Regions of reduced cortical magnetization transfer ratio detected in MS patients using surface-based techniques

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Introduction: The multiple sclerosis imaging community still struggles with the *in vivo* detection of cortical grey matter lesions. While newer sequences can help identify a small fraction of the cortical pathology present, subpial demyelination appears to be largely undetectable [1]. This is despite the fact that these cortical lesions are the most common subtype when sampled at autopsy and tend to extend over multiple gyri, following the shape of the cortical mantle [2]. The problem with conventional imaging of subpial cortical demyelination is that these lesions do not appear to be associated with an appreciable influx of inflammatory cells or edema, and consequently show little alteration of T2 or T1 relaxation times. An additional challenge is the complex geometry and thinness of the cortex, which induce variable amounts of partial volume at the cortical boundaries. Magnetization transfer imaging has been shown to be sensitive to changes in myelin content in white matter [3]. Based on this, we quantified the extent of subpial decreases of magnetization transfer ratio (MTR) of the cortical grey matter, which may indicate regions of cortical demyelination, in groups of MS patients and healthy controls. To increase our sensitivity, we exploited the knowledge gained from pathological studies of the unique geometry of these lesions, and carried out our analyses on two-dimensional parametric surface models of the cortex, instead of the three-dimensional voxel-wise analyses traditionally used.

Methods: Patients - MR scans were obtained for a previous study of patients recruited from the MS Clinic of the Montreal Neurological Institute and Hospital and studied in the Magnetic Resonance Spectroscopy Unit. In the current retrospective analysis, of all eligible progressive MS (MS) patients with a baseline scan, 12 were included after quality control. Twelve normal controls (NC) were then selected from all baseline scans such that both groups were appropriately age and sex matched. Subject demographics can be seen in Table 1.

MRI protocol - All subjects were scanned at the Montreal Neurological Institute on a 1.5T Philips ACS II scanner (Philips Medical Systems, Best, the Netherlands). Oblique axial T1-weighted images were acquired parallel to the antero-posterior commissural line, using a spoiled gradient-recalled echo sequence (TR= 35 ms, TE = 10 ms, 256x256 matrix, 250 mm field-of-view, 60 slices, 3mm thickness, 1 signal average). Images were acquired without and with a 1.2 ms on-resonance, bipolar (1-2'-1) magnetization transfer pulse (20 μT RF field strength) placed just before each slice-selective excitation.

MRI analysis - To calculate the MTR for each patient, the MT image volume acquired with the saturation pulse (Sat) was first linearly registered (mritoself, McConnell Brain Imaging Centre) to the volume without the saturation pulse (NoSat). The MTR image volume was then calculated as: 100 * (NoSat – Sat)/ NoSat, using an appropriate threshold to eliminate spuriously large percent differences of small values in the noise outside the tissue.

Cortical reconstruction was performed by using the T1w image volume (NoSat) as input into the Freesurfer image analysis suite (v4.0.5), which is documented and freely available for download online (http://surfer.nmr.mgh.harvard.edu/). Intermediary surfaces were then created from the generated pial and white matter surfaces. The information from the MTR image volume was then computed for every vertex on each surface, and blurred along the surface with a 10mm FWHM kernel. To facilitate group comparisons, the cortical models were registered to a spherical atlas which utilizes individual cortical folding patterns to match cortical geometry across subjects [4]. With this matched, t-statistics for the MTR value at each vertex were computed and then thresholded for significance using a false discovery rate of 0.05.

Results and Discussion: MS vs. NC revealed large regions with significant decreases in MTR values, which are visible on multiple surfaces (Figure 1). In addition, they appear to be more widespread on outer surfaces compared to more medial ones. This agrees with postmortem findings on subpial demyelination, in which pathology is more prevalent on the superficial layers of the cortex [5]. These biologically plausible findings are promising and suggest that this approach may be able to detect subpial demyelinating lesions. Further validation studies against postmortem material are planned.

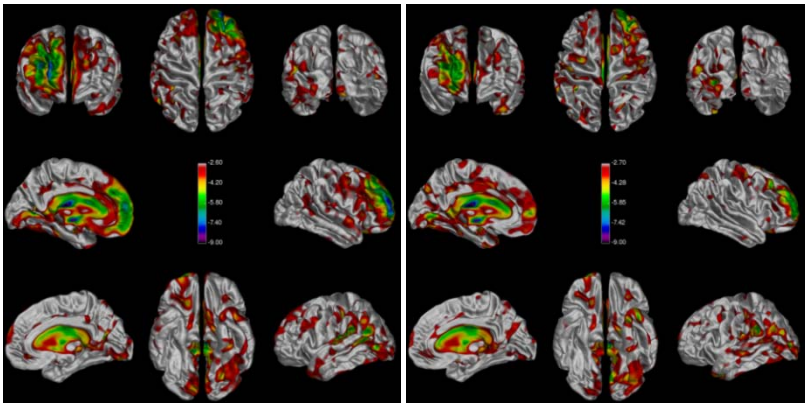

Figure 1 – Group differences in the MTR values of MS versus NC.
(left) pial surface, (right) midway between the pial and white matter surfaces.

Table 1 – Subject demographics

	MS	NC
Sex (F/M)	8/4	8/4
Mean Age (range)	47 (30-62)	44 (28-60)
Mean EDSS (range)	5.9 (3.5-8)	-
Mean DD (range)	14 (3-26)	-

EDSS: Kurtzke Expanded Disability Status Scale
DD: disease duration, in years

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