

# Abnormal White-matter Rich-club Organization in Obsessive-Compulsive Disorder

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## Background

In the normal functioning brain, information is integrated and communicated throughout distant and/or segregated regions quickly and efficiently.

Key players in this process are network *hubs*, regions densely interconnected with each other forming a “rich-club” within the brain<sup>1</sup>. Alterations in rich-club organization interfere with higher-order cognitive processes and are common to several psychiatric and neurological conditions.

A few studies examining white-matter alterations in obsessive-compulsive disorder (OCD) suggest decreased efficiency of information transfer across widespread regions in the brain<sup>2,3</sup>. However, whether this might be linked to alterations in the rich-club organization remains unclear<sup>4,5</sup>.

### Aim of the project

To investigate rich-club organization and rich-club connectivity as potential markers of OCD.

- [1] van den Heuvel MP et al. 2012. Proceedings of the National Academy of Sciences 109, 11372–11377.  
 [2] Zhong Z et al. 2014. Progress in Neuro-Psychopharmacology and Biological Psychiatry 51, 39–50.  
 [3] Reess TJ et al. 2016. Translational Psychiatry 6(9), pp.e882–e882.  
 [4] Peng Z et al. 2021. NeuroImage: Clinical, 32, p.102808.  
 [5] Zhou C et al. 2021. Brain Imaging and Behavior, 15(2), pp.700–710.

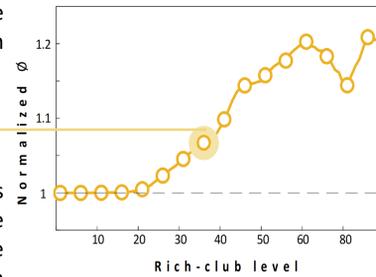
## Methods

The structural connectome of **28 unmedicated OCD patients**, **8 of their unaffected siblings (SIB)** and **28 healthy controls (HC)** was reconstructed using diffusion-weighted imaging and probabilistic tractography. A brain network was constructed, with regions as its *nodes* (N=250) and the reconstructed streamlines as its *edges*.

## Rich-club organization

### UNWEIGHTED ( $\emptyset$ ) =

extent to which hubs preferentially create connections between them.



### WEIGHTED ( $\emptyset^w$ ) =

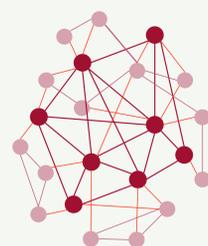
extent to which hubs preferentially allocate the strongest weights to the connections between them.

This is calculated over a range of rich-club (RC) levels.

## Nodes & Edges classification

Network nodes:

- RICH-CLUB** = top 16% most highly connected regions displaying rich-club organization at the group level
- NON-RICH-CLUB** = all other nodes



Network edges:

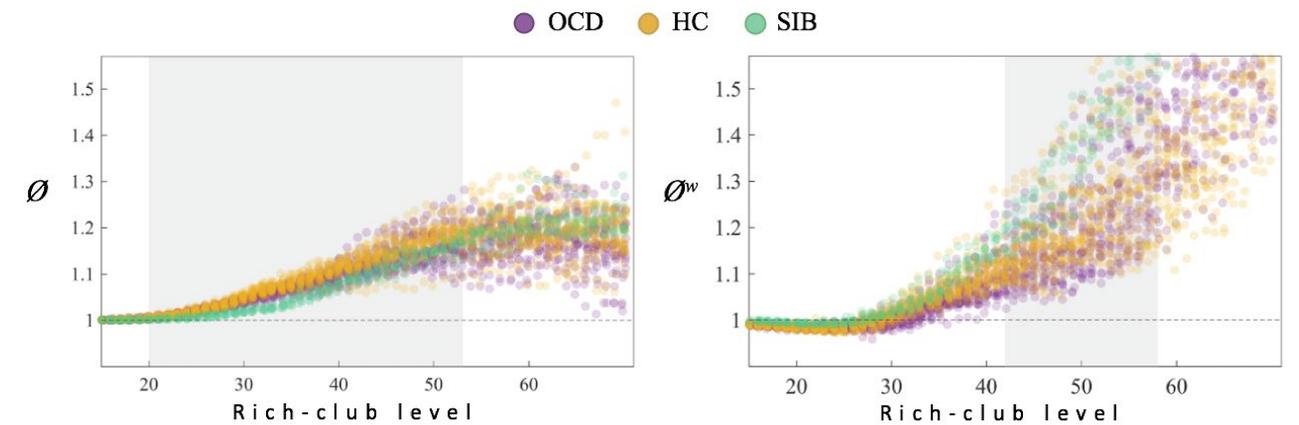
- RICH-CLUB** = connections between rich-club nodes
- FEEDER** = connections between rich-club & non-rich-club nodes
- LOCAL** = connections between non-rich-club nodes

### Connectivity DENSITY =

ratio of the connectivity strength (i.e., sum of edges) of each connection class to the connectivity strength of the whole brain

Ordered differences between  $\emptyset$  and  $\emptyset^w$  rich-club organization, rich-club, feeder and local density of the three groups were assessed using the Jonckheere-Terpstra test (50'000 permutations). False-discovery rate correction (q=0.05) was applied to account for multiple comparisons.

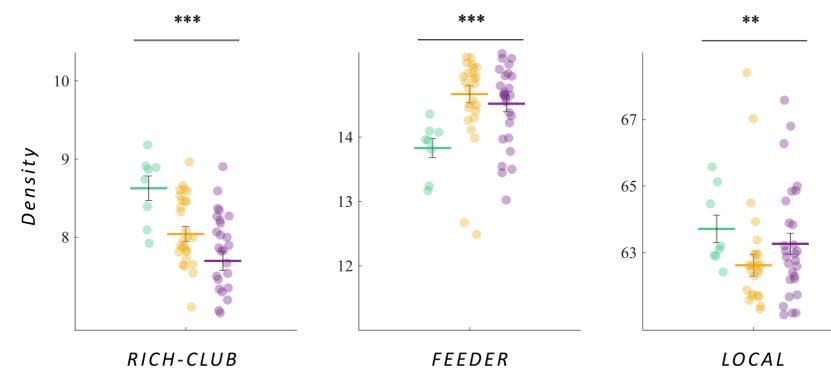
## Results



Individual normalized unweighted ( $\emptyset$ , left) and weighted ( $\emptyset^w$ , right) coefficients are plotted for OCD patients (purple), unaffected siblings (green) and healthy controls (yellow) for different RC levels. The grey shaded areas indicate significant ordered differences between groups, with HC > OCD > SIB unweighted (RC level = [20,53], q<.05) and SIB > HC > OCD weighted (RC level = [42,58], q<.05) rich-club organization.

Consistent with previous reports, rich-club nodes (selected at the top 16%) included:

- CORTICAL NODES** Precuneus, inferior parietal lobule, insula, cingulate gyrus, superior temporal lobe, fusiform gyrus, occipital cortex
- SUBCORTICAL NODES** Hippocampus, thalamus, caudate, putamen



Compared to HC, OCD patients displayed significantly reduced rich-club density (p<.001), and a slight increase in the density of local connections (p=.052).

Siblings displayed the highest and lowest (never intermediate) values across the different connection classes (\*\*\*, p<.001, \*\*, p<.01).

## Conclusions

These results suggest a topological shift of connections and their weights away from the rich-club, resulting in weaker structural connectivity between network hubs. Preliminary findings concerning the unaffected siblings stimulate further research into familial vulnerability or resilience to developing the disorder.

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