Frontal White Matter and Cognitive Development in Adolescence

M. Luciana[1], C. Hooper[1], H. Conklin[1], K. O. Lim[2,3]
[1]Dept. of Psychology, University of Minnesota, Minneapolis, MN, United States, [2]Dept. of Psychiatry, University of Minnesota, Minneapolis, MN, United States, [3]CMRR, University of Minnesota, Minneapolis, MN, United States

Introduction: Cognitive impairment has been observed in psychiatric disorders including deficits in working memory tasks in schizophrenia and decision making tasks in substance abuse. Our behavioral data suggest that during adolescence, there are distinct developmental trajectories in performance between a working memory task (self-ordered search task) versus a decision making task (Iowa Gambling Task-IGT). Adolescence is a period of brain maturation, especially of white matter[1]. Differential regional white matter maturation has been observed during this period of development. In this pilot study, we sought to examine whether developmental trajectories in task performance seen in adolescence are associated with measures of white matter maturation obtained with diffusion tensor imaging (DTI).

Methods: MRI data were collected using a Siemens 3T Trio whole body scanner with the standard single channel head coil. DTI data was collected using a pulsed gradient, single shot EPI imaging sequence which used two spin echos to minimize eddy current effects. Twelve non-collinear gradient directions with three averages were collected with the following parameters: B =1000, TR=11.5sec, TE=111msec, sixty four slices, 2mm thick, 128x128 matrix, 256mm FOV, Acq Time < 8 min. After inspection of the image data for gross movement and other artifacts, the diffusion tensor was computed from the data using a custom program written in IDL (Research Systems Inc). The resulting data were AC-PC aligned using the FLIRT program from Oxford (http://www.fmrib.ox.ac.uk/). Circular regions of interest of standard size were placed by a trained operator bilaterally in the frontal white matter in axial slices corresponding to Z=-6, 0, 6, 12, 18, 24 mm in relation to the AC-PC plane. The B=0, T2 weighted image was used for ROI placement and the operator was blind to subject identity. Left and right regions were averaged for each level.

Results: Imaging and cognitive data from 12 right-handed normal healthy subjects, between the ages of 10 and 16 were available for analysis. Significant associations were found between cognitive performance and mean white matter diffusion in several frontal regions. A high number of errors on the self-ordered search task was associated with high levels of mean diffusion at Z=0mm (at the AC-PC plane: Spearman's r=.65, p<.05) as well as Z=6mm (6mm above AC-PC plane, Spearman's r=0.56, p=.06). In contrast, a high relative number of good (advantageous) choices on the IGT was associated with low mean diffusion at Z= -6mm (Spearman's r= -.53, p<.10) and also with low mean diffusion at Z= 6mm (Spearman's r=-.69, p<.05). Fractional anisotropy measures yielded relatively few significant correlations in the predicted direction, although high anisotropy (indicating greater white matter integrity) at Z=0mm, 6mm, and 12mm above the AC-PC plane was associated with better performance on the digit span backward test (Spearman's r's=.50 to .68, p's range from .01 to .10).

Discussion: These findings suggest a region of white matter integration, 6mm above the AC-PC plane, that is commonly associated with performance on complex measures of self-organization. In addition to being associated with performance on these tasks, mean white matter diffusion in this area of the PFC declined with increasing age (r=-.70, p=.01). Thus, as mean diffusion of white matter tracts decreases in medial-dorsal and medial-ventral PFC, performance on the IGT improves. Similarly, as mean diffusion decreases in the medial regions of the PFC, performance on the self-ordered search task improves. These data suggest that mean diffusion of white matter may be a useful measure for examining relationships between white matter status and cognitive development during adolescence.

References: [1] Schmithorst VJ et al., Radiology 2002 222(1):212-8.
(Supported by DA-015330, MH-060662, P41 RR08079, MIND Institute)