Instantaneous and Causal Connectivity in Resting State Brain Networks Derived from fMRI Data

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Introduction

Previous studies have investigated functional connectivity (FC) in resting state networks (RSNs) such as default mode network (DMN) [1,2], hippocampal cortical memory network (HCMN) [3], dorsal attention network (DAN) [3] and fronto-parietal control network (FPCN) [3]. However, comprehensive effective connectivity (EC) analysis of these networks has been lacking primarily because their directional connectivity architecture is unknown and hence model driven methods cannot be applied. On the other hand, data driven methods such as Granger causality (GC), though not requiring *a priori* assumptions, are influenced by the zero-lag correlation in RSNs [4]. Therefore, in this work, we applied a new framework developed by us, correlation-purged Granger causality (CPGC), which is capable of reliably inferring causality without interference from correlation, to investigate the effective connectivity of the aforementioned RSNs in a multivariate fashion.

Methods

Resting state EPI data was acquired from 26 healthy subjects using a Siemens Tim Trio scanner. After routine pre-processing, the ROIs corresponding to the 4 RSNs were identified using previously published co-ordinates [1,3]. The mean time series from the ROIs were fed into the CPGC model [4] in order to derive both the instantaneous correlation and effective connectivity in the networks. The instantaneous correlation between the ROIs was displayed on a force-directed layout (FDL) [5] and significant ($p<0.05$) bidirectional and unidirectional causal paths were overlaid on the FDL. The unidirectional paths were obtained by determining whether the difference between the bidirectional paths between a pair of ROIs was significant.

Results and Discussion

Fig.1 shows the bi-directional and unidirectional causal paths overlaid on the FDL. The distance between ROIs on the FDL is proportional to their instantaneous correlation and the green paths denote the most significant correlations ($p<0.001$). It is evident that causal paths existed between ROIs whose signals are not synchronized. This demonstrates the ability of CPGC to infer causality effects which are not influenced by correlation. It can be seen that DAN ROIs are grouped together and away from the rest of the networks; this is expected because the externally directed DAN is anti-correlated with other internally directed RSNs such as DMN and HCMN. DMN ROIs, especially posterior cingulate (PCC) and posterior inferior parietal lobule (pIPL), are not only correlationally equidistant from most other ROIs but also are bidirectionally causally connected to the rest of the networks and hence act as transit hubs. The hippocampus (HF) receives a large number of inputs, possibly reflecting memory encoding. However, there are no unidirectional outputs from HF and therefore, memory retrieval may be routed via PCC. Anterior prefrontal cortex (aPFC), the seed of FPCN, receive inputs from middle temporal area (MT) and insula, likely indicating information about the external environment and homeostatic salience, respectively, being relayed onto aPFC. Since the aPFC is known to be at the apex of the control hierarchy [3], it is likely to integrate the various types of information that it receives. Our results not only emphasize the importance of PCC, pIPL and HF during resting state, but also lend credence to the hypothesis that aPFC-seeded FPCN controls the competing internally- and externally- directed RSNs [3]. Also, the results show that there is extensive causal interaction between RSNs, necessitating a multivariate analysis framework in order to gain complete understanding.

Conclusions

We have investigated the effective connectivity of RSNs without interference from zero-lag correlation. Our results suggest extensive causal interactions between RSNs with the PCC and pIPL acting as major transit hubs. In addition, our results also support the role of FPCN in the control of DMN and DAN.

References

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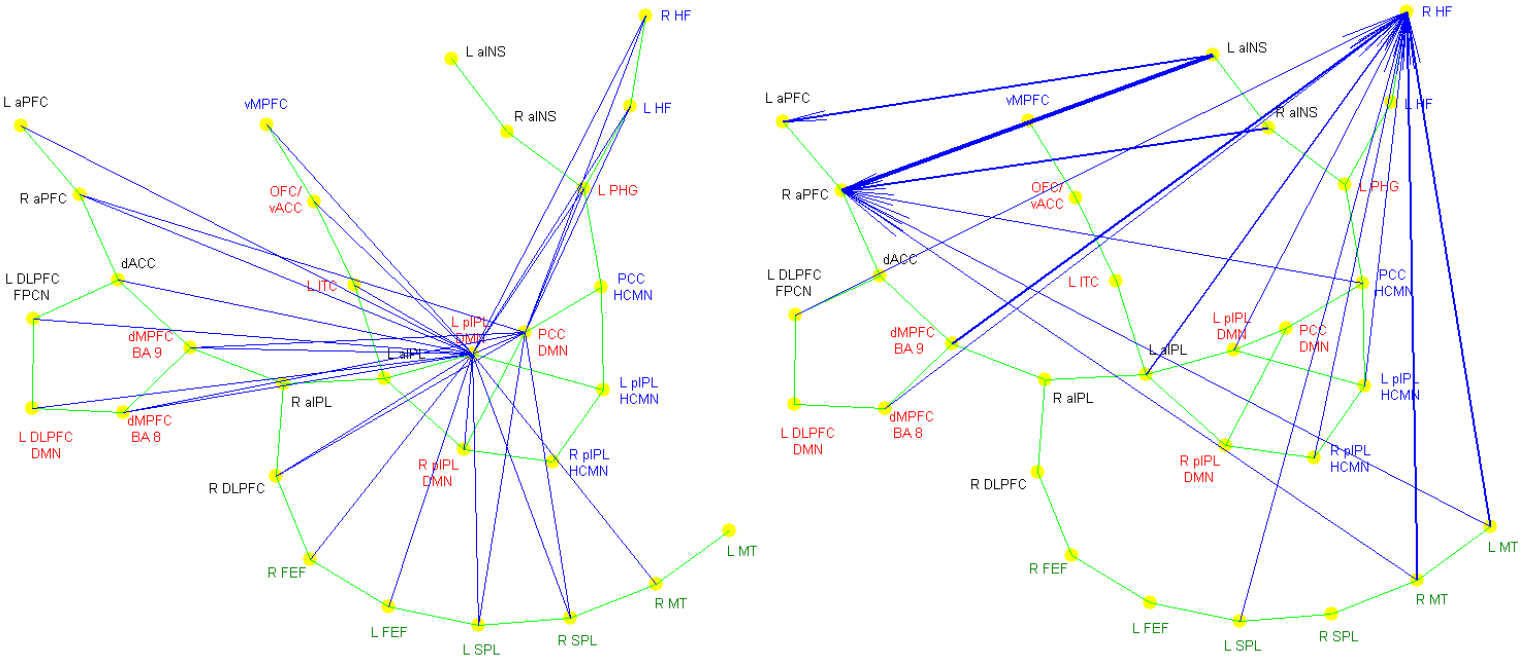

Figure 1 *Significant bidirectional (left panel) and unidirectional (right panel) causal paths (blue lines) overlaid on the force directed layout (FDL). On the FDL, yellow blobs represent ROIs and green paths the significant instantaneous correlation between them. The correspondence between ROI colors and the RSNs is as follows. Red: DMN, Green: DAN, Blue: HCMN and Black: FPCN. ROI abbreviations are as follows- L: left, R: right, BA: Brodmann area, p: posterior, a: anterior, d: dorsal, v: ventral, PCC: posterior cingulate, IPL: inferior parietal lobule, OFC: orbitofrontal cortex, ACC: anterior cingulate cortex, MPFC: medial prefrontal cortex, DLPFC: dorsolateral prefrontal cortex, HF: hippocampal formation, MT: middle temporal area, FEF: frontal eye fields, SPL: superior parietal lobule, PFC: prefrontal cortex, INS: Insula*