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Diffusion Tensor MR Imaging of Gray Matter in Different Multiple Sclerosis Phenotypes

In this issue of the *AJNR*, Bozzali et al describe an application of diffusion tensor imaging (DTI) in the evaluation of gray matter abnormality in different clinical phenotypes of multiple sclerosis (MS). The authors describe an automated technique, based on fractional anisotropy thresholding (1), to segment the cerebral gray matter and determine mean diffusivity (*D*) changes. Diffusion tensor MR imaging has been used extensively to evaluate cerebral white matter in normal development and in many disease states (2). As discussed in this article, DTI is emerging as a tool in the evaluation of gray matter abnormalities as well.

Numerous reports of MR imaging studies in the literature have documented that the normal-appearing white matter, as seen on conventional MR images in patients with MS, can indeed be abnormal. MR techniques such as diffusion-weighted imaging, magnetization transfer imaging (MTI), and MR spectroscopy have been proven to be sensitive and robust methods for detecting and quantifying these changes in MS. Recently, increased attention has been paid to MR investigations of the gray matter, in addition to the white matter. Postmortem studies have long shown that MS lesions, while predominantly found in the white matter, are also seen in the gray matter (eg, corticomedullary junction, cortex, deep gray matter) (3). Conventional MR imaging provides limited information regarding the cerebral gray matter, and long-TR sequences are generally used to determine if abnormally high signal intensity is present. Techniques such as diffusion-weighted imaging and MTI have the potential to overcome these limitations and improve our understanding of the pathophysiology of MS.

In the current study, gray-matter *D* histograms in different MS phenotypes (relapsing remitting [RRMS], secondary progressive [SPMS], and primary progressive [PPMS]) and healthy control subjects were compared. The results of this study show that the *D* histograms in the cerebral gray matter in all patients with MS were greater than that of healthy control subjects. These values were greater in patients with SPMS than in those with RRMS. Interestingly, the authors report that all of the *D* histogram–derived metrics did not differ in patients with RRMS, compared with those in control subjects. Previous MTI studies in which gray matter was segmented in patients with MS have revealed a gray matter abnormality in this phenotype (4). Perhaps the results of the current study reflect the particular patient population included in the RRMS subtype, because postmortem studies have revealed that gray matter involvement is highly variable among patients with MS. Patients with SPMS in the current study significantly differed from the control subjects; these differences may have been related to the greater T2 lesion volume reported. Differences in *D* histograms were found between the two major progressive forms of the disease; these findings implied that gray matter is more severely affected in those with SPMS than in others. The greater range of histogram values found in SPMS may indicate a more heterogeneous profile of gray matter lesions.

As the authors discuss, a limitation of this segmentation technique is that fractional anisotropy thresholding may theoretically lead to the classification of abnormal subcortical white matter as gray matter pixels that contribute to the *D* histogram changes. Partial-volume effect from the CSF might also contribute to increasing *D* values. This effect might be more prominent in patients with SPMS because the authors report decreased mean brain volumes in these patients.

Conventional MR imaging, even quantitative imaging, is flawed by the inability to consistently correlate the results with disability (5, 6). One important aspect of studying the gray matter in patients with MS is attempting to elucidate the pathophysiology of cognitive impairment in MS (abnormalities in recent memory, abstract reasoning, sustained attention, and information processing speed) (7). Demyelination and axonal degeneration have been attributed to the disruption of neural connections among cortical association areas and between cortical and subcortical structures (8). The results of the current study show that gray matter pathology in the patients with SPMS is more extensive than that in patients with RRMS. This finding may help explain the pronounced cognitive and neuropsychological impairment usually seen in patients with SPMS.

The pathogenesis of gray matter abnormality in MS is still unknown. A combination of factors are likely to be responsible for the gray matter disease, including focal lesions in the gray matter and neuronal cell-body disorders secondary to axonal destruction in white matter lesions that result in retrograde degeneration. The ability to determine the full extent of the pathologic changes in MS with imaging is important for many reasons, including the determination of the prognosis and response to therapy, the design of new therapies, and the monitoring of disease activity, particularly when one considers the dynamic nature of the disease. We should continue to develop and val-

idate new MR methods of probing the microstructural cerebral architecture that can provide insight into understanding the pathophysiology of MS.

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References

1. Cercignani M, Bozzali M, Iannucci G, Comi G, Filippi M. **Magnetization transfer ratio and mean diffusivity of normal appearing white and grey matter from patients with multiple sclerosis.** *J Neurol Neurosurg Psychiatry* 2001;70:311–317
2. Pierpaoli C, Jezzard P, Basser PJ, Barnett A, DiChiro G. **Diffusion tensor MR imaging of the human brain.** *Radiology* 1996;201:637–648
3. Brownell B, Hughes JT. **The distribution of plaques in the cerebrum in multiple sclerosis.** *J Neurol Neurosurg Psychiatry* 1962;25:315–320
4. Ge Y, Grossman RI, Udupa JK, Babb JS, Kolson DL, McGowan JC. **Magnetization transfer ratio histogram analysis of gray matter in relapsing-remitting multiple sclerosis.** *AJNR Am J Neuroradiol* 2001;22:470–475
5. van Walderveen MA, Barkhof F, Hommes OR, et al. **Correlating MRI and clinical disease activity and clinical disease activity in multiple sclerosis: relevance of hypointense lesions on short-TR/short-TE (T1-weighted) spin-echo images.** *Neurology* 1995;45:1684–1690
6. Fulton JC, Grossman RI, Udupa J, et al. **MR lesion load and cognitive function in patients with relapsing-remitting multiple sclerosis.** *AJNR* Am J Neuroradiol 1999;20:1951–1955
7. Peyser JM, Rao SM, La Rocca NG, et al. **Guidelines for neuropsychological research in multiple sclerosis.** *Arch. Neurol* 1990;47:94–97
8. Comi G, Filippi M, Martinelli V, et al. **Brain magnetic resonance imaging correlates of cognitive impairment in multiple sclerosis.** *J Neurol Sci* 1993;115:S66–S73