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The Impact of Multiple Sclerosis Lesion Tract Burden on the Cortex

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INTRODUCTION

- Multiple sclerosis (MS) is an immune-mediated degenerative disease affecting the central nervous system and is characterized by inflammatory and demyelinating lesions (Roosendaal et al., 2009)
- Although these lesions are prominently localized to white matter, there are also lesions in the cortical grey matter, which are much harder to detect with conventional MRI
- Furthermore, white matter lesions may have diaschisis effects on connected cortical areas.
- Understanding the spatial relationship between white matter lesion burden and changes in the cortex could yield new insight into the pathophysiology of MS
- In this work we sought to determine if the lesion burden in white matter tracts is correlated with various MR measures in the adjacent cortex

METHODS

- 202 relapsing remitting MS (RRMS) patients (151-F, mean age 44, ranging from 23 to 60) receiving an approved disease modifying therapy were scanned on a 3T MR scanner (GE Discovery 750)
- 3D T1w and FLAIR images were acquired with isotropic 1 mm and 1 x 1 x 4 mm resolutions respectively
- DTI data were acquired with a 45-direction b=1000 protocol, 2 mm isotropic resolution
- MT contrast was generated using an RF pulse 1600 Hz off-resonance, 1 mm x 1 mm x 2 mm
- For each subject, all images were registered to the T1w for using ANTs (Advanced Normalization Tools v2.1. 2018)
- WM lesions were segmented on the FLAIR images using a lesion predication algorithm in the LST toolbox of SPM (Schmidt et al., 2012)
- The John Hopkin's University (JHU)-DTI atlas (Wakana et al., 2007) was registered to each subject, and FreeSurfer was used to segment the cerebral cortex (FreeSurfer v6.0.0. 2018)
- Two expert viewers assigned the DK-atlas cortical regions to corresponding tracts, as shown in Figure 1
- Several lesion burden features were considered: percent of tract with lesion, the lesion mean MD, FA, and MTR
- The relationship between these measures and the following cortical measures were examined: cortical thickness, MD, FA, and MTR

RESULTS

- Figure 2 shows scatter plots of each lesion burden feature vs. each cortex feature
- No combination showed a significant correlation
- Although there is some kurtosis in the two-dimensional relationships, this is mostly in a single parameter direction, rather than with both parameters, indicating a skew in the underlying features, further indicating that there is no dependence
- Although not shown here, the log percent lesion volume of the tract yielded a more normal two-dimensional distribution
- In general, both the tract burden and cortex features were within the expected ranges of previous studies

CONCLUSIONS

- Our results suggest that there is little impact on the cortex of increasing lesion burden in the connected white matter tract, and that white matter and grey matter pathology evolve independently
- Although some studies have indeed found non-local effects of brain lesions, with the measurements reported on here, we do not see a diaschisis effect
- Further considerations of how to define tract and cortical pathology burden will be investigated to strengthen this study

