Multi-tracer model for staging cortical amyloid deposition using PET imaging

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Abstract:

Objective: To develop and evaluate a model for staging cortical amyloid deposition using PET with high generalizability.

Methods: 3027 subjects (1763 Cognitively Unimpaired (CU), 658 Impaired, 467 Alzheimer's disease (AD) dementia, 111 non-AD dementia, and 28 with missing diagnosis) from six cohorts (EMIF-AD, ALFA, ABIDE, ADC, OASIS-3, ADNI) who underwent amyloid PET were retrospectively included; 1049 subjects had follow-up scans. Applying dataset-specific cut-offs to global Standard Uptake Value ratio (SUVr) values from 27 regions, single-tracer and pooled multi-tracer regional rankings were constructed from the frequency of abnormality across 400 CU subjects (100 per tracer). The pooled multi-tracer ranking was used to create a staging model consisting of four clusters of regions as it displayed a high and consistent correlation with each single-tracer ranking. Relationships between amyloid stage, clinical variables and longitudinal cognitive decline were investigated.

Results: SUVr abnormality was most frequently observed in cingulate, followed by orbitofrontal, precuneal, and insular cortices, then the associative, temporal and occipital regions. Abnormal amyloid levels based on binary global SUVr classification were observed in 1.0%, 5.5%, 17.9%, 90.0%, and 100.0% of stage 0-4 subjects, respectively. Baseline stage predicted decline in MMSE (ADNI: *N*=867, *F*=67.37, *p*<0.001; OASIS: (*N*=475, *F*=9.12, *p*<0.001) and faster progression towards an MMSE≤25 (ADNI: *N*=787, *HRstage1*=2.00, *HRstage2*=3.53, *HRstage3*=4.55, *HRstage4*=9.91, *p*<0.001; OASIS: *N*=469, *HRstage4*=4.80, *p*<0.001).

Conclusion: The pooled multi-tracer staging model successfully classified the level of amyloid burden in >3000 subjects across cohorts and radiotracers, and detects pre-global amyloid burden and distinct risk profiles of cognitive decline within globally amyloid-positive subjects.

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