Interrogating Longitudinal Structural Network Topology in Alzheimer's Disease

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BACKGROUND

• Neurodegenerative diseases are network disorders that lead to complex progressive changes to structural & functional brain connectivity [1].

PURPOSE & HYPOTHESIS

• **Purpose:** To investigate longitudinal network changes in Alzheimer's disease (AD) using graph topological measures & structural connectomes.

• **Hypothesis:** Patients with AD will show significant network alterations compared to normal control (NC) and mild cognitive impairment (MCI) patients.

STUDY COHORT

	AD (N=44)	MCI (N=114)	NC (N=77)	χ^2, *p*
Gender (M:F)	16:28	40:37	42:72	4.98, *p*=0.084
APOE4 (0:1:2)	16:23:5	51:25:1	50:50:114	16.49, *p*=0.002
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	***p***
Education	15.45 (2.9)	16.39 (2.8)	15.89 (2.7)	0.190
Age	74.79 (8.7)	73.07 (5.6)	72.91 (7.3)	0.307

Table1. Demographics for AD, MCI and NC patients.

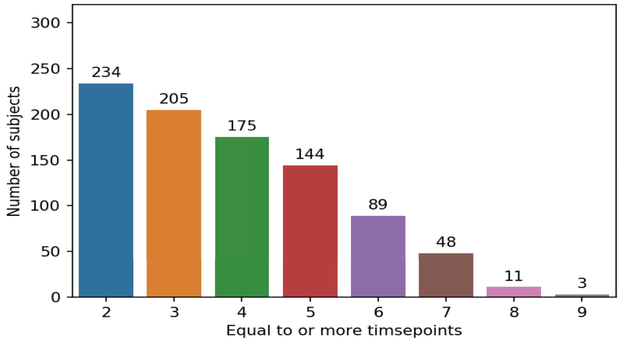

Fig 1. Subjects having N longitudinal diffusion MRI timepoints or more

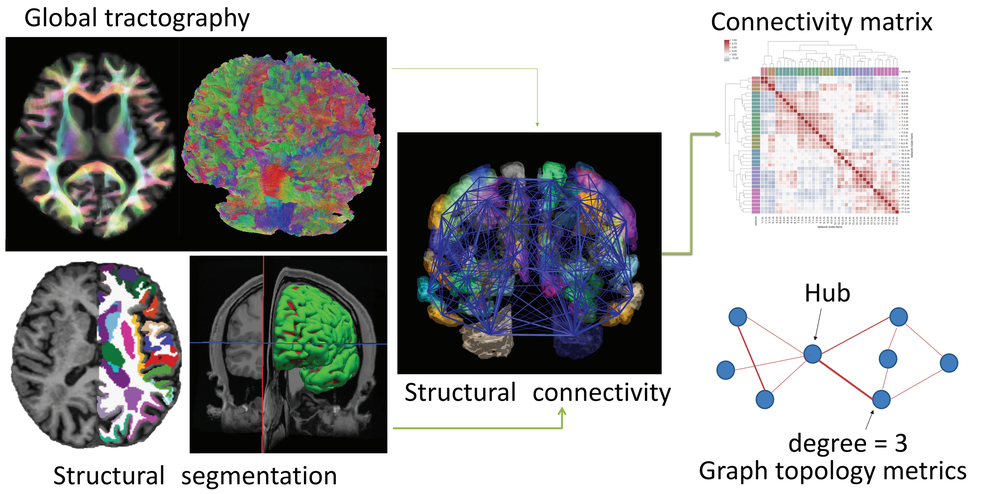

Fig 2. Optimized diffusion pipeline with Graph topology metrics.

