White Matter Hyperintensity Trajectories in Patients With Progressive and Stable Mild Cognitive Impairment

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- Alzheimer Disease Neuroimaging Initiative (ADNI) dataset
- Four groups: Amyloid positive vs negative, and progressors vs stable
- Tracked over ~6 years
- LARGE sample (n = 820).
- Also monitored APOE4 status and other factors that might influence risk of progression
- Amyloid negative stable had least baseline white matter hyperintensities (WMH) compared to amyloid positive stable and amyloid positive progressors
- Amyloid positive progressors had the greatest degree of WMH change, and amyloid negative stable the least
- Hypertension is a critical factor impacting the risk of progression.
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Figure 1: Boxplots showing baseline WMH distributions (log transformed) across diagnostic groups for each lobe. Baseline WMH distributions (log transformed) across diagnostic groups for each lobe. The first and second rows show the log transformed WMH loads for each group by lobe. Amyloid positive (AP+) progressor, amyloid negative (AP-) progressor, amyloid positive (AP+) stable, and amyloid negative (AP-) stable. WMH = white matter hyperintensity.
Figure 2: Longitudinal change in total and regional WMH volume by group. Longitudinal WMH distributions (log transformed) across diagnostic groups for each lobe. The first and second rows show the log transformed WMH loads for each group by lobe. Amyloid positive (AP+) progressor, amyloid negative (AP-) progressor, amyloid positive (AP+) stable, and amyloid negative (AP-) stable. WMH = white matter hyperintensity
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- Mild cognitive impairment (MCI) clinical category for cognitive impairment without the activities of daily living impairment characteristic of dementia

- Many contributors to MCI – including treatable causes:
  - Sleep apnea, hearing loss, anticholinergics, CNS depressants, medical conditions, psychiatric disease

- Neuropathologic contributors:
  - Nonamnestic MCI:
    - Lewy body disease
    - Atypical AD variants: posterior cortical atrophy, dysexecutive, IvPPA
  - Vascular disease
  - Amnestic MCI:
    - Alzheimer’s disease
    - LATE disease

- Roughly 5-10% of patients convert from MCI to dementia per year

- Trying to predict who will convert remains difficult
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- Clinical practice – concern for who is going to progress, and how

- Imaging markers seem to predict this in a logical manner, as vascular factors are well known to associate with progression, particularly for Alzheimer’s
  - Pattern and topography of these imaging markers seems important

- Modifiable risk factors are of particular importance

- Hypertension appears to emerge as a critical factor here, which can be addressed
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UNKNOWNNS

- Type of vascular disease: small vessel, lacunar infarct, cerebral amyloid angiopathy, etc
- APOE4 load – 1 vs. 2 copies: relationship to cerebral amyloid angiopathy
- What about tau?
- Does treatment of hypertension actually change the course, not just correlate with it?
- How various treatments interact with the course of WMH will be of interest
- Implications for practice