

Intro to Cognitive Neuroscience

Alzheimer's disease

Dementia

- A family of diseases that are characterized by cognitive and behavioral deficits involving some sort of permanent damage to the brain.

- Dementias affect ~4 million people in the U.S. (6% - 8% of people over age 65)

Alzheimer's disease

- First described in 1907 by Alois Alzheimer as “a strange disease of the cerebral cortex”.
- Accounts for 50% - 70% of all dementias.

AD diagnostic criteria

- Multiple cognitive deficits, including
 - Memory impairment
 - At least one of: aphasia, apraxia, agnosia, or disturbance in executive function.

AD diagnostic criteria

- Significant impairment in functioning, involving a decline from previous level.

- Gradual onset and continuing cognitive decline.

AD diagnostic criteria

- Requires neurological evidence (from autopsy) for a definitive diagnosis

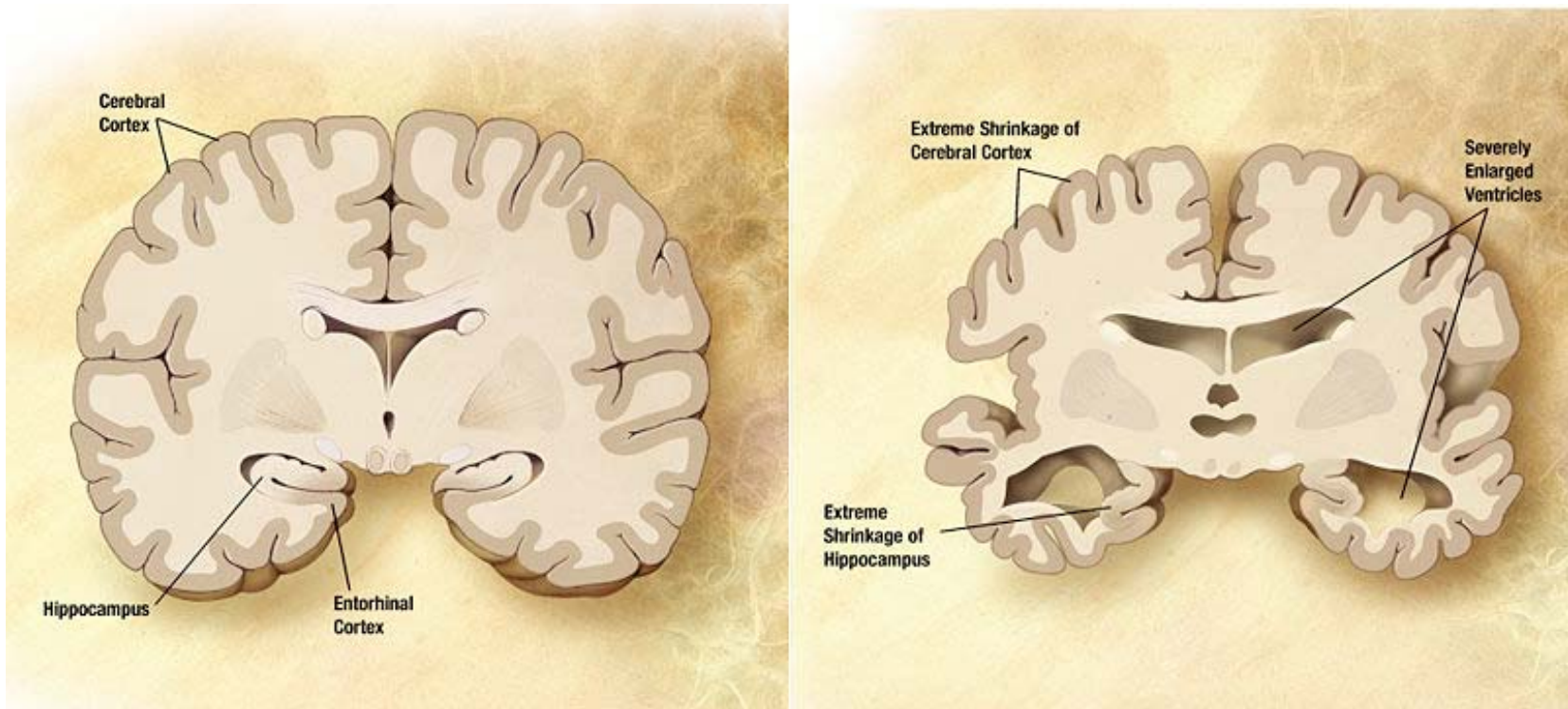


Image courtesy of the National Institute on Aging

- Normal vs. AD brain - some macro scale differences

Neurological changes

- Two characteristic changes at the cellular level:
- Senile plaques - made up of small (35 - 40 amino acids) peptide fragments called amyloid-beta.

