INTEGRATION AND SEGREGATION NETWORK ANALYSIS OF RESTING-STATE MEG IN PARKINSON'S DISEASE

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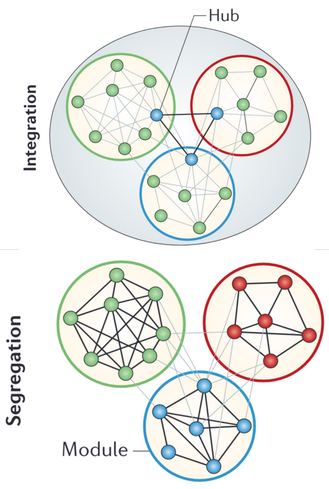
1. BACKGROUND

Parkinson's disease (PD) induced loss of dopaminergic neurons results in chronic decrease in dopamine levels throughout the brain, especially in the **cortico–basal ganglia–thalamic network** [1]. **How cortical networks are altered in PD remains poorly understood.** Here, we focus on **MEG cortical activity** to characterise fast timescale changes in this network using graph theory. Global graph measures indicate a general increase of **functional connectivity (FC)** in early PD stages followed by a decrease later in the disease course [2]. In a longitudinal study, PD patients were shown to have decentralised and less integrated functional networks compared to healthy controls (HC), correlating with motor and cognitive symptoms [3]. Much less has been done concerning **local network properties** which we explore here and interpret in the context of **integration and segregation (I-S)**. I-S balance quantifies the complementary ability of brain regions to communicate globally (integration) and perform localised computations within modules (segregation).



Adapted from [4].

2. APPROACH

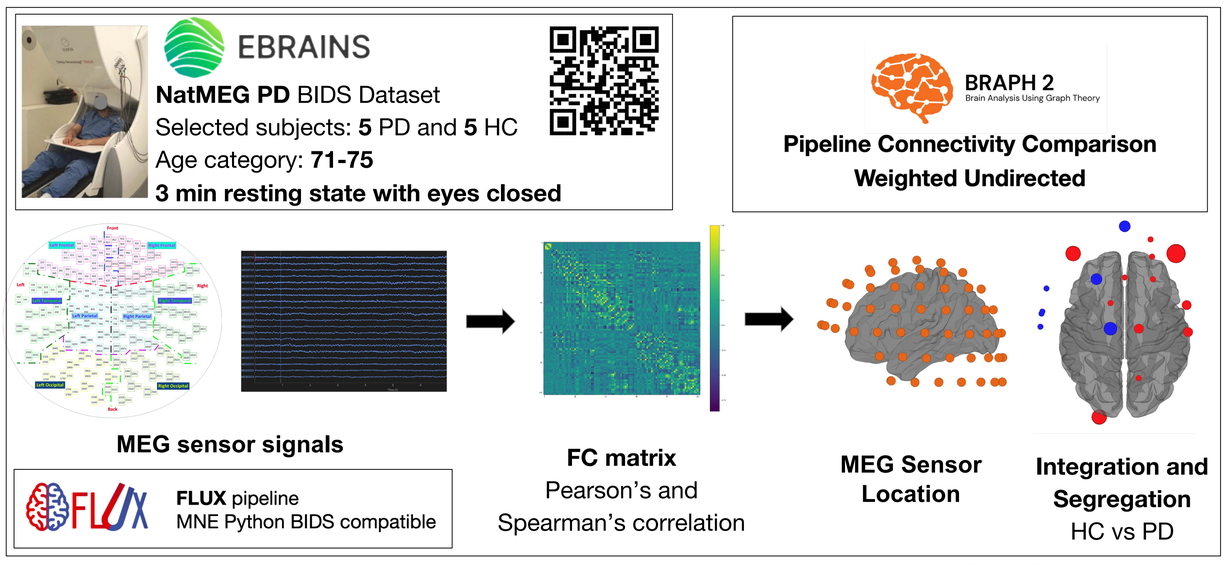


Fig.1 *Pipeline overview*

3. RESULTS

Results were computed from root mean squares (RMS) of gradiometers resulting in 102 timeseries.

