**INTRODUCTION**

Alzheimer’s disease (AD) is a progressive neurodegenerative disorder. Mild cognitive impairment (MCI) is a transitional stage between healthy aging and overt AD, with 10-25% converting to AD every year [1]. To boost power for drug trials aiming to resist disease progression, it is important to know which factors influence rates of brain tissue loss. We set out to detect sex- and age-related differences in atrophic rates in a large cohort of subjects scanned twice 1 year apart.

**METHODS**

**MRI scans:** Baseline and 1-year follow-up MRI scans were acquired from N=684 subjects
- 144 probable AD patients; age at baseline: 76.5±7.4 years
- 336 probable MCI patients with amnestic MCI: 76.0±7.2 years
- 202 healthy elderly controls (CTL); 77.0±5.1 years

**Brain atrophic rates:** 3D maps of atrophic rates were created using an image analysis technology termed tensor-based morphometry (TBM). General linear regressions were used to assess factors influencing or related to brain atrophic rates in Alzheimer’s disease and normal aging. These correlations were subsequently evaluated by cumulative distribution functions (CDF) to determine if they were significant after controlling for multiple comparisons.

**RESULTS**

- **Brain atrophic rates linked to CSF biomarker levels**
  - Brain atrophic rates correlated with baseline clinical measures
  - Atrophic rates were most strongly correlated with the ADAS-cog, LM-m, and AVLT-S scores at baseline
  - Brain atrophic rates were correlated with CSF biomarker levels, but more weakly than clinical correlations

- **Brain atrophic rates correlated with cognitive decline in 1-year**
  - Atrophic rates were most strongly correlated with the ADAS-cog, LM-m, and AVLT-S scores at baseline
  - Anatomical changes over time were also highly correlated with ongoing changes in clinical measures

- **Brain atrophic rates correlated with baseline clinical measures**
  - Atrophic rates were most strongly correlated with the ADAS-cog, LM-m, and AVLT-S scores at baseline

- **Brain atrophic rates linked to CSF biomarker levels**
  - Brain atrophic rates were correlated with CSF biomarker levels, but more weakly than clinical correlations

**CONCLUSION**

- **Sex differences linked to CSF biomarker levels**
  - TBM is a sensitive, high-throughput biomarker for tracking disease progression in large imaging studies
  - Sub-analyses focusing on women or younger subjects gave improved sample size requirements for clinical trials.

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**Image 1:** Brain atrophic rates linked to CSF biomarker levels

**Image 2:** Brain atrophic rates correlated with cognitive decline in 1-year

**Image 3:** Brain atrophic rates linked to CSF biomarker levels

**Image 4:** Brain atrophic rates correlated with baseline clinical measures

**Image 5:** Brain atrophic rates correlated with cognitive decline in 1-year

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