# Whole Brain Parcellation Based on Group-ICA of Tractography Connectivity Maps Shows Differences in Schizophrenia Subjects and Healthy Controls

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**Target audience:** The paper is useful to those developing brain structural connectivity mapping methods based on diffusion imaging data and its clinical applications.

**Purpose:** We demonstrate that data-driven group-ICA can parcellate whole brain based on connectivity maps obtained from probabilistic tractography into meaningful white matter tracts and gray matter cortical regions without a priori specified ROIs. We show next that this brain parcellation can be used to look for connectivity differences between healthy controls (HC) and schizophrenia subjects (SZ).

**Methods**: Diffusion data on 64 HC (mean age 35.3 ± 11.0) and 64 SZ (mean age of 38.8 ± 13.3) was collected on a 3T Siemens Trio scanner at 2mm resolution with 30 gradient directions and b-value = 800 s/mm$^2$. Voxel-to-voxel connectivity maps were calculated by probtrackx/FSL for each subject at 5mm resolution. Down-sampling reduced the voxels and the connectivity matrix to a manageable size. The connectivity map gives the number of fibers connecting any two vertices. We used a space-by-space group-ICA [1] on the connectivity maps (PCA-ICA) as the clustering method to obtain 30 components, followed by back-reconstruction for subject specific maps. A similar approach has been applied before to parcellate cortical regions [2], to parcellate thalamus [3], and these methods are reviewed in [4].

**Results:** Whole brain connectivity maps were dominated by white matter and their connections to the cortical regions because of stronger connectivity within the white matter. All the maps obtained here overlap substantially with some of the principal tracts in the JHU atlas. Unlike resting-state functional connectivity maps which can contain distant and separate regions of the brain, these structural connectivity maps tend to be tighter clusters.

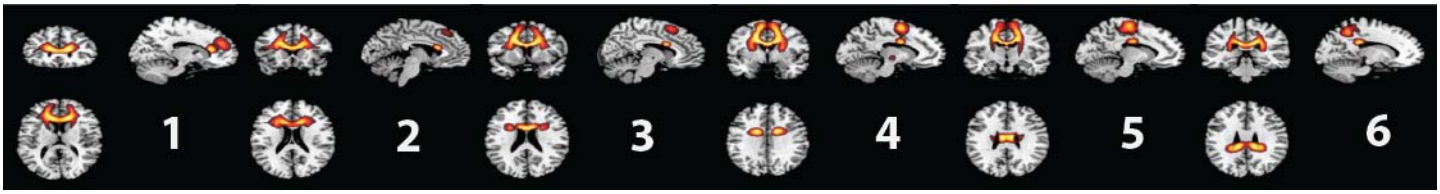


**Fig 1. Corpus callosum with its connections to cortical regions was segmented into six clusters by this method. This is similar to what has been reported before by streamline tractography and more interactive segmentation [5].**

A subset can be extracted from a larger connectivity map to focus on regions of specific interest. As an example we extracted the connectivity map for the gray matter cortical regions from the whole brain connectivity map. 30 clusters were then extracted from these connectivity maps. By doing this we were able to parcellate regions that were excluded previously because of their mutual weaker connectivity. The multi-modal nature of the parcellation in Figure 2 (small distinct clusters) indicates that a higher-order model (ie 75 or more components) might be useful for parcellating cortical regions.

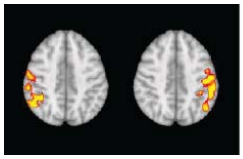

**Fig 2. Two similar cortical components on either hemisphere.**

Back-reconstruction provides a connectivity map (CM) and a conjugate-connectivity map (CCM) for each subject. The CCM corresponds to the reduced matrix axis in a typical fMRI ICA analysis. All our group differences were in the CCMs and they seem to have better discriminating capability between the SZ and HC groups. The statistical differences were tested with age as a covariate. The significant regions were adjusted for multiple comparisons at FDR corrected $p<0.05$ and cluster size > 5 voxels. A decreased significant connectivity was seen in CCM for forceps major, left cortico-spinal tract, left uncinate fasciculus (Fig. 3) and left inferior fronto-occipital fasciculus. An increased significant connectivity was found in the CCM of anterior thalamic radiation.

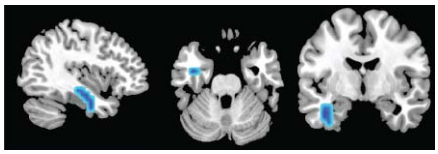

**Fig. 3. The decreased connectivity in SZ for the uncinate fasciculus region.**

**Conclusions.** Connectivity maps obtained from data-driven analysis of probabilistic tractography can be used to parcellate the brain and then identify connectivity based group differences. Future work may extend these methods to combine with other measurements, e.g. fractional anisotropy and/or fMRI to better characterize brain networks.

**References.** 1) Calhoun et al. Human Brain Mapping, 2001. 2) Jbabdi et al HBM 17th Meeting, 2011.3) O'Muircheartaigh et al. Neuroimage 2010. 4) Cloutman et al. Frontiers Neuroanat. 2012. 5) Hofer and Frahm Neuroimage 2006.