

## Independent component analysis of DTI metrics in multiple sclerosis

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**TARGET AUDIENCE:** Physicists and imaging analysis experts working with diffusion weighted imaging and advanced methods of analysis, neuropsychologists with an interest in the mechanisms of cognitive dysfunction, clinicians with an interest in multiple sclerosis and other white matter diseases.

**PURPOSE:** To investigate whether: (a) independent component analysis (ICA) applied to diffusion tensor imaging (DTI) data is able to reveal patterns of covariance between specific white matter (WM) tracts in multiple sclerosis (MS) patients, and (b) whether the microstructural variance associated with specific independent components predicts cognitive performance in these patients.

**INTRODUCTION:** DTI parameters reflect the microstructural organization of WM tracts. The majority of structural imaging studies treated DTI measurements from different WM tracts as if they were independent. However, recent studies demonstrate that ICA is able to reveal specific patterns of covariance between fractional anisotropy (FA) values across WM tracts in the healthy population<sup>1</sup>. In the present study, for the first time, we extended this approach to patients with multiple sclerosis (MS) in order to examine specific patterns of correlation in FA across WM matter tracts. Each pattern (or cluster) is represented by an independent component. Each component is formed by a pattern of FA variation across the sample, and by an anatomical map indicating what tracts are better represented by that pattern. Therefore, we also examined whether, in patients, the pattern of FA variation across the sample associated with specific components could predict cognitive performance.

**METHODS:** Thirty patients with secondary progressive MS (SPMS) (20 women, mean age 54 yrs, range 36-65) underwent diffusion weighted imaging on a 3T scanner. After correction of movement and eddy current distortions, the tensor model was fitted on a voxel-by-voxel basis using DTIFIT from the FMRIB's Diffusion Toolbox. FA maps were processed using Tract-Based Spatial Statistics (TBSS) in order to obtain a skeletonised map for each patient. The 30 skeletonised maps were decomposed into 18 spatially independent components (ICs) using ICA implemented in the Group ICA fMRI Toolbox (GIFT) and the FastICA algorithm. The resulting spatial maps of the ICs show voxels for which the FA values within each map co-vary across individuals. ICs were assigned to 5 classes following Li et al<sup>1</sup>. Five cognitive domains that are commonly affected in MS patients were assessed. For each cognitive domain, single test scores were transformed into z-scores and averaged. Linear regression was used to investigate the association between a cognitive score and the across-subject FA covariance associated with each IC in a given class.

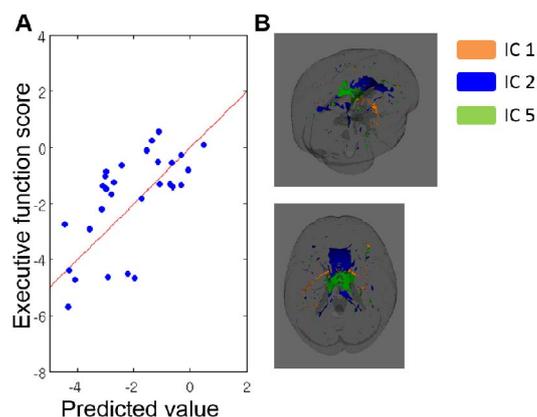
**RESULTS:** Of the 18 ICs, 15 were associated with clearly recognisable WM tracts. We grouped the components in separate classes, depending on the type of tract. Class I, the supratentorial commissural tracts, included 3 components (IC1, IC2, IC5) and was mainly represented by the anterior commissure and corpus callosum. Class II, the supratentorial projection tracts, included 5 components (IC6, IC8, IC10, IC14, IC18), encompassing the corticospinal tract, optic radiations and anterior thalamic radiations. Class III, the neocortical association tracts, included 2 components (IC4 and IC11), corresponding to the superior and inferior longitudinal fasciculus. The last class, the limbic association tracts, consisted of 3 components (IC3, IC12 and IC17) and was mainly represented by the cingulum. Additionally, we found 2 components (IC7 and IC15) largely overlapping with the uncinate fasciculus. The linear regression model for class I was significant for executive function ( $p = 0.015$ ,  $R^2 = 0.325$ ) (Fig. 1A), verbal memory ( $p = 0.036$ ,  $R^2 = 0.276$ ) and working memory ( $p = 0.0004$ ,  $R^2 = 0.5$ ). The largest coefficient was associated with IC1 (Fig. 1B).

**DISCUSSION:** The resulting spatial maps of the IC reveal clusters of WM voxels for which the FA values co-vary across patients. Most of the extracted components showed interpretable spatial patterns, and we were able to identify in this group of patients the same ICs as previously described in healthy subjects<sup>1</sup>. It is thought that these clusters of WM tracts may indicate similarities in the evolution of microstructural integrity and in the function of specific white matter tracts, which belong to the same pattern. In MS patients this could also indicate a similar degree of degeneration in clusters of WM tracts. Interestingly, the pattern of FA variation in the supratentorial commissural tracts, belonging to Class I, was associated with performance on tests of executive function, verbal memory and working memory tests.

**CONCLUSION:** This study maps microstructurally correlated white matter regions in MS patients and suggests that ICA can detect patterns of correlation in FA which may be useful to understand the mechanisms of cognitive dysfunction in SPMS.

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**REFERENCES:** 1) Li Yo, Yang FG, Nguyen CT, et al. Independent component analysis of DTI reveals multivariate microstructural correlations of white matter in the human brain. *Human Brain Mapping* 2012;33(6):1431-1451.



**Fig. 1 |** Scatterplots of the actual cognitive scores against the values predicted by the linear regression models based on the across-subject FA trends associated with class I (B), the supratentorial commissural tracts. The red line shows the  $y=x$  line.