Diffusion Tensor MRI and Cognitive Function in Normal Ageing

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Introduction

Some cognitive functions change with age, but the biological bases 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]. White matter lesion (WML) load on structural MRI correlates inconsistently with cognition. Diffusion Tensor MRI (DT-MRI) reflects more subtle white matter tract deterioration. The diffusion of water molecules can be characterised by two scalar parameters: 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 [1,2]. Some small studies have suggested a relationship between these DT-MRI parameters and both ageing and cognition.

We report the largest study to date of DT-MRI parameters and cognition in elderly volunteers with a very narrow age range. We hypothesise that (1) worse cognitive function would be associated with higher WML load, and (2) worse cognitive function (particularly executive function) would be associated with increased <D> and decreased FA.

Methods

Subjects: 115 volunteers were recruited from the community, providing 105 usable scans. 72 (68.6%) were female, mean age 78.4 (SD 1.5) years. All were relatively healthy and living independently.

Cognitive tests: Subjects took the following cognitive tests: National Adult Reading Test (NART) – a measure of prior cognitive ability; Mini Mental State Examination (MMSE) – a measure of global cognitive function; verbal fluency (VF) – a measure of executive function; Moray House Test No 12 (MHT) – a measure of verbal reasoning; Raven's Progressive Matrices – a measure of non-verbal reasoning.

MRI Scans: Structural MRI and DT-MRI were performed on a GE Signa LX 1.5T scanner. Structural scans were rated semi-quantitatively for periventricular lesions (PVL) and deep white matter lesions (DWML) using the Fazekas scale. For DT-MRI, regions-of-interest (ROI) were placed on normal-appearing white matter on T_2-weighted images in frontal and occipital regions, and centrum semiovale [2]. These ROI were then transferred to the <D> and FA maps. Informed consent and local ethics committee approval were obtained.

Results

Cognition and white matter lesions: Associations between WML load and cognitive test score were all in the expected (negative) direction ($\rho \sim 0.0$ to -0.15), with MMSE reaching statistical significance ($\rho = -0.23$, $p = 0.02$).

Cognition and DT-MRI: <D> was generally negatively correlated with cognitive test score ($r \sim -0.02$ to -0.26), and FA positively correlated ($r \sim -0.07$ to 0.25). The pattern was more consistent for <D> than FA. There was a statistically significant association ($p < 0.05$) between <D> and VF in all brain areas ($r \sim -0.22$ to -0.27); between <D> and MMSE in centrum semiovale ($\rho = -0.21$), and between <D> and MHT occipitally ($r = -0.21$). The only statistically significant association for FA was occipitally with VF ($r = 0.25$, $p = 0.01$). When corrected for potential confounders (age, sex) these associations were attenuated. Significant correlations remained occipitally for VF and both <D> (frontal $r = -0.20$, $p = 0.053$; occipital $r = -0.26$, $p = 0.012$) and FA ($r = 0.22$, $p = 0.03$).

Conclusions

This is the largest study to date reporting structural MRI, DT-MRI and cognitive function data in a typical community dwelling group of older people, with a narrow age range. In this cohort, white matter lesion burden was not significantly correlated with cognitive test score. Using DT-MRI, <D> was more consistently associated with cognitive ability than FA, in particular with verbal fluency. Executive function may be the cognitive domain most sensitive to cortical disconnection. DT-MRI, in particular <D>, is useful in investigating the ultrastructural changes underlying cognitive ageing.

References

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