Longitudinal study of functional brain network reorganization in clinically isolated syndrome

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Background

There is a lack of longitudinal studies exploring the topological organization of functional brain networks at the early stages of multiple sclerosis (MS) that could help to understand cognitive compensation.

Objectives

To assess potential **brain functional reorganization at rest in patients with CIS** (PwCIS) after **1-year of evolution** and to characterize the dynamics of functional brain networks at the early stage of the disease.

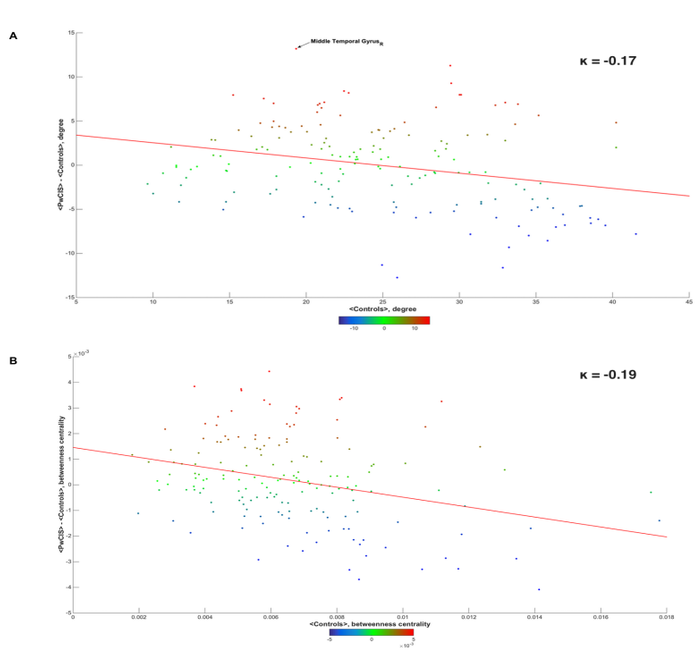
Methods

- 41 patients recruited less than 6 months after a CIS with at least two asymptomatic cerebral lesions on FLAIR and 19 HC matched for age, sex and educational level.
- 3T brain MRI scan including 3D T1-weighted images, FLAIR and Resting-State functional MRI were acquired at <u>baseline</u> and <u>1-year</u> after.
- Attention, working memory (WMem), episodic memory (EMem), executive functions (EF) and information processing speed (IPS) were assessed by a neuropsychological battery.
- Destrieux parcellation was obtained using FreeSurfer 5.3.
- Graph-based network measures calculated: Global efficiency (Eglob), Local efficiency (Eloc), Betweenness centrality (BCN) and Degree (Deg).
- Hub disruption index (κ) of each measure was estimated as the slope of the following graph:

$$(\text{Network\_Measure}_{subject} - \text{Network\_Measure}_{ControlMean}) = f(\text{Network\_Measure}_{ControlMean})$$

- Connectivity measures were compared globally with Hub disruption index, and locally in different regions of the brain.
- Correlations between cognition and connectivity were computed at baseline and longitudinally (accounting for age, sex and level of education).

Figure 1. Hub disruption index of PwCIS at baseline



Hub disruption index of (A) degree (B) betweenness centrality.
Red denotes an increased degree in the PwCIS compared to HC; blue denotes a decreased degree in the PwCIS compared to HC.

Conclusions

- For the first time, **dynamic changes** of functional brain networks are observed in CIS patients → The pattern of functional connectivity reorganization **remained the same during the first** year but tended to be **more pronouced at 1-year**.
- At the first stage of the disease, regional reorganization of connectivity is associated with **the maintenance of normal global efficiency and cognition** suggesting a **compensatory effect**.

Literature

Bullmore E, Sporns O. Complex brain networks: graph theoretical analysis of structural and functional systems. Nat Rev Neurosci 2009.
Fleischer V, Radetz A, Ciolac D, et al. Graph theoretical framework of brain networks in multiple sclerosis: A review of concepts. Neuroscience 2017.
Rubinov M, Sporns O. Complex network measures of brain connectivity: Uses and interpretations. Neuroimage 2010.

Results

Patients mean age was 38.3 years with 78% females. 64% of patients had a high level of education.

❑ **<u>Functional connectivity</u>**

➢ <u>Baseline</u>

- The hub disruption indexes of <u>degree</u> and <u>betweenness centrality</u> were significantly <u>negative</u> at baseline in patients ($p<0.001$ and $p<0.05$, respectively) **(Figure 1)** → meaning that the hubness tended to decrease mainly in the hub regions and tended to increase mainly in the non-hub regions → Regionally, these alterations were mainly driven by increased hubness in the right middle temporal gyrus **(Figure 3)**
- No global efficiency differences were observed between the patients and the HC → **compensatory effect**

