White matter hyperintensity burden is associated with reduced parietal lobe white matter integrity

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Background

Subclinical brain lesions, detected as white matter hyperintensities (WMH) on T2-weighted MR images, are ubiquitous in older adults (**Figures 1 and 2**), and there is strong evidence of their detrimental influence on cognition (Deary et al. 2003, Gouw et al. 2006) and emotional health (Godin et al. 2008).While it is known that they are associated with vascular risk factors (Murray et al. 2005), there is debate on the exact pathology of WMH (Young, Halliday & Kril 2008). Diffusion tensor imaging (DTI) measures the small scale integrity of white matter, by quantifying the fractional anisotropy (FA) of tissue water diffusion (**Figure 3)**. DTI is potentially a powerful tool for investigating the white matter damage associated with WMH burden.

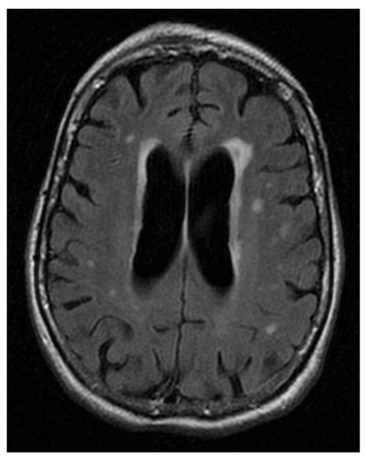

Figure 1. Axial FLAIR MRI showing a brain with low hyperintensity burden.

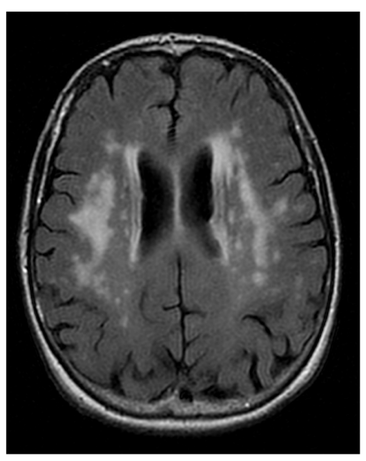

Figure 2. Axial FLAIR MRI showing more marked Hyperintensity burden.

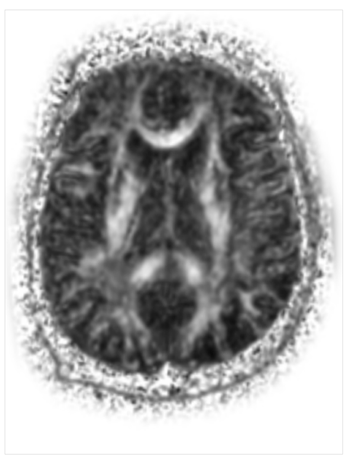

Figure 3. Example of a brain FA map of a healthy individual. Brighter areas represent higher FA.

Purpose

To describe the relationship between brain WMH burden and FA in a cohort of healthy people in late midlife. This study tested the hypothesis that greater WMH burden would be inversely correlated with FA and that there would be regional correlation of these metrices.

Methods

Participants

102 normal people (age range 67-69) were recruited for a brain MRI study of WMH and FA. All participants were members of the Aberdeen 1936 Birth Cohort.

MRI imaging and processing

MRI was carried out on a 1.5T NVi scanner (GE, Milwaukee, USA) using T2 axial, FLAIR, 3D T1 and DTI sequences. T2 weighted and FLAIR images were analysed for WMH using a modified Scheltens' scale (Scheltens et al. 1993). The DTI images were processed by affine registering each directional DTI image to the non-directional image. FA maps were then generated using DTIStudio (Jiang et al. 2006). Using the Wake Forest pick atlas tool (Maldjian et al. 2003) regions of interest of the whole brain (WFB) and the major cerebral lobes (temporal, occipital, parietal and frontal) were created. The T1 image of each volunteer was scalp stripped and then segmented (using FSL (Smith et al. 2004) tools BET and FLIRT). The grey and white matter segments were summed to create a volunteer brain mask (VB). Using the ITK (Yoo et al. 2002) demons non-linear registration algorithm the WFB image was registered to the VB image. The transformation field was applied to each of the other lobe masks. The non-directional DTI image was registered to the T1W image and the transform applied to the FA map. This gave volunteer specific masks for the major lobes. In this way the lobe masks could be directly applied over the FA maps.

Statistical analysis

Correlation between WMH score and FA was tested by Pearson's correlation. Analysis was performed on the whole brain and on the frontal, parietal, occipital and temporal lobes independently.

Results

Table 1 demonstrates Pearson correlations between WMH burden and tissue FA. FA was inversely correlated with WMH score in the parietal lobe of the brain (p=0.009, r= -0.27) but not in the frontal, occipital, temporal lobes or in the whole brain (p>0.05).

Brain region	Metric	Mean	SEM	r	p-value
Frontal Lobe	WMH	3.09	0.16	-0.08	0.45
	FA	0.26	0.00		
Parietal Lobe	WMH	2.30	0.19	-0.27	0.01
	FA	0.23	0.00		
Temporal Lobe	WMH	1.14	0.16	-0.01	0.94
	FA	0.25	0.00		
Occipital Lobe	WMH	0.56	0.13	-0.12	0.24
	FA	0.25	0.00		
Whole Brain	WMH	7.09	0.00	-0.15	0.14

Table 1. Summary table of WMH burden and FA values, and the correlation between these metrices in 4 brain regions and the whole brain.

Discussion

The strengths of this study are MR images from a well characterised cohort of similar age. A weakness is the assessment of WMH by a semi-quantitative visual scale, subject to ceiling effects and observer variability. However, this does not negate the positive association found here.

Visible WMH are thought to represent ischaemic change in brain tissue and result from demyelination and microinfarction secondary to arteriolosclerosis (Pantoni, Garcia 1997). It is likely that such changes represent late stage ischaemia and subvisible changes precede development of WMH. Our results support this hypothesis in the parietal lobes, but not in other brain regions. Lack of correlation in other regions may be due to lack of anatomical matching of WMH and DTIStudio regions of interest. Alternatively, regional measures may be insensitive to FA differences in and around lesions typically 3-10 mm in diameter. Future work correlating WMH and FA measures at a voxel level may prove more informative.

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