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Connectomics based multi-modal graph measures in Bipolar Disorder

Aleksandar Tenev[a], Slobodan Kalajdziski[a], Dejan Gjorgjevikj[a], Ljupco Kocarev[b], Eduard Vietac*, Dina Popovic[c**], Luis Pintor[c], Pablo Villoslada[c], Vesna Prčkovska[c]

[a] Faculty for Computer Science and Engineering, Sts. Cyril and Methodius University, Skopje, R.Macedonia
[b] Macedonian Academy of Sciences and Arts, Skopje, R. Macedonia
[c] Center for Neuroimmunology, Department of Neurosciences, IDIBAPS, Hospital Clinic, Barcelona, Spain
[c*] Clinical Institute of Neuroscience, University Hospital Clinic of Barcelona, Barcelona, Spain.
[C**] Bipolar Disorders Program, Institute of Neurosciences, University Hospital Clinic of Barcelona, Barcelona, Spain.

INTRODUCTION

Bipolar disorder (BD) is a type of a mood disorder characterized by extreme mood swings, including both manic and depressive episodes commonly accompanied by psychosis. These types of disorders are characterized by specific brain regions that are integrated within large-scale intrinsic connectivity networks. By means of resting state fMRI (RS-fMRI) we can investigate the differences in these networks compared to healthy controls. Diffusion Spectrum Imaging (DSI) is the state-of-the-art MRI imaging technique that can quantify tissue properties in the white matter, as well as provide information of the white matter tracks. By employing connectomics-based approach and combining both RS-fMRI and DSI modalities we provide deeper understanding of BD by identifying the main brain regions involved in abnormal activity present in patients with BD and the network disruptions that might cause the relapsing course of the disease.

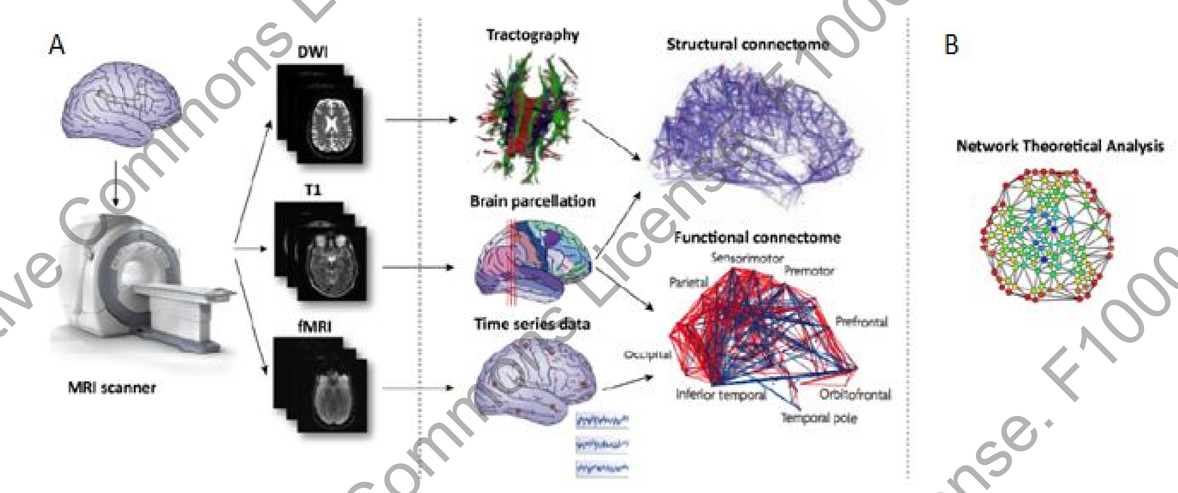

Figure 1: The functional connectivity (FC) and structural maps are weighted undirected graphs in which the weights are Pearson's correlation coefficients and number of fibers, respectively. We applied graph theory algorithms to calculate some of the graphs topological measures such as strength, local clustering coefficient and centrality of a node

