Cognitive Ageing and White Matter Integrity: a Diffusion Tensor and Magnetisation Transfer MRI Study

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Introduction

Retaining the integrity of the brain's white matter might be important for successful cognitive ageing [1]. There are associations between the number of white matter lesions (*e.g.* Fazekas scores) and cognitive test scores [2]. Diffusion tensor MRI (DT-MRI) can provide more sensitive indicators of the state of cerebral white matter. Mean diffusivity (<D>) and fractional anisotropy (FA) are found to correlate significantly with cognitive ability in old age, especially with tests of executive function [3]. On the other hand, one study suggested that DT-MRI parameters correlate with life-long cognitive traits rather than cognitive ability in old age specifically [4].

Here we test the hypothesis that white matter integrity as measured by DT-MRI and magnetisation transfer MRI (MT-MRI) is related to cognitive ability in youth and old age [5]. In MT-MRI, a saturation pulse is used to selectively saturate the bound proton pool, giving rise to contrast that reflects differences in the resonant properties of free and bound protons. The magnetisation transfer ratio (MTR), which expresses the magnitude of this effect, therefore reflects the amount and nature of macromolecular structures in a given brain volume, and can indicate white matter structural damage resulting from myelin loss. DT-MRI and MT-MRI are therefore complementary imaging modalities in that they provide measures of white matter tract integrity.

Methods

Subjects: 40 (21 men, 19 women) surviving participants of the Scottish Mental Survey of 1932 were studied.

Cognitive tests: Subjects IQ was tested at age 11 in June 1932 using the Moray House Test (MHT). In 2004, at age 83, they took a battery of mental tests to assess: premorbid ability (National Adult Reading Test; NART), working memory (Letter-Number Sequencing; LNS), executive function (Verbal Fluency; VF), non-verbal reasoning (Raven's Progressive Matrices; RPM) and processing speed (Digit Symbol; DS).

MRI acquisition: All MRI data were obtained using a GE Signa LX 1.5 T clinical scanner. The MRI examination consisted of a fast spin-echo (FSE) T_2-weighted sequence, a FLAIR T_2-weighted FSE sequence, and MT-MRI and DT-MRI protocols. To provide near whole brain coverage, 28 contiguous axial slice locations with a FOV of 240 × 240 mm and thickness 5 mm were imaged using the T_2-weighted FSE sequence. All subsequent sequences shared these contiguous slice locations, FOV and slice thickness. The MT-MRI protocol consisted of two standard SE sequences; one with a MT saturation pulse and one without. The MT pulse was a single sinc-shaped pulse of duration 16 ms and peak amplitude 1.3 times higher than that of the 90° pulse applied 1 kHz from the water resonance. The acquisition parameters for these SE sequences were an acquisition matrix of 256 × 128, and TR/TE of 1730/20 ms. In the DT-MRI experiment, diffusion-weighted (DW) images were acquired using a single-shot spin-echo echo-planar (EP) imaging sequence. Sets of axial DW-EP images (b = 0 and 1000 s/mm^2) were collected with diffusion gradients applied sequentially along six non-collinear directions. Five acquisitions consisting of a baseline T_2-weighted EP image and six DW-EP images were collected per slice position. The acquisition parameters for the DW-EP sequence were an acquisition matrix of 128 × 128 (zero filled to 256 × 256), and TR/TE of 8000/97.4 ms.

Image processing: Maps of <D>, FA and MTR (= $100\{M_0\text{-}M_s\}/M_0$, where M_s and M_0 are signal intensities with/without the saturation pulse) were generated for each slice in every subject on a voxel-by-voxel basis.

ROI analysis: Values of <D>, FA and MTR were obtained for normal-appearing frontal and occipital periventricular white matter and centrum semiovale from multiple 5.625 × 5.625 mm (6 × 6 voxels) regions-of-interest (ROI). The observer was blind to the clinical status and cognitive function of participants.

Results

Values of <D>, FA and MTR in the three regions studied are shown in Table 1. FA in the centrum semiovale correlated positively and significantly with all of the cognitive test scores, between r = 0.36 (p = 0.02) and r = 0.56 (p < 0.001). <D> in the centrum semiovale and frontal areas correlated, respectively, at r = –0.35 and r = –0.35 (both p = 0.03) with LNS, and r = –0.36 (p = 0.02) and r = –0.46 (p = 0.003) with VF. MTR in the occipital white matter correlated r = 0.32 with LNS (p = 0.04).

	Frontal white matter	Occipital white matter	Centrum semiovale
<D> (× 10^{-6} mm^2/s)	857 ± 39	801 ± 36	761 ± 31
FA	0.32 ± 0.03	0.41 ± 0.04	0.44 ± 0.05
MTR (%)	33.9 ± 0.9	33.0 ± 0.7	33.2 ± 0.8

Discussion

The results replicate other studies which find that DT-MRI indices are related to life-long cognitive traits and also to tests of executive function. We also find associations with a test of working memory (LNS), an ability that is especially close to general cognitive function. A new finding here is that MTR is related to a test of working memory. As far as we are aware, this is the first report of a MT-MRI measure being related to cognitive ability in normal cognitive ageing. However, caution must be exercised due to the number of cognitive test scores performed and MRI parameters used in the correlations. Nevertheless, these results indicate that the integrity of the white matter is an indicator of cognitive ability. Replication studies with larger samples are now required.

References

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