

## SHORT REPORT

## Does hemispheric dominance influence brain lesion distribution in multiple sclerosis?

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### Abstract

To evaluate whether hemispheric lesion distribution in multiple sclerosis is related to the uneven interhemispheric localisation of cerebral function, a 10 item self administered questionnaire evaluating hand preference and supratentorial brain MRI was obtained in 23 patients with clinically definite multiple sclerosis. The mean degree of hand preference was +74 (range -86 to +100). The median lesion volumes were 7275 (range 1045-22 440) mm<sup>3</sup> for the left hemisphere and 5385 (range 1010-19 490) mm<sup>3</sup> for the right hemisphere. The degree of hand preference correlated with the index of interhemispheric lesion distribution ( $P = 0.02$ ). The data suggest that local events, possibly related to specialisation of hemispheric function, might be responsible for the increased vulnerability of the dominant hemisphere to the pathological process of multiple sclerosis.

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Keywords: multiple sclerosis; hemispheric dominance; magnetic resonance imaging; hand preference

Multiple sclerosis is a multifactorial disease in which immunological factors and endocrine circuits are believed to play an important part in the development of lesions.<sup>1</sup> Immune and endocrine circuits are regulated in specialised brain regions that are mainly located in the dominant hemisphere. Rodents with experimental ablation of the left hemispheres had a significant decrease in number and functionality of circulating immune cells compared with animals with contralateral ablation.<sup>2</sup> Interhemispheric differences not only affect the neuroimmunoenocrine functions but, in humans, also seem to influence the distribution of neuronal cell degeneration within the CNS.<sup>3</sup>

Magnetic resonance imaging is effective in evaluating the lesion load and distribution in multiple sclerosis.<sup>4</sup> To assess whether the interhemispheric distribution of multiple sclerosis lesions may be influenced by the uneven interhemispheric localisation of cerebral functions, we measured the MRI lesion volume in the brain hemispheres of patients with

multiple sclerosis and assessed the correlation with the degree of hand preference.

### Methods and results

We evaluated 23 patients (seven men and 15 women; mean age 34.7 (range 18-54) years) with clinically definite multiple sclerosis (mean duration of the disease 9.3 (range 2-19) years, mean expanded disability status scale score 3.0 (range 1.0-5.5)) admitted to the clinics of Department of Neurology, University of Milano, San Raffaele Scientific Institute between 1 January 1994 and 30 June 1994. To investigate hand preference, a 10 item self administered questionnaire was used.<sup>5</sup> Briefly, each patient was asked to mark a "+" in the appropriate column if the activity was preferentially carried out using one hand, a "++" if in no way the other hand would be used, and a "+" in both columns in case of indifference on which hand to use. Hand preference was calculated by subtracting the number of + signs in the column of the left hand from the number of + signs in the column of the right hand and dividing the difference by the total number of + signs and multiplying the result by 100. The calculated hand preference varies from -100 (extreme left handedness) to +100 (extreme right handedness). At the time the hand preference questionnaire was completed, a supratentorial brain MRI was obtained with a 1.5 T machine. A 2000/50 SE sequence was used with 5 mm contiguous axial slices oriented parallel to the bicommissural line. The image matrix was 256 × 256 pixels with a field of view of 22 cm. The quantitative semiautomated assessment of the lesion load involved simple threshold segmentation, firstly to isolate the brain from the surrounding tissue, then to identify the white matter hyperintense lesions. A manual review was always performed to correct any error in lesion detection and to calculate the lesion load for each hemisphere. Lesion volume was obtained by simply multiplying lesion areas by slice thickness.<sup>6</sup> Measurements on MRI were always made by the same observer (MF), who was unaware of the hand preference of the patients. The index of interhemispheric lesion distribution (ILD) was calculated according to the following formula:  $ILD = (R - L/R + L) \times 100$  in which R was the lesion volume

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in the right hemisphere and L the lesion volume in the left hemisphere. The correlation between the degree of hand preference and index of ILD was evaluated by the Spearman rank correlation coefficient.

The mean degree of hand preference was +74 (range -86 to +100). These values are comparable with those obtained in a healthy Italian population.<sup>5</sup> The median lesion volumes were 7275 (range 1045-22 440) mm<sup>3</sup> for the left hemisphere and 5385 (range 1010-19 490) mm<sup>3</sup> for the right hemisphere. A significant direct association was found between the degree of hand preference and the index of ILD (Spearman rank correlation coefficient = 0.5; P = 0.02).

### Discussion

In patients with multiple sclerosis longitudinal MRI studies showed that, at the same time, brain lesions behave differently in different regions of the CNS.<sup>7</sup> The finding that new lesions appear while others are shrinking or disappearing indicates that local events might be involved in lesion formation.<sup>4</sup> Our finding that hand preference is directly associated with interhemispheric lesion distribution in multiple sclerosis (for example, an increased degree of right handedness is positively associated with higher values of interhemispheric lesion distribution) suggests that local events, related to hemispheric function specialisation,<sup>2</sup> might be responsible for the increased vulnerability of one of the two hemispheres to the pathological process of multiple sclerosis. The different vulnerability of the two cerebral hemispheres has been already proposed for Alzheimer's disease. A reduced frequency of left handedness was reported in patients with Alzheimer's disease (2.6%) compared with an age matched population (11.1%) and patients with depression (13.7%).<sup>3</sup>

It is difficult to predict which factors might operate in protecting or exposing cerebral hemispheres to autoimmune (or degenerative) processes. Neuroimmunoendocrine circuits, which are relevant in multiple sclerosis

pathogenesis,<sup>1</sup> are known to have a different hemispheric distribution and might be responsible for interhemispheric differences in lesion formation in multiple sclerosis. Moreover, haematogenous factors (effector lymphocytes, cytokines, immunoglobulins, etc) might be differently supplied to the hemispheres as a result of different blood perfusion occurring during hemispheric activation.<sup>8</sup> Immunological factors with potential demyelinating effects are indeed driven to the CNS by the blood stream in animal models of multiple sclerosis and in patients with multiple sclerosis.<sup>9</sup>

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