

Sex differences in structural connectivity-based AD pathology in the Indiana Memory and Aging cohort

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Introduction

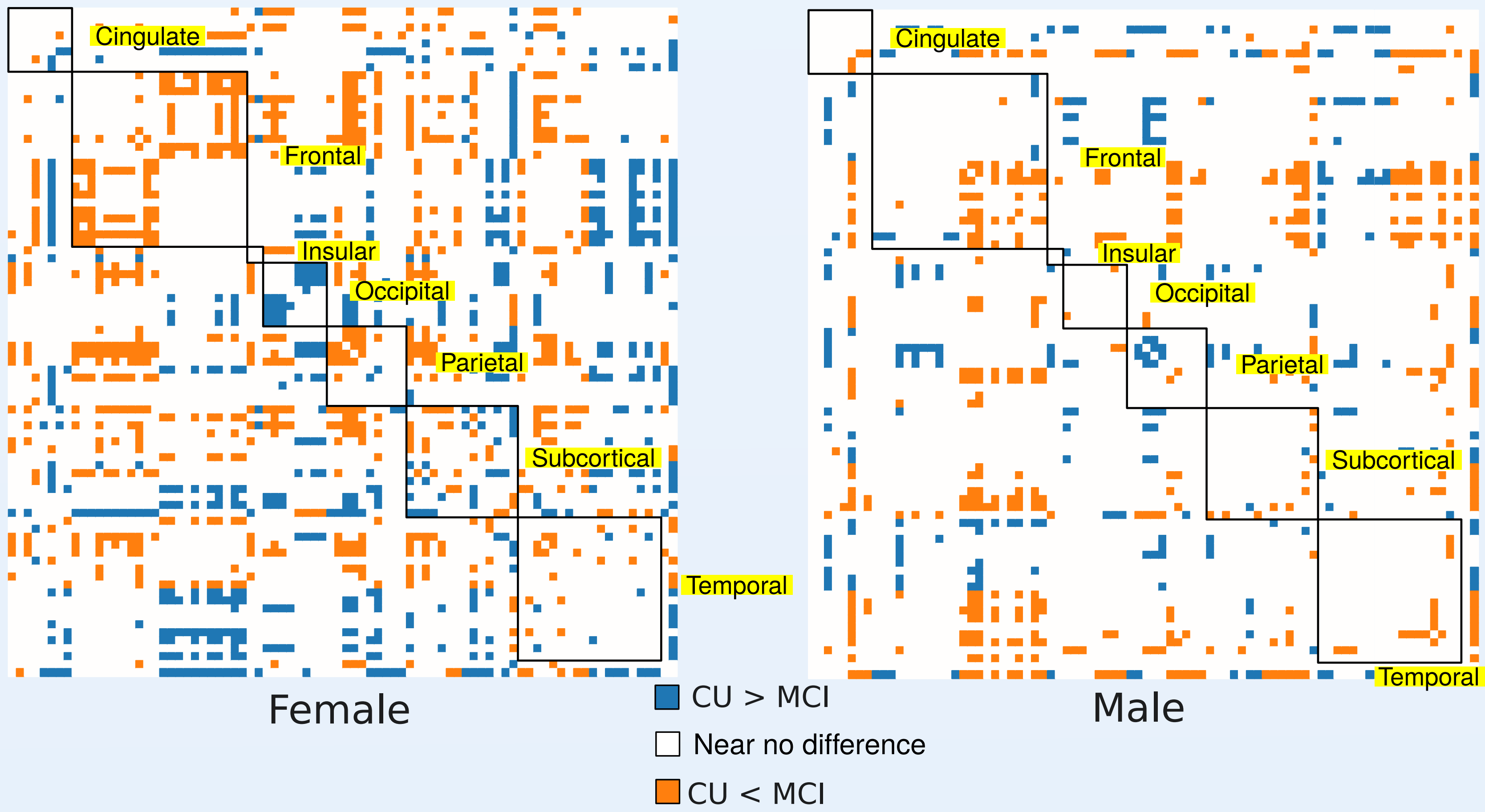
- It is known that 2/3rds of people with Alzheimers disease (AD) are women.
- Mild cognitive impairment (MCI) is a precursor to AD and offers valuable insights into early cognitive changes.
- Orientation Dispersion (OD) is a summary statistic derived from diffusion MRI data which estimates the variation in neurite fanning. OD has been found to be impacted by AD, and displays sex differences in both healthy, and individuals with AD.

