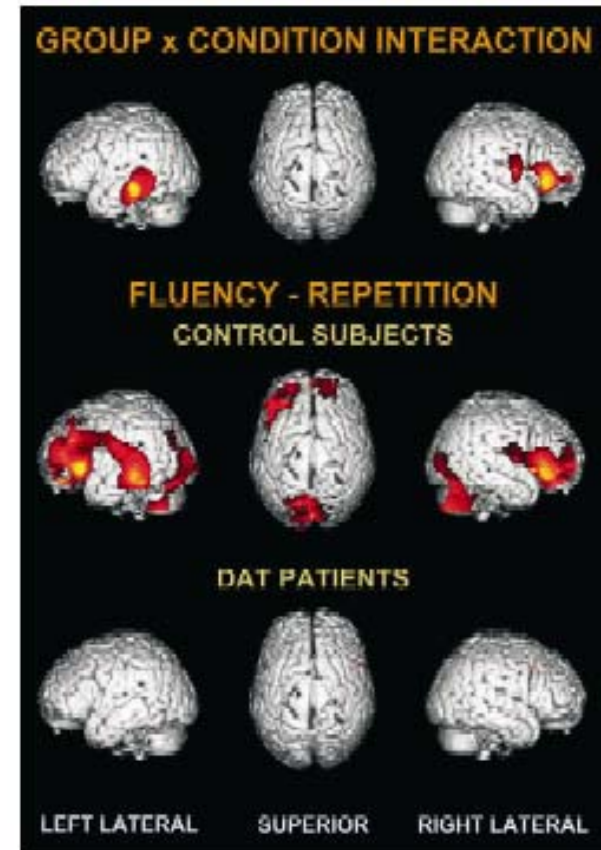
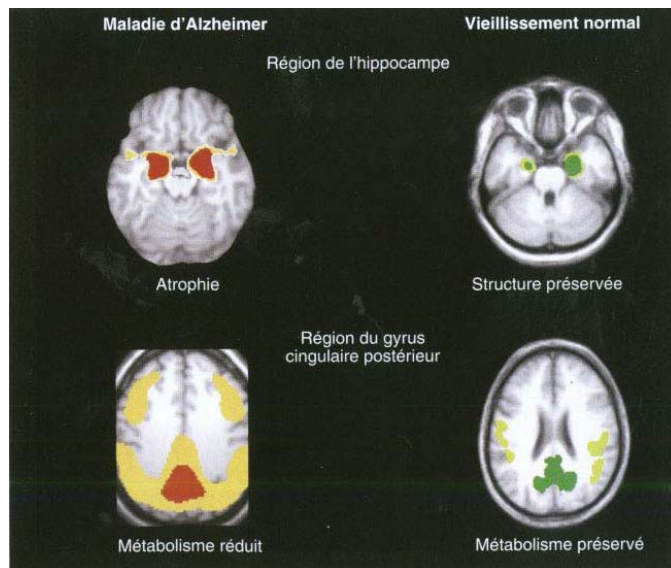
 - Amyloid peptides