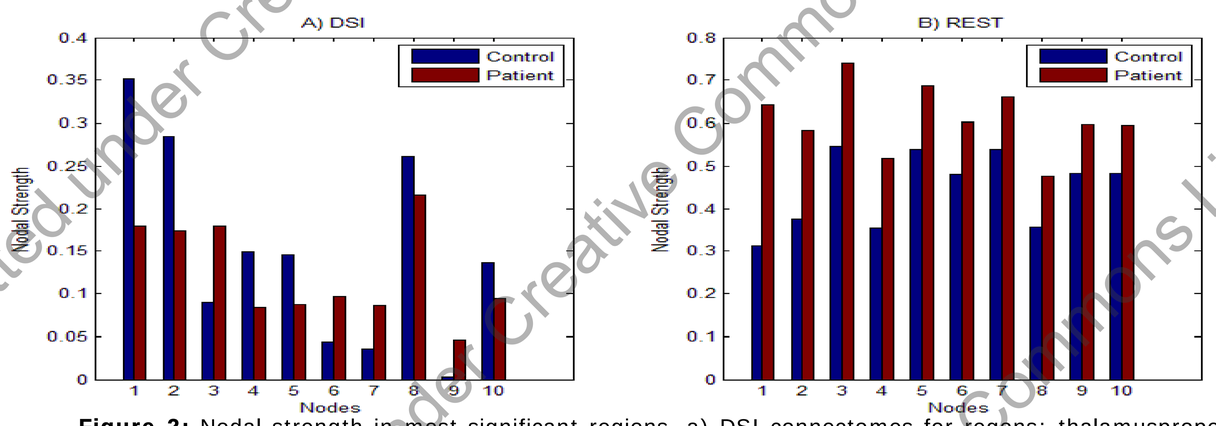

Figure 2: Nodal strength in most significant regions. a) DSI connectomes for regons: thalamusproper-1, rostralmiddlefrontal-2, palidum-3, precuneus-4, caudalmiddlefrontal-5, inferiortemporal-6,7, thalamusproper-8, temporalpole-9, caudalmiddlefrontal-10. b) RS-fMRI connectomes for regions: lateralorbitofrontal -1, caudalmiddlefrontal-2, superiortemporal-3,5 lateralorbitofrontal-4, supramarginal-6, insula-7, cuneus-8, medialorbitofrontal-9, transversaltemporal-10.

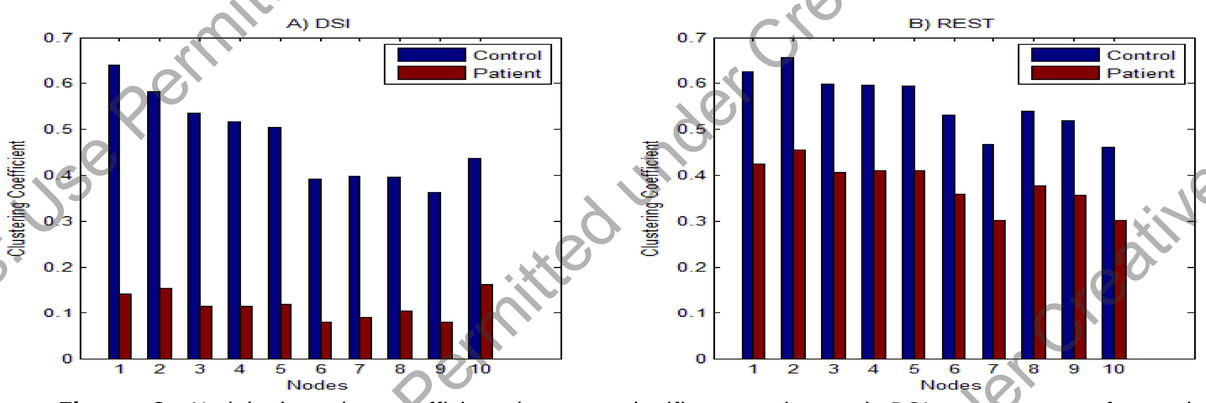

Figure 3: Nodal clustering coefficient in most significant regions. a) DSI connectomes for regions: precentral-1,2,rostralanteriorcingulate-3, caudalanteriorcingulate-4, superiorfrontal-5, paracentral-6, rostralmiddlefrontal-7, parsopercularis-8,thalamusproper-9, inferiorparietal-10. b) RS-fMRI connectomes for regions: superiorfrontal-1, rostralanteriorcingulate-2,3, accumbensarea-5, inferiortemporal-6, parsorbitalis-7, caudalanteriorcingulate-8, parsopercularis-9, rostralmiddlefrontal-10.

