Characterisation of brain white matter lesion severity with multi-parametric MR imaging: The Lothian Birth Cohort 1936

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Introduction

The Lothian Birth Cohort 1936 (LBC1936) is a unique group of 1091 healthy people who undertook IQ testing at age 11 and are returning for testing again in old age [1]. The current tests includes comprehensive magnetic resonance imaging (MRI) to assess how changes in the brain, and particularly in white matter, relate to cognitive changes observed in older age.

White matter lesions (WML) commonly seen in MR brain images of older people are related to various disorders including cerebrovascular disease. In this work we use multi-parametric MRI, including diffusion MRI, to assess the severity of WML observed in MRI data of LBC1936.

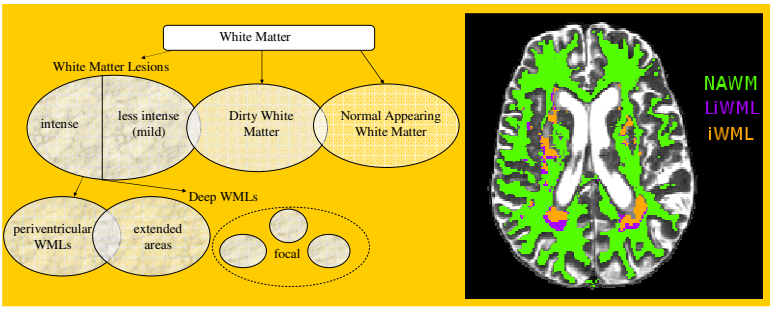

Figure 1. Classification of white matter; Normal appearing white matter (NAWM), less intense white matter lesions (LiWML) and intense white matter lesions (iWML)

Methods

MRI data from 44 participants from the LBC1936 study (age 72-73; 22 men) was used, comprising T2-weighted and fluid-attenuated inversion recovery MRI (FLAIR), diffusion MRI, T1-mapping and magnetization transfer MRI

We created mask images of intense (iWML) WML, as those observed in both T2-weighted and FLAIR images, and less intense (LiWML) WML, as those observed in FLAIR images only. The remaining WM tissue was classified as normal appearing white matter (NAWM), see Figure 1.

Diffusion fractional anisotropy (FA), mean diffusivity (MD), axial and radial diffusivity (Lax, Lrad), magnetization transfer ratio (MTR) and longitudinal (T1) relaxation time parametric maps (Figure 2) were calculated and masks were transferred to these maps using the FLIRT linear registration tool (FSL).

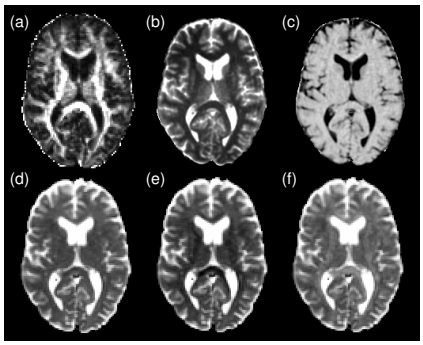

Figure 2.

Examples of parametric maps from a LBC1936 participant:

(a) FA, (b) T1, (c) MTR, (d) MD, (e) Lrad and (f) Lax

Mean values of each parameter were compared across the three white matter classes using ANOVA and post-hoc analysis with Tukey multiple comparisons of means. Effect size was assessed with Cohen's d.

	FA		T1		MTR	
Tissue	p adj	Cohen's d	p adj	Cohen's d	p adj	Cohen's d
LiWML - iWML	< 0.001	2.73	< 0.001	-2.19	< 0.001	0.94
NAWM - iWML	< 0.001	3.84	< 0.001	-1.96	< 0.001	1.53
NAWM - LiWML	0.66	0.18	0.86	0.12	0.02	0.60
	MD		**Lrad**		**Lax**	
Tissue	p adj	Cohen's d	p adj	Cohen's d	p adj	Cohen's d
LiWML - iWML	< 0.001	-1.84	< 0.001	-2.22	< 0.001	-0.97
NAWM - iWML	< 0.001	-3.62	< 0.001	-3.93	< 0.001	-2.81
NAWM - LiWML	< 0.001	-2.13	< 0.001	-1.67	< 0.001	-2.62

Large effect; Medium effect; Small effect

Table 1. Post-hoc tests of differences between tissue classes

Results

- ANOVA showed significant differences in all parameters between iWML, LiWML and NAWM (p<0.001).
- Post-hoc tests (Table 1) showed that FA decreased while MD, Lax and Lrad increased significantly in iWML compared with NAWM.
- MD, Lax and Lrad also increased significantly in LiWML, taking intermediate values, Figure 3
- MTR was reduced in iWML, and in LiWML to a lesser level.
- FA and T1 values did no change in LiWML.

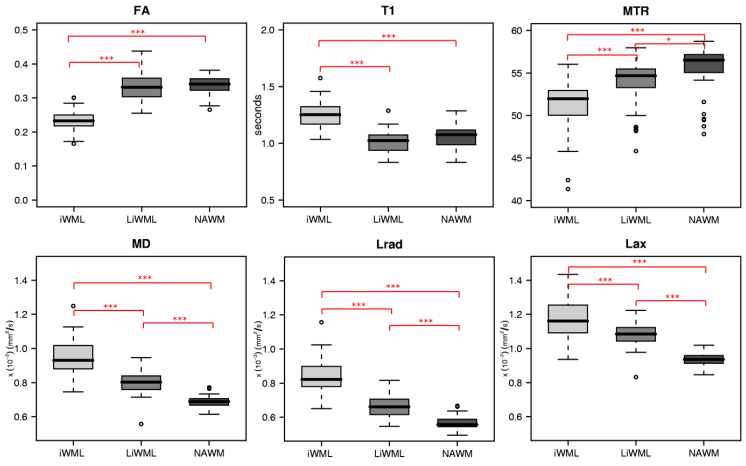

Figure 3. Boxplots of imaging parameters measured in the three white matter classes; *** = p<0.001; * = p<0.05

Discussion and conclusions

In a sample of LBC1936 subjects we found that both MD and MTR are more sensitive to early changes in white matter, as they change significantly in less severe lesions (LiWML). FA (commonly used to assess white matter integrity) and T1 (a marker of free water content) only showed changes in the more severe lesions (iWML).

This multi-parametric approach enables characterisation of WML severity and provides imaging markers for processes underlying WML progression in sequential studies.

References: [1] Deary IJ, et al 2007, BMC Geriatr 7:28.

Acknowledgements:

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