Segmentation and characterisation of white matter tracts in late childhood and adolescence

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Introduction

There have been few studies using diffusion MRI based tractography to look at the normal development of specific tracts during late childhood and adolescence. However, there is some evidence for the existence of relationships between diffusion parameters, especially fractional anisotropy (FA) and mean diffusivity (MD), and age or gender (e.g. [1]). In addition, previous work has suggested there may be lateral asymmetries in white matter properties at this age. Our contributions in this work are: (1) to demonstrate that a recently developed method for automated tract segmentation [2,3] is applicable to data acquired from children; and (2) to investigate the diffusion properties of a set of tracts segmented in this way.

Methods

Data were acquired from 27 subjects in late childhood or adolescence (13 male, mean age 11.4 ± 3.0 yr, age range 7.1–18.6 yr). All subjects were healthy, without any neurological, psychiatric or developmental problems, and none had any MR-visible structural abnormalities. An unpaired *t*-test showed no significant age difference between the males and the females ($P = 0.53$). Each subject underwent a diffusion MR protocol on a Siemens Avanto 1.5 T clinical scanner. Echo-planar diffusion-weighted images were acquired along 20 noncollinear directions at a *b*-value of 1000 s mm^{-2}, along with a *b*=0 image. This protocol was repeated three times during the scan session, and the data combined without averaging. Reconstructed image resolution was 2.5 x 2.5 x 2.5 mm.

Correction for eddy current induced distortions, brain extraction, and calculation of diffusion tensor FA and MD values was carried out using FSL tools (http://www.fmrib.ox.ac.uk/fsl). The tractography algorithm used was the multicompartment version of FSL ProbTrack [4], which allows for the presence of two white matter fibre populations in each voxel. The probabilistic neighbourhood tractography (PNT) technique [2,3] was used to select seed points for segmentation of the corpus callosum genu, cingulum bundles (CBs) and pyramidal tracts (PTs) in each subject. This fully automated approach is based on a probabilistic model of tract shape variability. Visitation maps were thresholded at the 5% level and binarised to produce the final tract segmentations. Statistical analysis of the mean FA and MD from within each segmented region was performed to investigate the effects of age and gender. We also investigated the diffusion properties of the tracts relative to one another.

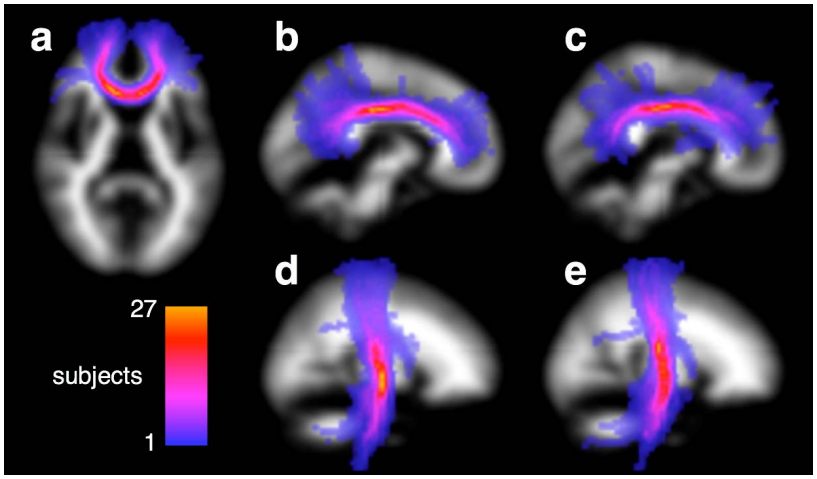

Fig. 1: *Group maps of the five tracts segmented across the data set: genu (a); left (b) and right (c) cingulum bundles; and left (d) and right (e) pyramidal tracts. Each subfigure is a maximum intensity projection, overlaid on a standardised white matter map in MNI space.*

Table 1: *Means and standard deviations of FA and MD within the five segmented tracts, across the data set.*

