

Research Highlights

Highlights from the latest articles in imaging



MRI techniques have become invaluable tools to investigate the characteristics and dynamics of multiple sclerosis (MS) pathology, as well as the effects of treatments. Here we present recent evidence supporting the use of conventional, as well as advanced, MRI methods as diagnostic and prognostic markers in MS.

Use of perivenous lesion appearance to distinguish multiple sclerosis lesions from asymptomatic white matter brain lesions

Evaluation of: Tallantyre EC, Dixon JE, Donaldson I *et al.*: Ultra-high-field imaging distinguishes MS lesions from asymptomatic white matter lesions. *Neurology* 76(6), 534–539 (2011).

In this article, we present recent evidence supporting the use of conventional, as well as advanced, MRI methods as diagnostic and prognostic markers in MS.

White matter (WM) inflammatory demyelinating lesions are often identified in MS patients as areas of hyperintense signal on T_2 -weighted MRI images. However, as other factors such as age or vascular pathology may also cause hyperintensities on T_2 -weighted MRI images, the specificity of these lesions for inflammatory demyelinating pathology is low. The high anatomical resolution of ultra-high-field (7T) MRI can contribute to identifying features of MS pathology, such as the perivenular localization of MS lesions, and, thus, help to identify MS lesions.

Using 7T T_2^* -weighted images, the study by Tallantyre *et al.* compared 28 clinically definite MS patients, two patients with clinically isolated syndromes (CIS) and 17 non-MS patients

with incidental WM lesions, with the aim to distinguish MS patients from non-MS patients based on the proportion of perivenous WM lesions visually identified.

Results from the study showed that WM lesions in MS patients were more likely to be perivenous than in the non-MS group (80 vs 19%, respectively). MS patients also had a higher proportion of perivenous lesions than CIS patients. Regression analysis showed that perivenous lesions were predictive of a clinically definite MS diagnosis when controlling for confounders such as lesion volume and location, age and gender. The cut-off for accurate diagnostic prediction of clinically definite MS in patients with WM lesions was the presence of more than 40 perivenular WM lesions.

Using the perivenous appearance of WM lesions in 7T T_2^* -weighted MRI, this study was able to accurately distinguish all patients with clinically definite MS from non-MS patients. The identification of true MS lesions on clinical 3T scanners with pathologically specific insights from ultra-high-field 7T MRI represents the next step of research, along with the assessment of the predictive value of perivenous lesions for conversion to MS in patients with CIS.

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Regional gray matter volume differences between neuromyelitis optica and MS

Evaluation of: Duan Y, Liu Y, Liang P *et al.*: Comparison of grey matter atrophy between patients with neuromyelitis optica and multiple sclerosis: a voxel-based morphometry study. *Eur. J. Radiol.* DOI:10.1016/j.ejrad.2011.01.065 (2011) (Epub ahead of print).

While previous studies using voxel-based morphometry (VBM) have investigated gray matter (GM) atrophy in various phenotypes of MS, differences in patterns of GM atrophy between neuromyelitis optica (NMO) and MS patients remain untested. The study by Duan *et al.* used VBM to identify localized differences in GM volume between patients with NMO and patients with MS, and to correlate

these differences with clinical measures, such as the Expanded Disability Status Scale, disease duration and brain lesion volume on T₂-weighted images.

In total, 26 NMO patients, 26 age- and sex-matched relapsing–remitting MS (RRMS) patients and 26 healthy controls underwent a structural MRI scan on a 1.5T system to obtain T₁- and T₂-weighted images. Lesion volumes were measured in each patient on T₂-weighted images, and regional GM volumes were determined from T₁-weighted images using an optimized VBM method.

While RRMS patients showed significant localized GM volume reductions in the thalamus, caudate, mammillary body, hippocampus and numerous cortical regions compared with the controls, NMO patients did not, suggesting that brain GM

is relatively spared in NMO. When the two patient groups were directly compared, RRMS patients showed significantly more GM volume loss in the thalamus, caudate, left parahippocampal gyrus, right hippocampus and right insula, suggesting that deep GM atrophy may be a distinguishing feature between RRMS and NMO patients. Although lesion volumes were quantified in both NMO and RRMS patients, only RRMS patients showed a negative correlation between T₂ lesion volume and volumes of the right caudate and thalamus bilaterally, suggesting a relationship between neural degeneration and lesion volumes in MS.