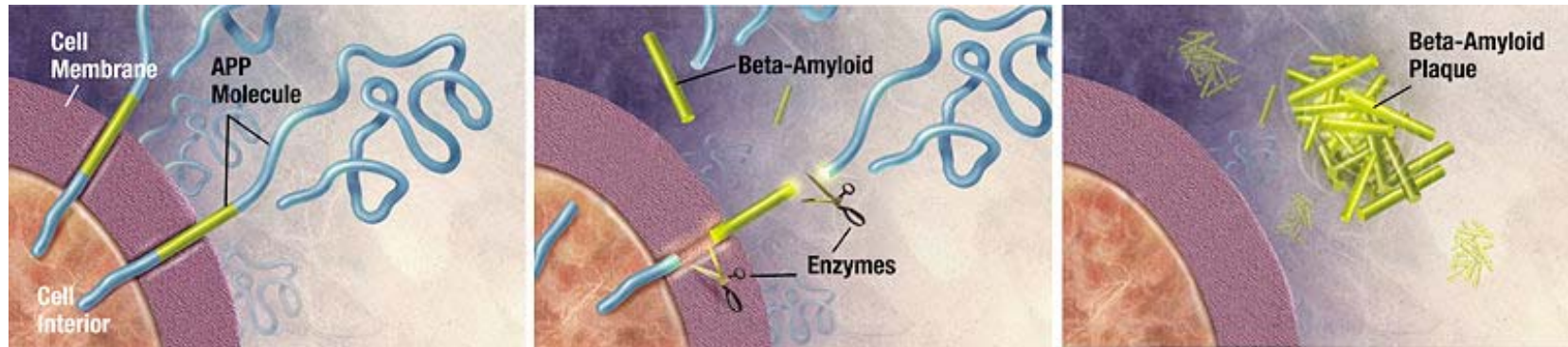


Image courtesy of the National Institute on Aging

Neurological changes

