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## White matter connectivity analysis in patients suffering from depression.

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## Introduction

- Major depressive disorder (MDD) is characterized by a profound dysregulation of affect and mood: cognitive dysfunction, insomnia, fatigue and appetite disturbance.
- Up to 80% of patients will suffer from a relapse.
- Understanding the neural correlates underlying the depression is critical for improving the efficacy of diagnostic and treatment strategies.
- Dysfunction of the circuits connecting frontal and subcortical brain regions, leads to a "disconnection syndrome" [1].
- Using graph theory-based analysis, we examined white matter changes in the organization of networks in patients suffering from depression.

## Network analysis:

- Computation of various metrics that characterize the global organization of anatomical networks
- Fiber density (number of fibers normalized by ROI volume) characterizes the strength of inter-regional connections.
- Regional nodal properties: Strength (reflects how the node is interacting with many other nodes in the network), Betweenness (in integrating dispersed networks) and Clustering (in local networks).
- Two-sample Student t-test between the two groups with age, gender, duration of disease and medication load [3] as nuisance covariates, combined with a permutation test.

## Material and Methods

### Data:

- LONGIDEP is a routine care cohort of patients suffering from MDD who underwent clinical, neuropsychological testing and imaging study.
- DTI scans: 30 directions using an EPI sequence with a b-value of 1000s/mm<sup>2</sup>.
- 20 MDD patients and 20 healthy controls (CTL) subjects.

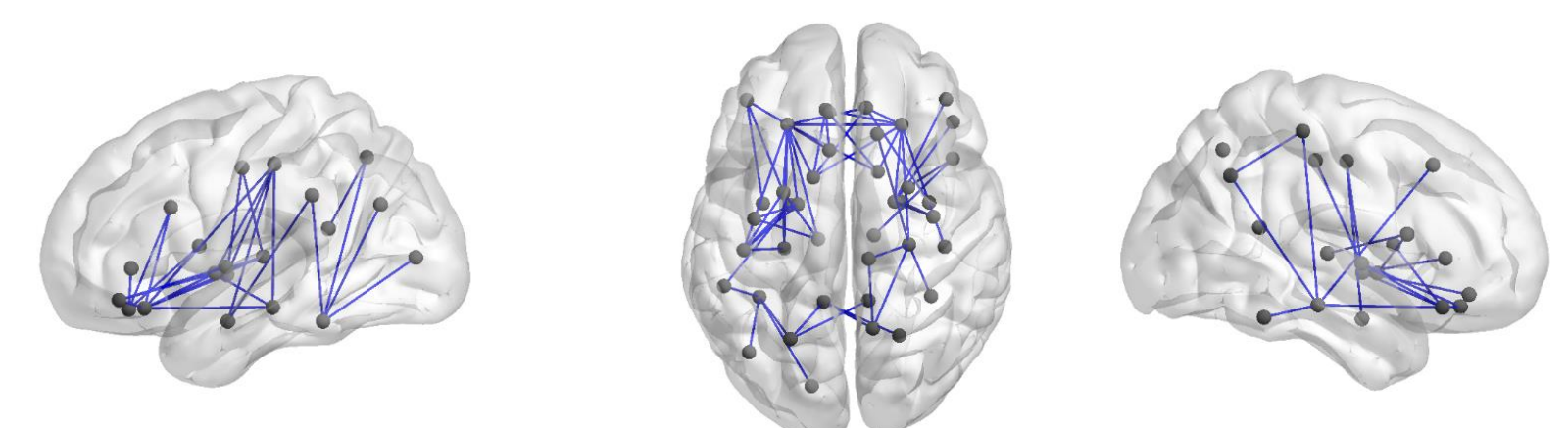
### Network node definition:

- Parcellation of the cerebral cortex into 66 cortical and 14 subcortical regions using Freesurfer image analysis [2].
- Each regions represents a node of the cortical network

