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Structural and Clinical Correlates of a Periventricular Gradient of Neuroinflammation in Multiple Sclerosis

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Study Question

Does innate immune cell activation in patients with multiple sclerosis (MS) decrease as the distance from the ventricular CSF increases, and is there a relationship between the periventricular gradient of neuroinflammation, microstructural damage and disability?

What Is Known and What This Paper Adds

Past studies have yielded evidence that MS-related microstructural damage is most severe in CSF-facing regions of the brain. This investigation's results suggest that in patients with MS, the innate immune cell activation predominates in periventricular regions, and is associated with microstructural damage and disability worsening.

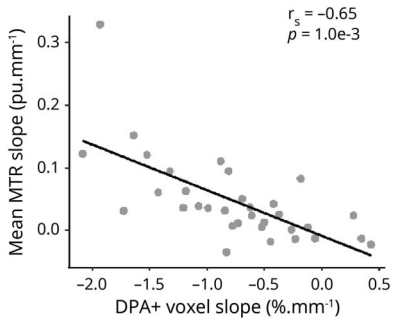
Methods

For this cross-sectional study, the investigators recruited 37 patients with MS, of whom 11 had relapsing-remitting MS and 26 had progressive MS, and 19 healthy controls (HCs). These participants underwent MRI and dynamic PET with [^{18}F]-DPA714, a TSPO radiotracer binding to innate immune cells. The investigators prepared voxelwise [^{18}F]-DPA714 distribution volume ratio (DVR) parametric maps, and they identified voxels characterized by innate immune cell activation (i.e., DPA$^+$ voxels) as those with DVRs that were ≥20% greater than their positional equivalents in the HCs' maps. The investigators segmented the white matter (WM) into 3-mm-thick concentric bands radiating out from the ventricular surface to the cortex, and for each band, they calculated the percentage of voxels that were DPA$^+$ and the mean magnetization transfer ratio (MTR), which served as a metric for microstructural damage. The primary outcomes were changes in DPA$^+$ voxel percentages and MTRs across the bands.

Results and Study Limitations

Compared with the HCs, the patients with MS had a higher DPA$^+$ voxel percentage and a lower mean MTR in the periventricular WM, and WM bands further from the ventricular surface had lower DPA$^+$ voxel percentages and higher mean MTRs. Decreasing DPA$^+$ voxel percentages correlated with increasing MTRs. The present study's limitations include the suboptimal specificity of TSPO tracers for innate immune cells and their lack of utility for differentiating between proinflammatory and regulatory innate immune cells.

Figure Correlation Between the Slopes for MTRs and DPA+ Voxel Percentages in WM Bands Radiating out From the Ventricular Surface



Study Funding and Competing Interests

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