Quantitative characterization of cortical pathology in multiple sclerosis using surface-based analysis of T2* relaxation at 7T

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Introduction. *In vivo* and *ex vivo* studies at ultra-high field (7T) MRI highlight the great sensitivity of T2*-weighted MRI to detect cortical lesions in multiple sclerosis [1, 2]. We recently combined T2*-weighted acquisition at 7T with surface-based analysis technique to study the distribution of subpial pathology in an MS population [3]. Here, in another MS group, we used a quantitative measure of relaxation rate, acquired using a 12-point sampling of the T2* tissue relaxation decay at 7T This technique allows us to investigate, in addition to focal lesions, more diffuse abnormalities, otherwise difficult to quantify using signal intensity measurements alone. Combined with surface-based analysis, this method also enables to study the spatial distribution of cortical MS changes across cortical regions, gyri and sulci, and their relation with clinical status.

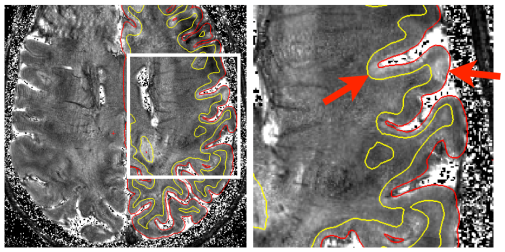

Fig1. T2* map of an MS patient showing a cortical lesion (arrow). Reconstructed pial (red) and WM (yellow) surface are overlaid.

Methods. *Subjects*. We recruited patients with clinically isolated syndrome (CIS, N=7) and with relapsing-remitting (RR) and secondary-progressive (SP) form of MS (N=11) and age-matched healthy controls (N=6). *Acquisition*. Subjects were scanned at 7T (Siemens Medical Solutions) using a head gradient and an in-house 32-channel coil. Protocol included a multiecho FLASH-T2* spoiled gradient-echo (*two slabs covering the supratentorial brain, TR=2020ms, TE=6.34+3.2n [n=1..12], resolution = 0.33x0.33x1 mm^3, 40 slices, matrix=576x504, BW=335Hz*) and a T1-weighted MPRAGE (*TR/TI/TE=2600/1100/3.26ms, 0.60×0.60×1.5 mm^3*). The same subjects were re-scanned at 3T (Tim Trio, Siemens Medical Solutions) to get a multiecho MPRAGE used for cortical surface reconstruction. *Processing*. Data were processed using Freesurfer [4]. Within-subject registration was done between the 7T FLASH scans and the 3T surface using robust boundary-based registration [5], then each surface was normalized to an average surface template. T2* maps were calculated on a voxelwise basis using least-squares fitting of the natural log of the data vs echo time. T2* signal was sampled between the white/grey matter interface and the midline of the cortical ribbon, then smoothed along the surface (FWHM=10mm). Mask of T2* increase was automatically generated by fitting a Gaussian curve to the histogram of the T2* map, and the value corresponding to P=0.05 (towards the upper tail) was used as a threshold to generate a binary mask. Normality of the data was assessed in all subjects (chi-square goodness-of-fit test, P<0.0001). Masks were summed across subjects to study the distribution of cortical pathology and the proportion of lesions in sulci/gyri. Spearman's correlations between T2* signal and clinical scores were also performed.

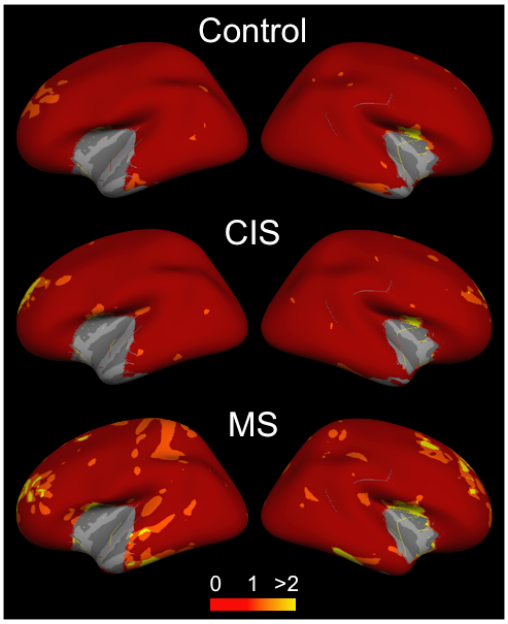

Fig2. Number of occurrence of cortical increase in T2*. Insula and superior temporal regions were masked due to extensive susceptibility artifacts.

Results. Cortical diffuse and focal pathology was visible on the T2* map (Fig1). Mean (±SD) T2* values in the whole cortex were 30.6±1.6ms in controls, 29.8±1.4ms in CIS and 31.6±1.8ms in MS patients. The cumulative distribution of T2* increases showed good consistency in each group, suggesting higher lesion load in CIS versus controls, and in MS patients versus CIS (Fig2). The proportion of identified lesions (*i.e.* significantly high T2* value per vertex) in sulci versus gyri was 54+/-3% in CIS (one-sample T-Test, P=0.01) and 58+/-7% in MS patients (P=0.004). Significant correlations were found between T2* value and sensory score in the lingual and postcentral regions (Fig3) and between T2* value and EDSS in the precuneus, superior parietal, middle temporal and lingual regions.

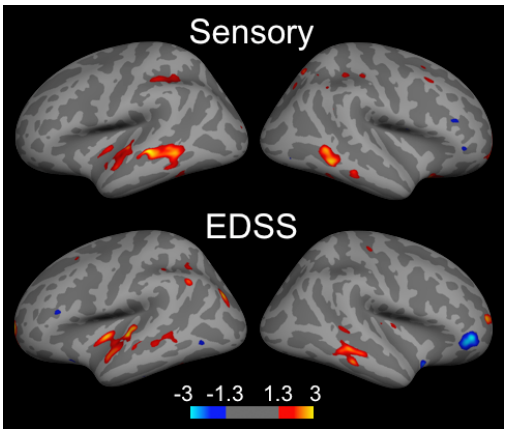

Fig3. $-\log_{10}$(P) associated with Spearman's correlations between T2* and clinical scores.

Discussion. This study reports a quantitative T2* increase in MS versus controls and CIS in frontal, parietal and temporal subpial regions, in accordance with previous results based on T2*-weighted signal at 7T [3]. This increase likely reflects disseminated cortical pathology described in post-mortem examination [6]. Sulci exhibited higher amount of pathology, confirming previous *ex vivo* study and validating the metrics used here in our study [6]. This technique has the potential to improve our understanding of the disease phenotypes via the discovery of specific quantitative biomarkers of cortical pathology in MS.

References.

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