R2, Field Dependent R2 Increase (FDRI) and Refocusing pulse time dependent R2 Increase (τDRI) in Multiple Sclerosis Compared to Healthy Controls

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Introduction: Hypointensity in the deep gray matter of Multiple Sclerosis (MS) patients was previously observed in 1.5T T2-weighted images [1,2], and was attributed to increased brain iron content from abnormal iron metabolism. It is expected that sensitivity for brain iron would increase by utilizing quantitative T2 measurements, especially at higher magnetic field strengths, which are more sensitive to sub-voxel susceptibility effects from paramagnetic iron. Observed relaxation rates $R2^+=1/T2^+$ depend on the field strength and on the acquisition method and can be approximated by [3]

$$R2^+ = R2_0 + \tfrac{1}{12}\gamma^2 G_{susc}^2(B_0,[Fe])D\tau^2$$

where G_{susc} is the local magnetic field gradient due to tissue susceptibility differences and depends on the field strength B_0 and iron concentration [Fe], D is the diffusion constant, τ is the time between refocusing pulses and $R2_0$ is the intrinsic relaxation predominantly reflecting tissue water content assumed to be independent on field strength. Thus sensitivity to iron susceptibility effects can be further increased by measuring the field dependent R2 increase $FDRI=R2^+(7T)-R2^+(3T)$. Alternatively, changes in $R2^+$ may also be measured for sequences with different τ at the same field strength, and a τ-dependent $R2^+$ increase ($\tau DRI= R2^+(\text{long }\tau)-R2^+(\text{short }\tau)$) may be calculated. Both methods were shown to be sensitive to brain iron content [4,5]. The aim of this study is to quantify MS-related changes in brain iron content by measuring T2, FDRI and τDRI.

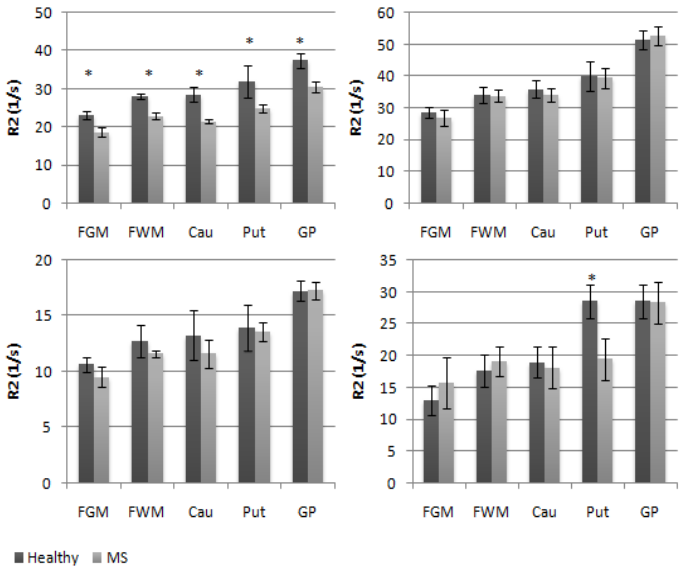

Figure 1: **$R2^+$ measured 3T (left) and 7T (right) with the Dual Echo Long τ (top) and GRASE short τ (bottom) sequences.**

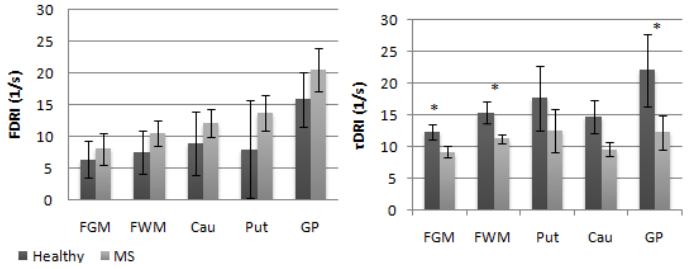

Figure 2: FDRI (left) and τDRI (right)

Methods: Two groups of 7 established MS patients (28-58y), and 7 healthy controls (32-56y) were imaged at 3T and 7T (Philips, Achieva). Dual Spin Echo (TR = 2000ms, TE = 10/50ms (7T) and 10/60ms (3T) and gradient-spin echo (GRASE) (TR = 2000, TE = 9 to 72ms, τ=9ms) were acquired with interpolated voxel sizes of $0.45\text{x}0.45\text{x}3.0\text{mm}^3$. Different brain regions, including frontal gray matter (FGM), frontal white matter (FWM), globus pallidus(GP, caudate (Cau), and putamen (Put) were manually traced, and $R2^+$ was calculated for each region. Average $R2^+$s for each sequence and field strength were computed for each brain region for the MS patients and healthy controls. FDRI and τDRI were computed from R2+ differences.

Results: Average $R2^+$ for MS patients and healthy controls for each brain region, both sequences and both field strengths are shown in Fig 1. For MS, $R2^+$ measurements are slightly lower (except for FGM and FWM at 7T), though the differences are statistically significant ($p<0.05$) only for 3D Dual echo. Fig. 2 shows Dual Echo FDRI and 3T τDRI data. FDRI was larger in all regions for the MS patients, whereas τDRI were smaller.

Discussion: Our study did not confirm the previous findings by Baksihi et al [1,2], as our $T2^+$ were generally longer in MS patients both at 3T and 7T. This may be explained by the fact that the measured $T2^+$ relaxation contains contributions from intrinsic $T2_0$ reflecting tissue water content and the susceptibility-diffusion term $\gamma^2 G_{susc}^2 D$. Due to demyelination in MS, free water may be increased and this may dominate the measured $T2^+$ thus obscuring effects from tissue iron. Both FDRI and τDRI difference methods remove the intrinsic $R2_0$ term, thus reflecting the susceptibility-diffusion term. The observed 40-80% increase in FDRI for MS may be indicative of brain iron increase in MS. In contrast, τDRI does not show an increase for MS compared to controls. This may indicate that differences in diffusion coefficients in MS patients conceal effects from iron susceptibility. Future studies need to explore the effects of water diffusion FDRI and τDRI.

References

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