Apparent Diffusion Coefficient in Children and Adolescents: Effect of Age and Correlation with Neuropsychological Measures of Frontal Brain Function.

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Introduction Diffusion tensor imaging[1] (DTI) provides a non-invasive technique for ascertaining information about white matter organization. There is increasing interest in studying neuropsychological correlates of DTI parameters, and the association of different brain regions with specific cognitive functions in various neurodevelopmental stages.[2-6] To determine structural correlates of neurobehavioral functioning, and to examine white matter maturation in children between 5 and 18 years, we obtained measurements of ADC bilaterally in 15 white matter tracts with a region of interest (ROI) based data analysis approach. The goals of our study were to evaluate 1) age-related differences in ADC; and, 2) correlation of neuropsychological measures of working memory and motor function with anterior white matter ADC.

Materials and Methods We examined 39 healthy children (17 female, 31 right handed, age range 5.5-18.3 years, mean age 13.0±3.8 years). Children were carefully screened for attention-deficit/hyperactivity disorder (ADHD), learning disability (LD) and other psychopathology. Images were acquired using the standard birdcage head coil on a 1.5 Tesla MR scanner. DTI data were acquired with a single-shot spin echo-echo planar sequence with 15 non-collinear diffusion gradient directions (b=1000 s/mm^2) and two b=0 mm/s^2 images. The following parameters were used: 24 axial slices, parallel to the anterior commissure – posterior commisure line, 96x96 acquisition matrix, FOV 240 mm, 5 mm slice thickness. ADC, FA and color maps were calculated from raw data using the in-house developed software DTI Studio (http://lbam.med.jhmi.edu). Polygonal ROIs that outlined each tract were drawn on the color maps two times by one operator and the measurements were averaged after overlaying the ROI on the FA and ADC maps. Fiber tracts examined included cerebral peduncle, temporal white matter, frontal white matter, anterior and posterior limb of the internal capsule, anterior white matter, temporo-occipital white matter, superior longitudinal fasciculus, corona radiata, superior fronto-occipital fasciculus, cingulum and centrum semiovale, and the genu, body, and splenium of the corpus callosum. All children were evaluated with a battery of 15 neuropsychological tests. Specific hypotheses have been developed regarding the relationship between neuropsychological test performance and ADC values in individual fiber tracts. In the initial analysis, we examined the relationship between two tests hypothesized to measure frontal lobe functioning and anterior white matter tracts: the Purdue Pegboard[7], a measure of manual dexterity and speed (left and right anterior white matter), and the Stanford Binet IV[8] (SB-IV) Bead Memory, a visual working memory task (right>left anterior white matter).

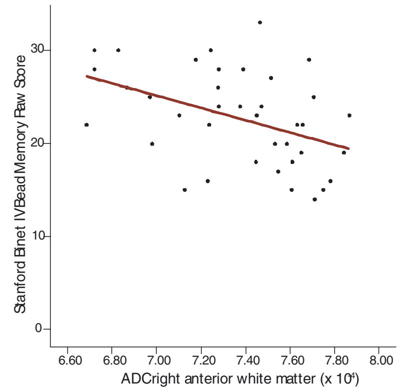

Fig. 1. Zero order correlation between ADC in the right anterior white matter and Stanford Binet IV Bead Memory raw scores.

Correlation analysis was performed to examine the relationship between ADC and age.

To evaluate the relationship between ADC and the two neuropsychological test scores, hierarchical regression was used, with age, gender and ADC entered in a fixed order as independent variables and the neuropsychological test raw score as dependent variable.

		B	R2 Δ	p
Bead Memory	Age	.444	.272	.003
	Gender	-.006	.000	.964
	ADC right anterior white matter	-.316	.094	.029*
Bead Memory	Age	.454	.272	.003
	Gender	-.009	.000	.949
	ADC left anterior white matter	-.249	.057	.093
Bead Memory	Age	.419	.272	.024
	Gender	.001	.000	.992
	ADC right temporal white matter	-.172	.019	.337
Bead Memory	Age	.521	.272	.003
	Gender	.004	.00	.978
	ADC left temporal white matter	-.001	.00	.995

Table 1: Results of hierarchical linear regression with Stanford Binet IV Bead Memory raw scores as dependent variable. ADC in the right anterior white matter has significant negative correlation with Bead Memory scores, corrected for age and gender. Left anterior white matter, and the temporal white matter bilaterally do not have significant association with SB-IV Bead Memory performance.

Results ADC decreased with age in 5 of 15 regions in the left hemisphere, namely, the corona radiata (r=-.531, p=.001), posterior limb of the internal capsule (r=-.441, p=.005), temporal white matter (r=-.440, p=.005), centrum semiovale (r=-.407, p=.010) and superior longitudinal fasciculus (r=-.350, p=.029) and in 3 regions in the right hemisphere: temporal white matter (r=-.594, p<.001), corona radiata (r=-.477, p=.002) and centrum semiovale (r=-.383, p=.016).

After controlling for age and gender, right anterior white matter ADC significantly predicted Bead Memory scores (R^2 change=.094, p=.029) (Table 1, Figure 1). In contrast, neither the left anterior white matter, nor the left or right temporal white matter ADC values were significant predictors of performance on Bead Memory.

The analysis for Purdue Pegboard (two hands trial) raw scores yielded no significant relationship to anterior white matter ADC.

Discussion Performance on SB-IV Bead Memory was better (higher raw scores) at lower ADC values in the right anterior white matter. Bead Memory requires visual working memory, a skill considered to be related to functioning in the dorsolateral prefrontal cortex (right greater than left).[9] This asymmetry is supported by our data that show less association of left anterior white matter ADC with Bead Memory. Temporal white matter as a region that was not expected to have influence on the examined visual working memory task, showed no association with Bead Memory. (Table 1)

In agreement with a previous study in 8 to 12 year old children, we detected a decrease of ADC in the corona radiata and the centrum semiovale.[6] However, the observed age-related differences were minimal, similar to the findings in the posterior limb of the internal capsule and temporal white matter.

Our DTI protocol is used in the MR examination of children that are also evaluated with MR spectroscopic imaging and volumetric MRI. As the total experimental time is long, a DTI protocol feasible in a short period of time is pertinent. This protocol takes 4 min and provides good quality, high in-plane resolution images, and a good reproducibility of the used polygonal ROI technique for ADC measurement.[10]

The presented findings further support association of white matter organization with performance on neuropsychological tests. It was shown that ADC reproduced the hypothesized hemispheric and regional location of white matter pathways of visual working memory function. Our approach might thus provide an objective tool to assess the maturity of anterior white matter pathways that contribute working memory function.

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