Material and Methods

- Cognitively Unimpaired (CU)
32 Female — 8 Male
- Subjective Cognitive Decline (SCD)
26 Female — 12 Male
- Mild Cognitive Impairment (MCI)
13 Female — 9 Male
- This study applies a latent space estimation (Wang et al., 2025) that captures group level connectivity trends using a bayesian MCMC algorithm that assumes connectivity induced elements to be realizations of random processes with noise.
- Preprocessed OD diffusion magnetic resonance imaging (dMRI) data using tau and amyloid measures, stratified into 84 regions was used as input into our model. Regions were reordered based on 8 anatomical lobes.

Results

- Males and females with the onset of MCI displayed increases and reductions in OD connectivity in different brain regions.
- In the frontal lobe, females tended to see increases in inter-hemispheric connectivity while males saw increases in intra-hemispheric connectivity within the right hemisphere.
- In the parietal lobe, females saw increases in connections within the left hemisphere, while males saw decreases.
- In the occipital lobe, we saw females display decreases in OD connectivity in inter-hemispheric connections, while males saw less significant changes.
- In the sub-cortical regions, females saw many significant changes, while males saw few regions with changes.
- In the temporal lobe, females saw connections within the left hemisphere that displayed increases to OD connectivity, while the males saw little changes except for connections with the right temporalpole and the right parahippocampal.



Strongest Decrease in Structural Connectivity for MCI group			
Female Group		Male Group	
Difference	Connectivity Edge	Difference	Connectivity Edge
0.0757	Right Entorhinal - Right Postcentral	0.0780	Left Frontalpole - Right-Parahippocampal
0.0648	Right Parahippocampal - Right Postcentral	0.0776	Left Entorhinal - Right Medialorbitofrontal
0.0644	Left Rostralmiddlefrontal - Right Entorhinal	0.0730	Lect Lateralorbitofrontal - Right Parahippocampal
0.0642	Right Entorhinal - Right Superiorfrontal	0.0723	Left Accumbens - Right Parahippocampal
0.0604	Right Entorhinal - Right Lateralorbitofrontal	0.0721	Left Entorhinal Right Lateralorbitofrontal
Strongest Increase in Structural Connectivity for MCI group			
Female Group		Male Group	
Difference	Connectivity Edge	Difference	Connectivity Edge
0.0616	Left Paracentral - Left Rostralmiddlefrontal	0.1446	Right Entorhinal - Right Parahippocampal
0.0593	Left Fusiform - Left Supramarginal	0.1183	Right Fusiform - Right Parahippocampal
0.0588	Right Accumbens - Right Temporalpole	0.1127	Right Lingual - Right Parahippocampal
0.0588	Left Rostralmiddlefrontal - Left Supramarginal	0.0989	Right Parahippocampal - Right Pericalcarine
0.0571	Left Fusiform - Left Temporalpole	0.0909	Right Isthmuscingulate - Right Parahippocampal

Conclusions

- Our results highlight the lobes and regions that display disparity between males and females with MCI.
- We found differences between males and females in the frontal, occipital, parietal, temporal lobes and the subcortical regions.
- We found the right parahippocampal to show the largest magnitude of increases in OD connectivity in males compared to females.
- Sex-specific differences in hemispheric asymmetry were observed across brain lobes.
- These differences suggest the key role OD connectivity plays in understanding the role sex has in MCI and further AD.

Additional Information

More information about the latent space model is available here:
<https://doi.org/10.1016/j.media.2024.103309>

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