FC WEIGHTS DISTRIBUTION

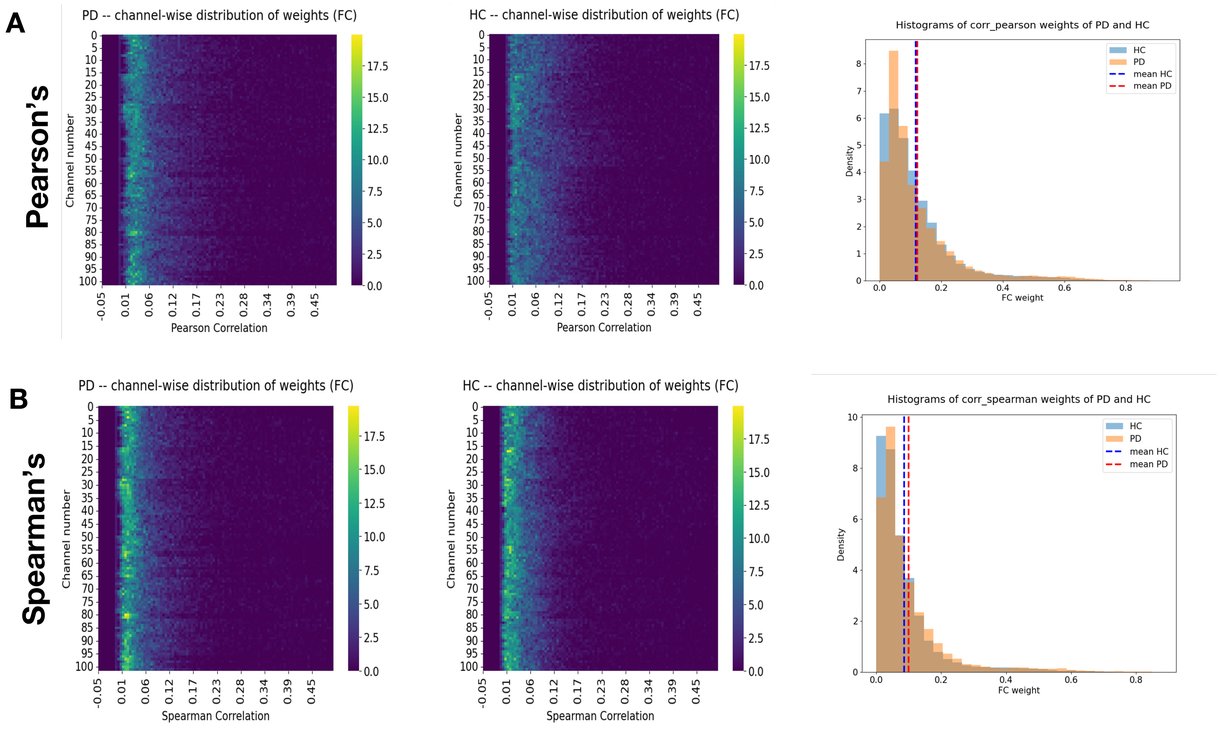
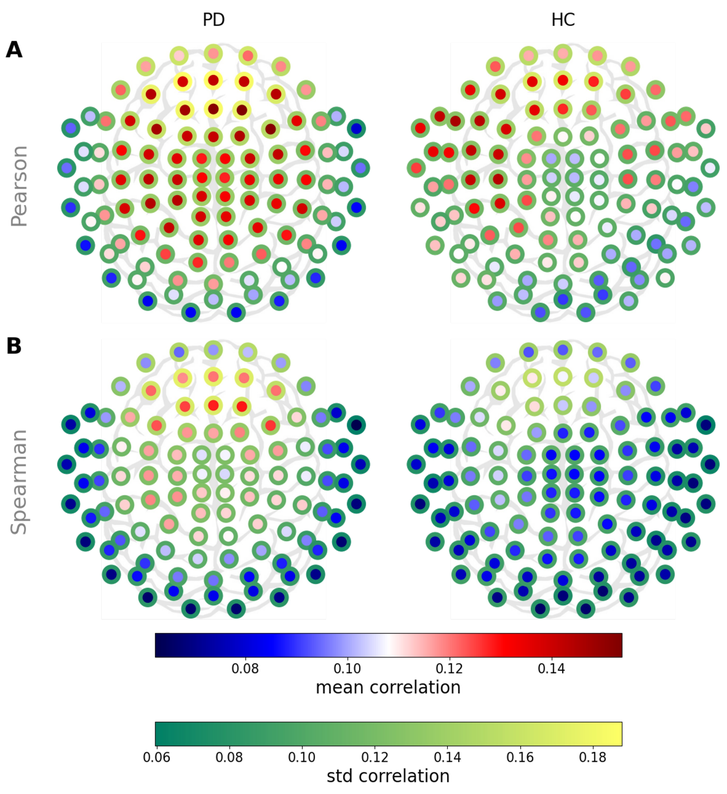