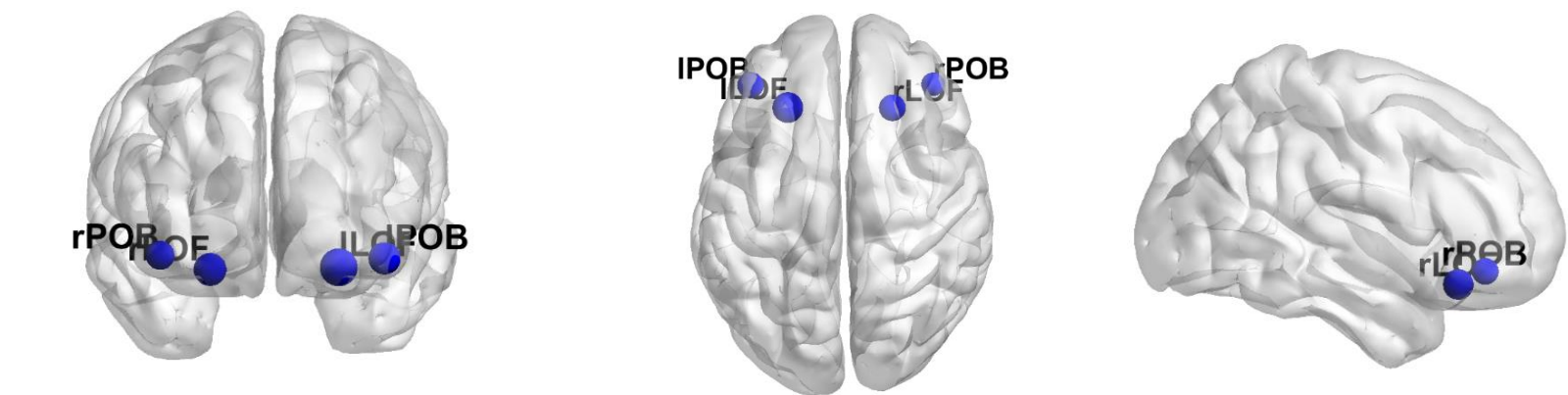
### Diffusion tractography:

- Fiber Assignment by Continuous Tracking (FACT) algorithm using Anima (<https://github.com/Inria-Visages/Anima-Public/wiki>).

