Difference Analysis of DWI and Cortical Thickness in the Alzheimer's Disease Connectome Project (ADCP)

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Background

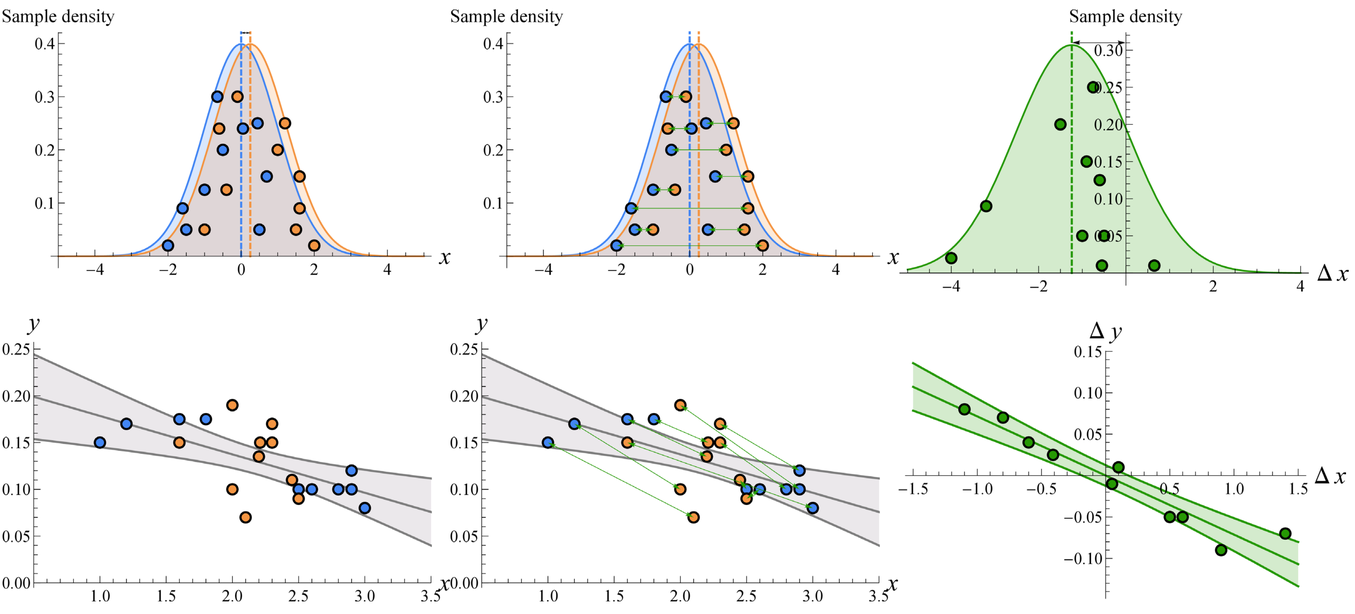
Diffusion weighted (DW) and T_1-weighted MRI data from the Alzheimer's Disease Connectome Project (ADCP) were analyzed to examine microstructural and cortical thickness differences among three diagnostic groups, **(1)** cognitively unimpaired (CU), **(2)** mild cognitive impairment (MCI), and **(3)** Alzheimer's disease dementia (AD) in two age categories for both the sexes.

Data

73 subjects underwent connectome quality MRI. **Left:** Sample sizes for each diagnostic group and sex in both the age categories. Numbers of samples (a) by diagnostic group: AD=18, MCI=25, CU=30, (b) by sex: female=37, male=36 and (c) by age category: younger=43, older=30. The sample sizes are balanced among the groups and the difference in the number of MCI between males and females in the older age category is the largest.

