Regional Age Related Changes in Fractional Anisotropy of the Brain in Cognitively and Developmentally Normal Children and Adolescents Using Diffusion Tensor Imaging and Tract Based Spatial Statistics (TBSS) at 3T

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Introduction: Fractional anisotropy (FA) has been considered a measure of axonal development, with higher FA values considered representative of greater axonal maturity. We studied a group of developmentally and cognitively normal children using diffusion tensor imaging (DTI) at 3T and Tract Based Spatial Statistics (TBSS) to evaluate the FA skeleton for age related changes in FA as a measure of axonal development.

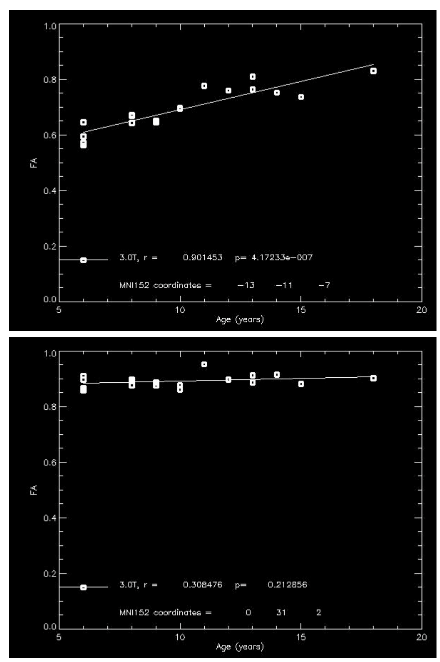
Materials and Methods: The investigation was prospective and IRB approved. 18 monolingual, English speaking, right handed control subjects (ages 6-18) underwent WISC-III or WASI, and tests of reading including Woodcock-Johnson Letter-Word Identification, and Woodcock-Johnson Word Attack. DTI was performed at 3T (Philips Achieva R2.5) using a 30 noncolinear gradient direction SS-EPI sequence [1], b=700, 56 sections, voxel size 2 mm, TR/TE=8237/74, acquisition matrix 128 x 128, 3 averages. Images were processed off-line using FSL (FMRIB [The Oxford Centre for Functional Magnetic Resonance Imaging of the Brain] Software Library, http://www.fmrib.ox.ac.uk/fsl) including BET to extract brain tissue and brain mask, eddy current correction and registration to the b=0 image volume, and DTIFit to reconstruct diffusion tensors and FA. Data from all subjects was aligned to a 9 year old control brain using a nonlinear registration and affine transformed into MNI152 standard space. The mean FA image was created and thinned to create a mean FA skeleton. Aligned FA data of the subjects was projected onto this skeleton and the resulting data were fed into voxelwise cross-subject statistics. Internally developed software written in IDL was used for ROI based parametric statistical analysis. ROI analysis was performed in the corpus callosum, posterior limb of the internal capsule (PLIC), superior (SLF) and inferior longitudinal fasciculus (IFO-ILF) and cingulum. FA values were plotted against age for each region and the slope of the line, and R-squared correlation calculated.

Results: Age-related increases in FA varied with location. The most marked changes in callosal FA were seen within the mid-callosal body (slope 0.016) with minimal changes in the callosal genu (slope 0.002) and splenium (slope 0.008). Age related changes in FA were seen in the PLIC (RT slope 0.0246, LT slope 0.020) and cingulum (slopes 0.016-0.023), SLF (slopes 0.009-0.014) and IFO-ILF (slopes 0.011-0.02) and were more marked in the left SLF (slope 0.014) than the right (slope 0.009).

Conclusion: DTI at 3T using TBSS in children known to be normal by extensive cognitive testing suggests white matter maturation proceeds at different rates in different parts of the brain and that normative FA values for older children and adolescents cannot be used for younger children.

Region	MNI location	R^2 Correlation	p value	slope	Group FA mean (SD)
Genu CC	0,31,2	0.095	0.213	0.002	0.892 (0.023)
Midbody CC	0,-13,27	0.347	0.010	***0.016***	0.619 (0.095)
Splenium CC	0,-36,18	0.378	0.006	0.008	0.866 (0.049)
RT PLIC	15,-11,-9	0.839	1.79E-07	***0.025***	0.719 (0.093)
LT PLIC	-13,-11,-7	0.811	4.17E-07	***0.020***	0.694 (0.079)
RT SLF	38,-22,29	0.258	0.031	0.009	0.503 (0.059)
LT SLF	-37,-23,30	0.552	0.0004	***0.014***	0.532 (0.067)
RT ILF-IFO	41,-36,-7	0.667	3.50E-05	***0.019***	0.625 (0.085)
LT ILF-IFO	-42,-40,-4	0.537	0.0005	0.011	0.634 (0.054)
RT ANT CINGULUM	11,37,7	0.658	4.40E-05	***0.019***	0.538 (0.079)
RT MID CINGULUM	10,20,24	0.646	5.70E-05	***0.016***	0.651 (0.068)
RT POST CINGULUM	8,-22,34	0.691	1.90E-05	***0.016***	0.532 (0.069)
LT ANT CINGULUM	-7,23,21	0.647	2.91E-05	***0.017***	0.644 (0.075)
LT MID CINGULUM	-7,2,33	0.690	1.58E-05	***0.019***	0.625 (0.083)
LT POST CINGULUM	-11,-44,23	0.808	4.17E-07	***0.023***	0.517 (0.089)

Fig 1. Regions of interest FA data with areas of greatest Slope (change in FA with age) highlighted



A.

B.

Fig 2. Plots of change in FA versus age in the PLIC (A) and callosal genu (B)

Reference:

[1] Jones DK, Horsfield MA, Simmons A. Optimal strategies for measuring diffusion in anisotropic systems by magnetic resonance imaging. Magn Reson Med 1999;42:515–525.