# Variation in DTI-FA as a Function of Age and Brain Region: Setting the Stage for Mild TBI

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**INTRODUCTION:** Mild traumatic brain injury (mTBI) is difficult to distinguish clinically from PTSD and is not detectable by clinical neuroimaging. Several groups have now shown diffusion tensor imaging to detect more severe TBI [1-3]. In order to increase the detection of axonal injury in mTBI, a comprehensive sampling of fractional anisotropy (FA) in healthy white matter was undertaken in order to define the limits of normal. These global and regional sampling distributions of normals allow for creation of probability maps of axonal injury.

**MATERIALS AND METHODS** Fifty healthy volunteers were recruited for a healthy aging study (age range = 19-81 yrs; 53.2 ± 18.9 M±SD; M/F = 17/33) and were imaged as a part of a multi-imaging protocol on a Siemens Sonata 1.5 T scanner. Single shot spin-echo planar DTI was acquired in six directions (resolution = 2x2x3mm; 33 axial slices; TR/TE = 5400/97 ms, and b values of 0 and 1000 sec/mm$^2$). DTI studio (http://www.mri.kennedykrieger.org) was used to create FA maps from diffusion images.

**Regional Analysis:**

*Normalization*: Each subject's FA map was spatially normalized to an in-house FA template using a non-linear warp, which was also weighted toward WM. The FA template was created by normalizing a single individual T1 image to the T1 template in SPM2 (http://www.fil.ion.ucl.ac.uk included in SPM2) and the resultant transformation matrix is used on the averaged FA image from 62 healthy volunteers (age range: 19-81yrs).

*Tissue class segmentation:* GM/WM/CSF contrast is very high on FA images and allows for robust tissue class segmentation. Automated segmentation using SPM2 produced tissue-class probability maps for each control FA image. A WM binary mask was created after thresholding P-map ($P \geq 0.55$). The WM mask was multiplied by the corresponding normalized FA image to create a WM-only FA image for each control.

*Transformation into ICBM_MNI space:* One control subject's normalized FA image was linearly warped to ICBM_MNI space using Landmarker (version 1.1, www.mristudio.org) with the transformation matrix then applied to all 50 subject's WM-only images. This was done to maximize the anatomical overlap between control images and the White Matter Parcellation Map (WMPM) in ICBM_MNI space comprised of 50 regions. Thresholding allowed for creation of individual or grouped regions of interest (ROIs) within ROIeditor (www.mristudio.org).

*ROI analysis:* Within DTI Studio, each ROI mask was applied to each subject's WM-only FA image**.** A voxel was only included for analysis if it was included in an ROI mask *and* in subject's WM-only FA image. For each ROI, we report the mean number of voxels for all 50 subjects, mean proportion of total voxels for a given ROI, the FA mean and standard deviation, the change in FA per decade of life span and significance of age effect. For the current abstract, bilateral ROI's were merged into a single ROI.

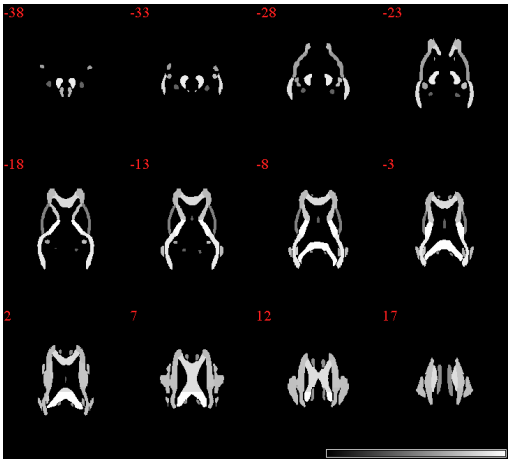
**RESULTS:** Table gives FA means and standard deviations by ROI as well as the effect of age on FA for a given ROI. Only 38 of the 50 total WMPM ROI's were adequately covered by scans. FA ranged between 0.56 (Splenium of CC) and 0.22 (Fornix). Larger regions demonstrated higher mean FA's ($R$=0.49; $P$<0.05, Spearman). 14 of 21 (67%) ROI's demonstrated a significant effect ($P$<0.05) of age on FA.

