Multimodal characterization and evolution of subtypes across the continuum of Alzheimer's Disease

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Heterogeneity of Alzheimer's disease (AD) is characterized with typical and atypical subtypes based on different neuroimaging biomarkers. While positron emission tomography (PET) imaging captures the neuropathological biomarker of neurofibrillary tangle burden, magnetic resonance imaging (MRI) allows to extract the neurodegenerative biomarker of brain atrophy. Subtypes identified on the basis of PET (e.g. measuring tau pathology) and MRI (e.g. measuring brain atrophy) vary by topographical distribution of the biomarkers, demographical, clinical and risk factors. Although the association between tau pathology and brain atrophy has been explored in the healthy and AD dementia populations in general, this association is not well-understood across the subtypes of AD.

We propose to use data from the Alzheimer's Disease Neuroimaging Initiative and explore how biomarkers from different modalities are related to each other and vary over time across the typical and atypical subtypes. In a cohort including AD dementia patients, prodromal AD patients and healthy individuals, we will identify subtypes using (a) tau PET, and (b) retrospective/prospective structural MRI. The convergence between tau PET-based subtype and longitudinal MRI-based subtype will be tracked for each individual. We hypothesize that the rate of convergence between subtypes identified using two neuroimaging modalities will differ across typical and atypical subtypes. This result will shed light on the poorly understood neurobiological mechanisms driving the subtypes. Additionally, by investigating the association between tau pathology and atrophy in subtypes across the AD continuum, we will highlight the unexplored difference between subtyping and disease staging. The overarching goal remains to identify subtype-specific patterns to aid disease-slowing or disease-modifying drug trials.