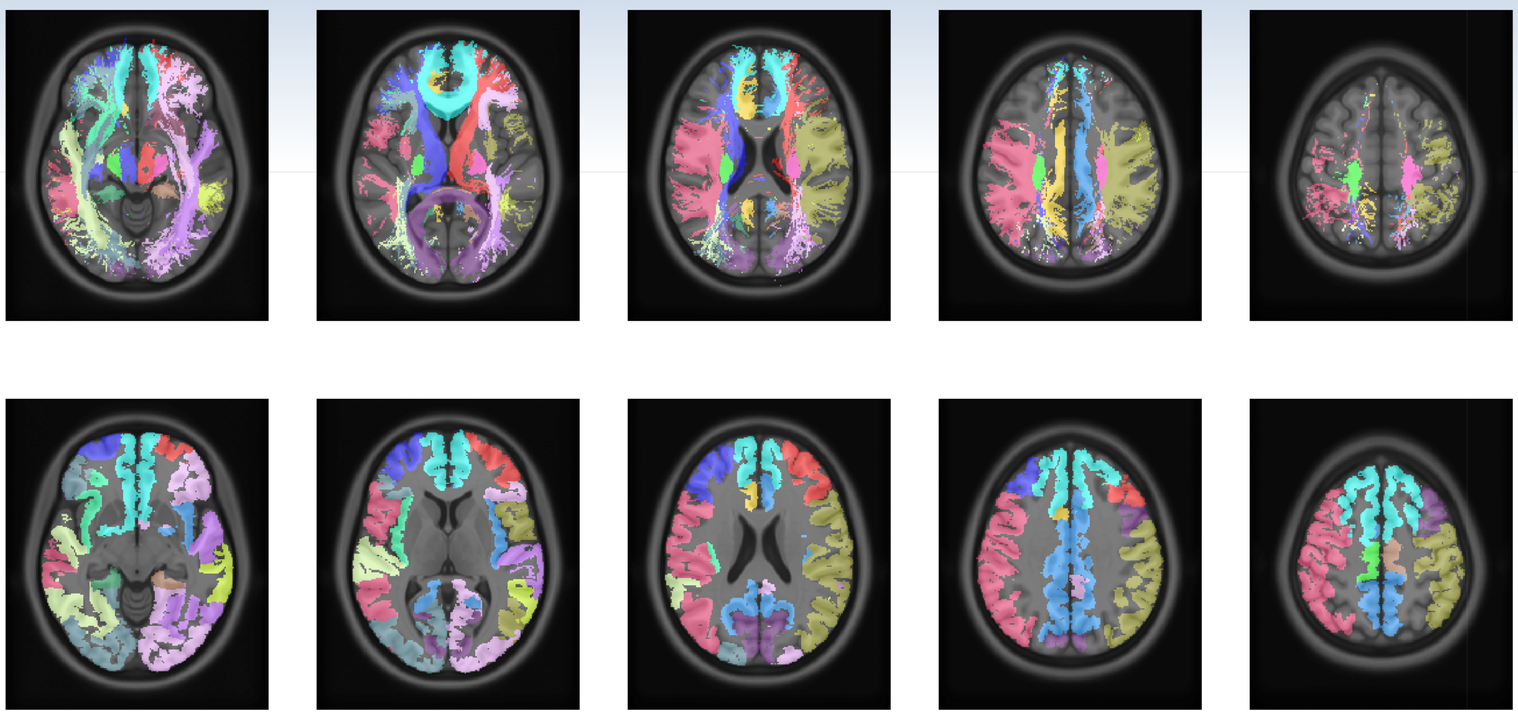

Figure 1: Atlases and cortical regions used in analysis. Upper row: tracts from the JHU-DTI atlas. Lower row: cortical regions assigned to each tract (matching colors).

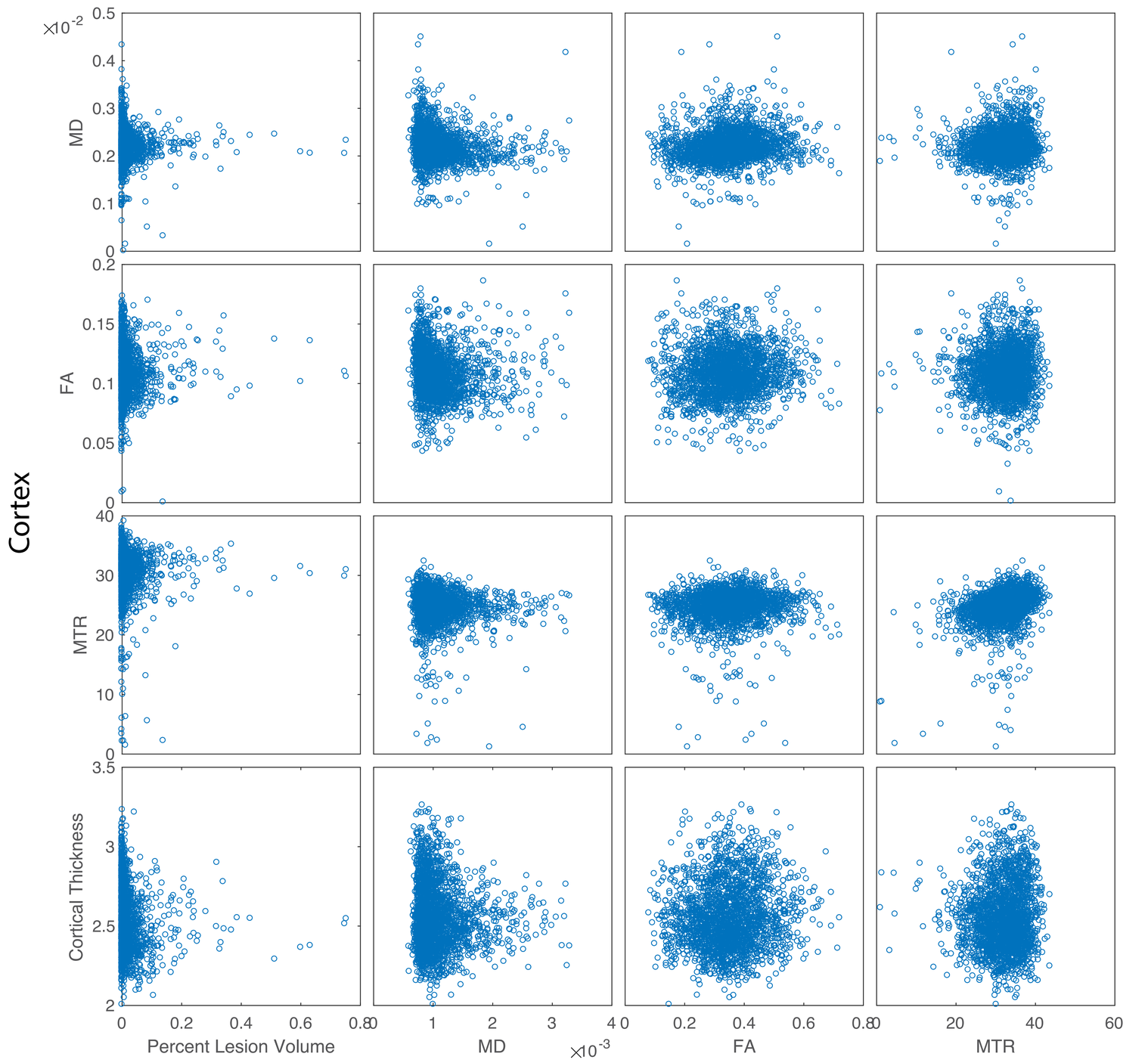

Figure 2: Cortex vs Lesion Burden. Four types of lesion burden: Percent lesion volume, average MD, average FA and average MTR of the lesions in the tract. There are also four cortical features, including average MD, FA, MTR and cortical thickness. No significant correlations are observed.

REFERENCES

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Looking west from Whitetooth Mountain, into Glacier National Park in Canada