# Functional relevance of cortical diffusion alterations in multiple sclerosis

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Target audience: Neuroradiologists and Clinical Neuroscientists

Purpose: Measurement of cortical proton diffusion properties provides a potential means to quantify cortical pathology in multiple sclerosis (MS). We hypothesise that patterns of regional cortical mean diffusivity (MD) will explain performance in different functional domains in MS. To test this hypothesis, we performed cortical surface-based mapping of partial volume corrected MD for a cohort of MS patients, with vertex-wise correlation between MD and functional performance in components of the MS functional composite (MSFC) [1] .

Methods: Forty MS patients (3 SPMS, 37 RRMS) underwent 3T MRI including MPRAGE and diffusion tensor imaging. Cortical segmentation was performed using FreeSurfer[2] with manual editing. Mean diffusivity (MD) maps were corrected for partial volume (PV) effects using the approach described by Koo et al [3]. PV-corrected MD values were sampled onto the cortical surface mesh. Multiple Sclerosis Functional Composite (MSFC), Benton Visual Retention Test (BVRT) and California Verbal Learning Test-II (CVLT-II) was performed in all subjects. Cognitive and imaging data from subjects in this cohort have been included in two previous reports [4,5,] but the cortical MD analysis and results presented here have not been reported previously. Vertexwise correlation between PV-corrected cortical MD and MSFC, the MSFC components (9 hole peg test (9-HP), 25-foot timed walk (25FTW) and Paced Auditory Serial Addition Test (PASAT)), BVRT and CVLT-II. A smoothing kernel of 20mm FWHM and multiple test correction was applied using false discovery rate (FDR).

Results: Surface based analysis revealed multiple significant negative correlations between MSFC and PV-corrected cortical MD at clusters in the left hemisphere (P<0.05, corrected, controlled for age) Figure 1. Significant positive regional correlations between cortical PV-corrected MD and 9-HP scores (including clusters in the left hemisphere hand motor area) Figure 2 and between PV-corrected cortical MD and 25-FTW were found Figure 3. Clusters showing negative correlation (P<0.005, controlled for age) between PV-corrected MD and the cognitive scores were found which included the left anterior cingulate cortex Figure 4, although only the correlations found for the BVRT survived multiple test correction.

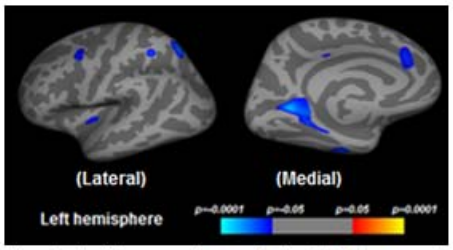


**Figure 1.** Significant negative correlation (P<0.05 corrected), controlled for age between MSFC scores and PV corrected cortical MD of the left hemisphere

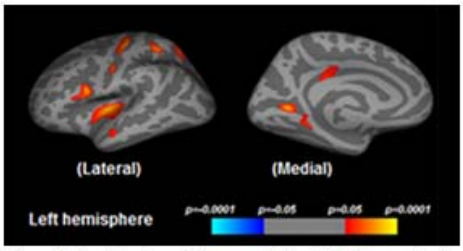


**Figure 2.** Significant positive correlation (P<0.05 corrected), controlled for age between PV corrected cortical MD of the left hemisphere and 9HPT scores

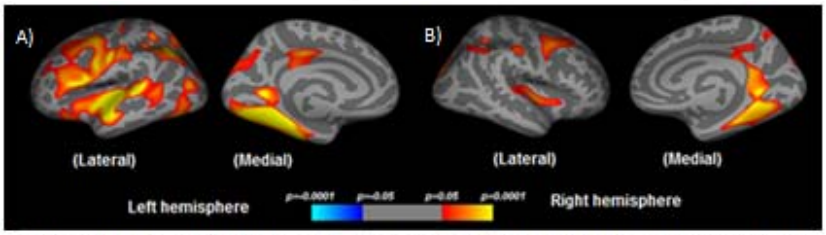


**Figure 3.** A) Left and B) Right hemispheres demonstrate significant positive correlation (P<0.05 corrected), controlled for age between 25FTW scores and PV corrected cortical MD

Discussion: In this study we demonstrate the functional relevance of cortical MD variability across the cerebral surface in MS patients, with differential patterns of MD variation relating to the MSFC and its component parts. The directions of the functional associations are as expected, with positive correlation between cortical MD and scores where a higher value indicates worse clinical status (9HPT and 25FTW). For BVRT the negative correlations are as expected given that a higher score indicates better cognitive status. A similar direction of correlation was found for PASAT and CVLT-II, although these surface based correlations did not survive the multiple test correction. To our knowledge, the surface-based approach that we employ to map the functional correlates of cortical MD change has not been applied previously.

Conclusion: Surfaced-based analysis reveals differential patterns of functionally-relevant regional cortical diffusion elevation between performance measures in different functional domains.

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