White matter structural correlates of cognitive performance in the temporal lobe projections

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Background: Various studies suggest that the ability to perform complex as well as simple cognitive tasks engages a network of brain regions, and the integration of information from different brain regions is mediated by the white matter (WM) fiber bundles connecting them. Aging is associated with reduced performance in various brain functions, as well as degradation of WM. Diffusion-tensor imaging (DTI) measures the displacement of water molecules *in vivo* non-invasively[5]. Aging is associated with an increase in water diffusivity, and a decrease in fractional anisotropy (FA), suggesting a decline in WM integrity[2,3].

Since the temporal lobe and its projections have various important functions, and these functions are known to deteriorate during aging, in this study we used the inter-subject variability in different cognitive domains to relate cognitive performance and WM integrity in five temporal projections: the uncinate fasciculus (UF), fornix, cingulum, inferior longitudinal fasciculus (ILF), and superior longitudinal fasciculus (SLF). We correlated between cognitive performances on different cognitive domains, including memory, executive function, information processing speed, and motor performance, with WM integrity, as measured by DTI indices, along the different temporal fiber tracts.

Methods: Subjects were 51 healthy volunteers, 25-80 y, all right handed. MR imaging was performed on a 3T (GE) MRI system. The DTI protocol consisted of 48 axial slices, with resolution of 2.5x2.5x2.5 mm^3, acquired for 19 gradient directions. The sequence was gated to the cardiac cycle with TR of 30 R-R intervals, and TE was 88ms. The duration of the entire MRI protocol was approximately 20 min. The DTI images were corrected for motion using SPM (UCL, London, UK) software. DTI was analyzed and calculation of ADC and FA maps was performed as described previously [1]. Tractography was applied using the principal eigenvectors and FA: the brute force FACT algorithm was used to generate the fiber coordinates[5], terminating at voxels with FA lower than 0.2 or following tract orientation change higher than 60°. The fiber masks of all subjects were registered to a fiber mask of one young subject. For each fiber track, fiber ROI was created that included only voxels containing fibers in 80% of the subjects. The same registration parameters that were created for each temporal projection were applied (right and left) on the DTI maps (ADC, FA, $\lambda 1$, $\lambda 3$).

Subjects also completed a battery of computerized tests (Mindstreams®, NeuroTrax Corp., NJ[4]) that evaluate performance across an array of cognitive domains. Factor analysis of 55 cognitive scores was performed and four cognitive domains were extracted - memory, executive function, information processing speed, and motor performance.

VBA analysis: multiple regression routine was performed using the SPM software, between the DTI indices (ADC, FA, $\lambda 1$, and $\lambda 3$) registered to the appropriate temporal projection, and scores in the four cognitive domains (executive function, information processing speed, memory and motor skills), with age as constant. The fiber ROI was used as a mask. The statistical threshold was set at $p<0.01$ uncorrected.

