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A CORTICOCENTRIC MODEL FOR MS PATHOGENESIS

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Background Degeneration of central nervous system normal appearing white matter (NAWM) underlies disability and progression in multiple sclerosis (MS). Axon loss typifies NAWM degeneration.

Objective To assess correlation between cortical lesion load and magnetisation transfer ratio (MTR) of the NAWM in MS, in order to test the hypothesis that cortical lesions cause NAWM degeneration.

Methods Nineteen patients with MS underwent 7T magnetisation-prepared-rapid-acquisition-gradient-echo (MPRAGE), and magnetisation transfer ratio (MTR) brain MRI. Cortical lesions were identified using MPRAGE and MTR images of cortical ribbons. White matter lesions (WMLs) were segmented using

MPRAGE images. WML maps were subtracted from white matter volumes to produce NAWM masks. Pearson correlation was calculated for NAWM MTR vs cortical lesion load, and WML volumes.

Results Cortical lesion volumes and counts all had significant correlation with NAWM mean MTR. The strongest correlation was with cortical lesion volumes obtained using MTR images ($r=-0.6874$, $p=0.0006$). WML volume had no significant correlation with NAWM mean MTR ($r=-0.08706$, $p=0.3615$).

Conclusion Our findings are consistent with the hypothesis that cortical lesions cause NAWM degeneration. This implicates cortical lesions in the pathogenesis of NAWM axon loss, which underpins long-term disability and progression in MS.