

Multi-Resolution Analysis of Brain Connectivity: Associations With PET-Based Alzheimer's Pathology

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Background

Identifying individuals at greatest risk for Alzheimer's disease (AD) at preclinical stages is critical for initiating early treatment. While amyloid accumulation is a primary pathological event in AD, loss of connectivity between brain regions is suspected of contributing to cognitive decline. Even though amyloid pathology is a feature of AD, its effect on connectivity has been difficult to measure in the preclinical (asymptomatic) stage of AD.

Methods

Cognitively asymptomatic participants from the WRAP study (N=135) underwent DTI imaging to assess structural connectivity and PiB PET to measure amyloid accumulation. Connectivity strengths were indexed by mean fractional anisotropy (FA) along tracts connecting 162 gray matter regions. We derived wavelet based multi-resolution connectivity signatures (WaCS) for each connection and modeled its relationship with amyloid accumulation (measured by PiB DVR) in 16 regions that accumulate amyloid plaque in AD. Linear modeling on WaCS yields the p-values.

Results

Amyloid burden was associated with extensive connectivity loss. For example, we found that amyloid deposition in left posterior cingulate is associated with connectivity loss between temporal and occipital regions even in this preclinical stage of AD. The p-values for WaCS for 15 (of 16) PiB-PET ROIs show advantages of multi-resolutional WaCS. For 12 (of 15) ROIs, the significance survives the Bonferroni corrected level. We detected 25 statistically significant (10 of 25 with very strong evidence at the Bonferroni corrected level of 0.01) associations between PiB ROIs and connectivity (7 unique edges).

Conclusions

While prior studies have failed to show a close association between amyloid deposition and structural brain changes, especially in preclinical AD, our new algorithm demonstrates the influence of amyloid burden on structural brain connectivity (in almost all regions implicated as important in AD). Our new results significantly enhance detection of amyloid effects on brain connectivity.