 - Tau protein hyperphosphorylated

MRI and AD: atrophy in the frontal cortex and in the hippocampus

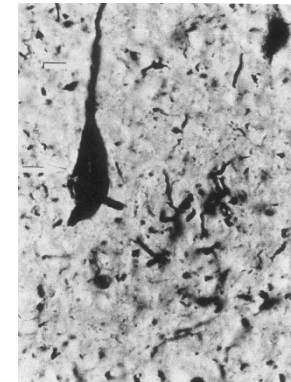
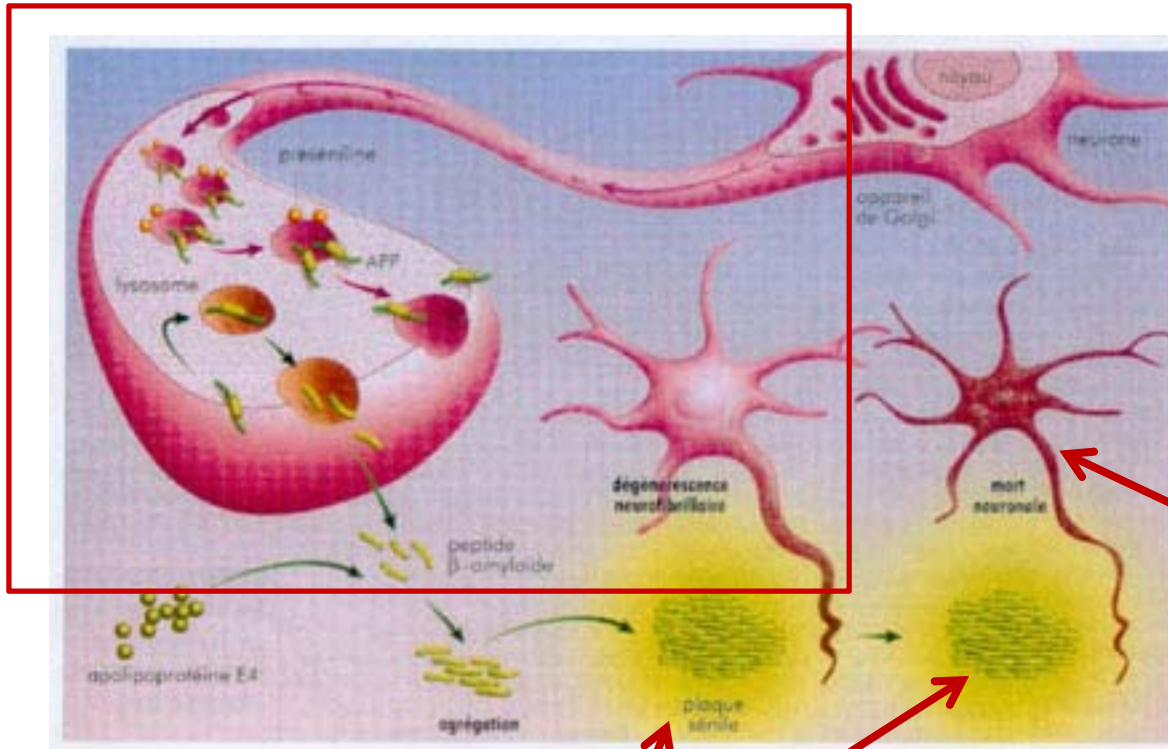


