T1rho MR is Sensitive to Changes in Normal Appearing White Matter and Gray Matter in Multiple Sclerosis

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Purpose

To determine if quantitative $T_{1\rho}$ MRI is sensitive to the demyelination process, or protein leakage found in the brains of Multiple Sclerosis (MS) patients[1], and to compare to normative values of $T_{1\rho}$ in white matter(WM) and cortical gray matter (GM).

Methods

Study Design

- Prospective Cross-Sectional Pilot Study
- 29 MS patients aged 30-60 (43.7 9.2)
- 18 age-matched controls
- MS patient sub-types of: Clinically *Isolated Syndrome (10)*, *Relapsing-Remitting (14), Primary Progressive (1)*, and *Secondary Progressive* (4) MS
- Data was acquired using a Philips 3T Achieva TX scanner and an 8-channel head coil
- Institutional Review Board (IRB) approval was obtained and all patients were consented

Acquisition

- Whole-brain $T_{1\rho}$-weighted images were acquired using a fluid attenuated variable flip angle 3D turbo spin echo technique (spatial resolution 1.8×1.8×1.8mm^3). Images were acquired with a spin lock frequency of 500Hz and spin lock durations of 0, 20, 40, 60, 80 and 100ms.

Analysis

- Each $T_{1\rho}$ map was calculated based on a single exponential fit to the co-registered $T_{1\rho}$-weighted images. The $T_{1\rho}$ map was then itself co-registered to a T_1-weighted 3D TFE anatomical scan. Using unified segmentation[2] (SPM8) of the T_1-weighted image, the $T_{1\rho}$ maps were segmented into WM and GM and spatially normalized to MNI space. Major WM tracts were defined using the JHU atlas[3], while cortical GM and juxta-cortical WM were defined by an intersection of the Harvard-Oxford cortical atlas (dilated by 5mm) with the subject-specific GM and WM masks respectively. In addition, 3D FLAIR (spatial resolution 1.2x1.2x1.2mm^3) and 3D DIR (spatial resolution 1.2x1.2x1.3mm^3) images were obtained for lesion identification.

Results

Cortical GM $T_{1\rho}$ values were higher in all MS groups compared to controls, although this did not achieve statistical significance. WM regions demonstrated significantly higher $T_{1\rho}$ values in all MS groups compared to controls. Juxta-cortical WM regions were higher in all MS groups, but did not prove significant in the CIS group. The new $T_{1\rho}$ technique produced high SNR whole-brain $T_{1\rho}$ maps. Figure 1 shows an example of the defined regions-of-interest using the WM/GM segmentation of T_1 weighted image and pre-defined MNI templates. The T_2 -FLAIR shows periventricular lesions that are clearly delineated on the $T_{1\rho}$ map . These lesions demonstrate substantially increased $T_{1\rho}$ (typically 100ms or greater) compared to the surrounding tissue (75-80ms); however, we subtracted the lesions out so that they did not artificially inflate the $T_{1\rho}$ values of the MS groups.

	Controls	CIS-MS	RR-MS	PP-MS	SP-MS	All MS
Sex	6F,11M	7F,3M	10F,4M	1F,0M	2F,*2M	20F,9M
Age (mean)	43.4 10.7	43.2 10.2	41.9 8.9	60	47 4.2	43.7 9.2
Cortical GM (ms)	78.3 1.1	79.0 1.2	79.0 1.2	79.9	78.8 2.2	79.0 1.6
p-value	-	0.185	0.098	n/a	0.661	0.075
WM Tracts (ms)	76.2 1.4	78.9 2.1	78.3 1.8	76.9	79.0 0.9	78.6 1.8
p-value	-	0.003	0.001	n/a	0.002	1.2×10^{-5}
Juxta-Cortical WM	75.1 1.0	76.0 1.3	76.5 1.5	75.5	76.9 0.2	76.4 1.3
p-value	-	0.065	0.005	n/a	1.1×10^{-6}	0.0005
EDSS Score Correlation w/ WM, GM, JC WM	-	0.14, 0.06,-0.17	-0.14, -0.50,0.18	n/a	-0.10, 0.85,0.52	-0.01, -0.36,0.03

Table 1. Subject demographics and T1rho estimates. (Mean±SD) RR=Relapsing remitting, CIS=Clinically isolated syndrome, PP=Primary progressive. Notes:1 Male SPMS withdrew for claustrophobia.; only 1 PPMS recruited no statistics available for subject.

Figure 1. (Left-scatter plot) T1ρ values of Controls and MS phenotypes vs. age.