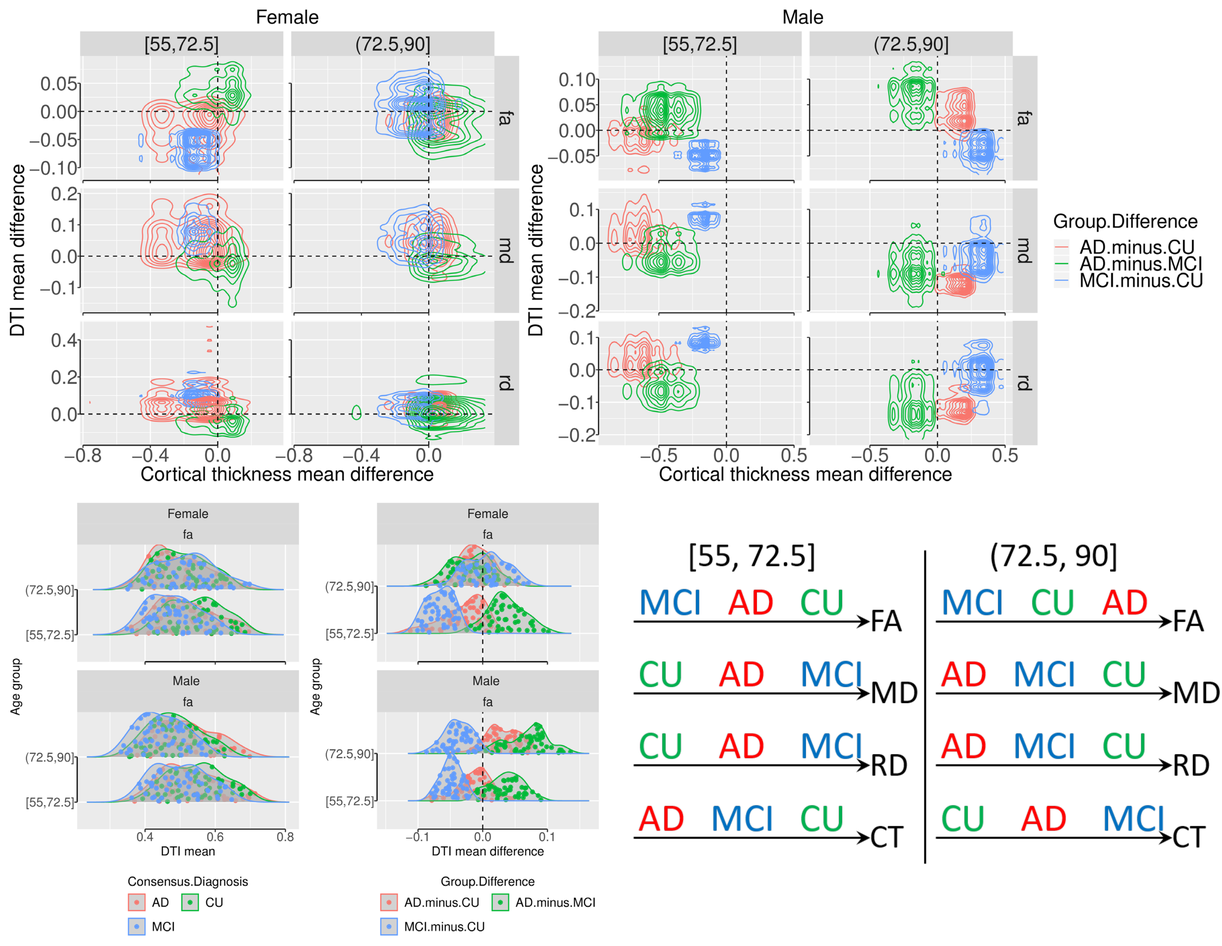
Methods

Diffusion tensor imaging (DTI) measures were estimated from the DWI data following eddy current and field inhomogeneity correction[1-3]. FreeSurfer based processing was used to estimate the cortical thickness. 48 white matter regions from the JHU DTI atlas[4] and cortical thickness in 34 gray matter regions from the Destrieux FreeSurfer cortical atlas[5] were examined. A difference analysis approach was applied to test for pairwise mean differences between the three diagnostic groups for each age category, and sex across all regions. Briefly, the difference analysis approach is performed as follows. First, the mean (across samples) of each measure is computed for each region in each diagnostic group, sex and age category. Therefore for each of the DTI measures, we would obtain 576 [=(# regions) 48 x (# diagnostic groups) 3 x (# sexes) 2 x (# age categories) 2] observations and for the cortical thickness we would get 408 [= 34 x 3 x 2 x 2] observations. Then for each region, sex and age category, we compute pairwise difference of these observations for the three diagnostic groups i.e. AD minus CU, AD minus MCI and MCI minus CU. Instead of performing the analysis directly on the distributions of mean measures in the regions, the analysis is performed on the distributions of these pairwise mean differences in all the regions *jointly*. Informally and intuitively, such pairwise differences can take advantage of the inherent dependencies among the data (in this case regional, sex and age category correspondences between samples) to better estimate the effects of interest[6].



Results

(1) White matter microstructural differences among the three groups (AD, MCI and CU) were observed among younger participants (55 to 72.5 years of age) while gray matter cortical thickness differences were observed among the older adults (72.5 to 90 years of age). Differences were also more pronounced in the males compared to females. **(2)** The difference analysis also showed greater sensitivity compared to traditional mean analysis approach.



Conclusions

(1) Diagnostic group differences in AD were identified in the bivariate space of white matter and gray matter imaging features (***derived using pairwise differences***). **(2)** Interestingly, among the **younger** participants, disease associated differences were prominent in **white matter**, while group comparisons among **older** participants revealed clearer **gray matter** differences. **(3)** Also, the "opposite" effects of increased FA, decreased MD, RD and increased cortical thickness for the AD group compared to the CU happen in the older age category. **(4)** Longitudinal data collection is needed to further examine the temporal trajectories of white matter and gray matter across the development of AD.

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Acknowledgements

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