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Brain signatures of chronic gut inflammation

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Introduction

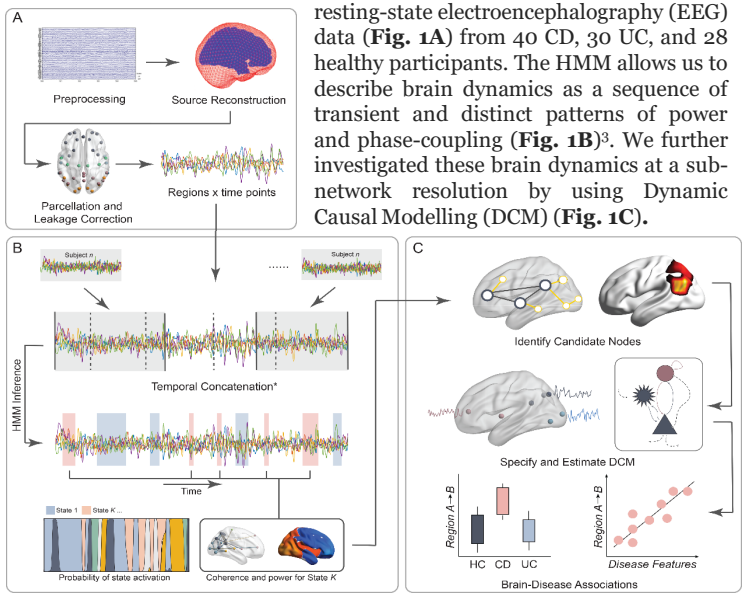
Gut inflammation is thought to modify brain activity and behaviour via modulation of the gut-brain axis[1,2]. However, how chronic and relapsing exposure to peripheral inflammation contributes to altered brain dynamics in Inflammatory Bowel Disease (IBD) is poorly understood.

Research Objective

In this study, we investigated whether Crohn's Disease (CD) and Ulcerative Colitis (UC) –characterised by long-standing and repeated exposure to systemic inflammation - were associated with alterations to spontaneous brain state dynamics.

Methods

We fit a Hidden Markov Model (HMM) to resting-state electroencephalography (EEG) data (**Fig. 1A**) from 40 CD, 30 UC, and 28 healthy participants. The HMM allows us to describe brain dynamics as a sequence of transient and distinct patterns of power and phase-coupling (**Fig. 1B**)[3]. We further investigated these brain dynamics at a sub-network resolution by using Dynamic Causal Modelling (DCM) (**Fig. 1C**).



Results: Brain States

Results from the HMM brain state assessment showed that resting-state EEG data was best described by six transient and recurring brain states, each with unique spatiotemporal profiles. The spatial maps of power and coherence networks were averaged across a wideband frequency range (1-30 Hz) (Fig. 2).

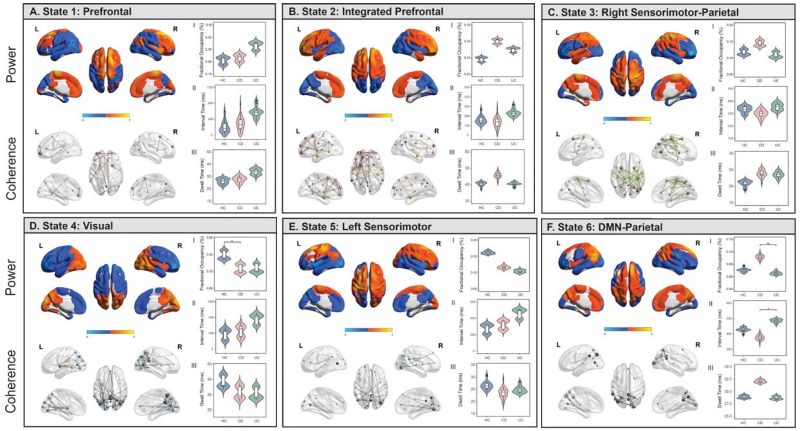


Fig 2. Brain states identified using Hidden Markov Modelling represent networks of power and spectral coherence. (**A-F**) Left panel shows wideband (1-30 Hz) power maps (top) and coherence networks (bottom) displayed for each state. (**A-F.I-III**) Comparison of temporal statistics between healthy controls (HC), Crohn's Disease (CD) and Ulcerative Colitis (UC) individuals for each state, after adjusting for age and sex. Permutation tests were performed to assess the null hypothesis of equality in temporal measures between groups. * denotes $p < 0.05$; ** denotes $p < 0.005$.

References

1. Bell, J. A. *et al.* Repeated exposure to systemic inflammation and risk of new depressive symptoms among older adults. *Translational Psychiatry* **7**, e1208-e1208, doi:10.1038/tp.2017.155 (2017).
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Results: Sub-network Assessment

To identify the key drivers of brain state differences, we performed a refined sub-network DCM analysis on communication between specific nodes within the *visual* (state 4) and *DMN-parietal* (state 6) states **(Fig. 3A).**

Using the time series from each candidate region, we performed a DCM for cross-spectral densities (CSD), which estimates the effective (directed) connectivity between network nodes (**Fig. 3B**). Results showed significantly stronger connectivity from the left insula to medial prefrontal cortex (mPFC) compared to HC and UC **(Fig. 3C-D).** Using a multiple regression, we provide preliminary support to suggest that chronic hyper-signalling between these regions co-occurs with disease duration in CD (**Fig. 3E**).

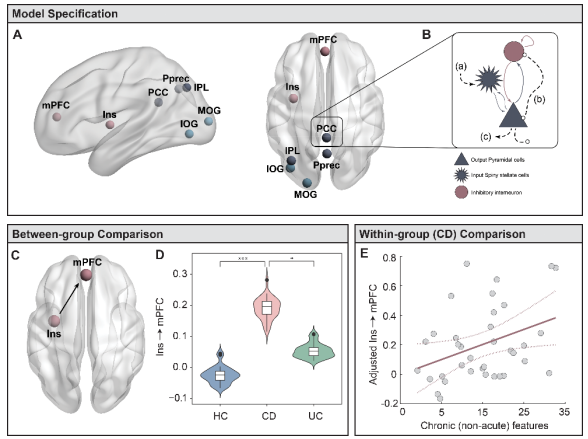

Fig 3. Targeted analyses of effective brain connectivity (Dynamic Causal Modelling, DCM). (A-B) Candidate regions were selected from the HMM brain states for a DCM analysis. (**C-D**) Results from a one-way MANCOVA, showing significantly stronger effective connectivity from the left insula to the mPFC in CD individuals. (**E**) Multiple regression in CD group testing whether disease duration or behavioural symptoms predict the strength of left insula to mPFC connectivity. * denotes $p < 0.05$; *** denotes $p < 0.0005$.

Conclusion

Using IBD as an ecologically valid model of chronic inflammation, we demonstrate that CD individuals exhibit alterations in brain states and patterns of effective connectivity supporting computations within internal, interoceptive mental states.