Altered brain perfusion and tissue injury in early multiple sclerosis assessed by ASL and MTR statistical mapping analyses

W. ZAARAOUI[1], F. REUTER[1], M. LEMAIRE[1], A. RICO[1], A. FAIVRE[1], V. CALLOT[1], I. MALIKOVA[1], E. SOULIER[1], S. CONFORT-GOUNY[1], P. J. COZZONE[1], J. PELLETIER[1], B. AUDOIN[1], and J-P. RANJEVA[1]

[1]Faculté de Médecine, CRMBM UMR CNRS 6612, Marseille, France

Background: Recent studies have evidenced the crucial role of perfusion alteration in multiple sclerosis (MS) [1, 2]. However, little is known about the relationships between hemodynamical parameters and local tissue damage encountered at all stages of the disease, and especially at the early phase.

Objective: To investigate the putative relationships between perfusion alterations and structural local white matter and grey matter impairments in early MS, we designed a MR protocol combining statistical mapping analyses of arterial spin labeling (ASL) data and magnetization transfer ratio (MTR) data obtained in 12 patients with clinically isolated syndromes (CIS) and 12 matched controls.

Methods: MR explorations were performed on a 3T Verio system (Siemens, Erlangen Germany) using a 32 channel head coil. Magnetization transfer ratio maps were obtained from two proton density weighted spoiled GE sequence (TE/TR: 4.5ms/750ms, 45 contiguous slices, thickness 3mm, RecFOV 320x240, matrix 256, without and with MT pulse). ASL was obtained with a pulsed-ASL sequence (PICORE Q2T) (TE/TR: 11ms/2545ms, 20 contiguous slices, 6mm thickness, TI1/TI2 700ms/1800ms, FOV 256x256, matrix 64, Tacq: 4min26). Raw data EPI images and corresponding reconstructed quantitative CBF maps were post-processed using Statistical Parametric Mapping (SPM5) to obtain statistical mapping analyses between patients and controls. Briefly, EPI images were spatially normalized in the MNI space and transformation was applied to the corresponding CBF maps. After smoothing (FWHM 8 mm), normalized CBF maps from all subjects were averaged to obtain a new CBF template. Then each individual CBF maps were spatially normalized according to this local CBF template. Between-group statistical mapping analysis (two-sample t test, $p<0.001$, $k=15$, uncorrected) was performed on the smoothed normalized CBF maps (FWHM 8mm). For analysis of MTR maps, T_2 lesions were delineated onto the T_2-weighted images by means of a semi-automated method. Mmt images were coregistered onto the T_2-weighted images and the mask of the T_2 lesions was subtracted from the coregistered Mmt to obtain the lesion-free Mmt image. Voxels of the T_2 lesion mask were set at a value corresponding to the mean voxel values of the lesion-free WM Mmt images and subsequently added to the coregistered lesion-free Mmt image. These modified Mmt images were then normalized in the Montreal Neurological Institute (MNI) space using the T_2 anatomical template provided by SPM5 software program and spatial transformation were applied to the MTR images. After segmenting the normalized modified Mmt images, the mask of the GM+WM (>0.9) was applied to the normalized MTR images. The resulting normalized tissue MTR images obtained were smoothed using a 8-mm Gaussian filter for the statistical analyses (two-sample t test, $p<0.001$, $k=15$, uncorrected). In order to determine relationships between local perfusion alteration and decreased MTR, a simple regression model was applied onto MTR maps using CBF values found to be abnormal (precuneus and splenium) ($p<0.05$, $k=15$).

Results: Significant decreased CBF was observed in CIS patients inside the precuneus (BA7) (Fig 1) and increased WM CBF was observed inside the splenium of corpus callosum (Fig 2). Relative to controls, decrease in MTR was observed in patients inside several white matter regions (fronto-occipital fascicle, longitudinal inferior fascicle and optic radiations) and in GM regions (thalamus, cingulate cortex and associative areas) (Fig 3) in accordance with previous studies in similar population [3]. Relationships between altered GM perfusion inside precuneus and local MTR decrease were restricted to neighboring destructurated regions including paracentral lobule and parietal WM (Fig 4). In contrast, altered WM hyperperfusion inside splenium was correlated with the MTR of spread destructurated areas including the right posterior thalamus, the right medium temporal gyrus, the left inferior and the right superior longitudinal fascicles, the right parietal WM, the right BA9/32 and the right BA37 (Fig 5).

Discussion and Conclusion: ASL and MTR statistical mapping analyses succeed to demonstrate altered brain perfusion and tissue destructuration in MS patients at the very early stage of the disease. Abnormal WM perfusion (splenium of CC) appear more correlated to a large-scale network of tissue injury (including large WM bundles and associative GM areas and nodes such as thalamus) compared to the abnormal hypoperfusion of the precuneus that appears correlated to a more restricted and closed areas. Ongoing works will aim at better characterizing these different patterns and their relative impact on clinical disability.

Fig 1: Decreased perfusion in CIS

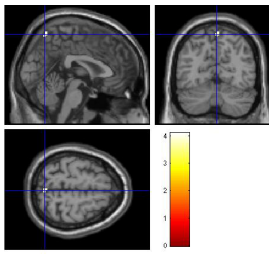


Fig 2: Increased perfusion in CIS

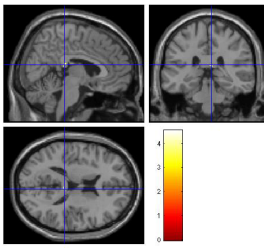


Fig 3: Decreased MTR in CIS

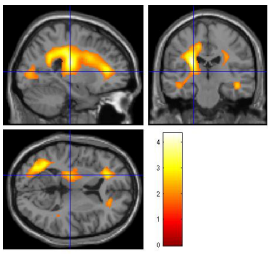


Fig 4: MTR=f(Perfusion Precuneus)

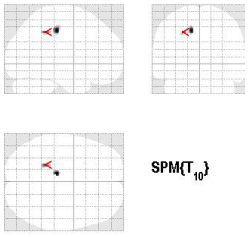
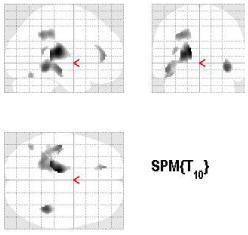


Fig 5 : MTR = f(Perfusion Splenium CC)



References :

1. Rashid W et al. J Neurol Neurosurg Psychiatry 2004;75
2. Varga AWet al. J Neurol Sci 2009;282
3. Ranjeva JP et al. Am J Neuroradiol 2005;26