Towards Standardizing a Framework for models of Alzheimer’s Disease

This symposium was conceived independently, but with the subsequent input, of:

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...who have developed a new Special Topics section for Alzheimer’s & Dementia to “assess the current state of knowledge related to the conceptual understanding of Alzheimer’s disease and dementia.”
Canonical AD: The Human Disease

*Where all models must start... or end up*

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Alzheimer’s Disease in relation to other etiologies

- Cerebrovascular
- Synucleinopathies
- Frontotemporal Degenerations
- CJD NAIM
- Other secondary etiologies
- Cogn Impt
- Alzheimer Disease
- Cogn Impt
- Cerebrovascular
Core neuropathologic features of AD

Arnold 1992
Variations in AD: Hippocampal sparing versus Limbic Predominant

Murray, Lancet Neurology 2011
Biomarkers of AD

- Elevated CSF tau
- Low CSF Amyloid
- Amyloid PET
- Temporo-parietal hypometabolism
- Volumetric MR
Sequential Biological & Clinical Changes in AD

Brain β-amyloidosis

Neurodegeneration

Symptoms of impaired thinking and memory

Severity

Years

Presymptomatic

Earliest symptomatic

Dementia
Age & Expression of Alzheimer Disease

1. Jorm, Neurology 1998
2. Jack, JAMA Neurol 2015
Relationship of dominantly inherited AD with genetic modifiers and “sporadic” AD

[Graph showing cumulative percent against age for different genetic markers: APP/PS1/PS2, APOE4, and Sporadic]
Amyloid → Neurodegeneration → Cognition
A sample of alternative models:
- Golde: Innate immunity
- Swerdlow: Energy homeostasis & the mitochondria
- Chui: Vascular mechanisms
- Iliff: Glymphatic system