Spatial clustering of white matter hyperintensities based on their microstructural abnormality

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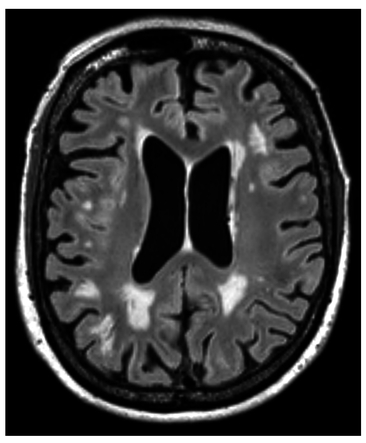
INTRODUCTION

- White Matter Hyperintensities (WMHs) are age-related magnetic resonance imaging (MRI) abnormalities widely recognized as markers of small vessel disease [1]
- Pathological substrates of WMHs depend on the spatial location of WMHs, with studies usually differentiating between periventricular and deep WMH [2]
- Spatial dynamics of WMH microstructure have never been characterized at a high spatial resolution

Objectives:

1. Characterize the MRI-derived microstructural abnormality of WMHs at a high spatial resolution (i.e., the voxel level)
2. Uncover data-driven spatial clusters of microstructurally-similar WMHs



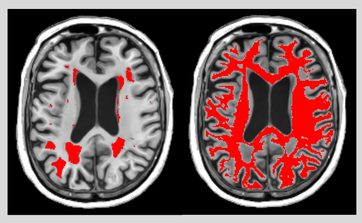
METHODS

Data

- 34,778 UK Biobank participants
- 7 MRI-derived microstructural properties
  - Diffusion-weighted imaging (DTI and NODDI)
  - Susceptibility-weighted imaging

Processing

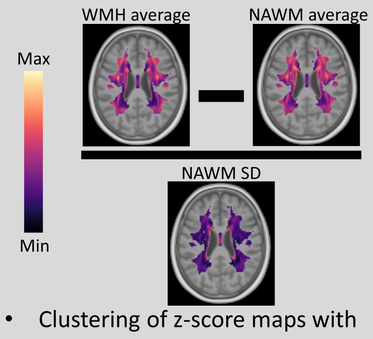
- Segmentation of WMHs and normal-appearing white matter (NAWM)