Tract	Mean±SD FA	Mean±SD MD, mm^2 s^{-1} (x 10^{-3})
genu	0.358±0.024	0.832±0.038
CB, left	0.317±0.045	0.810±0.041
CB, right	0.299±0.042	0.796±0.042
PT, left	0.408±0.045	0.871±0.046
PT, right	0.421±0.053	0.830±0.065

Results

Fig. 1 shows group maps of the five tracts of interest, after affine transformation into MNI standard space. This figure shows the degree of similarity between segmentations of each tract across the group. In each case the core of the pathway closely follows the known anatomy, and there is a high degree of symmetry between equivalent tracts in the left and right hemispheres. The means and standard deviations of FA and MD for each tract are shown in Table 1. We investigated the effects of age and gender on FA and MD in each tract individually, using ANCOVA. No significant age effects were found, although there was a significant effect of gender on FA in the left cingulum ($F = 5.10$, $P < 0.05$; boys mean = 0.338, girls mean = 0.298). There were no significant interaction effects.

Fig. 2 shows a plot of FA against MD for all the tracts of interest. Linear regression lines are shown for each tract individually, over the range of FA values observed in each case. A distinction between the tracts can be clearly made out. Multivariate ANOVA showed a significant effect of tract (genu/CB/PT; Wilks' lambda = 0.172, $P < 0.001$) and of hemisphere (left/right; lambda = 0.850, $P < 0.001$) on FA and MD, when taken together. There was also a trend towards an interaction between gender and hemisphere (lambda = 0.939, $P = 0.05$). Examining FA and MD separately, we found the effect of tract for both measures, but the effect of hemisphere only for MD. In addition, the interaction between gender and hemisphere was significant in both cases ($F = 5.28$ for FA, $F = 5.09$ for MD, both $P < 0.05$). No other interaction effects were significant. In light of the lack of age-related effects seen above, age was not used as a covariate in this analysis.

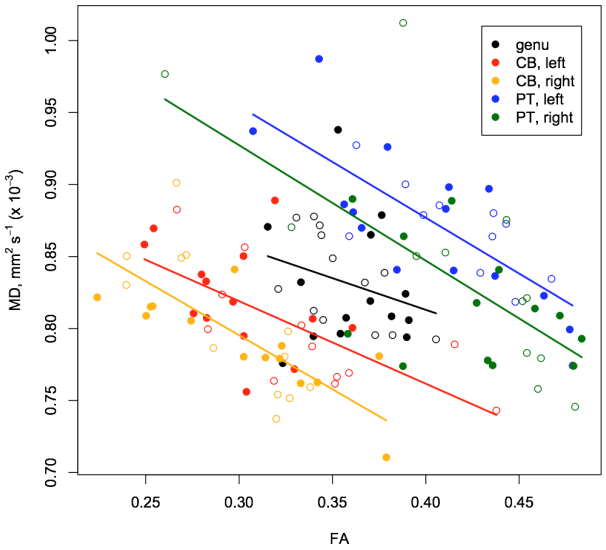

Fig. 2: *FA against MD within the five segmented tracts. Open circles represent males and closed circles females. A linear regression line is shown for each tract separately.*

Discussion

We have demonstrated that the PNT technique, based on a tract shape model, can be used to segment tracts in diffusion MR images of children's brains without intervention. We showed group maps of a set of five tracts which follow the known anatomy of each structure. We also found substantial differences between the diffusion properties of these tracts, and a lateralisation effect which appears to be partly modulated by gender, suggesting that young males and females may have different degrees of lateralisation to their white matter (some evidence for such a gender difference has been found in adults, e.g. in [5]). While we did not find significant effects of age, such effects may become apparent on investigation of additional tracts, or in a larger subject population.

Acknowledgment: This work was supported in part by the British Medical Research Council, through Programme Grant No. G0300117.

References: [1] Eluvathingal, T.J. et al., *Cereb Cortex* **17**:2760 (2007); **[2]** Clayden, J.D. et al., *IEEE Trans Med Imag* **26**:1555 (2007); **[3]** Clayden, J.D. et al., in revision at *NeuroImage*; **[4]** Behrens, T.E. et al., *NeuroImage* **34**:144 (2007); **[5]** Catani, M. et al., *Proc Nat Acad Sci USA* **104**:17163 (2007).