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Complex network analysis of brain functional connectivity under a multi-step cognitive task

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HIGHLIGHTS

- We analyze the functional connectivity of behavioral brain activity.
- The brain organization is a generic small-world and scale-free network.
- The functional connectivity differentiates from the order of behaviors performed.
- The functional connectivity is strongly correlated with activated ROIs.

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ABSTRACT

Functional brain network has been widely studied to understand the relationship between brain organization and behavior. In this paper, we aim to explore the functional connectivity of brain network under a *multi-step* cognitive task involving consecutive behaviors, and further understand the effect of behaviors on the brain organization. The functional brain networks are constructed based on a high spatial and temporal resolution fMRI dataset and analyzed via complex network based approach. We find that at voxel level the functional brain network shows robust small-worldness and scale-free characteristics, while its assortativity and rich-club organization are slightly restricted to the order of behaviors performed. More interestingly, the functional connectivity of brain network in activated ROIs strongly correlates with behaviors and is obviously restricted to the order of behaviors performed. These empirical results suggest that the brain organization has the generic properties of small-worldness and scale-free characteristics, and its diverse functional connectivity emerging from activated ROIs is strongly driven by these behavioral activities via the plasticity of brain.

1. Introduction

Human brain, consisting of billions of neurons and synapses, is perhaps the most complex system ever known. Its structural (or anatomic) and functional organization both behave as complicated connectivity in the view of graph and have been widely investigated via complex network theory in the neuroscience community. Plenty of works focus on

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the topological properties of structural and functional brain networks derived from diffusion MRI, functional MRI (fMRI), electroencephalograph (EEG), magnetoencephalography (MEG), and multielectrode array (MEA) data [1–6]. These networks show both the generic small-worldness [7] and scale-free characteristics [8] independent from the physiological and pathological states [9–13]. And, they also suggest high topological efficiency, robustness, modularity and rich club of hubs [14–21].

It is also well known that a human brain is a physically expensive system to built and run, that is, the adaptive responses (e.g., the capacity for information processing) of a brain network are constrained by its wiring costs [14,15,22–25]. In other words, the macro-scale functional response of human brain emerges from the synergistic dynamics of micro-scale coupled neurons. Thus, the links between the brain structure and function can be suggested by the neurons' dynamic activities. For example, Honey et al. firstly used a computational approach to relate the functional response of *resting-state* brain activity to the underlying structural connectivity and find there are structure–function correlations at multiple temporal scales [26]. Furthermore, they demonstrate that although the resting-state functional connectivity frequently exists between spatially distributed regions without direct structural edges, its strength, persistence and spatial statistics are constrained by whole structural organization [27]. Similar result is also found in Refs. [25,28].

We have known that the structural and functional connectivity are characterized by common features, and the functional connectivity is also correlated with the structural one even when the brain activity evolves in the resting state. However, insofar as we know, how the multi-step behavioral activities affect the emergence of functional connectivity and how its functional features involve with the structural organization have not yet been comprehensively studied by using complex network theory. Herein, complex network based approach is applied to analyze the functional connectivity when the brain activates under a multi-step cognitive task. The functional brain networks are constructed at voxel and ROI (i.e., region of interests, functional area of structure organization) levels from the high spatially and temporally resolved fMIR dataset. We find that at voxel level the functional brain network shows a number of the statistic features, such as small-worldness, scale-free characteristics, assortativity and rich-club organization, which are trivially affected by the order of behaviors performed. More interestingly, at ROIs level, some statistic features of functional brain network are obviously restricted to the order of behaviors performed and correlated with these activated ROIs. These empirical results suggest that the brain organization has some generic properties and the diverse function connectivity emerging from activated ROIs is strongly driven by these human behaviors via the plasticity of brain.

2. Materials and method

2.1. Materials

The benchmark StarPlus fMRI dataset is collected by Just and his colleagues in the $*/+/\$$ experiment at the Center for Cognitive Brain Imaging of Carnegie Mellon University [29–31]. In this cognitive experiment, there are two different sessions for each individual subject. The difference of the two sessions is the distinct order of behaviors performed that involve semantical and symbol stimulus. These two sessions are, respectively, divided into four independent blocks, and each one was composed of a number of trials. More specifically, each trial consisted of cognitive and rest segments. In the cognitive segments of the first session, subjects are presented with a sentence (semantic stimulus) on a screen such as "It is true that the star is below the plus" for 4 s; then the sentence is replaced with a black screen for another 4 s; finally subjects are shown with a picture (symbol stimulus) depicting the geometric arrangement of the symbols $*$ and $+$, and the subjects should quickly judge whether the sentence describes the picture correctly or not by pressing a button with the choice "yes" or "no". Once the judgment is made or lasted more than 4 s, the picture would be removed from the screen. Before repeating the next trial, there is a 15-s rest segment. The second session has the similar procedure by simply switching the order of presenting sentence and the picture.

The fMRI images were collected every 0.5 s with the resolution $64 \times 64 \times 8$. Thus, there are around 54 images (27 s) available for each trial. A total of twenty trials are implemented for each subject in each session. We denote the two sessions as P (a picture presented before a sentence) and S (a sentence shown before a picture), respectively. For each session, the block was made up by several (4 or 8) continuous trials and thus contained rest segments between adjacent trials.

Additionally, the cognitive experiments engaged several functional areas of cerebral cortex (i.e., structural organization of brain), such as visual area for the sentence/symbol reading (occipital lobe), spatial visualization (inferior parietal sulcus, e.g. LIPS and RIPS) and recognizing (inferior temporal, e.g. LIT, RIT, LT and RT), Broca area for language processing (left inferior frontal gyrus, e.g. LIFG), Wernicke area for semantic analyzing (middle and superior temporal gyrus, angular gyrus, e.g. LTRIA and RTRIA), motor area for the button pressing (supplementary motor area, e.g., SMA, LDLPFC and RDLPFC), etc. Therefore, the voxels (i.e., 3-dimension pixels) of fMRI images were anatomically allocated into 25 ROIs. Based on that, the functional connectivity of brain network constructed from these fMRI time series can be investigated at both small (voxel) and large (ROI) levels.

2.2. Functional brain network construction

The functional brain networks are extracted from the fMRI time series. At time t, the fMRI images of brain activity are measured by a group of voxels. Thus, the voxel time series $T(t, v)$ characterize the functional changes of cerebra cortex,

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