Neural correlates of cognitive impairment phenotypes following a COVID-19 infection

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Motivation

- Subjective complaints regarding **cognitive function impairment** following a **COVID-19** infection is a well-known phenomenon that can last for over a year[1].
- **Neurocognitive clinical evaluations (NCE)** performed on patients with such subjective complaints have revealed low scores in **memory, executive control and attention.**
- Here, we look into the **neuroanatomical substrate** of these patients by analyzing functional magnetic resonance imaging scans of their brains during the resting state **(rs-fMRI).**
- We compare them to a balanced **control group** that have not had a COVID-19 infection at the time of study and had average scores in their NCEs.
- Our objective is to identify **neural activity patterns** that characterize the outcomes of these clinical evaluations.

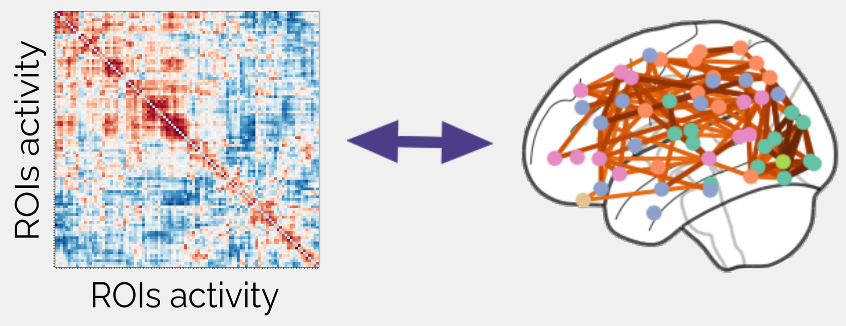
Methods

Dataset

Group	Females	Males	Mean age
post-COVID	32	10	56 +/- 12
Control	25	19	59 +/- 10
Total	57	29	58 +/- 11

- None had preexisting cognitive-related issues.
- rs-fMRI scans comprised sessions of 7 minutes (205 timepoints), with a voxel size of 3mm^3, and structural MRI scans (T1) with voxel size 2mm^3.
- The T1-weighted image was spatially normalized and aligned to a brain template using fMRIPrep[2]
- BOLD coordinates were then aligned to those of the T1-w.

- For each group, we parcel their brain scans into **400 brain regions** of interest **(ROIs)**[3]. These ROIs comprise **7 different functional networks**[4].
- By computing the **correlation** between the activity of these ROIs, we are able to build a **connectivity matrix (connectome)** that depicts the overall interconnectivity of the networks.



- We can then compute **graph measures** on each individual and average **across groups.** These measures characterize the **topology** of their functional networks.

Statistical analysis

Thresholding

- To perform a more robust analysis, we compute the connectivity measures on **each individual** on several **connection densities.**
- For a given network G = (V, E), we define $G_t = (V, E_t)$ as the spanning subgraph of the network that contains the **top *t* weighted edges:**

$$E_t \subseteq E \wedge (\forall e \in E \setminus E_t, e_t \in E_t) |w(e_t)| \geq |w(e)|$$

$$|E_t| = t * \frac{N(N-1)}{2} \qquad (0.05 \leq t \leq 0.40)$$

where w corresponds to the correlation coefficient and N is the number of nodes (ROIs) in the network.

Significance tests

- Wilcoxon rank-sum tests between the groups' measurements are performed at each value of *t*. A **black line** indicates **significant regions (p < 0.01).**

Connectivity measures

Network efficiency[5] characterizes small-world networks, such as the brain, which are both both globally and locally efficient.

- **Global Efficiency:** it is defined as the reciprocal of the harmonic mean of the network's path lengths. It is interpreted as the efficiency of **information exchange** in a parallel system.

$$E_{glob} = \frac{1}{N(N-1)} \sum_{i \neq j} \frac{1}{l_{ij}}$$

where N is the number of nodes in the network and l_{ij} is the shortest path length from node i to node j, as weighted by the correlation coefficients.

