Tract-specific white matter integrity and cognitive ability in youth and old age

S. Muñoz Maniega[1], L. Penke[1], J. D. Clayden[2], C. Murray[1], M. E. Bastin[1], A. J. Gow[1], J. M. Wardlaw[1], and I. J. Deary[1]

[1]University of Edinburgh, Edinburgh, United Kingdom, [2]Institute of Child Health, University College London, London, United Kingdom

Introduction

The aim of this work is to understand how brain white matter integrity contributes to age-related cognitive decline in humans. The Lothian Birth Cohort 1936 (LBC1936) is a unique cohort of 1091 healthy people who undertook IQ testing at age 11 and again at age 70 [1]. Using contemporary brain MRI (at age 72), including diffusion tensor imaging (DTI), we examined how white matter integrity relates to cognition in these subjects. We used fractional anisotropy (FA) and mean diffusivity (MD), calculated with tractography techniques, as markers of white matter integrity.

Methods

The first 192 participants from the LBC1936 cohort (age 72) were included in the current analysis; no patient had a history of dementia (MMSE > 23). DTI was performed with a 1.5T GE MRI scanner comprising diffusion-weighted images (b=1000s/mm^2) in 64 non-collinear directions, and 7 T_2-weighted images (b=0); with a resolution of 2×2×2 mm^3. Data were pre-processed and diffusion tensor parameters estimated using FSL tools [2]. We used BEDPOST/ProbTrack [3] with a two-fibre model and 5000 streamlines to estimate the tracts of interest. A novel unsupervised tract segmentation method [4], based on a neighbourhood tractography approach [5], was used to select equivalent tracts of interest in each subject. This technique optimises the choice of seed point by estimating the best matching tract from a series of candidates against a reference tract which was derived from a white matter atlas [6]. White matter connections in the brain thought to be affected by age were segmented: callosal fibres (genu and splenium of the corpus callosum), and frontal white matter connections bilaterally such as the anterior thalamic radiations, cingulum bundles, uncinate and arcuate fasciculi. Tract-averaged mean FA and MD were correlated (Pearson's r) with six cognitive variables: IQ at ages 11 and 70 (Moray House Test [1]), IQ change (11-70), and factors representing general cognitive ability (g), processing speed (g_{speed}) and memory (g_{memory}) at age 70.

Results

The automatic tractography technique worked in the vast majority of subjects. Figure 1 shows projections of the resulting tracts in one subject. All tracts were visually checked and only those following the expected path were used in the analysis. FA and MD outliers with ±3 SD from the population mean were also excluded.

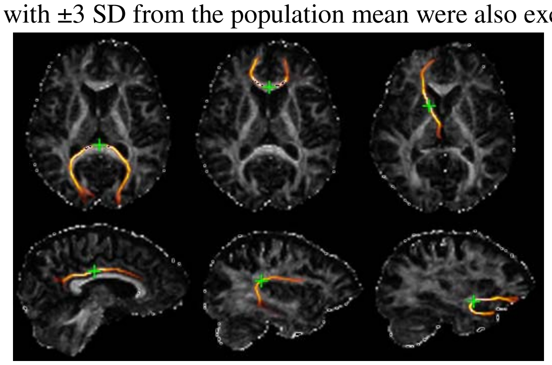

Figure 1: Tract segmentations obtained in one subject. From left to right, top row: splenium and genu of the corpus callosum and right anterior thalamic radiation; bottom row: right cingulum, arcuate and uncinate fasciculi. Seed points in green.

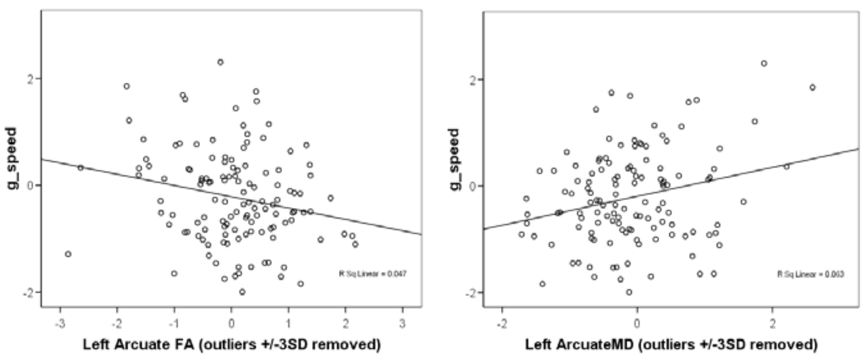

Figure 2: Scatter plots of left arcuate FA and MD versus the general processing speed factor at age 70 (FA and MD values are z-standarised). Higher values of g_{speed} indicate slower reaction times.

These preliminary results show correlations of cognitive performance with tract-averaged diffusion parameters mainly in fronto-temporal and parietal connections. Age 11 IQ was significantly correlated with FA in the left uncinate fasciculus, r=0.27 ($p < 0.01$) and age 70 IQ correlated with left uncinate fasciculus FA (trend) and MD, r=0.15, -0.19 ($p < 0.1$ and $p < 0.05$). Processing speed (g_{speed}) at age 70 correlated with FA and MD for arcuate fasciculi bilaterally, r=-0.24, 0.16 ($p < 0.01$ and $p < 0.1$) for right arcuate, and r=-0.22, 0.25 ($p < 0.05$ and $p < 0.01$) for left arcuate; Figure 2. No other significant effects were found between other white matter tracts or cognitive variables. Only right-handed subjects were used in the analysis; controlling for gender did not affect these results.

Discussion

Recent tractography studies showed correlation between uncinate fasciculus FA and intelligence scores in both children [7] and healthy young adults [8], suggesting that the uncinate fasciculus is part of the neural basis for intelligence. Our results corroborate this finding by showing that the relation is maintained from age 11 to age 70. We also found that mental speed in old age is related to arcuate fasciculus integrity, as predicted by the parietal-frontal integration theory of intelligence [9].

1. Deary IJ, et al 2007, BMC Geriatr. 7: 28.
2. FMRIB, Oxford, UK; http://www.fmrib.ox.ac.uk/
3. Behrens TE et al 2007, NeuroImage. 34:144–155.
4. Clayden JD et al. NeuroImage, under review.
5. Clayden JD et al. 2007, TMI. 26:1555-1561.
6. Mori S et al. 2005, Elsevier.
7. Constable RT et al. 2008, Pediatrics. 121:306-316.
8. Yu, C et al. 2008, NeuroImage 40:1533–1541.
9. Jung RE et al. 2007, Behav Brain Sci. 30:135-187.

Project funded by Help the Aged and Medical Research Council. MRI data acquired in the SFC Brain Imaging Research Centre (http://www.sbirc.ed.ac.uk/) and processed using TractoR libraries (http://code.google.com/p/tractor/).