- Non-linear registration to a custom UK Biobank template

Analysis

- Spatial normalization with expected NAWM microstructure at each voxel



- Clustering of z-score maps with spectral clustering

RESULTS

Fig. 1. Average WMH microstructural abnormality maps

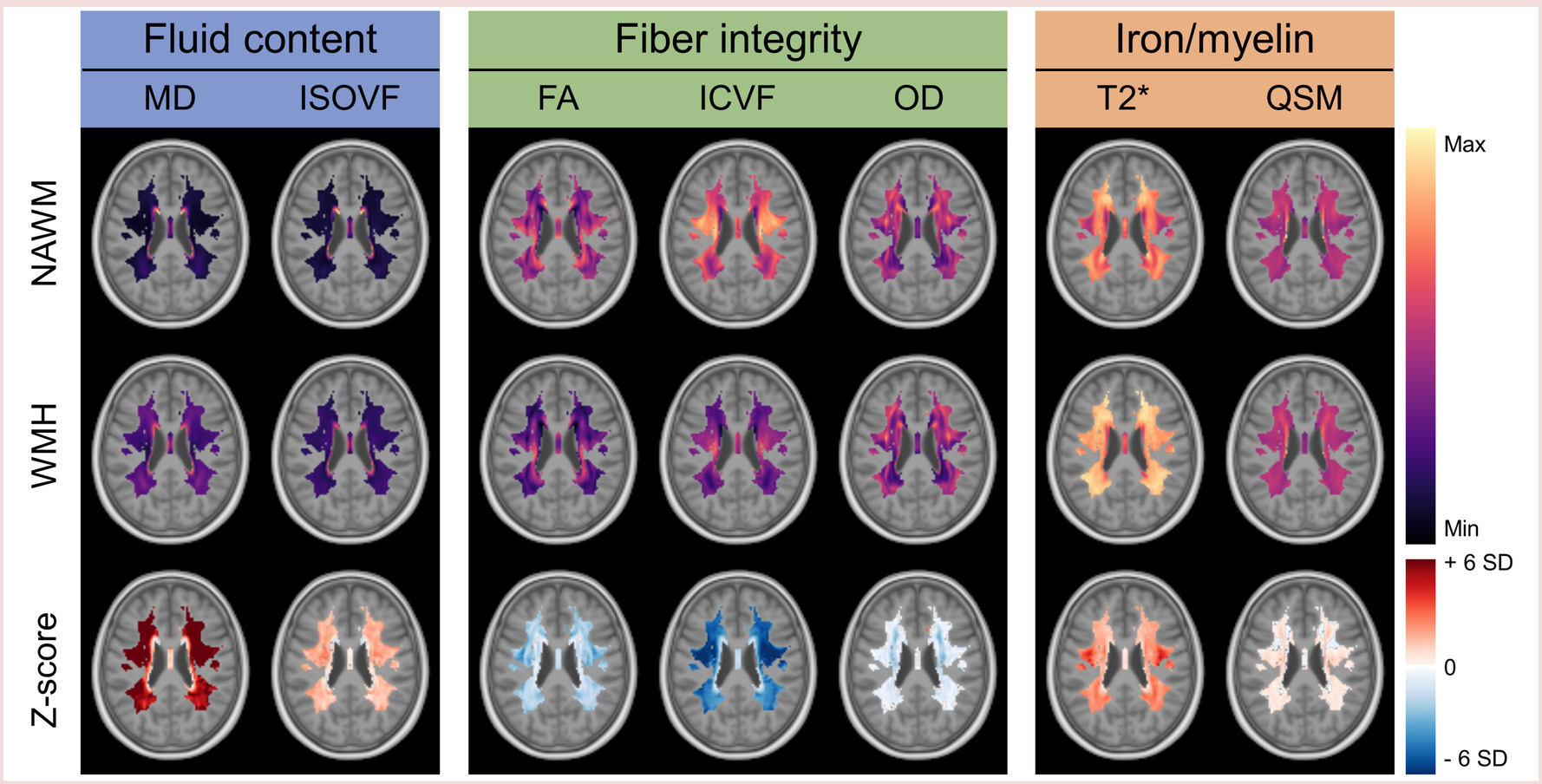


Figure 1. The between-subject voxel-wise averages for each microstructural metric for the two white matter tissue types (first row: NAWM; second row: WMH) are first computed, only including voxels where the prevalence of NAWM labels across subjects is more than 5000 and the prevalence of WMH labels is more than 50. Secondly, voxel-wise z-scores are computed from these maps, with regions in red showing higher microstructural values in WMH compared to NAWM and the opposite pattern for regions in blue. Each column represents a microstructural metric, which are grouped by biological sensitivity: blue for fluid-senstive metrics, green for fiber-sensitive metrics, and orange for iron- and myelin-sensitive metrics.

Fig. 2. Spatial clusters of microstructurally-similar WMHs

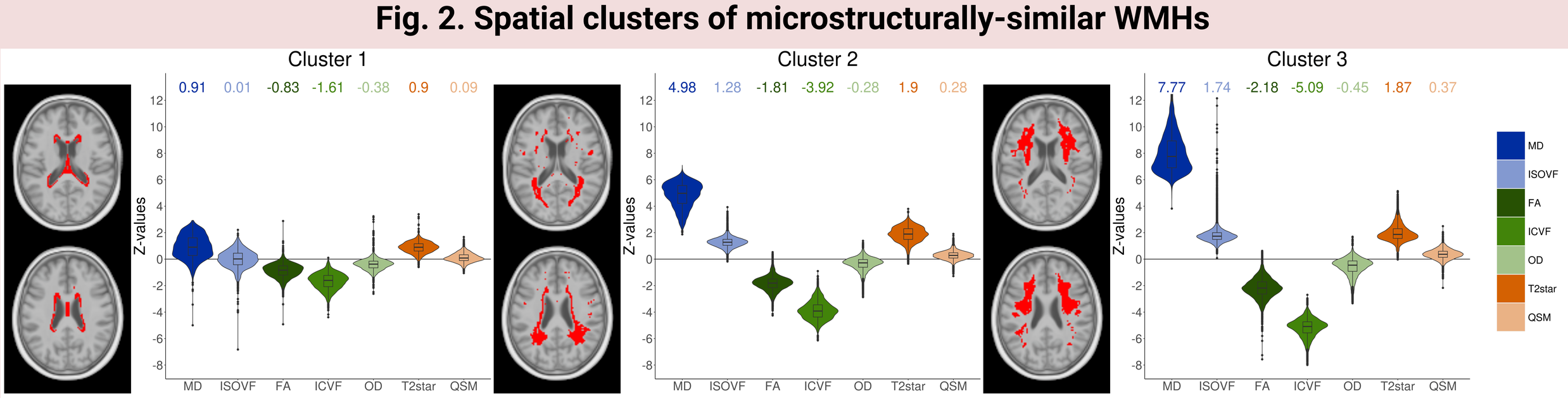


Figure 2. The red overlay on the brain image represent the locations of the voxels within each cluster in template space and the violin plots represent the microstructural abnormality distributions of voxels included in the clusters. The median values of those distributions are shown.

CONCLUSION

- Using a parcellation-free approach in a large aging cohort, we described the spatial dynamics of WMH microstructural abnormality
- WMHs in different areas showed a similar pattern of microstructural abnormality, indicating a continuum rather than a clear differentiation.
- WMHs in anterior regions showed higher abnormality for fluid- and fiber-sensitive metrics compared to posterior regions

References and abbreviations

[1] Wardlaw et al., *The Lancet Neurology,* 2019
[2] Kim et al., *Biological Psychiatry*, 2008

Abbreviations: white matter hyperintensities (WMHs), normal-appearing white matter (NAWM), diffusion tensor imaging (DTI), neurite orientation and dispersion density imaging (NODDI), mean diffusivity (MD), fractional anisotropy (FA), intracellular volume fraction (ICVF), isotropic volume fraction (ISOVF), orientation dispersion (OD), quantitative susceptibility mapping (QSM)