# Fiber tractography in healthy adolescents: an automated approach

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**Overview**: White matter (WM) development across the life span has been studied using both structural imaging and, more recently, diffusion tensor imaging (DTI)[1]. Although the current literature is still limited, available reports suggest DTI is sensitive to age-related changes in WM integrity through childhood and adolescence. One primary measure of interest is fractional anisotropy (FA), which reflects the directional portion of water diffusion. Region of interest, voxel-wise, and, to a lesser extent, fiber tractography have all been used to quantify developmental changes in WM microstructure[2,3]. Traditional tractography analyses using manually defined seed regions and inclusion criteria can be time consuming and are also susceptible to rater bias. The goal of the current study was to apply an automated probabilistic tractography method to a large sample of healthy pre-adolescents, adolescents and young adults. We hypothesized age-related increases FA in a number of tracts, especially in those involving frontal connections.

**Method**: One hundred forty-four healthy individuals, ages 9-23, participated in the study. Participants underwent a structured interview to confirm study eligibility and exclude individuals with histories of DSM-IV axis I disorders, drug use, severe medical problems, history of head injury, mental retardation, learning disabilities, and MRI contraindications. Participants were scanned on a Siemens Trio system using an 8 channel head coil. The scanning protocol included a T1-weighted MPRAGE scan, a 12 direction DTI scan, and a GRE field map sequence. T1-weighted images were processed using the FreeSurfer software package[4], generating both gray matter and white matter (WM) parcellations. WM ROIs from the FreeSurfer parcellation were aligned to the Johns Hopkins University tractography atlas and regions showing high overlap with the distal ends of tracts from the JHU atlas were selected as seed and target regions for tractography. The FMRIB software library[5] was used to conduct probabilistic fiber tractography in the cingulum bundle(CB), cortico-spinal tract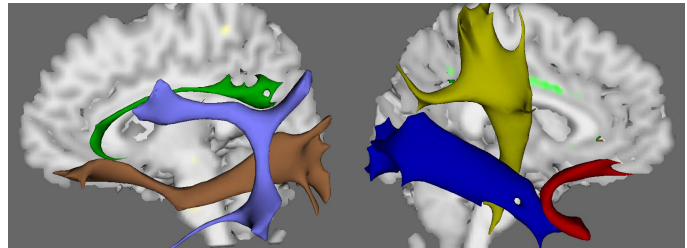(CST), inferior fronto-occipital fasciculus(IFOF), inferior longitudinal fasciculus(ILF), superior longitudinal fasciculus (SLF), and uncinate fasciculus(UNCI) (see Figure 1.). Mean FA was computed for each tract and the continuous relation between age and FA was examined with Pearson correlations. To further assess age-specific changes, participants were divided into four age groups (9-11y/o, 12-14y/o, 15-17y/o and 18-23y/o) and univariate ANOVAs with age-group and gender entered as between subjects factors were run on each tract.
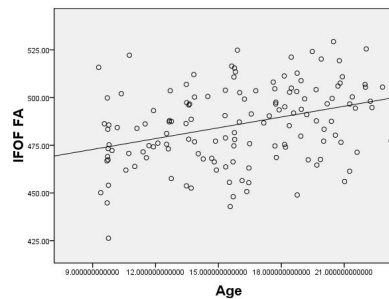


Figure 1. Left panel, green is CING, brown is IFOF, and blue is SLF. Right panel, yellow is CST, dark blue is ILF, and red is UNCI.



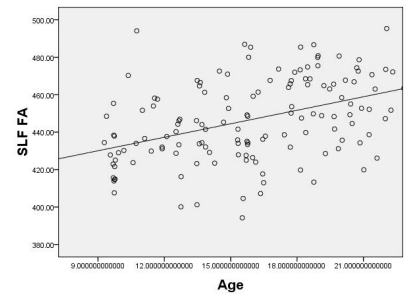Figure 2. Inferior Fronto-Occipital Fasciculus FA with Age



Figure 3. Superior Longitudinal Fasciculus FA with Age

**Results**: Fractional anisotropy in the CING, IFOF (Figure 2) and SLF (Figure 3) correlated positively with age ($p < 0.01$ in each tract). Tukey HSD post-hoc tests confirmed age-group differences were between the 18-23 year-olds and the 9-11 year-olds in the CING, IFOF and SLF, with the oldest group showing higher FA. Post-hoc tests also revealed differences between the 18-23 year-olds and the 12-14 year-olds in both the IFOF and SLF, with the oldest group having higher FA.

**Discussion**: This study examined a large number of healthy children, adolescents and young adults using DTI and a fully-automated probabilistic fiber tractography method. The data show age-related increases in WM microstructure in the CING, IFOF and SLF, suggesting continued changes in white matter in these tracts, until approximately 15 years of age.

**References: 1.)** Sullivan E. and Pfefferbaum, A. (2006). Neuroscience and Biobehavioral Reviews, 30:749-761 **2.)**Eluvathingal, T.et al., (2007). Cerebral Cortex, 17:2760-2768. **3.)** Bonekamp, D, et al, (2007). Neuroimage, 34:733-742. **4.)** http://surfer.nmr.mgh.harvard.edu/ **.5)** Smith, S. et al. (2004). NeuroImage, 23(S1):208-219 (www.fmrib.ox.ac.uk/fsl)