A Multivariate Approach Reveals Interactions of Brain Functional Networks During Resting and Goal-Directed Conditions

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Introduction

The brain is intrinsically organized by functional networks. However, most of the brain functional imaging studies thus far have largely focused on the interaction of different brain regions instead of among different brain networks. In this study, a multivariate approach was developed to discern the interaction of five predefined brain functional networks, including the default (D), fronto-parietal control (FPC), motor-sensory (MS), visual (V), and language (L) networks during resting, movie watching and finger tapping, respectively. The ability to elucidate the interaction of different brain networks and assess the dynamic perturbations of their interactions under different cognitive statuses should complement our understanding of brain functional interaction on a regional level and offer a more comprehensive insight into how the brain works at a different scale.

Methods

19 healthy subjects (age 25~33, 7F) were recruited in this study. Informed consent was obtained from all participants. T1 images were acquired with TR=1820ms; TE = 4.38 ms; inversion time = 1100ms; 144 slices; and voxel size = 1x1x1mm3. For the rfcMRI studies, a T2*-weighted sequence was used with TR = 2sec, TE = 32 ms; 33 slices; and voxel size = 4x4x4 mm3. This sequence was repeated 150 times for each experimental condition, including resting, continuous finger tapping and watching a movie clip. After time shifting, rigid body registration, spatial smoothing (6-mm full width at half maximum Gaussian kernel) and low pass filtering (<0.08Hz), the rfcMRI data was normalized to the MNI template using the transformation field acquired from T1 nonlinear registration. Subsequently, whole brain parcellation (90 ROIs) was then achieved usin the prior labeled atlas.

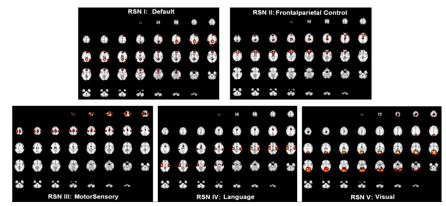

Figure 1. Spatial maps of five defined networks.

Principal component analysis (PCA) was followed by independent component analysis (ICA) to obtain a set of 29 aggregate independent components. The functional network definition is based on the template matching method [1]. Specifically, the templates containing the bilateral pre/post central gyri, bilateral occipital gyri, bilateral superior temporal gyri, bilateral anterior cingulate gyri/anterior prefrontal cortex, and bilateral medial superior frontal/bilateral posterior cingulate were used to find the best matched independent compoents for the MS, V, L, FPC, and D networks, respectively. Spatially unconnected regions (Z>1) within each network were extracted as individual ROIs and the median time course of each ROI was calculated for network analysis.

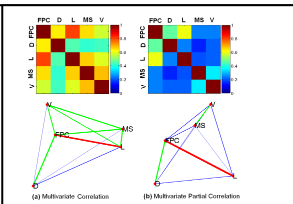

Figure.2 Network interaction patterns during resting state.

To quantify network level interaction, a canonical correlation [2] measure between two multivariate vectors was used. Note this network correlatio (NCC) ranges between 0 and 1 with 0 indicating no dependence and 1 indicating full dependence between these two sets of variables. Partial correlation is a measure of correlation between two random variables, while controlling for a set of other variables, with which one could determine what the correlation would be if the influence from the "mediator" has been removed. For univariate statistics, partial correlation between two random variables ***x*** and ***y*** controlling for another set of independent covariate ***z*** can be computed as the Pearson's correlation between the residuals ε_x and ε_y from two linear regression equations $x = x_0 + \beta_1 Z + \varepsilon_x$ and $y = y_0 + \beta_2 Z + \varepsilon_y$. Since the primary focus of this study is to depict correlation between two sets of variables, the above computational procedures need to be generalized to accommodate the multivariate property of this problem. For two sets of vectors $X = [x_1,..., x_m]^T$, $Y = [y_1,..., y_n]^T$, the previous two equations can be written as $X = X_0 + \mathrm{B}_1 Z + E_x$; $Y = Y_0 + \mathrm{B}_2 Z + E_y$, where E_x and E_y are the residual vectors of X and Y, respectively, after regressing on the variable set of Z. Subsequently, the canonical correlation coefficient of E_x and E_y can be calculated to represent the network partial correlation (NPC) between the two sets of variables (networks) X and Y. After calculating both NCC and NPC, the significance of each network-level interaction was tested using a surrogate data approach [3]. To detect possible perturbations across three different cognitive states, paired t-test was conducted on the Fisher's Z transformed correlation/partial correlation values to find significant interaction changes.

	Movie watching vs resting			Finger tapping vs resting		
	Connections	Changes	p-value (uncorrected)	Connections	Changes	p-value (uncorrected)
NCC	MS-V	Decrease	0.012	MS-V	Decrease	0.039
NPC	MS-V	Decrease	0.016	MS-V	Decrease	0.002
				D-MS	Decrease	0.027
				L-MS	Increase	0.016

Table.1 Observed changes associated with different brain states.

Results

The spatial maps of the five defined networks are presented in Fig.1. For resting condition, the averaged group correlation matrices (upper panel) and the corresponding spring embedding representations (lower panel) are shown in Fig. 2. The colors of the edges indicate statistically different grouping based on Tukey's method (p<0.05). Here, we define the L, MS and V as the outer-directed networks since they mainly interact with the external world. In contrast, we consider the D network as the inner-directed network. With NCC, the FPC-L exhibits the highest connection strength and with the exception of FPC-D, the interactions between the D and the outer-directed networks (D-L, D-MS, and D-V) are ranked the lowest, suggesting a minimum interaction between functionally dissimilar networks. Conversely, the interaction among the outer-directed networks is strong. Furthermore, the relatively strong interaction pattern of FPC-D together with the strong interactions between FPC and the remaining networks seem to suggest the "bridging" role of FPC network. The NPC interaction patterns (Fig. 2b) appear similar to that of NCC: the FPC-L interaction is ranked as the highest (red) and the interaction between the inner- and outer-directed networks remains minimal. However, the interactions of FPC-MS, FPC-V, L-MS, and L-V, which are ranked at the middle (green) using NCC now become the lowest (blue) using NPC suggesting noticeable mediation effects.

For the exploration of possible perturbations during differtn brain states when compared with resting, movie watching led to a significantly reduced MS-V interaction while finger tapping resulted in significantly reduced interaction of MS-V and MS-D and increased interaction of MS-L as shown in Table.1.

Discussion

In this study, using a newly developed multivariate approach, we demonstrate that the five pre-defined functional networks remain highly interacted during the resting condition. Our results also demonstrate that there is a minimum interaction between the inner- and outer-directed brain networks although the FPC appears to serve as the pathway linking the two systems which is independent of the experimental conditions imposed in our studies. In addition, with respect to the resting condition, the interaction patterns are modified in the presence of goal-directed tasks; a more remarkable modification is observed during finger tapping than that during passive movie watching. To the best of our knowledge, the newly developed approach represents the first reported results on a direct assessment of brain network interactions during resting as well as goal-directed tasks.

References

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