Future work will expand these results longitudinally to correlate brain GM atrophy with clinical changes in NMO and MS, and to examine the contribution of spinal cord pathology to these results.

Relationship between diffusion tensor imaging parameters and spinal cord histology in MS

Evaluation of: Klawiter EC, Schmidt RE, Trinkaus K *et al.*: Radial diffusivity predicts demyelination in *ex vivo* multiple sclerosis spinal cords. *Neuroimage* 55(4), 1454–1460 (2010).

Multiple sclerosis is an inflammatory disease of the CNS, which involves demyelination, axonal loss and gliosis. Diffusion tensor imaging (DTI) can provide information about CNS structural architecture and integrity by measuring the diffusion of water molecules parallel (axial diffusivity) or perpendicular (radial diffusivity) to the axons. Previously, brain DTI has been used in combination with neuropathology in *ex vivo* studies

to improve our understanding of the structural imaging correlates of *in vivo* MS pathology.

The study by Klawiter *et al.* examined the cervical spinal cord of nine MS patients and five controls to determine the correlation between histopathology and DTI parameters, including axial and radial diffusivity. A 4.5T scanner was used to acquire diffusion-weighted images and T₂-weighted images of the spinal cord. Regions of interest, including WM tracts and visible lesions, were identified in both the MRIs and the fixed spinal cord slices. The MRIs were registered to the fixed slices, and the DTI parameters, as well as the amount of demyelination and axonal count, were quantified for each region of interest.

Comparison between histological and DTI measures showed that increased radial diffusivity correlated with the level of demyelination, even when controlling for axonal loss. DTI was also able to distinguish between normal-appearing WM and areas of demyelination in the MS spinal cord. However, in contrast to previous studies, decreased axial diffusivity did not correlate with higher levels of axonal loss, possibly because of processes of gliosis accompanying the neuropathological remodeling of chronic MS lesions. However, DTI parameters were altered in MS patients compared with controls, even in areas of normal-appearing WM, suggesting the presence of diffuse abnormalities even in the least-affected regions of MS spinal cords.



Correlation between infratentorial lesion load and risk of falls in MS patients

Evaluation of: Prosperini L, Kouleridou A, Petsas N *et al.*: The relationship between infratentorial lesions, balance deficit and accidental falls in multiple sclerosis. *J. Neurol. Sci.* 1504(1–2), 55–60 (2011).

Damage to sensory integration pathways in MS can lead to a lack of balance and falls, resulting in a high level of morbidity. Clinical measures and demographic information, as well as disability scales, have been used with minimal success in discriminating between patients who are more and less likely to fall. This study quantified balance stability in patients with MS by using static posturography, and related it to structural MRI damage in infratentorial regions involved in balance control in order to identify patients at high risk of falls.

Static posturography was performed on 31 MS patients with balance problems. Patients stood on a force platform. The displacements of the center of pressure (COP) during standing and the velocity

of these displacements quantified balance stability. A 1.5T MRI scanner was used to obtain T_2 - and T_1 -weighted gadolinium-enhanced images. Lesion volume was calculated on the T_1 and T_2 images in infratentorial regions of interest.

Patients who reported at least one fall in the past 6 months ('fallers') had a greater T_2 lesion volume in the brainstem and middle cerebellar peduncles (MCPs) than 'nonfallers'. The fallers also had less balance stability than the nonfallers. Brainstem T_2 lesion volume in all subjects correlated significantly with the velocity and COP displacement on the force platform. MCP and brainstem T_2 lesion volume, as well as the COP displacement with the patients' eyes closed, were most predictive of the number of falls in the past 6 months.

The MCPs and the brainstem include WM pathways, connecting the spinal cord and cerebellum to brain regions. Therefore, damage to these regions can affect control of balance more than damage to other brain regions. Their assessment in MS patients may be useful for an earlier identification of patients at risk of falls.