- A-beta plaques

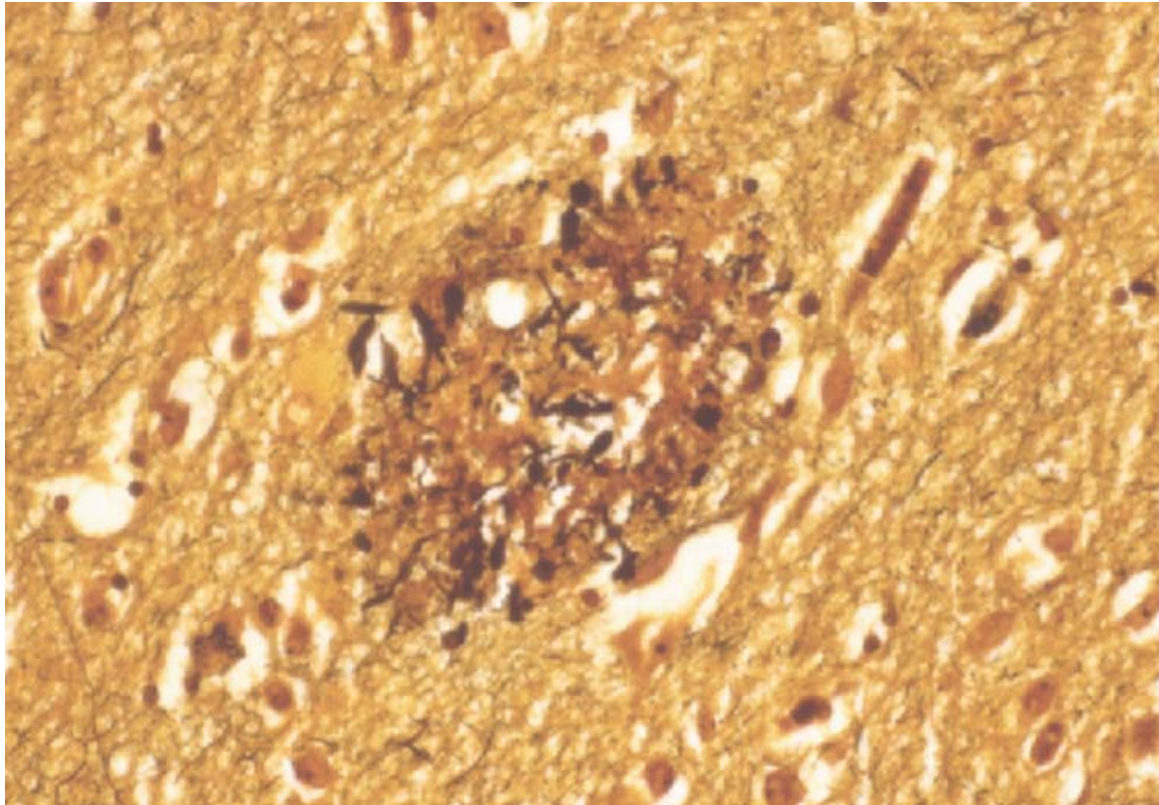
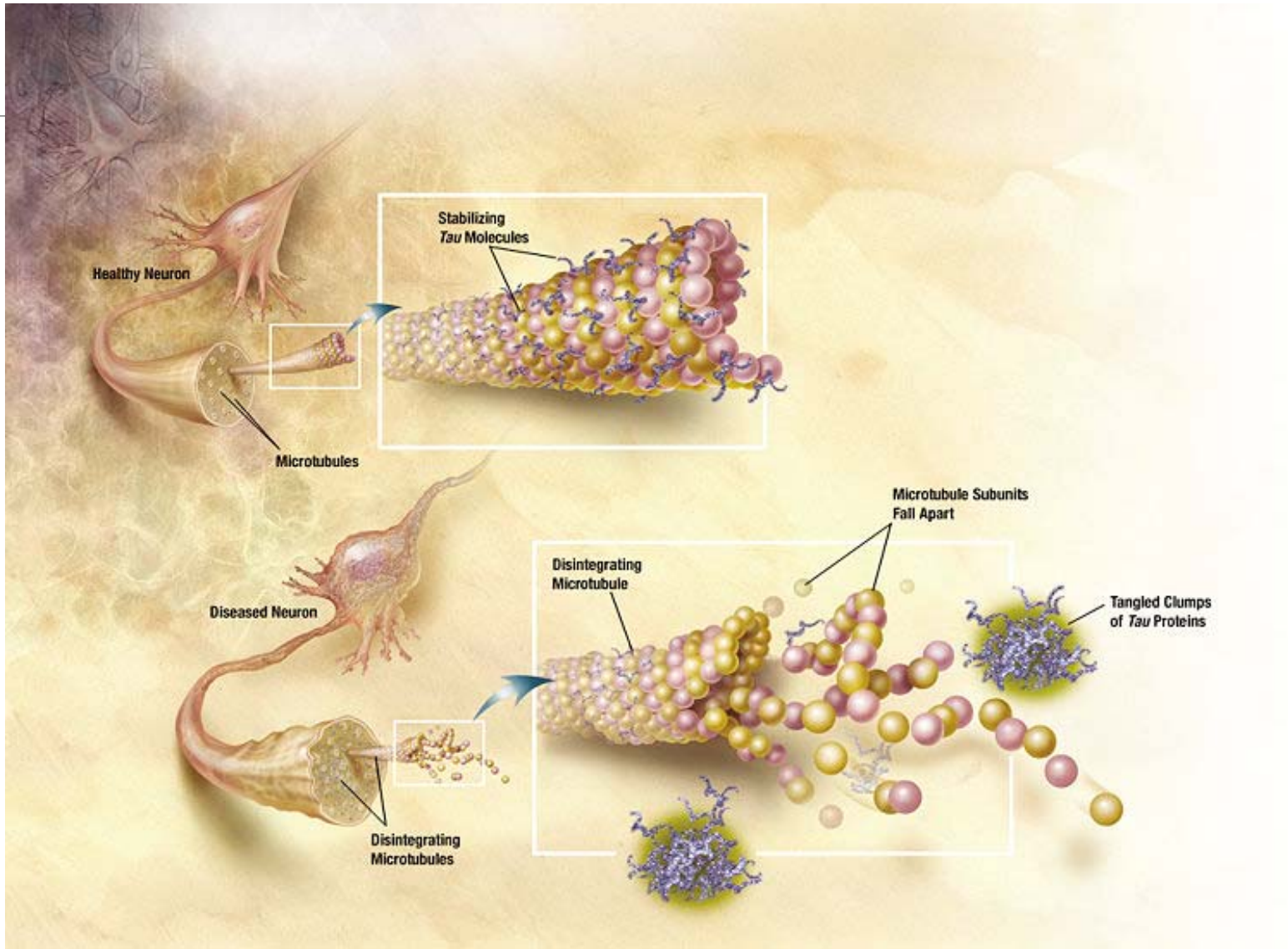


