What drives MRI-measured cortical atrophy in multiple sclerosis?

Popescu, MD*[1], V., Klaver, R., MSc*[2], Voorn, P., PhD[2], Galis-de Graaf[2], Y., Knol, D.L., PhD, [3] Twisk, J.W.R., PhD[3], Versteeg[1], A., Schenk, G.J., PhD [2]; Van der Valk, P., PhD[4], Barkhof, F., PhD[1], De Vries, H.E., PhD[5], Vrenken, H., PhD[1,6] and Geurts, J.J.G., PhD[2]

[1]Department of Radiology and Nuclear Medicine, [2]Department of Anatomy & Neuroscience, [3]Department of Epidemiology and Biostatistics, [4]Department of Pathology, [5]Department of Molecular Cell Biology and Immunology, [6]Department of Physics and Medical Technology, VU University Medical Center, Neuroscience Campus Amsterdam, The Netherlands

*both authors contributed equally

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.