DTI Demonstrates Non-linear White Matter Tract Development from Childhood to Adulthood

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INTRODUCTION: Brain maturation is a complex process that continues throughout childhood and adolescence into adulthood. White matter tracts provide the connections necessary to integrate information from spatially segmented brain areas. Previous studies have shown age-related changes in white matter tracts during adolescence using voxel-based morphometry[1, 2] (VBM) and region-of-interest (ROI) analysis[3, 4]; however, these methods are limited, since VBM assumes linear changes while ROI analysis is constrained to white matter tracts that are easily identifiable on two-dimensional images. Tractography, using diffusion tensor imaging (DTI), is an excellent tool for studying white matter maturation, allowing for non-linear analysis, as well as examination of white matter tracts that are not easily delineated on two-dimensional maps. In addition, tractography is more reproducible and less user-dependent than ROI analysis[5, 6], and has shown promise for studying white matter development in infants[7, 8]. The purpose of this study was to examine white matter tract maturation from early childhood to adulthood, using a semi-automated tractography algorithm designed to logistically permit the extraction of multiple white matter tracts in a very large DTI data set (i.e. 237 subjects).

METHODS: This study included 237 subjects aged 5-41 years (121m/116f) with no history of neurological disease or injury. All scans were performed on the same 1.5T Siemens Sonata scanner 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 and 6 directions, 6:06 minutes long. Images were normalized to a template with tensor reorientation. Tractography was performed in ExploreDTI using a semi-automated method developed specifically for this project. Seeding, inclusion, and exclusion regions were selected on the FA map template and automatically mapped to each normalized brain. Tractography was used to identify ten major white matter tracts: the cingulum, fornix, corticospinal tract, superior and inferior longitudinal fasciculi, superior and inferior fronto-occipital fasciculi, uncinate fasciculus, and genu and splenium of the corpus callosum. Average values of fractional anisotropy (FA) and mean diffusivity (MD) over the entirety of each tract were correlated with subject age using non-linear regression, yielding time constants that indicate rate of development.

RESULTS: Non-linear regression revealed significant age-related changes in both FA and MD of all tracts except the fornix, which shows significant changes only of MD with age. Increases of FA and decreases of MD follow a monoexponential curve, with rapid development occurring in childhood and leveling off into adulthood. Development rates were seen to vary among tracts (see Figure 1), with tracts reaching 63% of their maximum FA values from age 5 with a range between 7-16 years, and reaching minimum MD values between 8-17 years. Overall FA increased by 11-18%, while MD decreased by 7-11%, from age 5 as a baseline.

DISCUSSION: As might be expected, we found that white matter tracts involved in basic processing develop faster and earlier than tracts involved in higher-level cognitive processes. The corpus callosum, which connects left and right hemispheres, and the inferior longitudinal fasciculus, involved in visual processing, develop early and rapidly, reaching 63% of their maximum FA values (from age 5) at 8 and 7 years, respectively. The cingulum and uncinate fasciculus, two important frontal connections, do not reach this point until 12 and 16 years, respectively. This study of the normally developing brain, one of the largest using DTI, has indicated a non-linear pattern of maturation from childhood to adulthood, which corresponds to cognitive and behavioral changes during the same period[9].

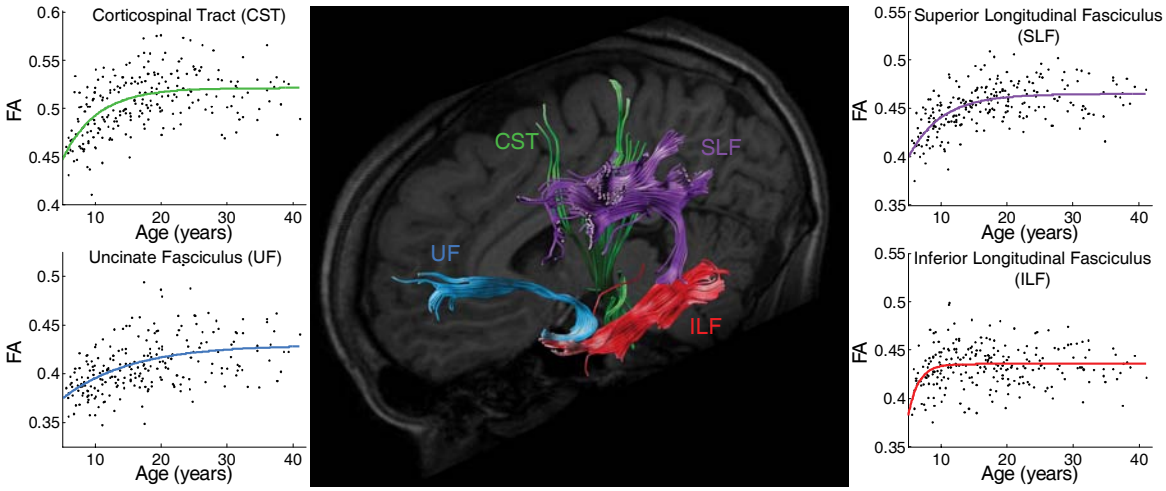

FIGURE 1: Considerable regional variation was seen in age-related FA changes for 237 subjects in nine of ten tracts measured (four are shown), although all nine followed a monoexponential pattern of development. Similar trajectories were seen for decreases of MD.

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