RESULTS

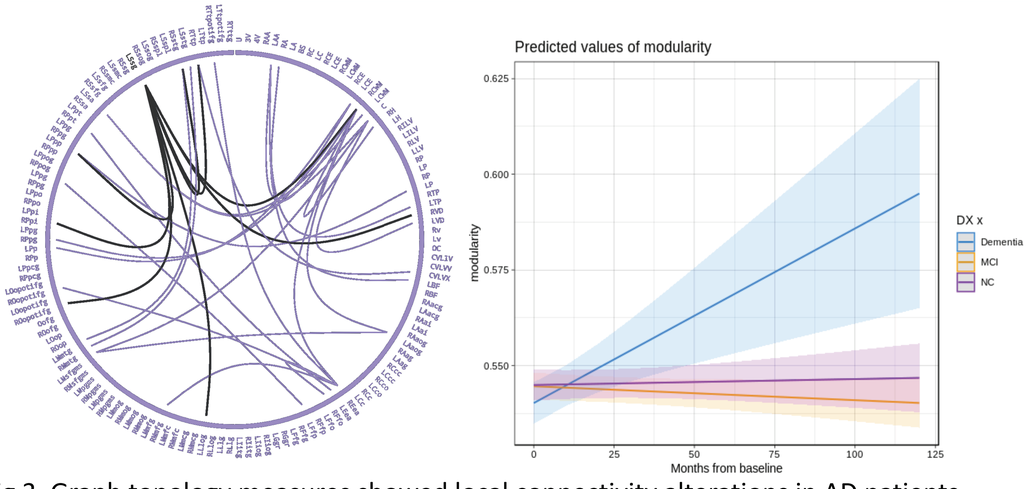

Fig 3. Graph topology measures showed local connectivity alterations in AD patients namely in the posterior cingulate cortex and significant increases in modularity longitudinally compared to NC and MCI (p=0.0058). Modularity is a measure of connectivity between brain modules (sub-networks), i.e. increased modularity implies decreased connectivity across brain regions of different modules.

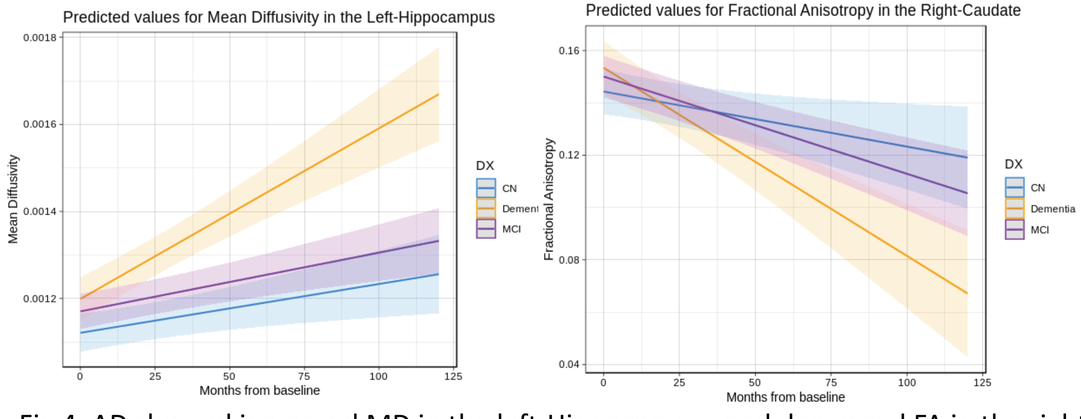

Fig 4. AD showed increased MD in the left-Hippocampus and decreased FA in the right-Caudate (p<0.001) across time compared to NC & MCI patients.

METHODS

• 235 ADNI subjects (77 NC, 114 MCI & 126 AD) were analyzed using optimized diffusion pipelines including eddy current correction with FSL [2] and anatomically constrained probabilistic tractography with MRtrix [3].

• Brain parcellation was performed using the MALPEM segmentation [4] and structural connectomes constructed & normalized.

• Graph topology measures were extracted using BCT [5]: modularity, efficiency & clustering. Diffusion metrics were extracted in WM and subcortical GM.

• Linear mixed effects models were used with fixed effects for time since baseline and diagnosis, their interaction & random effects for subject, accounting for age, gender, education & ApoE4 status.

CONCLUSION

Our preliminary results:

• Revealed breakdown of long-range connectivity between brain regions of different modules.

• Showed longitudinal diffusion changes in hippocampus & caudate between groups.

• Confirmed previous cross-sectional findings [6].

Future work will investigate the association of of these changes with cognitive performance.

References:

1. Biswal et al. 2010
2. Jesper et al.. 2016
3. Tourniet et al. 2007
4. Ledig et al. 2005
5. Robinov et al. 2010
6. Pereira et al. 2016

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