## **Theme: Cognitive Neuroscience**

## Studying effective connectivity using DCM and PEB with simultaneous EEG-fMRI task data in Multiple Sclerosis

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## Abstract:

Damage to the myelin sheath in Multiple Sclerosis (MS) disrupts structural pathways essential for neuron communication, leading to complex functional changes in brain networks and making MS a disconnection and network disorder. Studying these functional network changes is crucial to further decipher symptoms like cognitive impairment and physical disability and to better understand disease progression. We acquired longitudinal EEG-fMRI data from 18 Relapsing-Remitting MS (RRMS) patients and 18 matched healthy controls (HC) during task performance at baseline (immediately after diagnosis) and follow-up (after ten months). Using Dynamical Causal Modelling and Parametric Empirical Bayes, we analysed effective connectivity in the network underlying biological motion processing and identified connections with strong evidence (Posterior Probability>0.95) to be altered by disease and over time. With Spearman correlations we assessed the association between connection strength of the altered connections and cognitive scores collected through the Brief International Cognitive Assessment for MS (BICAMS) scale. Our findings revealed connections in MS that changed over time differently from HC, with some increasing at follow-up only (rOCC-IMTC, rOCC-rSTS), and others only at baseline relative to HC (IMTC-rOCC). These connections were also positively associated with cognition at follow-up, suggesting early adaptive compensatory mechanisms that may help preserve cognition. Some connections, like IMTC-rOCC appeared to approximate healthy values over time (alterations only in baseline), possibly due to treatment or natural progression, though this effect may be temporary. Importantly, connections that seemed unaffected at baseline (rOCC-IMTC, rOCC-rSTS) but became altered at follow-up in MS and correlated with cognition suggest potential biomarkers of disease progression, highlighting brain areas more likely to undergo changes in the future and may help predict future symptoms.

**Keywords:** Multiple Sclerosis, Effective connectivity, DCM, PEB, EEG-fMRI, Biological Motion