Tissue Perfusion Changes and Neuropsychological Impairment in Multiple Sclerosis

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Background: Cognitive impairment is common in multiple sclerosis (MS) and has a relevant impact on patients'social and occupational life. Abnormalities of cerebral blood flow have long been acknowledged in MS and advances in perfusion MRI allow their assessment *in-vivo*. This study aimed to investigate the relationship between regional perfusion changes and neuropsychological dysfunctions in patients with relapsing-remitting (RR) and primary-progressive (PP) MS.

Methods: Absolute cerebral blood flow (CBF), blood volume (CBV) and mean transit time (MTT) were measured in the NAWM and deep GM (Fig. 1) of 32 MS patients and 11 healthy controls using dynamic susceptibility contrast enhanced (DSC) T2*-weighted MRI. A comprehensive neuropsychological (NP) test-battery was administered to all patients. Raw NP scores were normalized using published norms and then converted to z scores based on the normal distribution. A mixed model analysis of covariance was performed for group comparisons in terms of perfusion measures in normal-appearing white matter (NAWM) and deep gray matter (GM). Pearson correlations were used to describe the association of perfusion metrics with NP scores.

Results: CBF and CBV values were significantly reduced in both NAWM and deep GM in MS patients compared to controls (p=0.01). In all patients, after adjusting for age, gender, disease duration and depression, deep GM CBF was significantly associated with Rey Complex Figure Test (RCFT)-Copy (r=0.5; p=0.001), deep GM CBV and NAWM CBV were significantly associated with Color-Word Interference Inhibition Switching test (D-KEFSIS) (r=0.4; p=0.008 and r=0.4; p=0.02). However, the only associations that remained significant after Bonferroni correction were between deep GM CBF and RCFT-Copy (r=0.5; p=0.006) (Fig.2) and deep GM CBV and D-KEFSIS (r=0.5; p=0.04)

Conclusion: Our results suggest a role for tissue perfusion impairment (not only in NAWN but also in deep GM) in neuropsychological dysfunction in MS. Larger-scale studies are needed to better characterize this association.

References: Rao S.M. et al., Neurology 1991; Rempp K. et al., Radiology 2004; Adhya S. et al, Neuroimage 2006.

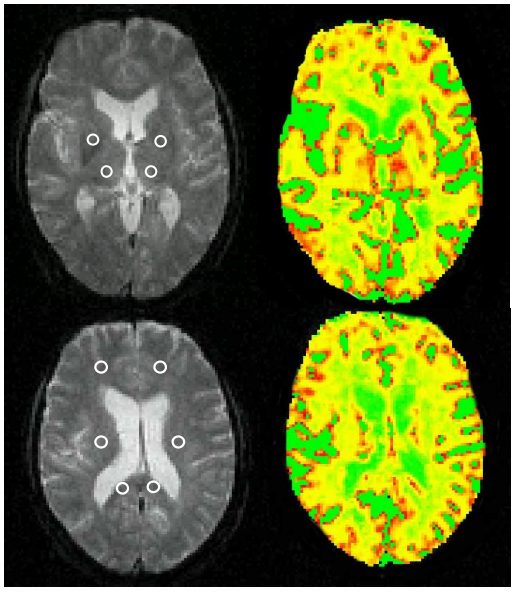

Fig. 1. Left: Axial gradient-echo echo-planar MR images from a MS patient. Circular ROIs are placed in the putamen, thalamus, frontal, periventricular NAWM and in the splenium of corpus callosum bilaterally. Each ROI has an in-plane resolution of 2 pixels **Right:** Axial color-coded CBF maps from the same patient.

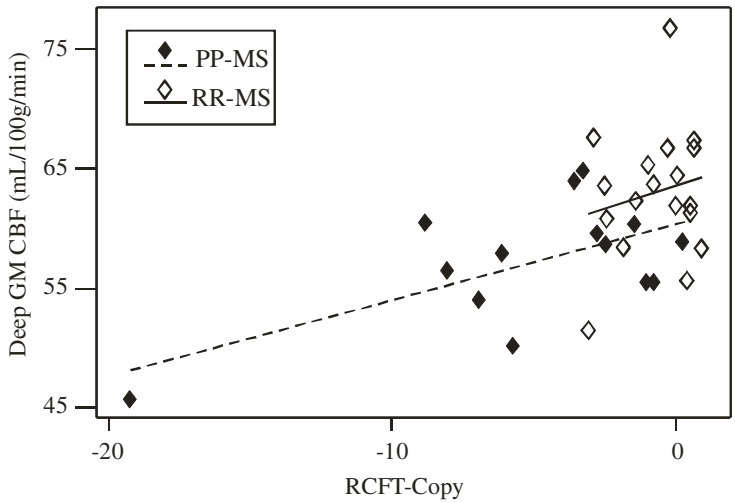

Fig. 2. Graph showing the correlation between deep GM CBF and the performance of PP-MS (♦) and RR-MS (◊) patients on the visual memory test (RCTF-Copy). Note that the Pearson Correlation test indicates a moderate correlation between the level of deep GM CBF and the memory test in the whole group of patients (r=0.5; p=0006) and a strong correlation in the PP-MS patients (r=0.8; p=0.002).