Mild Cognitive Impairment and Biomarkers

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Spectrum from Normal Aging to Dementia

Function vs. Age

- Normal
- Mild cognitive impairment (MCI)
- Dementia
What is a biomarker?

- Variables (physical, chemical, or anatomical) that can be measured in a person and reflect the state of the disease

- Eg. blood, CSF (spinal fluid), functional brain scans, MRI scans
Alzheimer Disease Pathology

Tau Tangles

Amyloid Plaques

Courtesy of Dr. Ian MacKenzie and Dr. Patrick McGeer UBC
Two Phases to Alzheimer Disease

1. Brain Amyloid Beta (Aβ) Deposition
   - Precedes clinical symptoms by 10 years
   - CSF Aβ ↓

2. Brain Neurodegeneration (MCI to AD)
   - Synapses are lost and tau ↑
   - Brain atrophies (shrinks)
   - Memory symptoms appear
Jack C, et al, Lancet Neurol, Jan 2010
Biomarkers Useful in MCI

- Spinal fluid: CSF tau / Aβ_{1-42} ratio
- PET amyloid: Presence of amyloid
- MRI atrophy: Hippocampal shrinkage, Ventricular enlargement
- Functional scan: FDG-PET or SPECT
High CSF p-tau/CSF $\beta_{1-42}$ Predicts Conversion from MCI to AD

PET amyloid & FDG imaging

Usefulness of Imaging Biomarkers

PET amyloid

MRI

Normal Pre-AD Early AD

Jack C, et al, Lancet Neurol, Jan 2010
CSF & MRI Utility in Memory Clinics

- Frequency of “Alzheimer-like” CSF
  - 30% in normal controls
  - 50% in subjective memory complaint
  - 68% non-amnestic MCI
  - 78% amnestic MCI

- Subjective complaints: CSF unhelpful
- aMCI + abnCSF: 50% convert to AD in 3 yrs
- aMCI + abnCSF + MTA: 94% convert
Does having a positive PET amyloid scan or CSF mean dementia will develop?

- Means the biological signature of AD
- Many elderly have positive markers and do not have dementia.....uncertain if they will
- CLINICAL expression of AD biological signature depends on other factors, such as cognitive reserve and vascular changes
Summary

• Biological signature of AD starts 5-10 years before symptoms, but when present in the elderly not everyone will develop dementia.

• CSF and PET amyloid scans will be valuable in younger patients to diagnose AD early.

• MRI hippocampal atrophy and FDG-PET are currently available useful predictors in MCI.