Principal Diffusion Direction in Relation to the Geometry of the Cortical Surface in Multiple Sclerosis

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Introduction. Pathologic and MRI studies in multiple sclerosis (MS) have provided evidence for the presence of lesions in the gray matter (GM). Diffusion anisotropy, obtained from diffusion tensor (DT) MRI, within cortical lesions was found to be increased in comparison with similar regions in the GM of healthy controls (HC) (1). Such an increase in diffusion anisotropy suggests the existence of a preferential directionality of the GM structure, which is usually not present in the normal GM because of cellular structures that run both parallel (dendrites) and perpendicular (neurons and their neuritis) to the cortex.

Objective. To evaluate the angle between the principal diffusion direction and the cortical surface in the cortex in patients with MS and in HC.

Methods. Using a 3.0 Tesla scanner, T_2-weighted, 3D T_1-weighted and DT MRI brain scans were acquired from 113 MS patients (21 benign [B] MS, 57 relapsing-remitting [RR] MS and 35 secondary progressive [SP] MS) and 35 HC. Expanded disability status scale (EDSS) score was assessed in all the patients. DW images were corrected for distortion induced by eddy currents, the DT was estimated by linear regression and the primary eigenvector derived. To compensate for distortions, the b=0 image was deformed to match the T_2-weighted image using an in-plane transformation (2) and the transformation was applied to the primary eigenvector field. GM was segmented from the 3D T_1-weighted using SPM8, after refilling of hypointense white matter lesions (3), and transformed to match the distortion-free b=0 image. GM maps were then skeletonized, the 3D vector field of normals to the cortical surface derived and smoothed (4). Finally, the angles (alpha) between the primary eigenvectors and the vectors normal to the cortical surface were calculated, as the arccosine of their scalar product. Since the absolute value of the arccosine function was considered, alpha ranges from 0 to 90 degrees, where 0 degree means that the dominant structures pass through the cortex perpendicularly and 90 degrees mean that they run parallel to the cortex. Normalized histograms of alpha within the skeleton of the cortex were calculated. These were averaged among subjects of the same phenotype and mean shape compared. Additionally, each histogram was fitted with a third degree polynomial curve and first derivative calculated: the value at a representative alpha of 10 degrees was extracted to be correlated with EDSS.

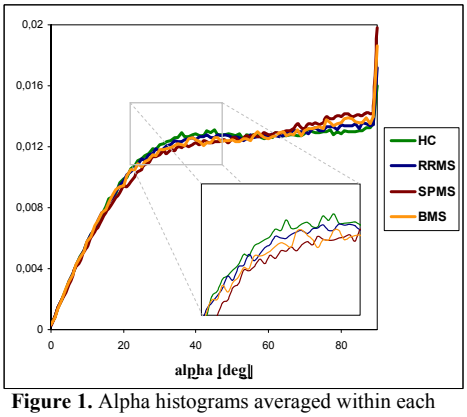

Figure 1. Alpha histograms averaged within each group. In the square, a detail is magnified.

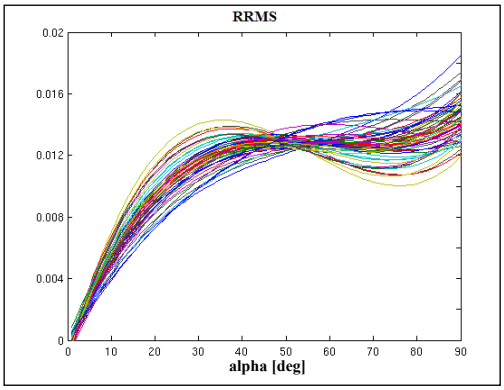

Figure 2. Plot of polynomial curves fitting alfa histograms of each RRMS patient.

Results. Average histograms of the alpha angles for the patient groups showed different behaviours, indicating that MS phenotypes in the more advanced phase of the disease have an increased number of voxels in the cortex with alpha close to 90 degrees (Figure 1). The plot of the fitted polynomial curves for each patient showed a spread of behaviours (Figure 2, for RRMS), that suggest several plausible parameters for the characterization. The derivative at 10 degrees correlated, albeit moderately (r=-0.42 for RRMS and r=-0.29 for all patients) with the clinical EDSS score (p=0.002) (Figure 3).

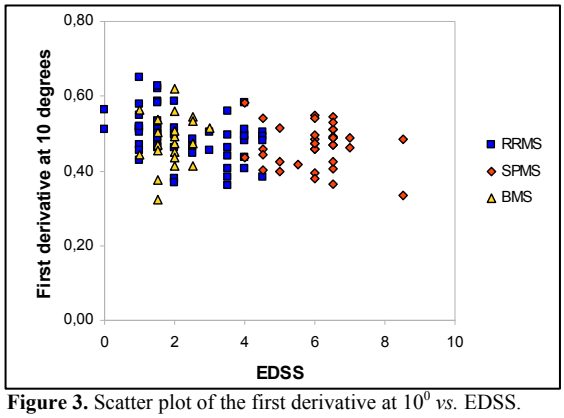

Figure 3. Scatter plot of the first derivative at 10^0 *vs.* EDSS.

Conclusions The study of the cortical structure through the analysis of the principal diffusion direction in relation to the geometry of the cortical surface could differentiate MS phenotypes. In MS patients, changes in diffusion anisotropy seem to be driven by a degeneration of the 'radial' component (towards the cortical surface) in the GM, resulting in a predominance of the parallel component.

References 1. Poonawalla AH et al. Diffusion-tensor MR imaging of cortical lesions in multiple sclerosis: initial findings. Radiology 2008;246:880-886. **2.** Rohde GK et al. The adaptive bases algorithm for intensity-based nonrigid image registration. IEEE Trans Med Imaging 2003;22:1470-1479 **3.** Chard DT et al. Reducing the impact of white matter lesions on automated measures of brain gray and white matter volumes. J Magn Reson Imaging 2010;32:223-228 **4.** Smith SM et al. Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. Neuroimage 2006;31:1487-1505.

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