Bernard et al., Neurobiol. Aging, 2007

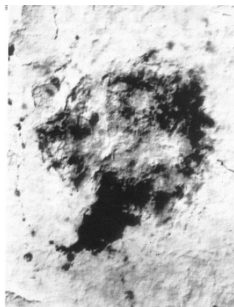


Slosman et al., Brain Res Rev, 2001

Cellular events

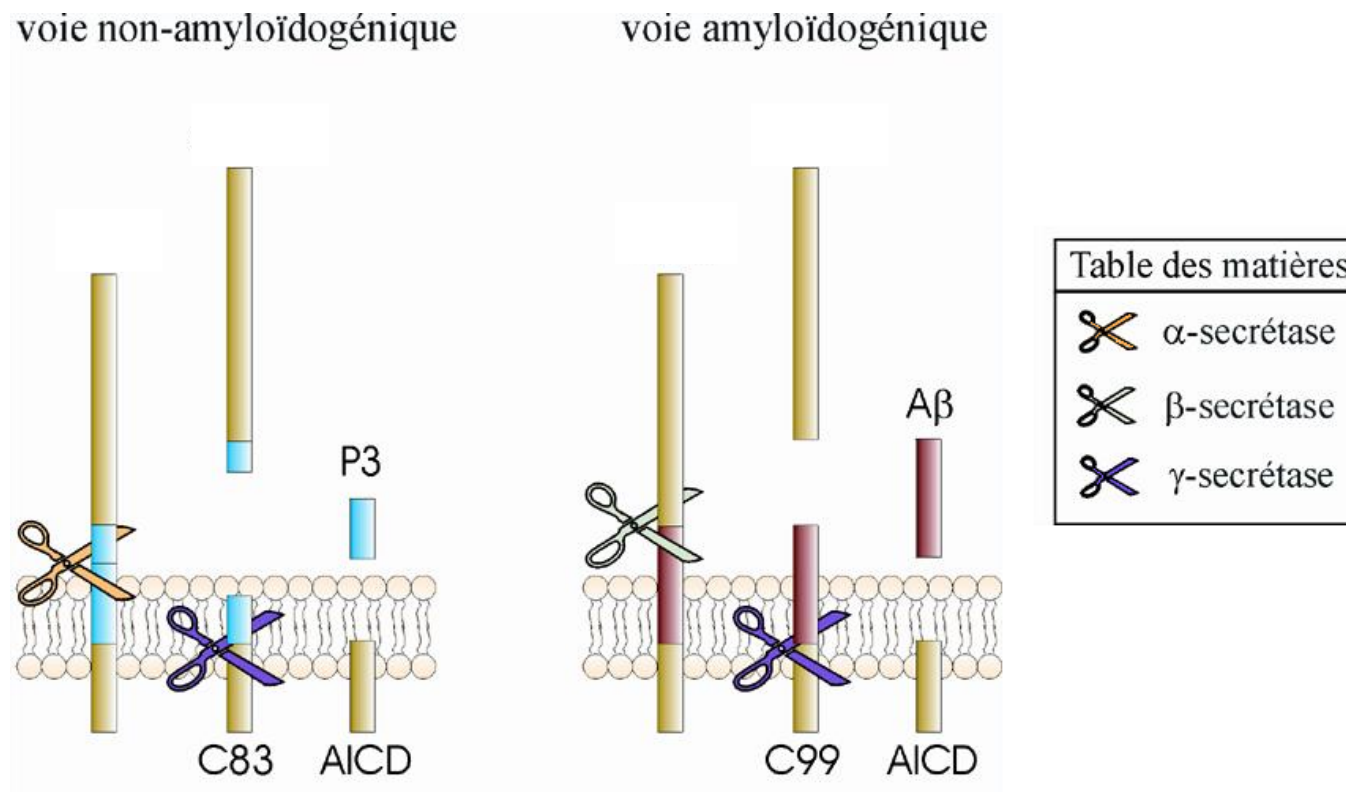


Neurofibrillary tangles



Amyloid plaques

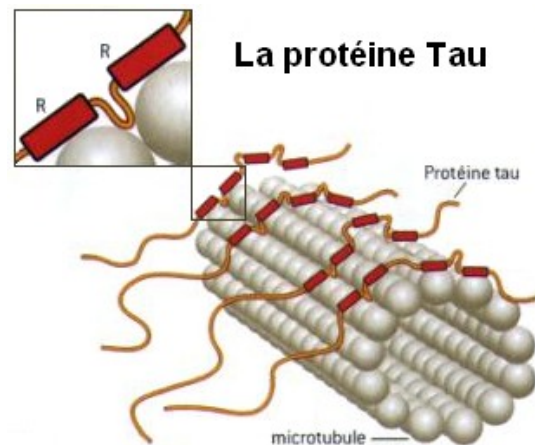
β -amyloïde peptide synthesis



The A β peptide is synthesized from APP a membrane protein.

Tau protein hyperphosphorylated

La protéine Tau hyperphosphorylée forme des agrégats qui induisent des dégénérescences neurofibrillaires .



- Atteinte du cytosquelette
- Altération du transport axonique
- Désintégration cellulaire

Les gènes de susceptibilité

Le site Alzheimer Research Forum,
repertorie les gènes impliqués dans la MA,
Site: www.alzgene.org

APO ϵ 4

CLU (APOJ),

CR1,

PICALM...