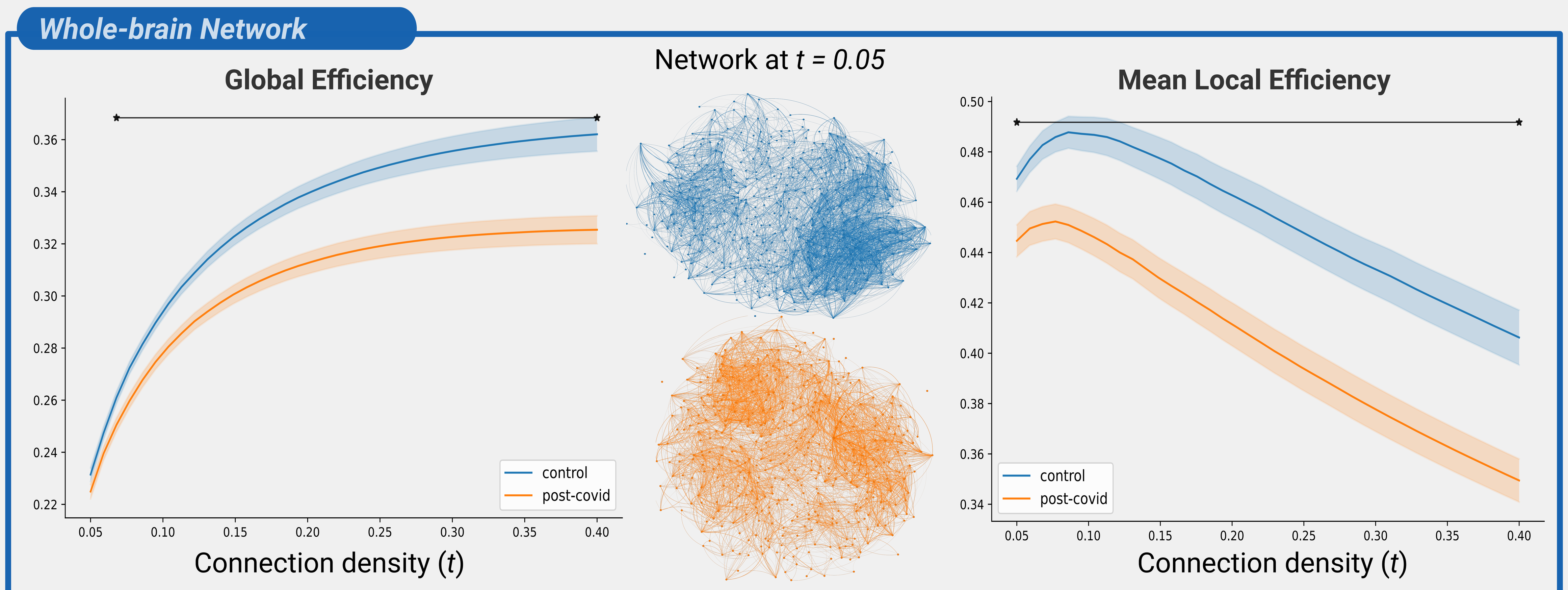
- **Local Efficiency:** it can be defined as the global efficiency computed on the neighbourhood of a given node. It reflects the extent of **integration** between the immediate neighbors of the given node.

$$E_{loc}(i) = \frac{1}{N_{G_i}(N_{G_i}-1)} \sum_{j,h \in G_i} \frac{1}{l_{jh}}$$

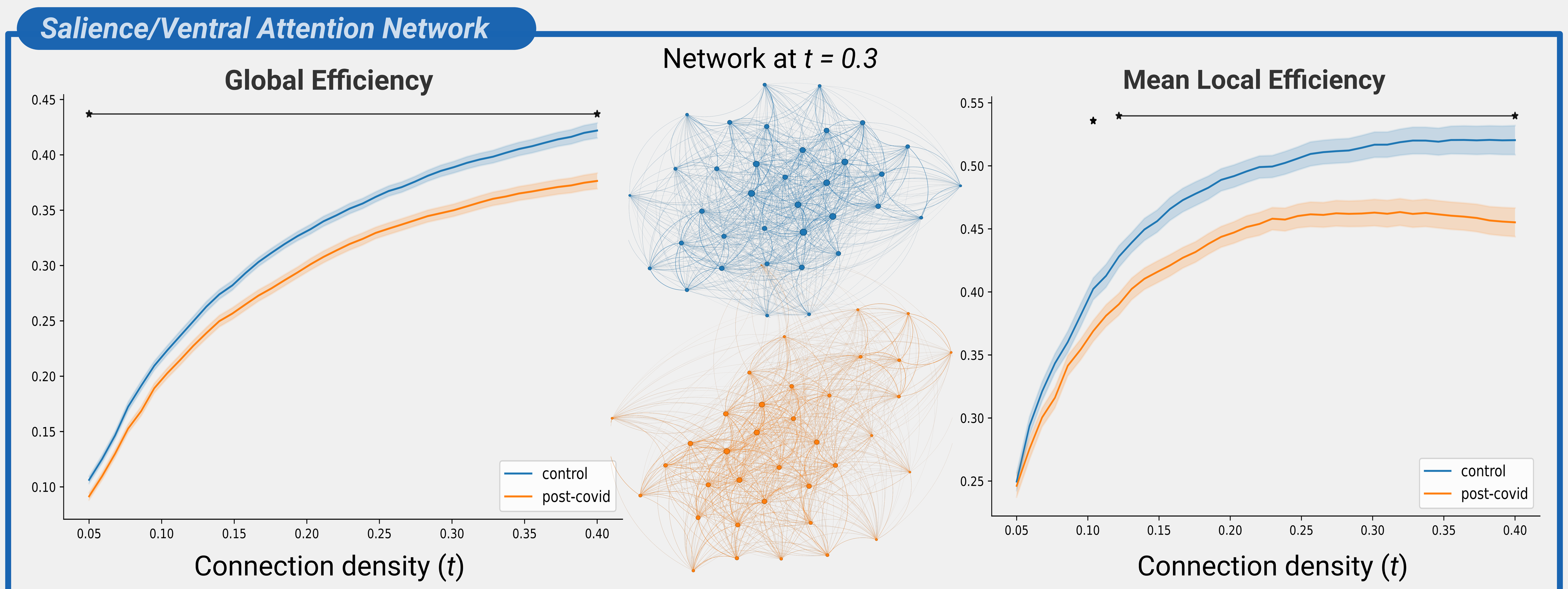
where G_i denotes the subgraph comprising all nodes that are immediate neighbors of the i_{th} node. We report the average over all nodes.