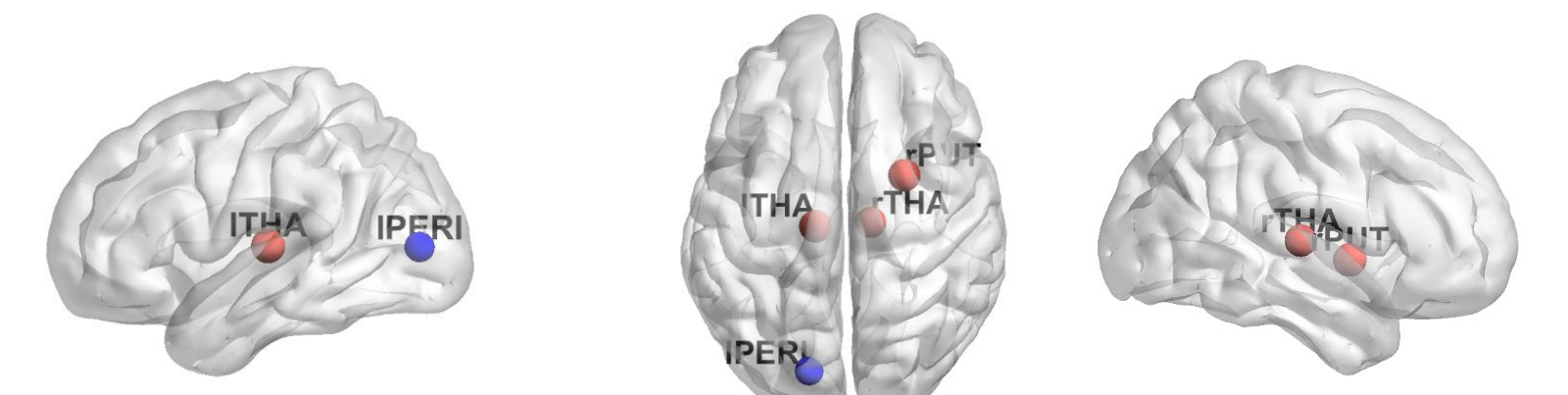
### Fiber density



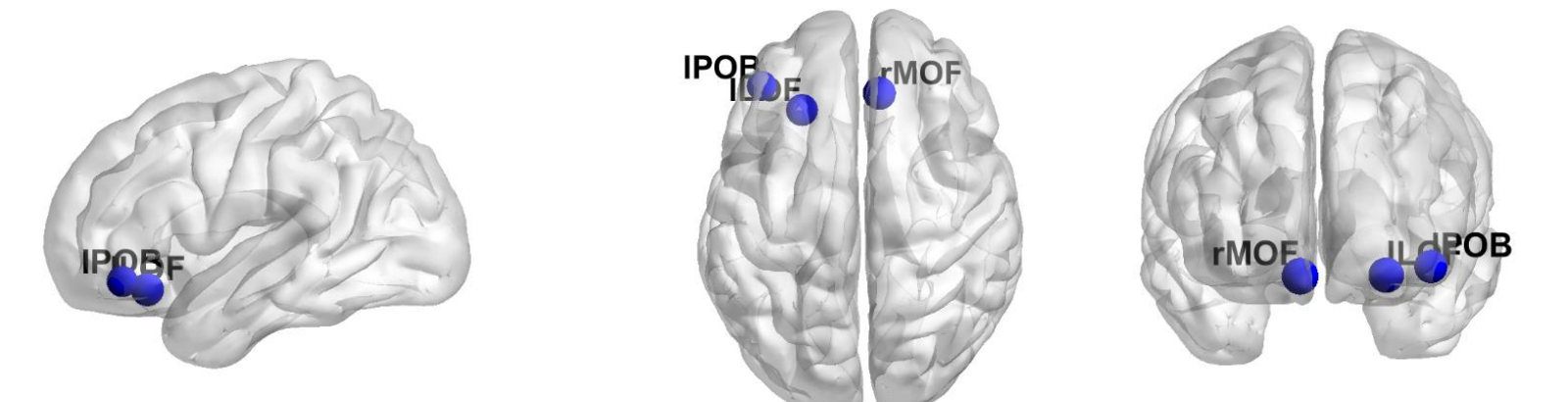
### Strength



### Betweenness



### Clustering



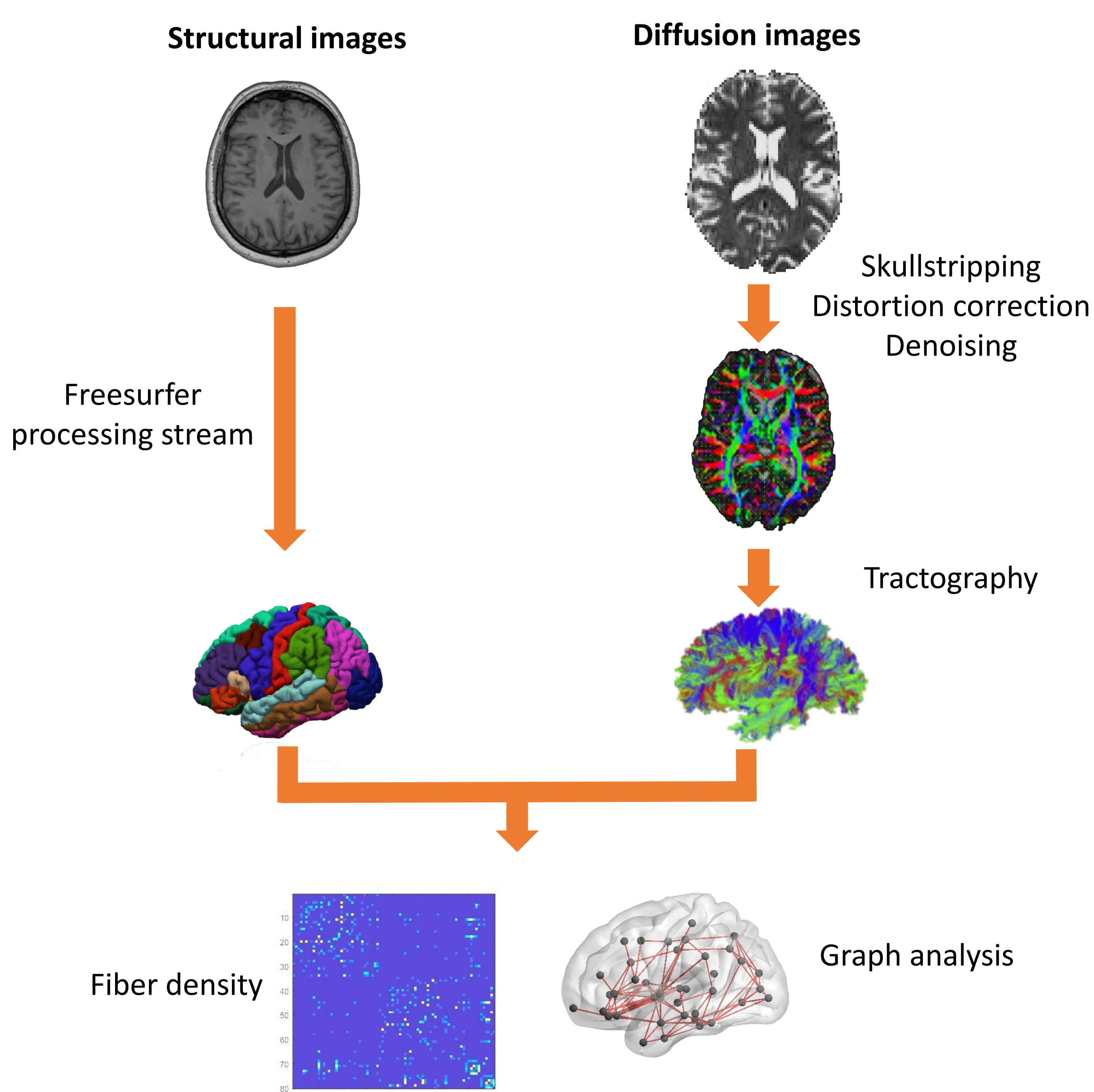
**Figure 2.** Regions exhibited significant between-group differences in regional nodal parameters between MDD and control groups. The blue color represented the higher values of regional nodal metrics in MDD group, and the red color represented the higher values of regional nodal metrics in CTL group ( $p < 0.05$ , with permutation test).

## Results

- Widespread white matter abnormalities in patients with MDD: reduced connection between the frontal and parietal lobes, and between the frontal pole and limbic regions
- In the frontal pole: reduced strength and reduced clustering
- Higher betweenness in right and left thalamus and in right putamen for MDD

## Conclusion

- Decreased fiber density in circuits connecting subcortical brain regions with the frontal and parietal cortex, supporting the theory of limbic-frontal circuit dysfunction in MDD.
- Less segregated network organization in the frontal lobe, implicated in abnormalities of emotion regulation and cognition in MDD.
- Thalamus and putamen: highly interactive regions that likely participate in more functional interactions.



**Figure 1.** Overview of the method

[1] Liao, Y., Huang, X., Wu, Q., Yang, C., Kuang, W., Du, M., ... & Gong, Q. (2013). Is depression a disconnection syndrome? Meta-analysis of diffusion tensor imaging studies in patients with MDD. *Journal of psychiatry & neuroscience: JPN*, 38(1), 49.  
 [2] N. Wiest-Daesslé, O. Commowick, A. Stamm, P. Perez, C. Barillot, R. Seizeur, S. Prima, Cortical surface-based analysis. I. Segmentation and surface reconstruction, *Neuroimage*, 9 pp. 179-194, 1999.  
 [3] Sackeim, H. A. (2001). Functional brain circuits in major depression and remission. *Archives of General Psychiatry*, 58(7), 649-650.