Bertram & Tanzi Genome wide association studies in Alzheimer's disease. Human Mol Genetics, 2009.

Lambert et al. Genome-wide association study identifies variants at CLU and CR1 associated with Alzheimer's disease. Nature Genetics, 2009.

Harold et al. Genome-wide association study identifies variants at CLU and PICALM associated with Alzheimer's disease. Nature Genetics, 2009.

GWA studies: analyse d'épidémiologie génétique par association des identifications génétiques avec des traits particuliers après séquençage à haut débit du génome et analyse informatique.

Risks of AD development

First factor: age

5% of parental inheritance

95% sporadic cases

Genes mainly implicated:

APP chromosome 21

PSEN1 chromosome 14

PSEN2 chromosome 1

TAU chromosome 17

(MAPT)

APOE ϵ 4 chromosome 19

Genes of susceptibility

CLU (APOJ)

CR1 & PICALM (2009)

Plus d'une 100 gènes répertoriés (Alzgene forum)

Drugs

Anti-cholinesterase activity:

- Tacrine (Cognex)

First drug used but removed for its liver toxicity

- Donezepil (Aricept)
- Rivastigmine (Exelon)
- Galantamine (Reminyl) (+ agoniste nicotinique)

Antagonist of NMDA receptor:

- Memantine (Ebixa)

Aging and ethics

Ethic dilemma: Predictive medicine,
Prediction of an AD at 20, 30, 40, 50 years for a precece diagnosis

Changes in brain functions

Loss of neurons
and glial cells



Memory loss
Spatial and temporal
disorientation

Loss of cognitive functions

Preserved functions



Senses
Emotion
Motricity

Desorientation
Loss of landmarks



Insecurity

Behavior changes

IX- Parcours de soins

Stabiliser

Médicaments

Accompagner

Le malade

La famille, l'aidant principal

L'équipe médicale

Mobiliser les capacités préservées

Les capacités sensorielles

L'ajustement émotionnel

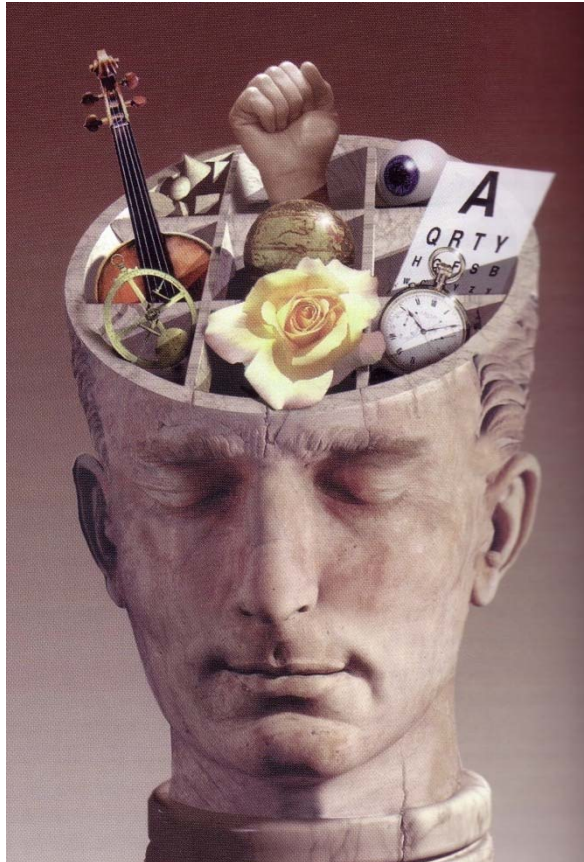
Améliorer la communication

Le mot, la voix,

le geste, le visage,

le corps

Mobiliser toutes les capacités cérébrales possibles



Autre espace-temps

Apaiser, reconforter

Encourager, renforcer

Ne pas s'acharner

Respecter