Relations between white matter integrity and working memory in children and adolescents

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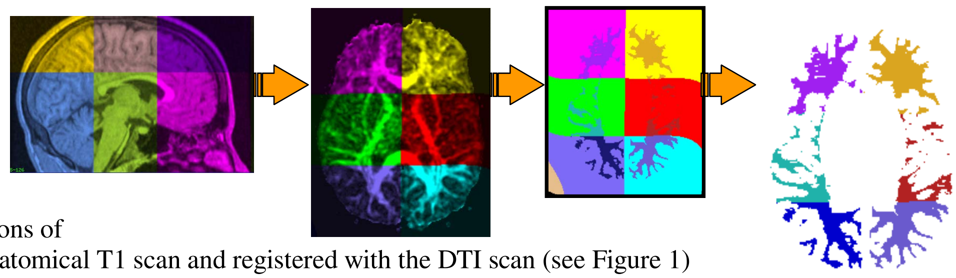
Introduction and Purpose: Based on volumetric studies, white matter development within the cerebral hemispheres tends to occur in a posterior to anterior trajectory. Although diffusion tensor imaging (DTI) has been used extensively to document overall white matter growth in children and adolescents, less attention has been given to differences in the rate of growth across various regions of the brain. The first goal of this study was to examine regional differences in the relations between age and a DTI index of white matter integrity (fractional anisotropy). Further, despite evidence that white matter plays a critical role in physiological mechanisms of brain maturation and neural signalling, evaluation of relations between white matter and cognitive function in children has only recently received attention. DTI indices of white matter integrity in a variety of brain regions predict intelligence, reading, cognitive control, and processing speed in children. Maturation of white matter, particularly in the frontal lobes, is likely important in the development of working memory, as increased efficiency of axonal and dendritic signal conduction may play a role in consolidating relevant neural networks. A second goal of this study was to test the relations between DTI indices of white matter, age, and working memory in typically developing children.

Subjects and Methods: Participants were 36 children and adolescents ranging in age from 6 to 17 years (mean = 12.04 S.D. = 2.66) with a mean IQ of 117 (S.D. = 13.06). Imaging data were acquired with a GE LX 1.5T MRI scanner using a single shot spin echo DTI sequence with an EPI readout (25 directions, TE/TR=0-79/8300 ms, 28 contiguous axial slices, 3 mm thick, 128 x 128 matrix, FOV = 26 cm, rbw = 125 kHz). Mean fractional anisotropy (FA) was calculated for 12 regions of hemispheric white matter defined on an anatomical T1 scan and registered with the DTI scan (see Figure 1) including left and right occipital (LO, RO), parietal-occipital (LPO, RPO), temporal (LT, RT), frontal-parietal (LFP, RFP), inferior frontal (LIF, RIF) and frontal (LF, RF) regions. The measure of working memory was the digit span task from the Wechsler Intelligence Scale for Children – Third Revision. First, FA across left and right hemispheres were combined for each lobar region and correlations were used to examine relations with age. Second, correlation and regression analyses were used to predict performance on the working memory task accounting for FA within each specific hemispheric lobar region and age. To control for multiple correlations, results were considered significant at $p < .01$. As fewer regression analyses were conducted, and they were only conducted when a significant correlation was present, results from the regressions were considered significant at $p < .05$.

Figure 1: Registration of T1 regional template with FA map and white matter mask to define regions.



Results: Mean FA for hemispheric white matter ranged from .48 to .53 (Table 1). When values across hemispheres were combined, the strongest increases in FA as a function of age were for regions of frontal-parietal and temporal white matter (rs < .62, ps < .001). Age related increases were also evident for inferior frontal, parietal–occipital, and occipital regions (rs < .47, ps < .01). Notably, the effect of age was significantly stronger for frontal-parietal white matter ($r = .68$) than for the posterior areas, including occipital and parietal-occipital regions (rs = .47), ps < .01. Age-related changes in FA were not evident for frontal white matter ($r = .39$, $p > .01$). Relations between FA and working memory were examined controlling for FSIQ. Performance on digit span increased with age and was related to multiple areas of white matter, including right occipital and frontal-parietal regions, and bilateral temporal, inferior frontal, and frontal regions (Table 1). Only FA for the bilateral frontal and right inferior frontal regions accounted for working memory skills after also accounting for age, $p < .05$. Although age continued to contribute to predicting working memory after accounting for FA within the bilateral frontal regions $p < .05$, it did not contribute to the model after considering FA within the right inferior frontal region.

Table 1: Mean FA and Correlations with Digit Span for hemispheric lobar regions

	LO	RO	LPO	RPO	LT	RT	LFP	RFP	LIF	RIF	LF	RF
Mean FA	.48	.48	.48	.49	.51	.51	.52	.53	.47	.47	.50	.50
Correlation with Digit Span	.41	.48*	.22	.42	.48*	.57**	.42	.44*	.52*	.55**	.50*	.57**

$p < .01$ ** $p < .001$

Conclusions: Consistent with prior volumetric studies, the growth of white matter appears greatest in frontal-parietal regions for children and adolescents. Indeed, the effect of age on FA was stronger for frontal-parietal white matter than posterior white matter in occipital and parietal-occipital regions. Greater changes in frontal and inferior-frontal white matter may be evident in samples of older adolescents and young adults. We also found that frontal white matter integrity is related working memory in typically developing children and adolescents. A novel finding was that only right inferior-frontal regions contributed uniquely beyond the effect of age in accounting for performance: age did not contribute to working memory when FA within this region was first included in the model. Considering we found that both FA in right inferior frontal regions and working memory increased with age, our findings are consistent with the growth of regional white matter organization as playing an important role in increased working memory with age.