Image courtesy of the National Institute on Aging

Neurological changes

- Two characteristic changes at the cellular level:
- Neurofibrillary tangles - tau proteins associated with the cytoskeleton.
 - Tau proteins become hyperphosphorylated and change shape, causing microtubules to disintegrate.



Neurofibrillary Tangles

Image courtesy of the National Institute on Aging

Neurological changes

- Two characteristic changes at the cellular level:
- Tau tangles - proteins associated with the cytoskeleton.

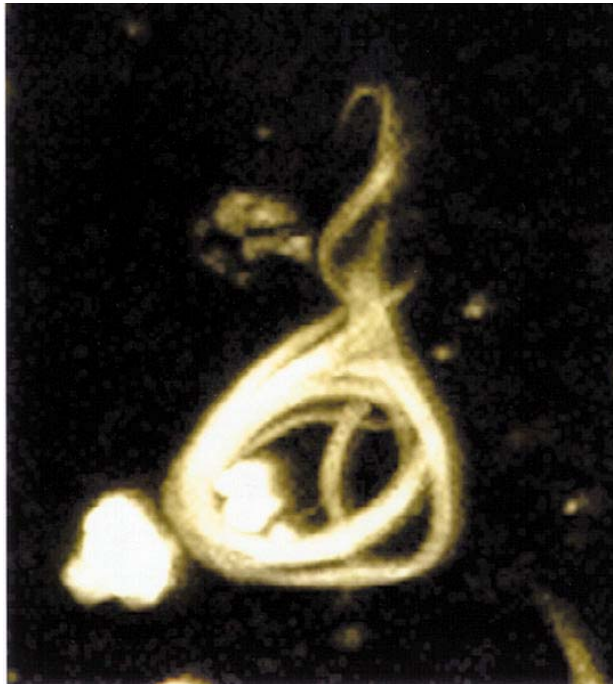


Image courtesy of the National Institute on Aging

Neurological changes

- Senile plaques and neurofibrillary tangles are characteristic of normal aging, but AD patients have more and in different locations.

- Both of these are protein-misfolding issues, so AD is classified as a proteopathy.

Causes

- Unknown, but some hypotheses:
 - Cholinergic hypothesis - AD is caused by reduced synthesis of ACh.
 - Most medications for AD are based on this hypothesis; treat symptoms but do not affect progression of disease.

Causes

- Tau hypothesis - tau protein abnormalities trigger the disease.
 - Supported by flaws in amyloid hypothesis, mostly.

Causes

- Amyloid hypothesis - amyloid-beta deposits are causative factor.
 - Majority of researchers support this hypothesis.
- Gene for APP is on chromosome 21 (chromosome that is tripled in Down syndrome, and DS patients almost always exhibit AD-like symptoms by age 40).

Causes

- Amyloid hypothesis - amyloid-beta deposits are causative factor.
 - Study by Holmes et al (2008). Stage 1 Clinical trial of a vaccine that removes amyloid-beta plaques.
 - Found no improvement in survival rates or dementia progression, despite effectiveness at clearing plaques.

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