HUB IDENTIFICATION IN DYNAMIC RESTING-STATE FUNCTIONAL CONNECTIVITY OF THE DEFAULT MODE NETWORK

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Introduction

The default mode network (DMN) has received considerable attention in the fMRI literature over the past decade, due to its prominent role in regulating resting-state brain activity. Whilst the majority of studies have considered stationary functional connectivity measured over scan durations of several minutes, more recently fMRI connectivity analyses have been applied which characterize dynamic connectivity patterns over shorter time periods [1]. In addition, graph theory has been shown to be a useful tool for characterizing brain networks and investigating neuroscientific questions[2], with the identification and characterisation of hubs being particularly important due to their likely role in integration of network activity. Previous studies applying graph theory to fMRI data have identified the posterior cingulate cortex (PCC) as a hub region of the DMN using stationary temporal correlation[3]. However it has not been shown whether the PCC remains a hub when functional connectivity is considered dynamically. The objective of this study was to investigate the dynamics of central nodes or hub regions within the DMN. To do this we applied degree centrality (using both binarised and weighted graphs) and betweenness centrality (both binarised and weighed graphs), two metrics frequently used to identify hub regions[4].

Material and Method

Eight healthy volunteers (5 male, 32±6yrs) underwent a 15 minute resting-state fMRI scan (3x3x4mm voxels, TR=2s, 450 volumes, FA = 80°). For functional connectivity analysis, data were motion corrected and confounds (white matter, ventricular and global signals) were regressed out. Previously, from a separate cohort of 55 healthy subjects (28 male, 25±4yrs), data from 6 minute resting fMRI scans (3x3x4mm voxels, TR=2s) were used to identify the DMN using independent component analysis (MELODIC), which was divided into eight ROIs. Sliding-windows of length 240sec were applied [1] to ROI timecourses with the maximum possible overlap (one data point (2sec) shift). For each window, the regularized inverse covariance [5] (RICOV) for a controlling parameter of one hundred [6] was applied to measure connectivity between DMN ROIs. RICOV values were averaged across subjects, forming an adjacency matrix of connections between each pair of DMN regions. Due to the controversial nature of theresholding, graph metrics for each adjacency matrix were integrated over a range of thresholds, from 0% to 100% of connections. For identification of DMN hubs, four different graph metrics were used: binarised and weighted degree centrality, and binarised and weighted betweenness centrality.

Results

For all four graph metrics, as mentioned in the introduction, the PCC was observed to have the highest centrality across the whole scan (Fig. 1). The integrated binarised degree centrality metric (Fig.1A), stayed in the range of 300 to 450 for the PCC, whilst values for other ROIs were much smaller, peaking at ~250 for the inferior parietal lobes (IPLs) and being lowest for the para-hippocampal nodes (50-100). Using a weighted matrix to compute integrated degree centrality the ordering of ROIs was preserved, with the PCC having the largest value and bilateral para-hippocampal ROIs having the lowest values across the scan. For both binarised and weighted matrices the degree centrality values were similar across bilateral pairs of DMN ROIs, however, right hemisphere ROIs (e.g. rMTL and rIPL) had larger values compared to left hemisphere ROIs. Similarly, for the integrated binarised betweenness centrality values (Fig 1B), the PCC had the largest value over the entire scan duration (exceeding 1400) while the other ROIs had values below 500. Also, using a weighted matrix to compute integrated betweenness centrality resulted in the same plot as that shown in Fig 1B.

Conclusion

These results support the use of dynamic functional connectivity measures to characterize brain networks. The PCC was reliably identified as the strongest hub within the DMN, in agreement with measures extracted from stationary functional connectivity. This was true based on degree centrality and betweenness centrality measures, which identify the most important nodes within a network. In contrast, the para-hippocampal ROIs had the smallest centrality values. For all four metrics this pattern was seen to occur throughout the duration of the scan. The degree centrality metric showed that bilateral ROIs had comparable degree magnitudes (using either weighted or binarised matrices) suggesting that these pairs of bilateral ROIs act in a similar way during the scan. Moreover, the similarity between binarised and weighted degree centrality shows that temporal correlation coefficients represent the strength of functional connections. Overall this work demonstrates the possibility of using dynamic functional connectivity to track brain network dynamics.

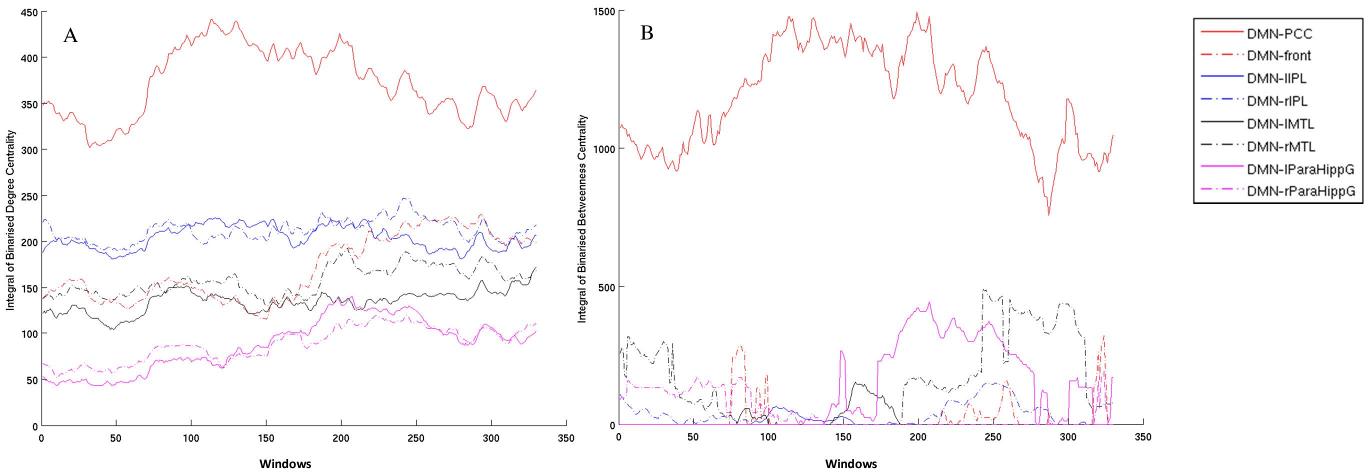

Figure 1: Integration of binarised degree centrality (A) and integration of binarised betweenness centrality (B).

References

1. Hutchison, R. Matthew, et al. "Dynamic functional connectivity: Promises, issues, and interpretations." NeuroImage (2013).
2. Bullmore, Ed, et al. Complex brain networks: graph theoretical analysis of structural and functional systems. Nature Rev Neuroscience10.3 (2009): 186-198.
3. Buckner, Randy L., et al. Cortical hubs revealed by intrinsic functional connectivity. The Journal of Neuroscience, 2009; 29.6: 1860-1873.
4. Freeman, L. C., Centrality in social networks: Conceptual clarification. Social Networks, 1978; 1, 215-239.
5. Friedman, Jerome, Trevor Hastie, and Robert Tibshirani. Sparse inverse covariance estimation with the graphical lasso. Biostatistics, 2009; 9.3: 432-441.
6. Stephen M Smith et al., Network modelling methods for fMRI. NeuroImage, 2011; 54(2):875-91.