# Hub Identification in Dynamic Resting-State Inter-Network and Intra-Network Functional Connectivity

Soroosh Afyouni[1,2], Joanne R Hale[2], Stephen D Mayhew[2], Theodoros N Arvanitis[1,3], and Andrew P Bagshaw[2]
[1]Institute of Digital Healthcare, WMG, University of Warwick, United Kingdom, [2]School of Psychology, University of Birmingham, United Kingdom, [3]Birmingham Children's Hospital NHS Foundation Trust, United Kingdom

## Introduction

Study of functional connectivity (FC) has received considerable attention in the fMRI literature over the past decade. Whilst the majority of studies have considered stationary FC measured over scans of several minutes, more recently fMRI connectivity analyses have been applied to characterize dynamic connectivity patterns over shorter time periods (Hutchison, 2013). In addition, graph theory has been shown to be a useful tool for characterising brain networks and investigating neuroscience-based questions (Bullmore, 2009), with the identification and characterization of hubs being particularly important due to their likely role in integration of brain activity. Previous studies have identified some ROIs as hub regions using stationary correlation (Buckner, 2009). However, it has not been shown whether these ROIs remain hubs in dynamic FC. The objective of this study is to investigate the dynamics of central nodes or hub regions on two scales; inter- and intra-network FC. To do this we applied degree centrality and betweenness centrality, two metrics frequently used to identify hubs (Freeman, 1978).

## Methods and Materials

Eight healthy volunteers (5 male, 32±6yrs) underwent a 15 minute resting-state fMRI scan (3x3x4mm voxels, TR=2s, 450 volumes). Data were motion corrected and confounds were regressed out. 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 behavioural networks using independent component analysis. Timecourses from 28 ROIs were divided into 330 sliding-windows of length 240s (Hutchison, 2013) and overlap of 238s. For each window, the regularized inverse covariance (Friedman, 1978) (RICOV) for a parameter of one hundred (Smith, 2011) was applied to measure FC between ROIs. Due to the controversial nature of thresholding, adjacency matrices were thresholded at a range of densities from 0-100%. Individual subject adjacency matrices were analysed for two FC regimes: 1) *Inter-network*. RICOV values of nodes in the same behavioural networks were summed producing a new adjacency matrix with dimensions corresponding to the 8 behavioural networks. 2) *Intra-network*. From inter-network analyses (Fig 1) the DMN was chosen as a network of interest. RICOV values of DMN nodes were selected, forming a DMN matrix. For both inter- and intra-network, degree and betweenness centrality measures (using both binary and weighted graphs) were computed, integrated over thresholds and averaged across windows.

## Results

Graph metrics of inter- and intra-network FC across subjects were summarized as boxplots. For inter-network connectivity, (Fig 1), the DMN had the largest value of degree centrality for both binarised and weighted networks. Also, betweenness centrality of this matrix showed the DMN as the most important network node, whilst the dorsal attention and saliency networks also had large centrality values.

Similarly, for intra-network connectivity, (Fig 2), the posterior cingulate cortex (PCC) was identified as the most important node, due to its high values of centrality. In contrast, the para-hippocampal ROIs have the smallest centrality values. Furthermore, centrality values of bilateral regions were fairly similar.

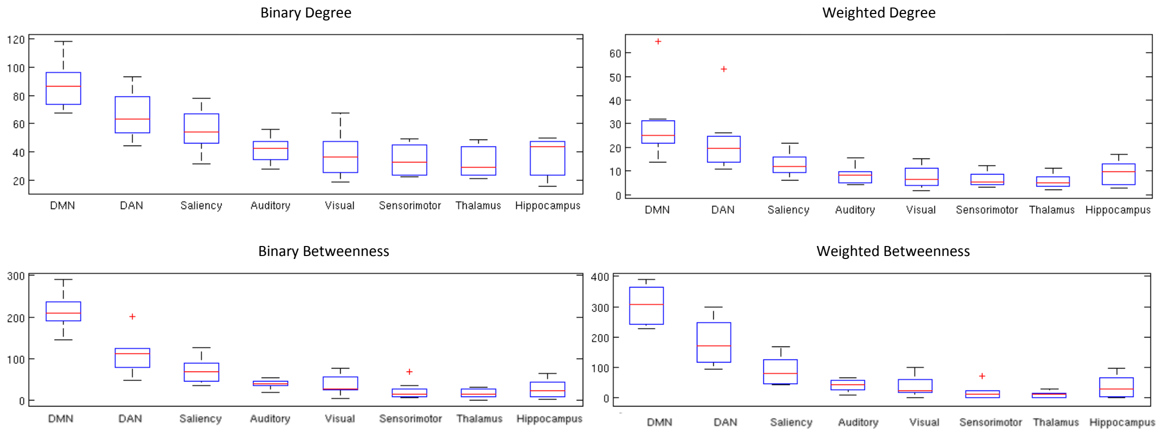

Figure 1: Binarised and weighted degree centrality (top) and binarised and weighted betweenness centrality (bottom) of inter-network connectivity. Results were shown in interquartile range and outliers were shown with a red cross.

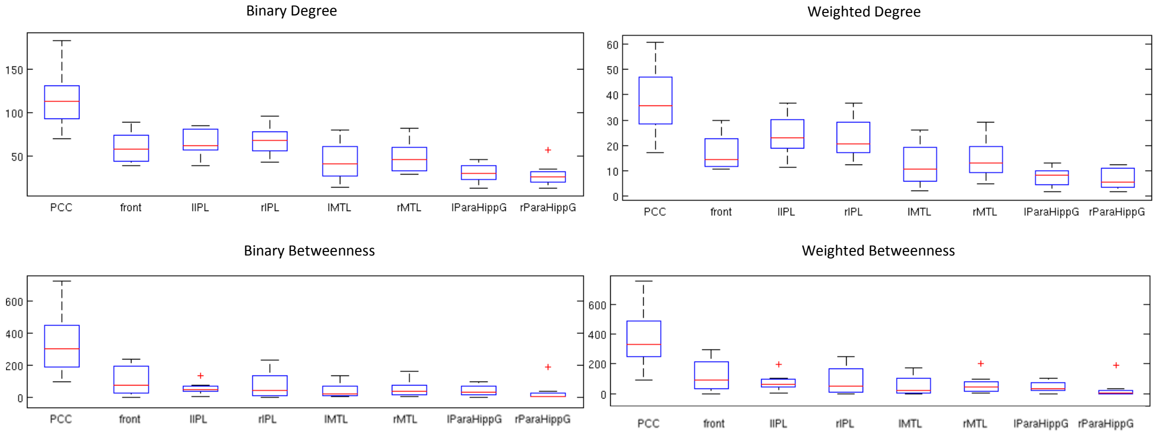

Figure 2: Binarised and weighted degree centrality (top) and binarised and weighted betweenness centrality (bottom) of intra-network connectivity. Results were shown in interquartile range and outliers were shown with a red cross.

## Conclusion

These results support the use of dynamic FC measures to characterize inter- and intra-networks of the brain. The PCC was reliably identified as the strongest hub in the DMN, in line with expectations (Buckner, 2009), and the DMN was identified as a hub in the inter-network analyses. This was based on degree and betweenness centrality measures, which identify the most important nodes in a network. While the PCC had the highest centrality values, the para-hippocampal ROIs had the smallest centrality values in intra-network DMN FC analysis. Also, 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.

## 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.