Fig.2 *Distribution of the weights channel-wise over HC and PD groups for Pearson's and Spearman's correlations which is then pooled over all the channels.*

- Compared to Pearson's correlation (PC), Spearman's correlation (SC) leads to a **more skewed distribution** of the FC's weights.
- **HC has broader distribution** (higher std) for PC not SC, std is **less regular over channels in PD**.
- Overall **weights did not decrease in PD**. Same results were found with different methods for computing the FC: the weighted phase lag index and the amplitude envelope correlation in beta band.

FC WEIGHTS TOPOGRAPHY

Fig.3 *Topography of the mean and the standard deviation of SC and PC over the RMS gradiometers' sensors.*



- Only looking at the **spatial distribution** of the weights shows some differences between PD patients and HC, especially in the **frontal and central parts** of the brain. These parts of the brain are the most (functionally) connected.
- Interestingly, PD patients seems to have a **more symmetric** FC topography.
- **Stronger FC in PD** is contradictory with previous results. Multiple reasons can explain this discrepancy like the number of subjects, sensor rather than source analysis, FC method.

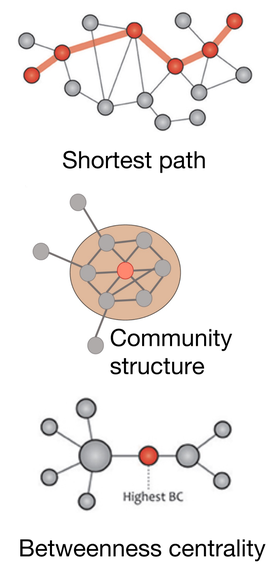
GRAPH MEASURES

All the graph measure computations were performed at the **nodal level**, meaning we get a value for each sensor (RMS gradiometer).

Integration is assessed by **path length** that is the averaged shortest distances from a node to all other nodes.

Segregation is assessed by **community structure** as a subdivision of the network into non-overlapping groups of nodes which maximizes the number of within-group edges and minimizes the number of between-group edges.

Finally, as a **centrality** measure we assess with **betweenness centrality** as the fraction of all the shortest paths in the graph that pass over a given node.