➢ <u>1 year</u>

- After 1 year, a similar pattern of brain network disruption was present in the patients, as the hub disruption indexes for degree and betweenness centrality were significantly negative ($p<0.00001$), but such reorganization appeared <u>more pronounced</u> than at baseline **(Figure 2)** → Regionally, these alterations were mainly driven by increased hubness in bilateral hippocampus, post-ventral cingulate gyrus, and left parieto-occipital sulcus and decreased hubness in the right middle occipital gyrus and the left posterior segment of the lateral fissure **(Figure 3)**
- No global efficiency differences were observed between the patients and the HC → **compensatory effect**

❑ **<u>Cognitive impairment</u>**

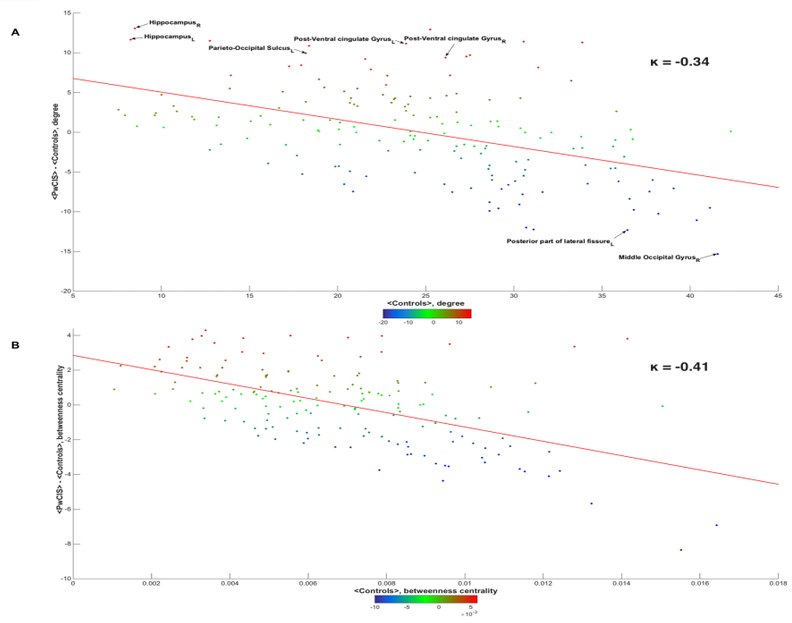
➢ <u>At baseline:</u> Only a moderate cognitive impairment was noticed at baseline, as only the computerized speed cognitive test (CSCT) and the brief visual memory test revised (BVMTR) were altered.

➢ <u>After 1 Year:</u> This cognitive impairment was no longer observed after 1-year as PwCIS showed no significant differences compared to HC.

❑ **<u>Relationships between network topology and cognition</u>**

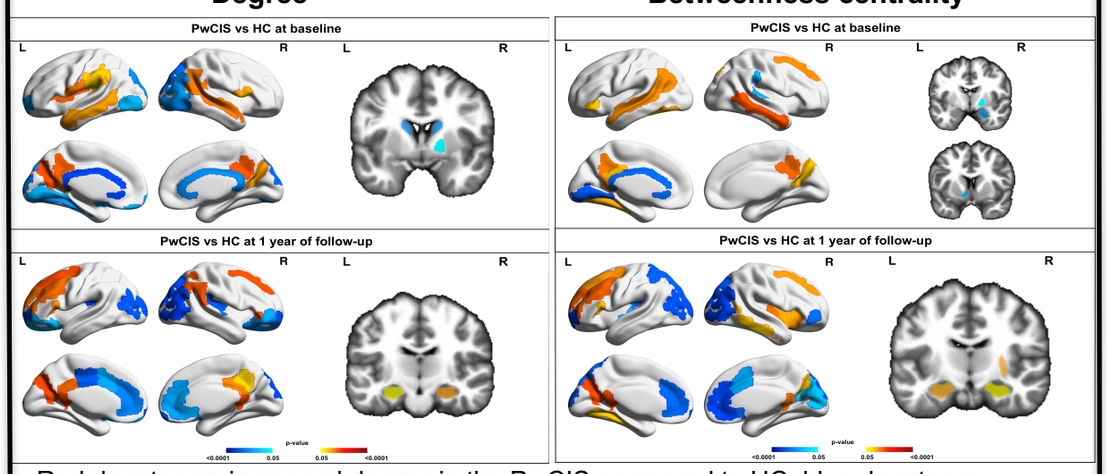
➢ Hub disruption index of betweenness centrality was observed to be correlated to delayed recall of the BVMTR (BVMTR-DR) as $r = -0.32$ and $p<0.05$ at 1 year → This indicates a more pronounced brain network reorganization as the cognitive performances are getting better.

Figure 2. Hub disruption index of PwCIS at 1-year



Hub disruption index of (A) degree (B) betweenness centrality.
Red denotes an increased degree in the PwCIS compared to HC; blue denotes a decreased degree in the PwCIS compared to HC.

Figure 3. Regional differences in degree and betweenness centrality between PwCIS and HC at baseline and 1-year



Red denotes an increased degree in the PwCIS compared to HC; blue denotes a decreased degree in the PwCIS compared to HC.