Detecting Early-stage and Preclinical Alzheimer’s Disease

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  - None

- Speaker’s Bureau(s)
  - None

- Editorial Duties
  1. *Alzheimer’s Disease and Associated Disorders*, Editor-in-Chief
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Chronic Disease Model of AD

Preclinical Phase
- Diffuse plaques
- Neuritic plaques, NFTs, neuron and synapse loss
- Cognitive impairment
- Functional loss

Clinical Phase
- Onset of symptoms
- Diagnosis
- Death

Genetic and environmental factors

Modified from Troncoso and Katzman
Appearance of Plaques and DAT

DAT = dementia of Alzheimer’s type.
Courtesy of Dr Mark Mintun.
An antecedent biomarker of disease is a characteristic that is objectively measured and evaluated that indicates a particular risk or likelihood that a clinically detectable disease will occur in the future.

In cardiovascular disease, LDL and HDL cholesterol levels indicate risk for atherosclerosis and angiography and cardiac imaging indicate the presence of atherosclerosis in coronary arteries.
Pathological Hallmarks of Alzheimer’s Disease

Aggregation and deposition of amyloid-β (Aβ) in plaques in human brain with Alzheimer’s Disease (extracellular Aβ)

Aggregation and buildup of hyper-phosphorylated tau in neurofibrillary tangles and neuropil threads in paired helical filaments (intracellular)
Candidate Biomarkers In AD

- Genetic: deterministic mutations; susceptibility factors (eg, apoE)
- CSF (Aβ/tau; other)
- Blood (plasma Aβ; other)
- -omics (eg, genomics, proteomics, metabolomics)
- Neuroimaging
  - Structural (regional or global)
  - MRS
  - Functional (fMRI, PET, SPECT)
  - Detect plaques/tangles
**CSF Biomarkers of AD**

**CSF β-Amyloid**
- Controls (n=72)
- Alzheimer Disease (n=131)

**CSF Tau**
- Controls (n=72)
- Alzheimer Disease (n=131)

*Published Aβ_{42}:
  - Sensitivity, 70-100%
  - Specificity, 40-90%

*Published Tau:
  - Sensitivity, 40-85%
  - Specificity, 65-85%

Based on clinical criteria*

MRI Volumetric Measures

Cerebral Binding of [$^{11}$C]PIB as a Candidate Biomarker of AD

Mean Cortical PIB Binding in DAT
Mean Cortical PIB Binding in Nondemented Controls (N=41)
PIB Binding and CSF Aβ₄₂ Levels Didn’t Consistently Correspond With Clinical Diagnosis: Implications for Possible Antecedent Biomarkers of AD

Immunization of Human Alzheimer’s Disease

Midfrontal

Parietal Cx

Immunized Case

Unimmunized Case

Biomarkers for Meningoencephalitis

Potential Roles for Validated Biomarkers for AD

- Diagnosis
- Monitoring therapeutic response
- Preclinical detection
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