

EDITORIAL COMMENTARY

Clinical and magnetic resonance imaging heterogeneity in multiple sclerosis

All clinicians who see patients with multiple sclerosis will be profoundly aware of the highly variable and unpredictable clinical course. Surprisingly, the mechanisms which account for clinical heterogeneity are poorly understood. A clearer understanding of these mechanisms is desirable, as it may open the way to new and more effective therapeutic strategies.

It is likely that pathological heterogeneity underlies the different clinical courses. A postmortem study comparing primary and secondary progressive multiple sclerosis has shown significantly less inflammation in the primary progressive group,¹ a finding which is supported by the paucity of gadolinium enhancing lesions seen in this subgroup.² Serial enhanced MRI has also shown less inflammatory activity in patients with benign MS, but greater numbers of focal enhancing lesions in those with active relapsing remitting or relapsing secondary progressive disease. Another striking finding from MRI has been the lower overall brain lesion load seen in primary progressive multiple sclerosis, but in the spinal cord, similar lesion loads are seen in all clinical subgroups.

In the present issue of the *Journal* (pp 153–7) there is a report from Japan describing differences in clinical and MRI findings in a group of Japanese patients with multiple sclerosis, when compared to white cohorts described in the literature.³ In particular, a higher proportion of Japanese patients have clinical and radiological involvement confined to the spinal cord and optic nerves, and although brainstem involvement is often seen clinically in both Japanese and white patients, the present study reports a somewhat lower frequency of clinically manifest cerebellar features and a much lower incidence of cerebellar lesions on MRI in the Japanese group. Although methodological

factors may contribute to these differences (for example, some previous studies in white patients may have included the cerebellar peduncles in the cerebellum), the authors argument that differences in lesion distribution may relate to genetic differences in the two ethnic populations is a plausible one.

Genetic factors may contribute to the variations in lesion site expression and they might also affect their pathological severity. The latter is probably more important in terms of clinical prognosis; in particular there is considerable evidence that axonal damage, inferred using putative MR markers, is more common in those with progressive forms of the disease.⁴ Whereas much work has been done looking at genetic factors involved in susceptibility to multiple sclerosis,⁵ rather less has been done in exploring genetic mechanisms which might affect the disease course. Further studies in this area should give fruitful insights, particularly if complemented by MR findings on the in vivo pathology.

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- 2 Thompson AJ, Kermode AG, Wicks D, *et al*. Major differences in the dynamics of primary and secondary progressive multiple sclerosis. *Annals of Neurology* 1991;29:53–62.
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- 4 Van Walderveen MAA, Kamphorst W, Scheltens P, *et al*. Histopathological correlator of hypointense lesions on T1-weighted spin echo MRI in multiple sclerosis. *Neurology* 1998;50:1282–8.
- 5 Sawcer S, Jones HB, Feakes R, *et al*. A genome screen in multiple sclerosis reveals susceptibility loci on chromosome 6p21 and 17q22. *Nat Genet* 1996;13:464–8.