

## **Outer and inner cortical MTR abnormalities in clinically isolated syndromes**

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### **BACKGROUND:**

Substantial pathology occurs in cortical grey matter (CGM) in MS, with lesions and neuroaxonal loss occurring preferentially in outer (subpial) CGM. In relapse-onset MS, cortical magnetization transfer ratio (cMTR) is abnormal, and more so in the outer compared with deeper cortical layers. It is not known whether earlier a similar gradient in cMTR changes occurs soon after the first symptoms of MS, or is only a feature of more long-standing MS.

### **OBJECTIVE:**

To investigate inner and outer cMTR changes in people soon after a clinically isolated syndrome (CIS) suggestive of MS, and compare cMTR abnormalities in those who remained CIS and those who developed MS within 15 years.

### **METHODS:**

Seventy-two people with optic neuritis (ON) underwent MRI scanning within 6 months of onset (mean age 33.4 years, 51 F) and were followed up 15 years later. Thirty-six healthy controls (HC; mean age 34.0, 24 F) were also scanned.

Using a 1.5T GE Signa scanner, proton-density/T<sub>2</sub>-weighted, T<sub>1</sub>-weighted images, and MTR data were acquired.

Segmentation of lesion filled T<sub>1</sub>-weighted images was performed using the Geodesical Informational Flows algorithm, and the cortex was subdivided into inner and outer bands by calculating the mid-harmonic location using the Laplace equation-based cortical thickness framework. Inner and outer cortical bands were co-registered to MTR data using NiftyReg, and a 90% threshold was applied to CGM probability maps to limit potential partial volume effects).

Between-group differences were examined using SPSS with one-way ANCOVA tests, adjusted for age, gender and brain parenchymal fraction.

### **RESULTS:**

The ON group had significantly lower outer and inner cMTR compared with HC, and the outer-to-inner cMTR ratio was also significantly lower in ON (all  $p < 0.001$ ).

In the ON group, compared with HC, inner and outer cMTR were lower both in those who developed clinically definite MS after 15 years ( $n=56$ ,  $p < 0.001$ ) and in those that remained CIS ( $n=16$ ,  $p < 0.05$ ). Compared with HC, the cMTR ratio was also significantly lower in MS ( $p < 0.001$ ) but not in the CIS group. The outer cMTR and cMTR ratio were both reduced in MS compared to the CIS group ( $p < 0.05$ ).

### **CONCLUSIONS:**

Gradients in cMTR abnormalities - with greater disease effects towards the surface of the brain - are seen soon after a clinically isolated ON, and appear to be related to the subsequent risk of developing MS. This suggests that outer cortex abnormalities are already present early in the course of MS.