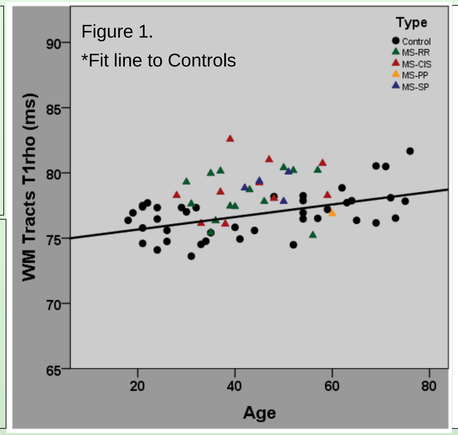
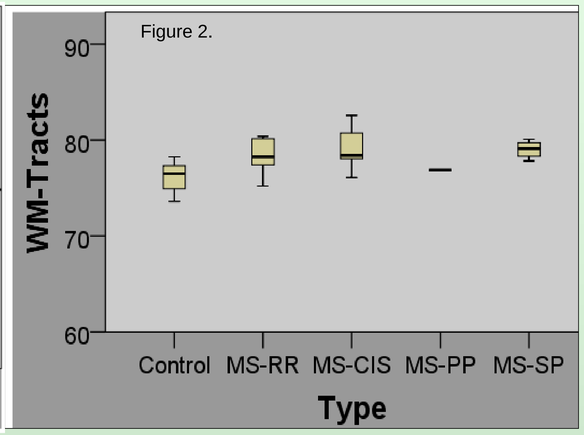


Figure 2. (Left-scatter plot) T1ρ values of Controls and MS phenotypes vs. age.



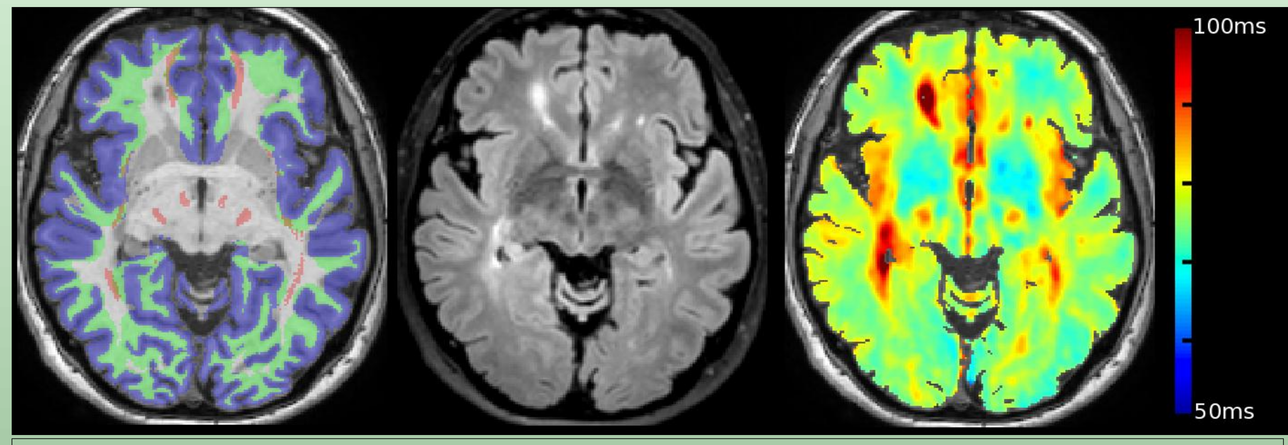


Figure 3. T1-weighted image showing segmentation of cortical gray matter (blue), juxta-cortical white matter (green) and major white matter tracts (forceps minor, cortico-spinal tract, anterior thalamic radiation, inferior longitudinal fasciculus, red);T2-FLAIR showing white matter lesions;T1rho map.

Discussion and Conclusions

$T_{1\rho}$ MRI has previously been shown to reflect the macromolecular content of biological tissue, due to chemical exchange. Limited brain studies have shown $T_{1\rho}$ to be sensitive to the changes associated with Alzheimer's and Parkinson's disease [4]. MS is known to cause disruption of the blood-brain barrier, which leads to increased levels of blood serum proteins in the brain [1]; this increase in protein content can increase chemical exchange locally. Abnormal epithelial tight junction (TJ) proteins found in MS could be a possible source of chemical exchange that is detectable with a quantitative MRI measure, like T1ρ. Our results demonstrate that both normal-appearing WM and juxta-Cortical WM have increased $T_{1\rho}$ values in MS compared to age-matched controls. GM did not achieve a statistical difference. Lesions have low signal intensity on the T1-weighted images, leading to their exclusion from the WM/GM masks generated by the segmentation. Thus, our results are not biased by lesion load, which would otherwise increase the $T_{1\rho}$ values within the defined regions. Including lesions in the analysis would likely increase differentiation between the MS and control groups due to their higher $T_{1\rho}$ values. In addition, although this study found significant differences between non-focal regions of interest in WM and JCWM, it is possible that specific brain regions show greater changes, which would improve the diagnostic utility of this approach. MS is known to result in early stage cortical lesions, although these lesions are often not visible on standard imaging [5,6]. $T_{1\rho}$ may provide a quantitative measure of juxta-Cortical WM changes that are not seen with other methods. While the differences in $T_{1\rho}$ values is relatively small (~1-2ms), our technique has sufficient sensitivity to detect this subtle change.

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