R2' is reduced in normal appearing white matter and lesions, and increased in the basal ganglia in patients with multiple sclerosis

D. J. Paling[1], D. J. Tozer[1], C. A. Wheeler-Kingshott[1], X. Golay[1], R. Kapoor[1], and D. H. Miller[1]
[1]Department of Neuroinflammation, UCL Institute of Neurology, London, United Kingdom

Introduction:

The presence of paramagnetic substances within the imaging voxel leads to magnetic field inhomogeneity at the mesoscopic level, leading to increase in the R2* (=1/T_2*) relaxation rate in MRI. The R2' rate constant, derived from subtracting R2 from R2*, describes the reversible part of the MR signal decay that originates solely from mesoscopic field inhomogeneities. As deoxyhaemaglobin is paramagnetic, its presence in vessels within the voxel leads to an increase in R2' proportional to the product of oxygen extraction fraction and deoxygenated blood volume.[1] R2' can also be increased by non-haeme iron deposition[2]. In this study we created whole brain R2' maps in patients with multiple sclerosis and healthy volunteers and interrogated them for significant changes that could indicate differences in metabolism or iron accumulation.

Methods

T2 and T2* weighted images were acquired in 7 patients with secondary and primary progressive multiple sclerosis, 6 females, 1 male with mean age 44, and 5 healthy volunteers, 3 males, 2 female with mean age 35. The study was approved by the local ethics committee.

MRI protocol

All MRI studies were performed using a 3 Tesla Philips scanner and a 32-channel receiver coil. For T2 determination a fast spin echo sequence was used, acquiring images at 7 different TEs (voxel size 1x1x2mm^3, FOV 240x180x152 mm^3, TE1 16ms, ΔTE 16ms, TR 5230ms, NEX 1, acquisition time 6 min 48s). For T2* determination a gradient echo sequence was used, acquiring images at 10 different TEs (voxel size 1x1x2mm^3, FOV 240x180x152mm^3, TE1 7.1ms, ΔTE 6.3ms, TR 5667ms, NEX 1, acquisition time 8 min 47s, SENSE=2). T2 and T2* maps were created using in house T2 mapping software. In house registration software was used to register subsequent echoes to the first echo in both the T2 and T2* weighted sequences, and register the T2 and T2* map together. R2' maps were created using the image algebra toolkit in JIM 5.0 (Xinapse Systems, www.xinapse.com) using the formula R2'=1/T2'=1/T2*-1/T2. Lesions, caudate and lenticular nuclei were identified using the first echo of the T2 weighted sequence using the region of interest toolkit in JIM. 26 anatomically defined regions of interest were placed in the normal appearing white matter; 4 in the temporal lobe, 10 in the frontal lobe, 6 in the occipital lobes and 6 in the parietal lobes. Statistical analysis was performed using Predictive Analytics Software 18 for Windows 7 (IBM, www.spss.com). Man Whitney U test was used to compare region R2' between groups.

Results

R2' was significantly reduced in MS lesions as compared to the normal appearing white matter (8.20 x 10^{-3} s^{-1} vs 9.77 x 10^{-3} s^{-1} , P<0.001). R2' was also significantly lower in the NAWM in patients with MS as compared to healthy control patients (9.77 x 10^{-3} s^{-1} vs 10.13 x 10^{-3} s^{-1} P=0.01). Increases in R2' were seen in the lenticular nucleus in patients with multiple sclerosis (14.57 x 10^{-3} s^{-1} vs 13.42 x 10^{-3} s^{-1}, P<0.001) and in the caudate nuclei (12.53 x 10^{-3} s^{-1} vs 10.53 x 10^{-3} s^{-1}, P<0.001)

Discussion

Increase in R2' within the caudate and lenticular nucleus may represent abnormal iron deposition which is recognised pathologically in patients with multiple sclerosis. As the contribution of deoxyhaemaglobin to R2' is proportional to the product of oxygen extraction fraction and deoxygenated blood volume, R2' reduction within lesions and normal appearing white matter may suggest a reduction in oxygen extraction fraction. However this finding could also represent a reduction in deoxygenated blood volume, or reduction in non haeme iron, possibly due to loss of iron containing oligodendrocytes due to ongoing demyelination. Future studies should investigate changes in R2' over time in acute lesions, or use modelling as proposed by other investigators to provide separate measures of oxygen extraction fraction and deoxygenated blood volume from R2'[1].

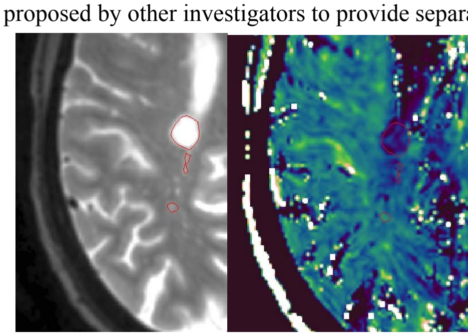
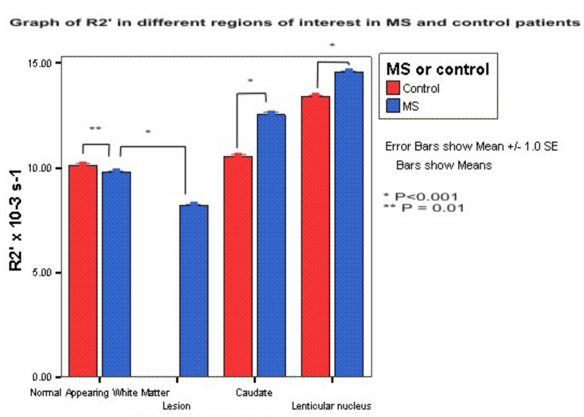


Fig 1. T2 weighted image (left) and R2' map (right), brighter colours denote increased R2'. Decrease in R2' can be seen in some of the outlined lesions with comparison to the normal appearing white matter.



1. He, X. & Yablonskiy, D.A. Quantitative BOLD: Mapping of human cerebral deoxygenated blood volume and oxygen extraction fraction: Default state. *Magnetic Resonance in Medicine* **57**, 115-126 (2007).
2. Brass, S.D., Chen, N., Mulkern, R.V. & Bakshi, R. Magnetic Resonance Imaging of Iron Deposition in Neurological Disorders. *Topics in Magnetic Resonance Imaging* **17**, 31-40 (2006).