Magnetization transfer and spin-lattice relaxation time measurements of white matter lesions in normal aging

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Introduction

Deep and periventricular white matter lesions are a common finding on T_2- and FLAIR-weighted MRI scans of older subjects, but their etiology and relationship to cognitive function remains unclear. The aim of this pilot study was to characterize differences in magnetization transfer ratio (MTR) and spin-lattice relaxation time (T_1) between macroscopically normal-appearing white matter (NAWM) and white matter lesions in a subset of participants of the Lothian Birth Cohort 1936 (LBC1936). These 1000+ subjects were born in 1936 and underwent cognitive testing in 1947 at age 11. Currently in their early 70s, the subjects have taken a battery of cognitive tests and are undergoing brain imaging.

MTR and T_1 are quantitative biomarkers of white matter integrity, with the former related to the degree of myelination and the latter to brain water content. In healthy, well myelinated white matter, MTR takes relatively high values (30 to 50 %), while T_1 is relatively low (0.7 to 1.0 s at 1.5 T). We therefore hypothesized that the MTR of white matter lesions would be lower and T_1 higher than in NAWM, indicating reduced white matter integrity and increased brain water content. Following previous work which indicated correlations between water diffusion parameters and MTR in white matter lesions [1], we also hypothesized that MTR and T_1 would be correlated in these lesions.

Methods

Subjects: Twenty participants of the LBC1936 underwent structural (T_2-, T_2*- and FLAIR-weighted), magnetization transfer (MTI) and T_1-mapping MRI protocols on a GE Signa LX 1.5T clinical scanner. These 20 subjects were randomly selected to be representative of the whole range of white matter lesion severity and hemosiderin deposits found in the first 350 subjects who were imaged.

MRI acquisition: Apart from the FLAIR sequence which had a slice thickness of 4 mm, all scans shared the same contiguous slice locations, field-of-view (256 × 256 mm), reconstructed acquisition matrix (256 × 256) and slice thickness (2 mm), giving co-registered volumes with resolution of 1 × 1 × 2 mm. The MTI protocol consisted of two standard spin-echo sequences; one with an RF saturation pulse applied 1KHz off-resonance and one without. The T_1-mapping protocol employed two fast spoiled gradient-echo sequences acquired with brain-optimized flip angles of 2 and 12° respectively [2].

Image processing: Using tools freely available in FSL (http://www.fmrib.ox.ac.uk), the structural, MTI and T_1-mapping sequences were pre-processed to extract the brain and remove bulk patient motion, with MTR and T_1 volumes determined as previously described for each subject [1,2]. After interpolation of the FLAIR volume to 1 × 1 × 2 mm resolution, regions of NAWM and white matter lesions were identified using the MCMxxxVI (1936) brain segmentation tool from the T_2*- and FLAIR-weighted volumes [3]. The resulting lesion and normal brain masks were applied to the MTR and T_1 volumes to determine values of these biomarkers in the two tissue types.

Statistical analysis: Values of MTR and T_1 for NAWM and white matter lesions were compared using an independent samples *t*-test, while bivariate correlations (Pearson's *r*) were used to investigate the relationship between MTR and T_1 in the two tissue types. All statistical tests were performed using SPSS 14.0 (SPSS Inc, Chicago, Ill, USA), with $p < 0.05$ being considered significant.

Results

Mean values of MTR and T_1 for the two tissue types are shown in Table 1; MTR is significantly greater in NAWM than white matter lesions, while T_1 is significantly lower (*cf.* Figure 1). In lesions, there is a significant correlation between MTR and T_1 ($r = -0.63$, $p << 0.01$), while there is no correlation in NAWM ($r = 0.13$, $p = 0.59$). These two correlations are significantly different at $p = 0.01$.

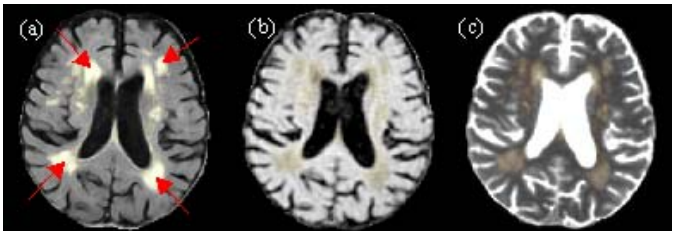

Figure 1: Maps of (a) FLAIR signal intensity, (b) MTR and (c) T_1. Regions of white matter lesions are overlaid in pale yellow on the maps and indicated by red arrows. Note the reduced MTR and increased T_1 in these regions compared with surrounding healthy tissue.

	Normal WM	WMLs	*p*
MTR	56.8 ± 1.9	49.6 ± 5.1	< 0.001
T_1	0.93 ± 0.12	1.35 ± 0.30	< 0.001

Table 1: Values of MTR (%) and T_1 (s) in normal-appearing white matter and white matter lesions (WMLs).

Discussion

This is the first study to measure simultaneously MTR and T_1 parameters in age-related white matter lesions and surrounding macroscopically normal-appearing white matter. Correlations between MTR and T_1 parameters were found in the former, but not the latter, indicating that white matter lesions are characterized by alterations in brain water homeostasis, reductions in white matter integrity and myelin injury. This allows quantitative MRI parameters to take a much wider range of values than in healthy tissue, where water content and the degree of myelination are held within relatively tight limits.

These results add to the previous observation that water diffusion parameters determined using diffusion tensor MRI and MTR are correlated in periventricular white matter lesions but not in surrounding healthy white matter [1]. These data further confirm the non-benign nature of these lesions and may shed light on their etiology. Analysis on the remaining participants of the LBC1936 is ongoing with the aim to confirm this finding and determine whether such correlations are useful in determining the severity and progression of white matter lesions.

References

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