Results

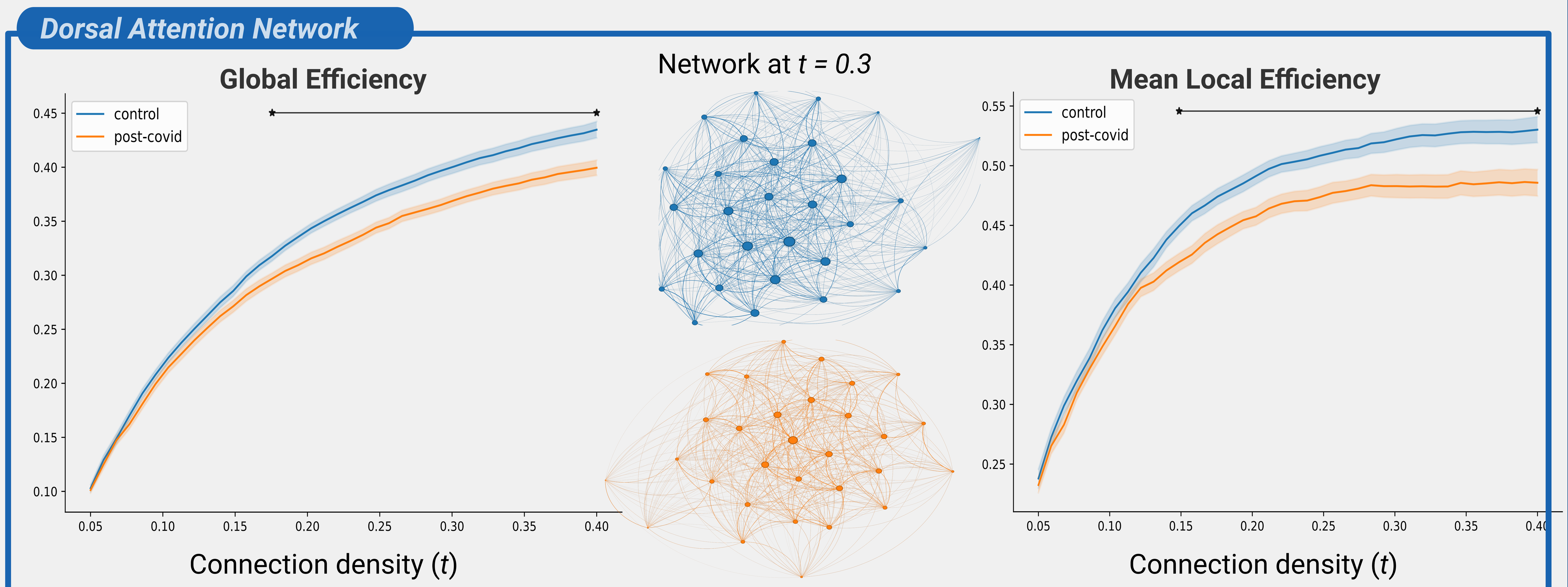
Whole-brain Network



Salience/Ventral Attention Network



Dorsal Attention Network



Conclusions

- Consistent with previous studies[6], there is a correlation between **cognitive phenotypes** and the **topological properties** of functional networks in the brain.
- The differences in the measurements are most prominent when looking at the brain as a whole. Notwithstanding, the **Dorsal and Ventral Attention (Salience) Networks**, followed by the Default Mode Network, have also displayed statistically significant differences.
- To sum up our analysis, we intend to thoroughly examine the results of the clinical evaluations and assess their **alignment with specific attention test scores.**

References

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