Diffusion Tensor Tractography of Corpus Callosum Development Across the Lifespan

S. Caverhill-Godkewitsch[1], C. Lebel[1], and C. Beaulieu[1]
[1]Biomedical Engineering, University of Alberta, Edmonton, Alberta, Canada

INTRODUCTION: Brain changes occur in a complex manner throughout life, and the corpus callosum (CC), a very important brain white matter pathway, is no different. Three previous studies used diffusion tensor imaging (DTI) to investigate fractional anisotropy (FA) and mean diffusivity (MD) changes in the CC across the lifespan. These studies (n=77, 82, 121) used region-of-interest analysis on a midsagittal slice to demonstrate U-shaped trajectories of FA and MD from 7-80 years[1-3]. Diffusion tractography, a powerful technique that allows for segmentation of the CC based on the unique target regions to which the fibers extend, has not yet been used to depict changes in the CC over the entire tract across the lifespan. The purpose of this study was to thoroughly examine CC development across a wide age range in a very large number of healthy subjects (n=313) using DTI tractography.

METHODS: This study included 313 subjects (164f/149m) aged 5-59 years with no history of neurological/psychiatric disease or injury. All scans were performed on the same 1.5T Siemens Sonata scanner using the same protocol. DTI was collected using dual spin echo EPI, 40 3mm slices (no gap), image matrix 96x128 zero-filled to 256x256, TE/TR = 88 ms/6400 ms, b=1000 s/mm^2, 8 averages, 6 directions, 6:06 minutes long. Deterministic tractography of the CC was performed manually in DTIStudio using one seeding region on a midsagittal slice and seven separate target regions bilaterally to segment the CC into regions ordered from front to back: orbital frontal (OF), anterior frontal (AF), superior frontal (SF), superior parietal (SP), posterior parietal (PP), temporal, and occipital[4] (see Fig.1). FA and MD were calculated for each region by averaging over the entire tract and quadratic curves were estimated with respect to age. Age of peak FA values and minimum MD values were determined for each tract.

RESULTS/DISCUSSION: FA and MD followed quadratic development curves, with FA increasing from childhood to adulthood, then decreasing; MD followed an opposite trend, decreasing until adulthood, and then increasing (Fig.1). Peak FA values were achieved between 26-35 years, while minimum MD values were reached from 30-44 years. Anterior (OF, AF) and posterior (occipital) regions reached peak FA values earliest, followed by the central (SF, SP, and PP) regions (see Fig.1 for exact peak ages). For MD values, similar trends were observed, with the occipital and OF regions achieving minimum MD first, followed by the temporal region, the AF and PP regions, and finally the SF and SP areas. MD minima were reached between 3-10 years later than peak FA values for each region. Initially, the highest FA values are in the occipital region, while the anterior areas show values slightly higher than the central section. At the end of this age range, however, after the anterior regions undergo a marked drop in FA values, the posterior CC has the highest FA, while the anterior CC has the lowest FA. MD values are fairly scattered at first, but at later ages, anterior regions have lower MD values than posterior areas, with the exception of the OF. Significant gender differences of FA and MD values were observed in the SF and SP regions, with males having higher FA (0.006-0.008 higher) and lower MD (0.015-0.02 x10^{-3} mm^2/s lower). Quadratic fits were highly significant for all 7 regions for MD and for 5 regions for FA, with the exceptions of PP and temporal.

DTI tractography has demonstrated quadratic development trends of FA and MD in the CC that peak between 26-44 years, confirming previous DTI findings[1-3]. The only previous DTI study to report developmental timings of CC subdivisions across the ages observed an anterior-to-posterior trend of maturation[2], similar to conventional MRI studies in children[5, 6]. Our results demonstrate an overall outer-to-inner development trend in which the anterior and posterior regions peak earlier than central areas, supporting previous reports of early development in the anterior CC, but also showing early maturation of the occipital region. However, the diffusion parameters were averaged across the entire CC tract, whereas other studies looked only at the central slice, so differences in timing may be due to the inclusion of voxels further from the midline. Future analyses will examine smaller central regions of the tracts to determine if the trends are the same. This study provides insight into white matter development in the CC across the age span.

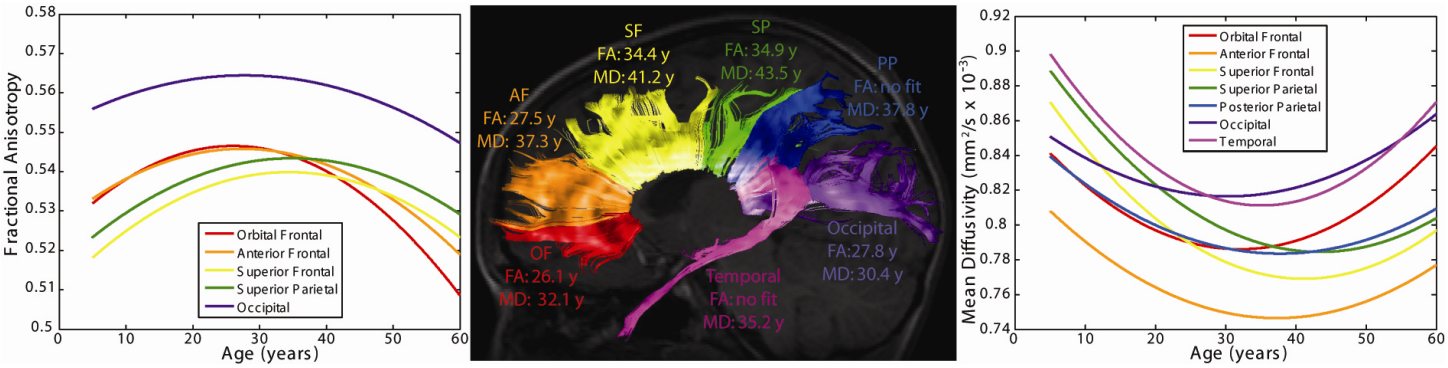

Figure 1: All seven subdivisions of the corpus callosum are shown here in a 9 year old male, with corresponding FA and MD vs. age plot. FA and MD followed quadratic development curves, with peak ages varying from 26-44 years, depending on the region. For all regions, MD minima were reached later than FA peak values.

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