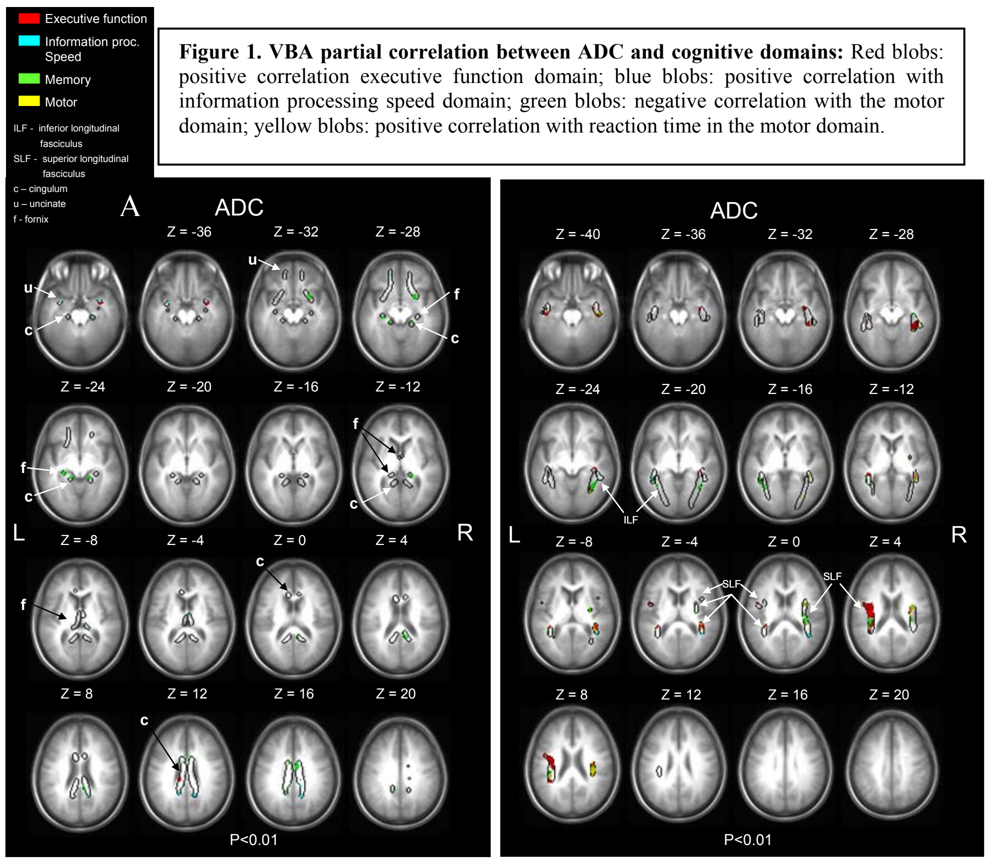

Figure 1. VBA partial correlation between ADC and cognitive domains: Red blobs: positive correlation executive function domain; blue blobs: positive correlation with information processing speed domain; green blobs: negative correlation with the motor domain; yellow blobs: positive correlation with reaction time in the motor domain.

Results: In Figure 1 we chose the ADC as a representative parameter. (Figure 1(A): cingulum, fornix and UF; figure 1(B): ILF and SLF).

Executive function domain is correlated with DTI indices in the right UF (ADC, $\lambda 3$) and in the left UF (FA, $\lambda 3$), right cingulum (FA, $\lambda 3$), left cingulum (ADC, $\lambda 3$), right ILF (ADC), right SLF ($\lambda 3$), left SLF (all indices). Memory domain is correlated with DTI indices in the right UF (ADC, $\lambda 1$ and $\lambda 3$), right fornix (ADC, FA), left fornix (ADC), right cingulum (ADC, $\lambda 3$), left cingulum (ADC, $\lambda 1$ and $\lambda 3$), right ILF (ADC, FA and $\lambda 3$), left ILF (FA, $\lambda 3$), right SLF ($\lambda 1$ and $\lambda 3$), left SLF (ADC and $\lambda 3$).

Information processing speed domain is correlated with DTI indices in the right UF (FA) right fornix ($\lambda 3$), left fornix, ($\lambda 3$), right cingulum (FA, $\lambda 3$), left cingulum (FA), right ILF (FA), left ILF (FA, and $\lambda 3$) , right SLF (FA, $\lambda 1$ and $\lambda 3$), left SLF (FA).

Motor domain is correlated with DTI indices in the right & left cingulum (all indices), right ILF ($\lambda 3$) right SLF (ADC, $\lambda 3$) and left SLF (ADC, FA and $\lambda 3$).

Discussion and Conclusions: The main finding of this study is that WM integrity is correlated with cognitive performance in a fiber specific manner. The fibers exhibiting substantial correlation in our study are known to play an important part in the corresponding functional domain. For example, the memory domain is known to be related to the temporal lobe, and indeed, it shows significant correlation in all temporal projections. The executive function domain, known to involve frontal and temporal regions, shows most significant correlations in the UF, SLF and cingulum, connecting the frontal lobe with the temporal lobe. Information processing speed, (in the present study we used a calculation task) known to involve the parietal regions, and indeed shows correlations in the cingulum and SLF, connecting parietal and temporal regions. It also showed correlation with ILF. The motor domain showed correlations in cingulum and SLF, which are proximate to motor fibers in the corona radiata. To conclude, using DTI tractography we can relate cognitive performance and WM integrity in the temporal projections. Using the methodology performed here, DTI tractography enables anatomical definition of region of interest for correlation analysis of any behavioral parameters with diffusion indices.

References: Basser PJ, Pierpaoli C. Magn Reson Med 1998;39(6):928-934. ; 2. Moseley M. NMR Biomed 2002;15(7-8):553-560.; 3. Sullivan EV, Pfefferbaum A. Eur J Radiol 2003;45(3):244-255.; 4. Dwolatzky, T et al.. BMC Geriatrics. 2003; 3:4.; 5.