Main Results

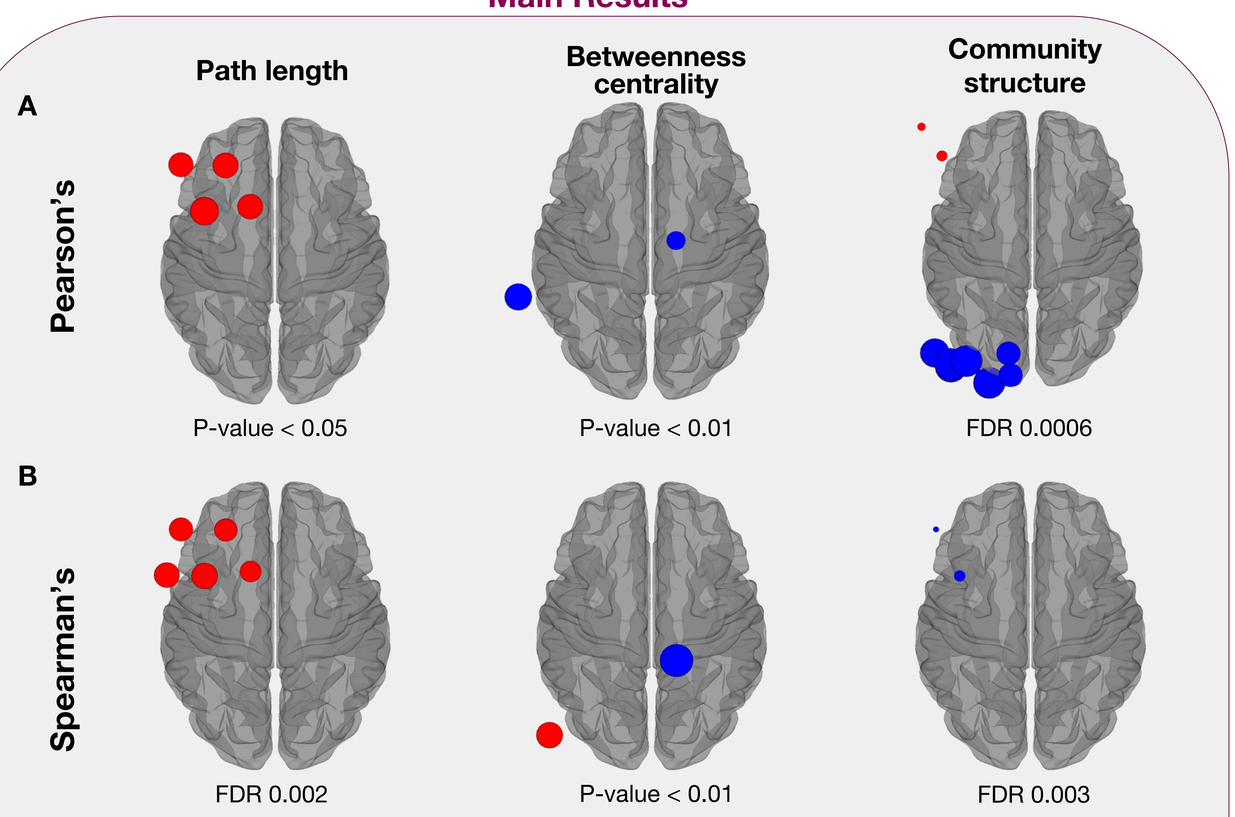


Fig.4 *Difference between HC and PD patient groups graph measures for SC and PC matrices. Only nodes with the most statistically significant difference are displayed on top of a brain template. Size is proportional to the difference.*

Interpretation

Pearson's correlation reflects the linear relationship between two signals whereas Spearman's correlation denotes the presence of monotonicity between them, it being linear or nonlinear. It is thus normal to get discrepancy between the results from these two FC methods. That said, **differences between PD and HC** are observed in interesting regions like **occipital (visual), frontal (cognitive) and temporal (sensorimotor)**. To be noted, these changes are mainly in the **left hemisphere**, to be expected as most subjects are right handed. These regions can be associated to classical PD symptoms like hallucinations for the visual cortex, motor disorders for the sensorimotor cortex and dementia for the frontal cortex.

Even at the nodal level, PD alters the I-S balance assumed to be present in HC. Some measures show compensation effects with increase somewhere and decrease elsewhere. Others follow a clear trend, like **path length overall decreases**. However only some nodes had a statistically significant difference between PD and HC as seen in Fig.4.

- Significant **decreased path length in PD** frontal areas suggest an **increase of integration** in these parts of the brain that have the larger weights, see Fig.3.
- **Increase of betweenness centrality** also points to an **increase of integration** but this time more in the temporal lobe which becomes more **central** in PD, possibly explaining motor issues.
- **Community structure increases** in the visual area suggest an **increase of segregation** possibly leading to a disability of dealing properly with visual inputs.

4. DISCUSSION

CONCLUSION

Our results highlight **important restructuring of functional connectivity** which is **lateralised** with a seemingly compensation phenomenon well illustrated by Fig.4. According to the proposed relationship of I-S balance with the **excitation-inhibition (E-I) balance** [5], changes observed here are in line with previous results suggesting E-I imbalance in PD cortex [6]. It also suggests that dopamine replacement therapy is not sufficient here to ensure a "healthy state" of the functional network in PD. Finally, one idea emerging from this study is trying to **recover I-S balance by non-invasive brain stimulation** for reducing some of the motor and non-motor symptoms.

PERSPECTIVES

- Performing source reconstruction and then source analysis.
- Look at different time lag in the FC computation.
- Go into the details of graph measures regarding nodes showing statistically significant difference.
- Link the results to the metadata to interpret them in a PD context.

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