Altered Hemodynamics of Cortical Lesions in Multiple Sclerosis: a Dynamic Susceptibility Contrast MRI study using a Kernel-Based Deconvolution Algorithm

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INTRODUCTION

Degenerative features in patients with Multiple Sclerosis (MS) have been identified in white matter and, more recently, in grey matter (GM), but mechanisms and causes of degeneration are still unclear. In particular, microvascular abnormalities have been observed in various MS subtypes, suggesting that vascular and perfusion factors may contribute to the pathogenesis of MS. We performed a Dynamic Susceptibility Contrast Magnetic Resonance Imaging (DSC-MRI) study in order to investigate the differences in cerebral perfusion in the Cortical Lesions (CLs) compared to the Normal Appearing Grey Matter (NAGM) in Relapsing Remitting Multiple Sclerosis (RRMS) patients. A deconvolution operation between the arterial input function (AIF) and the voxel concentration of contrast agent (C(t)) must be preformed to obtain the residue function (R(t))[1] and from there the Cerebral Blow Flow (CBF) [1]. In this study we use a Kernel-Based algorithm developed by De Nicolao et al. called Stable Spline [2,3] that provides more accurate and more physiological R(t) estimates than SVD and cSVD [4,5].

MATERIALS AND METHODS

19 RRMS patients have been considered (F/M= 14/5; mean age= 36±11; mean disease duration= 10±8; mean EDSS score=3.5±1.3). All the acquisitions have been performed on a Philips Achieva 1.5T. The DSC-MRI (TR 1.375 s, TE 40 ms, FOV 230x230 mm, voxel size 1x1x6 mm) data have been used to compute the Cerebral Blood Flow (CBF), Volume (CBV) and the Mean Transit Time (MTT). The AIF has been automatically extracted as reported in [5]. The Double Inversion Recovery (DIR) (TR 15631 ms, TI1, 325 ms, TI2 3400 ms, FOV 230x230 mm, voxel size 1x1x3 mm) sequence has been used to identify CLs and the T1-weighted images (TR= 25ms, TE=4.6ms, FOV=230x230 mm, voxel size 1x1x1 mm) have been used to identify the NAGM (i.e. grey matter without CLs). All the images have been moved to the DSC-MRI space using FSL (FMRIB Software Library, v4.1). The CLs detection has been manually detected by a blinded trained physician and GM segmentation has been automatically performed by Statistical Parametric Mapping (SPM v. 8). CLs areas have been subtracted from GM maps in order to keep only NAGM ones. CBF, CBV and MTT mean values on CLs have been computed for each subject and compared to his/her NAGM ones. Kolmogorov-Smirnov test has been used to infer statistical significance.

RESULTS

In total, 81 CLs have been found in the considered patients (mean=4.9±3 lesions per subject). We identified two distinct CLs population based on CBF values, ipoperfused and iperperfused CLs. In particular, 74 over 81 CLs are ipoperfused when compared to the NAGM (Fig. 1), with a decreased CBF (-53±21%; p<0.001). In addition, these 74 CLs present also a significant reduction in the CBV (-45±24%; p<0.001) and a significant increase in MTT (+58±105%; p<0.001). The remaining 7 CLs have been classified as iperperfused. They present a higher CBF (+39±30%) and CBV (+11±23%) than the NAGM ones, and a slightly reduced MTT (-2±73%). However, probably due to the small size of the iperperfused CLs population, only CBF shows to have a statistical significant difference (i.e. p < 0.05) from those of NAGM. Figure 2 shows the boxplot of the percent difference of CBF and CBV estimates in iperperfused and ipoperfused CLs population.

DISCUSSION

In [4] SS algorithm has been applied to simulated and clinical data providing better results compared to the most used methods. In this study the same algorithm has been used to study the haemodynamic parameters in RRMS patients. In iper, ipoperfused CLs and NAGM, R(t) reconstructed by SS does not present the oscillations typically present in SVD or cSVD results, providing a more physiological and regular shape. Our results show that the ipoperfused CLs present also a reduced CBV and an increased MTT when compared to the NAGM, thus suggesting a neuronal damage and loss with a reduction in the tissue's metabolism. On the other hand, iperperfused CLs are characterized by a higher CBV and a lower MTT than the NAGM, in agreement with an increased metabolism. This confirms several neuropathological observations showing a subgroup of active CLs characterized by a high degree of inflammatory cells which are characterized by a high metabolism. Further studies are required to better understand the relationship between such microvascular disturbance and the CLs activation in MS.