What drives MRI-measured cortical atrophy in multiple sclerosis?

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Research question and background
Cortical atrophy, assessed with magnetic resonance imaging (MRI), is an important outcome measure in multiple sclerosis (MS) studies. However, the underlying histopathology of cortical volume measures is unknown. We investigated the histopathological substrate of MRI-measured cortical volume in MS using combined post-mortem imaging and histopathology.

Methods and tissues used
MS brain donors underwent post-mortem whole-brain in-situ MRI imaging. After MRI, tissue blocks were systematically sampled from the superior and inferior frontal gyrus, anterior cingulate gyrus, inferior parietal lobule, and superior temporal gyrus. Histopathological markers included neuronal, axonal, synapse, astrocyte, dendrite, myelin, and oligodendrocyte densities. Matched cortical volumes from the aforementioned anatomical regions were measured on the MRI, and used as outcomes in a nested prediction model.

Results and conclusion
Forty-five tissue blocks were sampled from 11 MS brain donors. Mean age at death was 68±12 year, post-mortem interval 4±1 hours and disease duration 35±15 years. MRI-measured regional cortical volumes varied depending on anatomical region. Neuronal density, neuronal size and axonal density were significant predictors of GM volume. In patients with long-standing disease, neuronal and axonal pathology are the predominant pathological substrates of MRI-measured cortical volume in chronic MS.