

Determination of inversely correlated resting state brain functional networks using cluster analysis

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Introduction

Brain function or activation is not localized to isolated areas of increased metabolism or blood flow but consists of networks of functionally connected regions. Even in a resting state several distinct brain regions have been identified as forming a functionally coherent unit[1]. Functional connectivity is defined here as time-synchronous behavior of the different nodes of the network. Here we sought to develop a technique to automatically detect networks that are functionally connected but are 180 degrees out of phase.

Background

Low frequency BOLD signal fluctuations have previously been observed in fMRI scans of the brain at rest.[2, 3]. One network that expresses these synchronous fluctuations consists of the posterior cingulate cortex (PCC), anterior cingulate cortex (ACC) and the inferior parietal cortex (IPC). Another network is the hand motor cortex as well as Broca and Wernicke's area[4]. Most of the previous investigations have been based on manually a priori selected ROIs and whole brain correlations. Cluster analysis has previously also been applied to resting state function as well as activation studies. Inversely correlated networks are an important aspect in the study functional connectivity. The prefrontal cortex has previously been reported as having a opposite functional time course with the PCC network [1].

Methods

Ten healthy volunteers (6 Males (mean age=27), 4 females (mean age=24)) with no history of major neurologic and psychiatric disease were recruited for the study. All MR scanning was performed on a Siemens Allegra 3T head dedicated scanner. Each volunteer received several anatomical scans including a BOLD sequence at the end and were told to relax with eyes closed. The subjects were naive as to which scan was the resting state fMRI scan. The protocol for the BOLD sequence was as follows: TR=2000, TE=30ms, Matrix Size=64x64, FOV=21cm, slice thickness = 3mm, gap=1mm. 70 time points were obtain. The BOLD scans were preprocessed using Brain Voyager 2000 (Brain Innovation B.V., Maastricht, The Netherlands): motion and slice time correction as well as spatial (6mm) and temporal smoothing (4s). The signal time courses were also converted to Z-scores for subsequent correlation computations. Cluster analysis was performed using in-house developed software in Matlab (The Mathworks Inc., Natick, MA). Cluster analysis was implemented using the K-Means algorithm with distance metric being the correlation between cluster center and time course. We have chosen the standard k-means algorithm over fuzzy cluster or hierarchical clustering algorithm because of its computational simplicity and fast convergence. We have limited the number of clusters to 10 based on the number of brain voxels and estimates from previous hierarchical clustering studies [5]. The software was designed to automatically report the maximally negatively correlated time courses between the 10 cluster centers.

Results

Several of the previously mentioned networks were consistently detected across all subjects. Inversely correlated networks between the PCC/ACC/IPC and the prefrontal cortex were also detected in 4 of the subjects (Figure 1).

Conclusions

Here we have presented a practical method to detect inversely correlated brain functional networks of the brain at rest. Not all subjects showed complementary networks which might be due to the nature of the random mental activity during the 'resting state'. But these complementary networks can be turned on by requiring the subjects to perform certain (such as working memory [1]) cognitive tasks. This measure of complementarity might add a new dimension to the conventional analysis of fMRI data.

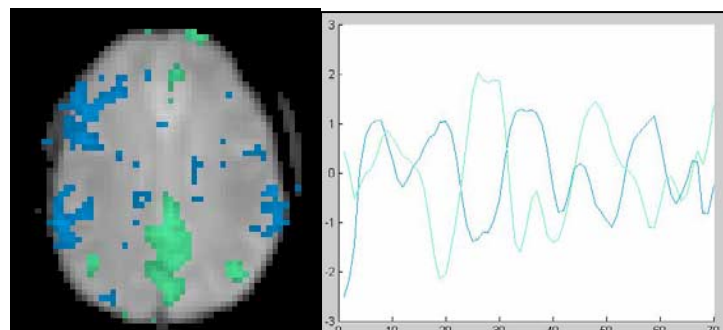


Fig. 1: (left) Shown are two clusters representing the PCC/IPC/ACC network and the prefrontal cortex ($p < 0.0001$); (right) The time course represented by the corresponding cluster centers.

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