Multi-modal investigation of the role of brain gyrification in Alzheimer's disease

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Background and aims

This study aims to investigate the interplay between Alzheimer's Disease (AD)-correlated alterations in surface-based morphometry (SBM)-derived indices such as Gyrification Index and other regional cortical properties, specifically cortical thickness and metabolic rate measured through PET-FDG, as well as structural covariance metrics such as nodal degree and clustering coefficient.

Materials and methods

The study included retrospectively collected 3-T 3DT1-weighted MRI and 18-F-FDG-PET data from two groups: patients with biologically defined Alzheimer's disease (AD, n=44, CDR global score ≤ 1) and controls (n=17). Subsets of both the AD patients (n=27) and the non-AD group (n=13) underwent a PET/CT with 18F-fluorodeoxyglucose imaging. Montreal Cognitive Assessment (MoCA) was used for cognitive screening purposes. A pipeline involving Statistical Parametrical Mapping (SPM)-based toolboxes, Computational Anatomy Toolbox (CAT) [2] and PETPVE12 [3] was used for preprocessing 3DT1 and FDG-PET scans, respectively. A Matlab script based on the methodology proposed by Liu et al. [3] was used to build single-subject structural covariance networks. The Matlab toolbox Graph Theoretical Network Analysis Toolbox (GRETNA) was used to calculate the nodal degree and clustering coefficient from the single-subject structural covariance matrices. Statistical analyses were performed with SPM12 and SPSS, using age and sex as covariates. Maps of cortical thickness and local gyrification index (GI) were obtained, as well as ROI-derived data for these metrics. The regional Standard Uptake Value ratio (SUVR) for PET-FDG images and the structural covariance parameters at the nodal level were analyzed with a ROI approach. Spearman's correlations were performed between ROI-derived data of insular gyrification index, cortical thickness, SUVR, nodal degree and clustering coefficient, as well as with MoCA, when available.

Results

Figure A and B show voxel-wise maps illustrating statistically significant decrease in the GI and in the cortical thickness, respectively, of AD compared to non-AD. In the voxel-wise analysis, the GI of AD showed a significant reduction in the left insula compared to non-AD (FWE p<0.050, corrected with TFCE (A).The ROI analysis further confirmed this finding, with a significant difference in the average insular GI between the two groups, while no other regions displayed notable changes in GI. The voxel-wise comparison for cortical thickness maps between the two groups showed a series of significant clusters in a wider series of regions including bilateral temporal and posterior parietal lobes (B). The ROI-based analysis revealed significant group differences in cortical thickness, with AD showing reduced thickness across all regions examined compared to non-AD. Metabolic uptake was also lower in the insula in AD. Insular GI correlated positively with insular metabolism (SUVR; R=0.370, p=0.021) (C), and MoCA scores (R=0.554, p=0.004) (D). No significant correlations were observed with CSF biomarkers. Inversely GI correlates with increasing nodal insular degree (E, F).

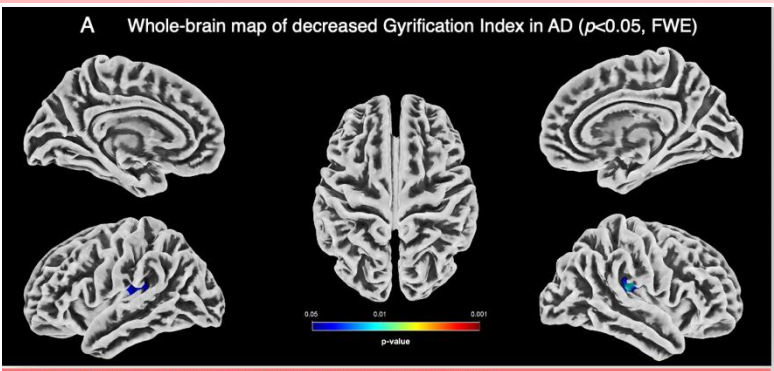


Figure 1A. Regional differences in GI between AD and non-AD subjects (p<0.05, FWE-corrected)

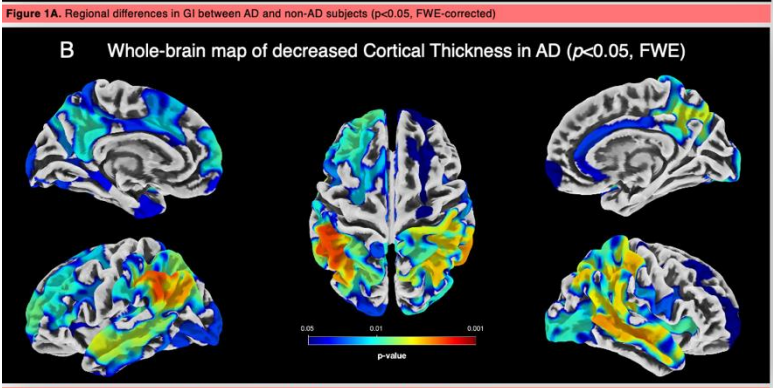
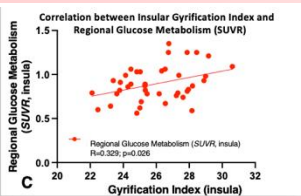
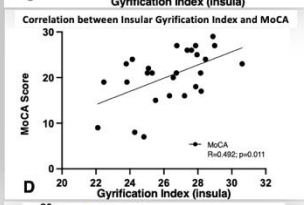
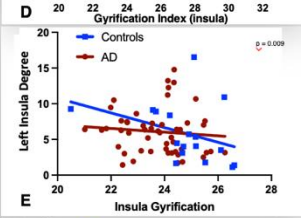
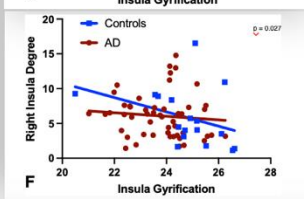


Figure 1B. Regional differences in CT between AD and non-AD subjects (p<0.05, FWE-corrected)









Conclusions

Our multi-modal imaging approach revealed localized changes in gyrification in individuals with AD, contrasting with the widespread brain atrophy typically observed in these patients. Importantly, the observed insular GI reduction was specific to the AD group when compared to individuals with non-AD cognitive impairment and a non-AD CSF profile. Notably, significant and clinically relevant correlations were found between GI and regional glucose metabolism as well as cortical thickness in the insula, suggesting a link to disease-related functional disruptions. Inversely, the inverse correlation with increasing nodal degree indicates compensatory connectivity changes not paralleled by clustering coefficient increases, reflecting a shift from small-world to more random network configurations.

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