Establishing the Structural Connectome as a Quantitative Imaging Biomarker: Application to Alzheimer's Disease

Monday, 12:15- 12:45 PM
Location: Learning Center, Hall D

PARTICIPANTS:

Jeffrey W Prescott MD, PhD (Presenter): Nothing to Disclose
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Jeffrey R Petrella MD: Advisory Board, Johnson & Johnson Speakers Bureau, Quintiles Inc Advisory Board, Piramal Enterprises Limited

PURPOSE

The current study analyzes structural connectome topological metrics and their reproducibility in the setting of Alzheimer's disease pathology.

METHOD AND MATERIALS

We studied 102 subjects enrolled in the multi-center biomarker study, the Alzheimer's Disease Neuroimaging Initiative (ADNI) 2 who had both DTI and florbetapir PET data. Subjects' T1 scans were automatically parcellated into cortical regions of interest. Standardized uptake value ratios (SUVr) were calculated from florbetapir PET scans for 5 cortical lobes (frontal, cingulate, parietal, temporal, and occipital). Structural connectome graphs were created from DTI scans, and connectome topology was analyzed in each lobe using graph theoretic metrics: strength, local efficiency, clustering coefficient, and betweenness centrality. Linear mixed effects models were fit to analyze the effect of florbetapir SUVr on the structural connectome metrics. In addition, reproducibility of the topological metrics was analyzed in the cohort of normal controls between baseline and 3 month scans.

RESULTS

There were strong, significant associations between florbetapir SUVr and structural connectome metrics in each of the 5 lobes. Increased cortical florbetapir SUVr was associated with decreases in strength (p = 0.00001), local efficiency (p = 0.00001), and clustering coefficient (p = 0.00006), but not betweenness centrality (p = 0.69). The best reproducibility between consecutive measurements for normal controls was 6% for strength, 16% for local efficiency, 13% for clustering coefficient, and 48% for betweenness centrality.

CONCLUSION

Increased amyloid burden is strongly associated with changes in the topology of the large-scale structural network architecture of the brain (the 'structural connectome'), even in the preclinical stages of AD. The most reproducible topological measurement studied was strength, while local efficiency and clustering coefficient had acceptable but not great reproducibility. These results
suggest that it may be possible to use structural network topology as an imaging biomarker of Alzheimer's disease, and therefore as a target for therapy early in the course of AD.

CLINICAL RELEVANCE/APPLICATION

These results suggest that it may be possible to use structural network topology as an imaging biomarker of Alzheimer's disease, and therefore as a target for therapy early in the course of AD.