Mapping Microstructural Correlations of White Matter in the Human Brain Using Seed-Voxel Correlation Analysis of DTI

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Introduction

Microstructural correlations reflect phylogenetic and functional similarities between different white matter pathways [1]. Independent component analysis (ICA) has been used on group DTI data to characterize the spatial co-variation of white matter microstructure across subjects [2]. In addition to ICA, seed-voxel correlation (SVC) analysis is often used to detect functional connectivity in resting state fMRI. These two methods are compared in a recent resting state fMRI paper finding complementary, as well as overlapping, information [3]. In this study, we demonstrate the first application of SVC to group DTI data in order to map white matter microstructural correlations. We directly compare these novel SVC results to those of ICA by using the dominant cluster of correlated voxels in each independent component (IC) spatial map as the seed region for SVC analysis.

Methods

200 normal adult volunteers (mean 26.4± 6.5 years, 108 men) underwent 3T DTI with 55 directions at b=1000. In FSL, FLIRT was used for motion correction, BET for brain extraction, and dtifit for fractional anisotropy (FA) calculation. Direct registration of individual whole-brain FA volumes to the FMRIB58 template was applied in TBSS and the mean FA image and the mean FA skeleton were computed. We performed spatial ICA on these skeletonized FA values as described in [2]. Due to our larger cohort, we estimated 50 ICs instead of the 25 ICs in [2]. Z scores were computed for each of the IC maps and were thresholded at 2.5 as in [2]. The seed regions for SVC were obtained from the largest cluster in each thresholded IC map. The FA values in the seed region were averaged and the Pearson correlation coefficient was computed between the seed and every voxel on the FA skeleton with FSL's General Linear Model [4]. The correlation maps were then transformed to Z score maps and thresholded at $p < 0.05$ after false discovery rate (FDR) correction for multiple voxel-wise comparisons.

Results

As in the recent ICA of DTI study [2], voxels with the strongest FA correlations in most IC spatial maps corresponded to anatomically distinct white matter tracts, tracts segments, and/or homologous pairs of tracts. In addition to the five main groups (commissural, projection, neocortical association, limbic, thalamus/brainstem, and cerebellar tracts) previously found, we identified another dominant feature that could be classified as prefrontal tracts, such as the anterior corona radiata. We found 36 IC maps where the FA correlations corresponded to meaningful anatomical white matter regions. The SVC and IC maps were similar for these 36 pairs, as shown in Figure 1, with SVC confirming the unilateral, bilateral and midline FA correlations previously shown with ICA [2]. We used weighted spatial correlation [3] between each IC and SVC map to create the similarity matrix shown in Figure 1. We place the IC maps along the x-axis and the SVC maps along the y-axis, hence this matrix is not symmetric. The high vales along the main diagonal demonstrate the SVC maps are most similar to their corresponding IC map. Figure 2 shows a corresponding pair of IC and SVC maps from each of these six groups; the seed region is shown in green for the SVC maps. In general, IC maps empirically thresholded at Z>2.5 exhibit more sparsity than the corresponding SVC maps, as can be seen from Figure 2.

Figure 1: Weighted Spatial Correlation

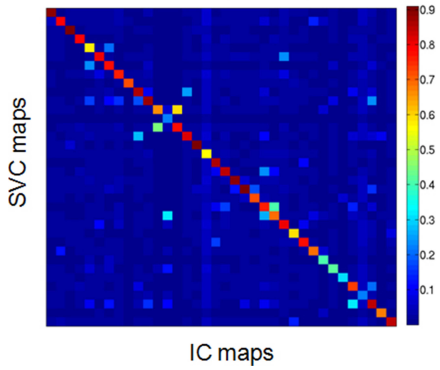
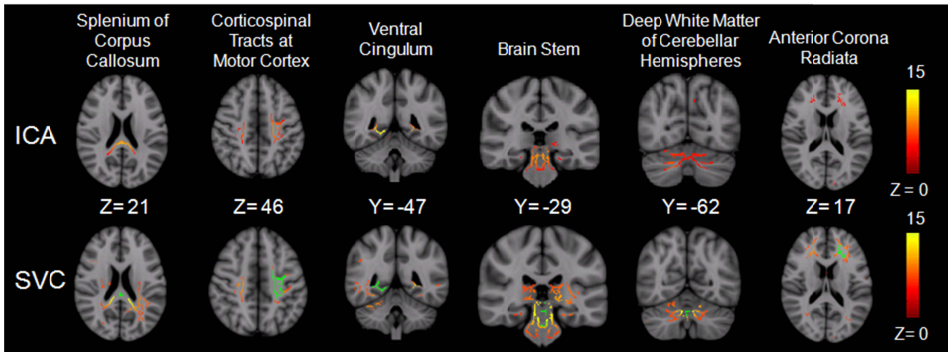


Figure 2: Example Pairs of IC and SVC Maps



Discussion

In this study, we extend the findings of [2] by performing a higher dimensional ICA decomposition of normal white matter, revealing additional spatial correlations of FA, such as in bilateral prefrontal fiber tracts, not found in the earlier study. However the main result of this investigation is to demonstrate that SVC can be used to map white matter microstructural correlations and produces results similar to ICA when the seed region is derived from ICA. Advantages of SVC over ICA include the ability to perform hypothesis-driven mapping of microstructural correlations of specific white matter regions and the ability to specify a principled statistical threshold for defining regions of significant correlations. As is the case for analyzing functional connectivity in resting state fMRI, ICA and SVC can play complementary roles in mapping white matter microstructural correlations from group DTI data.

References

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