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.


  • Found no improvement in survival rates or dementia progression, despite effectiveness at clearing plaques.
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