Effects of baseline regional amyloid deposition patterns on subsequent accumulation

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**Background:** Cortical summary measures of amyloid depend on the choice of regions to include in calculations and ignore potentially meaningful information in disproportionate amyloid deposition between specific regions. We define a set of “uptake patterns” that are independent of assumptions of reference region, regions of interest, or positivity threshold, and examine the utility of these patterns in predicting subsequent amyloid accumulation.

**Methods:** Each uptake pattern was derived from the partial volume-corrected florbetapir means of 46 bilateral Freesurfer-defined brain regions. We fit an Infinite Gaussian Mixture Model (IGMM) to uptake patterns calculated from 1067 baseline florbetapir PET scans in the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database, belonging to 368 Cognitively Normal (CN), 304 Early Cognitive Impairment (EMCI), 250 Late Cognitive Impairment (LMCI), and 144 Alzheimer’s Disease (AD) subjects. The IGMM clustered scans into 16 uptake patterns, each representing a distinct regional profile. We tested the efficacy of uptake patterns as predictors of longitudinal amyloid accumulation in normal and MCI subjects by fitting linear regression models to annualized amyloid change, as measured by cortical summary SUVR using a composite reference region (whole cerebellum, brainstem/pons, and subcortical WM).

**Results:** We examined cortical summary SUVRs for the 14 baseline florbetapir patterns with at least 2 members. Applying a previously-validated positivity threshold revealed that 5 patterns were expressed predominantly by florbetapir- subjects, 3 patterns by a combination of florbetapir- and florbetapir+ subjects, and 6 by florbetapir+ subjects. Low-SUVR patterns exhibit dominant uptake in cerebral and cerebellar WM, while high-SUVR patterns are dominated by the frontal, parietal, and cingulate cortices (Fig 1). Linear regression analyses revealed that increased probability of membership in several uptake patterns was associated with subsequent amyloid change, even after correcting for baseline cortical summary SUVR and other demographic variables (Fig 2). 3 uptake patterns predicted relative increases of 0.01 to 0.02 SUVR/year, while one uptake pattern predicted a relative decrease of 0.02 SUVR/year.

**Conclusions:** These findings suggest that expression of specific uptake patterns provides predictive information about amyloid accumulation that is not available using global amyloid measures, and which would aid in identifying subsets of individuals at higher risk of accelerated accumulation.