**Table.** *Fractional Anisotropy (FA) by Region of Interest (ROI).*

| ROI | Nvox | %/vox | Mean | St.Dev | Δ/10 yr. | *P* |
|---|---|---|---|---|---|---|
| CC (Splenium) | 12,729 | 0.99 | 0.563 | 0.05 | -0.0080 | 0.027 |
| IC (Retrolent.) | 3,111 | 1.00 | 0.549 | 0.03 | -0.0046 | 0.209 |
| Post. Thal. Rad. | 3,975 | 1.00 | 0.522 | 0.03 | -0.0080 | 0.002 |
| IC (Post. Limb) | 3,386 | 0.98 | 0.507 | 0.03 | -0.0051 | 0.111 |
| Sagittal Stratum | 2,230 | 1.00 | 0.497 | 0.03 | -0.0050 | 0.119 |
| CC (Body) | 13,711 | 0.99 | 0.494 | 0.04 | -0.0093 | 0.005 |
| IC (Ant. Limb) | 2,708 | 0.99 | 0.488 | 0.04 | -0.0060 | 0.018 |
| CC (Genu) | 8,851 | 0.99 | 0.486 | 0.05 | -0.0104 | 0.003 |
| SFO | 507 | 1.00 | 0.443 | 0.04 | -0.0087 | 0.008 |
| Cor. Rad (Sup.) | 7,504 | 1.00 | 0.435 | 0.02 | -0.0016 | 0.367 |
| SLF | 6,606 | 0.99 | 0.425 | 0.04 | -0.0087 | 0.002 |
| Cor. Rad. (Post.) | 3,721 | 1.00 | 0.423 | 0.03 | -0.0028 | 0.152 |
| Tapetum | 598 | 0.98 | 0.423 | 0.10 | -0.0181 | 0.042 |
| Cor. Rad. (Ant.) | 6,851 | 1.00 | 0.412 | 0.03 | -0.0073 | 0.001 |
| Stria Term. | 1,125 | 0.96 | 0.395 | 0.05 | -0.0107 | 0.005 |
| Uncinate Fasc. | 378 | 0.95 | 0.358 | 0.06 | 0.0025 | 0.032 |
| IFO | 1,949 | 0.92 | 0.353 | 0.05 | -0.0059 | 0.101 |
| Cingulum\ CG | 2,547 | 0.92 | 0.322 | 0.05 | -0.0064 | 0.082 |
| Ext. Capsule | 3,650 | 0.81 | 0.287 | 0.04 | -0.0072 | 0.016 |
| Cingulum\ Hipp. | 1,196 | 0.83 | 0.219 | 0.04 | 0.0011 | 1.4E-5 |
| Fornix | 659 | 0.73 | 0.216 | 0.09 | -0.0225 | 0.001 |

A total of 38 ROI's were reduced to 21 with bilateral ROI's merged into a single ROI. Key: Nvox = number of voxels; %/vox = mean proportion of total possible voxels in ROI; Δ /10 yr. = change in FA per decade; *P*= Probability of age effect on FA; CC = Corpus Callosum; IC = Internal Capscule; SFO = Superior Frontal Occipital Rad = Radiata; SLF = Superior Longitudinal Fasciculus; IFO = Inferior Frontal; Occipital Fasciculus; CG = Cingulate Gyrus; Hipp.=Hippocampus.

**Figure.** *Map of Mean FA by Region of Interest.*




For this image, the brightness (gray) scale indicates FA magnitude for a given ROI. Values range between 0.563 and 0.216. Note the relatively higher FA (brighter) in posterior ROI's (see table for details).

**CONCLUSIONS:** Mild TBI requires exquisitely sensitive brain imaging and image processing to differentiate from normal. We found regional variation in FA as well as the effect of age. These findings suggest that DTI, and more specifically FA, applied to TBI will be rendered more sensitive and specific when taking into account this regional variation. Our laboratory is already using this normative data to enhance diagnosis of mild TB

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