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Surface-based parcellation and vertex-wise analysis of ultra high-resolution ex vivo 7 tesla MRI in Alzheimer's disease and related dementias

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Introduction: MRI is the standard modality to understand human brain structure and function in vivo (antemortem). Decades of research in human neuroimaging has led to the widespread development of methods and tools to provide automated volume-based segmentations and surface-based parcellations which help localize brain functions to specialized anatomical regions. Recently ex vivo (postmortem) imaging of the brain has opened-up avenues to study brain structure at sub-millimeter ultra-high-resolution revealing details not possible to observe with in vivo MRI. Unfortunately, there has been limited methodological development in ex vivo MRI primarily due to lack of datasets and limited centers with such imaging resources. Therefore, in this work, we present one-of-its-kind dataset of 82 ex vivo T2w whole-brain hemispheres MRI at 0.3 mm^3 resolution spanning Alzheimer's disease and related dementias. We developed a fast and easy-to-use automated surface-based pipeline to parcellate ultra-high-resolution ex vivo brain tissue at the native subject space resolution using the Desikan-Killiany-Tourville (DKT) brain atlas. This allows us to perform vertex-wise analysis in the template space and thereby link morphometry measures with pathology measurements derived from histology.

Methods: We perform structure-pathology association analysis in a large dataset of ultra-high-resolution 0.3 mm^3 T2w 7T MRI scans of whole brain hemispheres from 82 brain donors with ADRD diagnoses, a first study of such scale conducted at this resolution. We present a new computational pipeline that performs automated segmentation and whole-hemisphere FreeSurfer DKT atlas parcellation of the cortex in native subject space at sub-millimeter 0.3 mm^3 resolution, a first large-scale surface-based scheme for ex vivo whole-hemispheres analysis in diseased population. We achieve this by adapting the surface-based pipeline in FreeSurfer with an initial subject-space topology-corrected WM segmentation derived from a deep learning-based segmentation model as developed (Fig. 1). We evaluate the framework by correlating cortical thickness with neuropathological markers implicated in AD (measures of p-tau, neuronal loss; global amyloid-β, Braak staging, and CERAD) and perform vertex-wise generalized linear modeling.

Results: Fig. 2 shows the Spearman's rho-value between the mean cortical thickness (mm) in each brain region (computed in subject space at native resolution) and five pathology measures: global ratings of amyloid-β, Braak staging, CERAD, and regional ratings of p-tau pathology and neuronal loss in the MTL, the region first implicated in AD. The analysis was covaried for age, sex and postmortem interval and corrected for multiple comparisons using Bonferroni method. Significant negative correlation was found in entorhinal, parahippocampal, medialorbitofrontal, temporal pole, inferior temporal and parietal lobes which are consistent with literature on progressive loss of cortical gray matter in AD.

Vertex-wise correlation between thickness and the neuropathology ratings was performed in MNI template-space by fitting a GLM at each vertex across the entire cohort with age, sex and PMI as covariates and corrected for multiple comparisons. Fig. 3 shows the t-statistics map on the pial and the inflated surfaces with the clusters outlined in white indicating regions where the significant strongest associations were observed surviving FDR correction. We observe that the strongest correlations were observed in MTL, the region associated with AD.

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