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Evolution of cortical lesions and domain-specific cognitive decline in multiple sclerosis

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Introduction:

The evolution of cortical lesions over time remains understudied, particularly in relation to cognitive decline, due to a lack of longitudinal data. Also, current knowledge of the impact of cortical lesions on specific cognitive domains is limited.

Objectives/Aims:

To identify temporal changes in cortical lesions and how these relate to decline in predefined cognitive domains during 10-year follow-up.

Methods:

In this longitudinal study, 96 people with MS (mean age 48.1 ± 10.2 years, 68 females) underwent structural 3T MRI (T1 and FLAIR) and neuropsychological assessment (expanded BRB-N) at baseline and 10-year follow-up. At both time points, cognitive functioning was evaluated based on neuropsychological tests reflecting seven cognitive domains. Cortical lesions were scored and segmented on artificial intelligence-enabled double inversion-recovery images at each time point. Annual change in cortical lesion count was calculated, and associated with baseline cortical and white matter lesion load and domain-specific annual change in *Z*-scores relative to healthy data during follow-up.

Results:

People with MS had a median cortical lesion count at baseline of 7 (range 0 – 73). During follow-up (mean 10.4 ± 1.2 years), cortical lesion counts increased by a median count of 4 (range -2 – 71) in the total cohort. Median annual change rate was 0.39 (range -0.20 – 7.58), with trends towards higher rates in cognitively-impaired MS at baseline (P=0.061). Both baseline cortical lesion count and baseline white matter lesion volume were significantly associated with annual cortical lesion increase (both P<0.001). Log-transformed annual increases in cortical lesion counts were significantly associated with the degree of annual overall cognitive decline (P=0.046), specifically in the executive functioning domain (P=0.007). Effects of cortical lesion count increases on cognition appeared independent of baseline white matter lesion volume (P=0.025), but dependent of baseline cortical lesion count (P=0.541). Decline in other cognitive domains did not show significant associations with cortical lesion count increases.

Conclusion:

Cortical lesion counts increased during 10-year follow-up. Increases were related to cognitive decline and specifically decline in executive functioning, independent of white matter lesion burden. Increases in cortical lesions may offer potential for uncovering cognitive heterogeneity among individuals with MS. Future analyses will additionally focus on the spatial evolution of cortical lesions in relation to cognition and grey matter neurodegeneration.

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