METHODS

1. We analyzed 5 BD patients in depressive phase with HDRS score >22 (4m, 1f, 58.4±6.9 years) and 5 healthy controls (4m, 1f, 34.4±6.7 years).
2. High-resolution three-dimensional T1-weighted MPRAGE images were acquired for anatomic reference (TR/TE=2200/3ms,FA=7o,1mm3 isotropic voxels).
3. Due to its sensitivity to pathology, T2-weighted scan was used in order to identify pathological findings (TR=3780ms,TE=96ms,FA=120o, voxel size 0.8x0.6x3.0mm, 3.0mm thick, 0.3mm gap between slices, 40 axial slices).
4. Functional resting state data (of 14 minutes) was acquired (TR/TE=2000/30ms,FA=85^o,3.0mm^3 isotropic voxels, 3.0mm thick, no gap between slices).
5. DSI data was acquired in the same scanning session with 515 gradient directions at a max b-value of 8000 s/mm^2 (TR/TE=8200/164 ms) and voxel size of 2x2x3mm^3 with a total acquisition time of 35.42 min.

In figure 1 we present schematic diagram of the pipeline for contruction of the structural and functional connectome from our data.

RESULTS

In fig. 2 we present the results from the nodal strength in both connectomes. We observe significant decrease in structural connectivity in BD patients in thalamus region, rostralmiddlefrontal and increase in pallidum region. In the resting state connectome we see increase of the node strength in all the regions for the patients. In fig. 3 we show similarly the regions where the difference in clustering coefficient is the most prominent between the two groups. We observe that in the presented regions we have generally lower clustering values in the patient diffusion data, which means that many of the structural links are missing or weaker in the patient group. It clearly coincides with the clustering coefficient of the functional data making it a potential biomarker and interesting measure to be examined in future for this disorder. Finally in fig.4 we present the nodal centrality or hubness in both modalities. We observe that the pattern in the REST data is varying. However, there is decrease of hubness in BD patients in putamen and precentral regions and increase in other regions depicted in DSI connectome.

DISSCUSION

This is a study that combines anatomical and functional connectivity graph based techniques in BD when the patients are experiencing a depressive episode. It is a pilot study with small number of subjects and therefore the results should be taken with care. However, here we identify per graph measure category the 10 most interesting anatomical regions in the structural and functional connectome that show significant difference between patient and control groups.

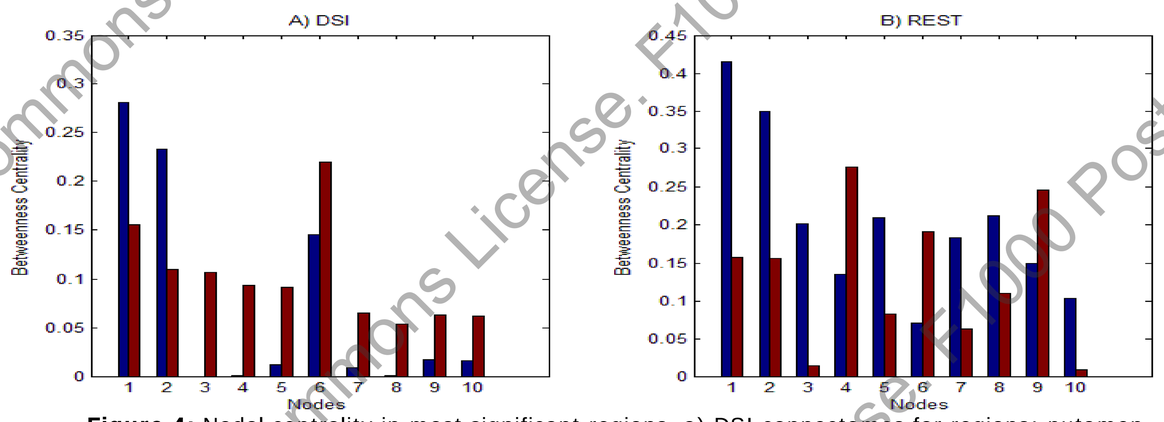

Figure 4: Nodal centrality in most significant regions. a) DSI connectomes for regions: putamen-1, precentral-2, inferiortemporal-3,8, lateraloccipital-4, postcentral-5, thalamusproper-6,paracentral-7, posteriorcingulate-9, caudalinteriorcingulate-10. b) RS-fMRI connectomes for regions: superiorfrontal-1, precentral-2, parsorbitalis-3, middletemporal-4, posteriorcingulate-5, lingual-6, inferiortemporal-7, precuneus-8, cuneus-9, palidum-10.

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