

**Title:** White Matter Integrity and General Cognitive Performance: a Tract-based Spatial Statistics approach.

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**Abstract:**

Diffusion Tensor Imaging (DTI) is a magnetic resonance imaging modality that allows the estimation of indices of white matter integrity (WMI; e.g., fractional anisotropy, FA). Some recent studies (Yu et al., 2008; Chiang et al., 2009; Penke et al., 2010) have related WMI to general cognitive performance, but only one of them (Chiang et al.) used a whole-brain, voxel-wise exploratory approach instead of studying a reduced number of tracts selected *a priori*. However, whole-brain DTI studies are affected by several well known problems, i.e. partial volume effects and arbitrary smoothing extent. The Tract-Based Spatial Statistics (TBSS; Smith et al., 2006) method is a robust alternative to traditional voxel-wise analyses that automatically extracts a group mean FA mask ("skeleton") representing the centers of the tracts across subjects. Further analyses are constrained to the skeleton, avoiding problems related to misalignment (especially relevant at the tracts' borders) and arbitrary smoothing (which is no longer necessary). In the present study, DTI was acquired in a sample of 102 normal subjects (44 men, 58 women, mean age = 19.83, SD = 1.64) to explore the relationships between WMI and cognitive performance. Diffusion tensors were computed from the diffusion-weighted images, and several scalar indices of WMI were obtained (FA; mean diffusivity, MD; axial diffusivity, AD; and radial diffusivity, RD). TBSS was applied to these images to obtain their skeletons. A total of nine cognitive tests were used to measure reasoning (Gf), verbal (Gc), and spatial intelligence (Gv). General performance scores were also obtained from PAF1. Statistical analyses were conducted using non-parametric inference, given the non-Gaussianity of the WMI scalars. Gc was significantly correlated with FA in females, but not in males, mainly in the splenium of the corpus callosum and in the right superior longitudinal fasciculus (corrected for multiple comparisons,  $P < 0.05$ ). Gf and FA were correlated in males, but not in females, in the right inferior fronto-occipital fasciculus (corrected for multiple comparisons,  $P < 0.1$ ). No significant correlations were found for MD, AD, and RD. Our results point to sex differences in brain structure and to the relevance of WMI for cognitive performance.

**References:**

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