White Matter Integrity and Cognition in Childhood and Old Age: A Diffusion Tensor MRI Study

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Introduction: Some cognitive functions change with age, but the biological basis of these changes are not well understood. One underlying process might be disruption of white matter fibre tracks connecting different cortical regions, so called cortical disconnection[1,2]. Subtle white matter tract deterioration can be identified using scalar parameters derived from the apparent diffusion tensor of water (**D**): the mean diffusivity (<D>) which measures the magnitude of water molecule diffusion, and the fractional anisotropy (FA) which indicates the coherence of diffusion. Low values of <D> and high values of FA indicate intact healthy coherent axons. Some studies have suggested a relationship between these DT-MRI parameters and both ageing and cognition[1,2] .

Here, in a unique cohort of healthy subjects in whom cognitive ability was measured at both age 11 and 83, we investigate the hypothesis that white matter tract integrity as measured by DT-MRI is related to cognitive ability in youth and old age.

Methods: 40 (21 men, 19 women) surviving participants of the Scottish Mental Survey of 1932 were studied. 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), global cognitive function (Mini-Mental State Examination; MMSE), non-verbal reasoning (Raven's Progressive Matrices; RPM), working memory (Letter-Number Sequencing; LNS), verbal memory (Logical Memory; LM), executive function (Verbal Fluency; VF), and processing speed (Digit Symbol; DS).

All DT-MRI data were obtained using a GE Signa LX 1.5 T clinical scanner. Diffusion-weighted (DW) images were acquired from 28 contiguous axial slice locations with a FOV of 240 × 240 mm and thickness 5 mm 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 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.

Values of <D>, FA for normal-appearing frontal and occipital periventricular white matter and centrum semiovale (CS) were measured in multiple 5.625 × 5.625 mm (6 × 6 voxels) regions-of-interest. The observer was blind to the cognitive function of participants and the purpose of the study.

Results: The principal results of this study, namely correlations (Pearson's r) between DT-MRI parameters and cognitive test scores, are shown in Table 1. Significant correlations ($p < 0.05$) are shown in bold.

	Frontal <D>	Frontal FA	Occipital <D>	Occipital FA	CS <D>	CS FA
Prior cognitive ability						
Age 11 IQ (MHT)	-0.13	0.24	0.08	0.17	-0.21	**0.37**
NART	-0.19	0.08	-0.08	0.03	-0.14	**0.42**
MMSE	-0.22	**0.32**	0.07	0.24	-0.13	**0.41**
Assessments of current cognitive ability						
RPM	-0.18	0.28	0.15	0.23	-0.27	**0.38**
LNS	**-0.35**	0.09	-0.04	0.28	**-0.35**	**0.41**
LM	-0.03	-0.09	0.06	-0.12	0.04	0.15
VF	**-0.46**	0.17	-0.18	0.16	**-0.36**	**0.56**
DS	-0.14	0.14	0.19	0.10	-0.24	**0.36**

Discussion: Table 1 shows significant correlations between FA in centrum semiovale and scores on psychometric tests of non-verbal reasoning, working memory, executive function and processing speed. These data also replicated the highly provocative finding that centrum semiovale FA correlates with IQ at age 11, and with an estimate of prior ability[2]. This study therefore not only provides further evidence for reduced white matter integrity being a basis for individual differences in cognitive ageing, but also that centrum semiovale FA may in part reflect some life-long association with cognition not just cognitive ability measured in old age.

References

1. O'Sullivan M, et al. *Neurology* 2001;**57**:632-638. 2. Shenkin SD, et al. *Neuroreport* 2003;**14**:345-349.

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