CORTICAL SURFACE BASED IDENTIFICATION OF BRAIN NETWORKS USING HIGH SPATIAL RESOLUTION RESTING STATE FMRI DATA

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ABSTRACT

Resting state fMRI (rsfMRI) has been demonstrated to be an effective modality by which to explore the functional networks of the human brain, as the low-frequency oscillations in rsfMRI time courses between spatially distant brain regions show the evidence of correlated activity patterns in the brain. This paper proposes a novel surface-based data-driven framework to explore these networks through the use of high resolution rsfMRI data. Guided by DTI defined fiber pathways and constrained by the gray matter, we map the rsfMRI BOLD signals onto the cortical surface generated by DTI-based tissue segmentation. We then use a data-driven affinity propagation clustering algorithm to identify these functional networks. Our experimental results demonstrate that the framework has high reproducibility and that several networks are detected reliably among individual subjects. Furthermore, our results exhibit that functional networks are highly correlated with structural connections. Finally, our framework is able to reveal visual sub-networks, indicating its potential role in sub-network exploration.

1. INTRODUCTION

The human cerebral cortex has distinct functional regions, which is usually known as functional segregation or specialization [1]. However, even simple cognitive function in the cerebral cortex involves a network of multiple distinct functional regions. Therefore, the identification of functional networks has been in active research. Recent functional MRI studies demonstrated that rsfMRI can be an effective approach to explore the functional networks of the cortex [2]. Partly due to the ease of data acquisition, rsfMRI is gaining wide popularity in the exploration of functional networks of the cerebral cortex.

Current studies on rsfMRI include model driven and data driven methods, many of which are volume-based methods. Although fruitful results have been generated, some limits still persist. For example, model driven methods often require a pre-defined seed region. The reconstructed functional network might heavily depend on the sizes and localizations of the seed regions. Volume-based data driven methods, such as independent component analysis (ICA) [3], treat the whole brain as a 3D image, usually neglecting the anatomical and biological differences between brain tissues.

In this paper, we propose a novel surface-based data-driven framework to explore the functional networks of whole brain using high resolution rsfMRI data. The core of this framework is to represent the cerebral cortex by the interface surface between white matter (WM) and gray matter (GM), and represent the GM BOLD rsfMRI signals on the cortical surface. To do so, we co-register the rsfMRI data and the DTI data, and map the original BOLD signals to the cortical surface generated by the WM segmentation from DTI data [5]. The mapping is guided by fiber tractography and constrained within the GM. Geodesic smoothing of signals on the cortical surface is performed to enhance the signal-to-noise ratio (SNR). After mapping the BOLD signals onto the cortical surface, we use a data-driven clustering algorithm to explore the functional networks of the cortex. In essence, this framework converts the 3D volumetric functional network exploration problem to a 2D cortical surface problem.

Three major advantages of the surface-based brain network identification are: 1) since the main generators of electrical brain activity captured by fMRI signal are known to be the pyramidal neurons of layer IV [4], the cortical surface-based mapping of rsfMRI BOLD signals should be a faithful representation of functional activity in the brain; 2) the complex and variable geometry of the cerebral cortex is well represented by the cortical surface. This facilitates the geodesical grouping of vertices into brain regions and networks, which is more biologically meaningful than that based on Euclidean distance; 3) by mapping the 3D volume onto the 2D surface, the network identification is better able to identify the meaningful voxels and the computational time is significantly reduced.

2. MATERIALS AND METHODS

2.1. Overview

To explore the functional networks, we used multi-modality datasets which included DTI and rsfMRI. As shown by the flow chart in Fig.1, we firstly used DTI data to generate the gray matter (GM) segmentation, the white matter and gray

matter cortical surface, and fiber tracts. We then registered the rsfMRI BOLD signals to DTI space, and, using the tracts as a guide, mapped the signals onto the cortical surface. It should be noted that this is the step which converts the 3D volume problem to a 2D surface problem, while also helping to better represent the BOLD signals on the surface through anatomical guidance. Finally, we used the affinity propagation clustering algorithm [7] to perform data-driven exploration of functional networks on the cortical surface.

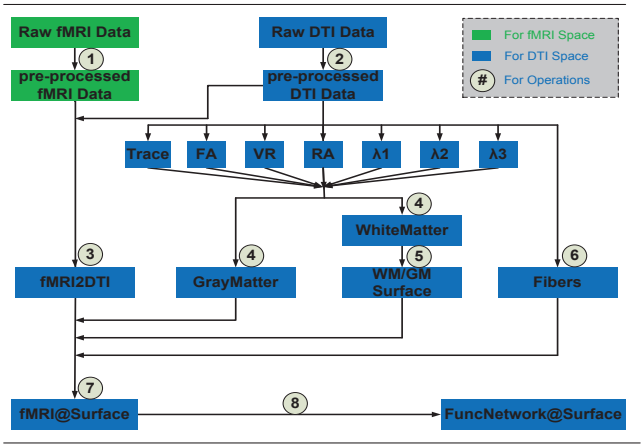

Fig.1. The flowchart of the framework. The steps are as follows: (1) and (2) are pre-processings (see 2.2 for details); (3) registration rsfMRI to DTI space; (4) segmentation of brain tissue using DTI data; (5) WM/GM cortical surface reconstruction; (6) fiber tratography; (7) fiber-guided mapping of BOLDs onto cortical surface; (8) affinity propagation clustering.

2.2. Materials, pre-processing, and generation of intermediate results

Nine volunteers were scanned in a 3T GE MRI system. Resting state fMRI data were acquired with dimensionality 128*128*60*100, space resolution 2mm*2mm*2mm, TR 5s, TE 25ms, and flip angle 90 degrees. DTI data were acquired using the same spatial resolution as the fMRI data; parameters were TR 15.5s and TE 89.5ms, with 30 DWI gradient directions and 3 B0 volumes acquired.

Pre-processings of the rsfMRI data included brain skull removal, motion correction, spatial smoothing, temporal prewhitening, slice time correction, global drift removal, and band pass filtering(0.01Hz~0.1Hz). For the DTI data, pre-processings included brain skull removal, motion correction, and eddy current correction.

After the pre-processing, fibers tracts, GM and WM segmentations, and GM/WM cortical surface were generated based on the DTI data. Fiber tracking was performed using MEDINRIA (FA threshold: 0.2; minimum fiber length: 20; sampled by 4). Brain tissue segmentation was conducted on DTI data by the method in [5]. Based on the WM, the cortical surface was reconstructed using the in-house software [6]. The surface has about 40,000 vertices.

2.3. Using DTI space as the standard space

Even though echo planar imaging (EPI) confers many advantages, the distortion inherent to it has always been a source of concern. There is currently no perfect solution to the problem. According to our experiment, distortion was still severe even whilst applying a distortion correction algorithm. For high-resolution fMRI data and DTI data, the distortion can lead to misalignment of GM and WM between fMRI/DTI and T1 data. Thus, registration of GM from T1 to fMRI may exhibit poor or incorrect correspondence (Fig.2).

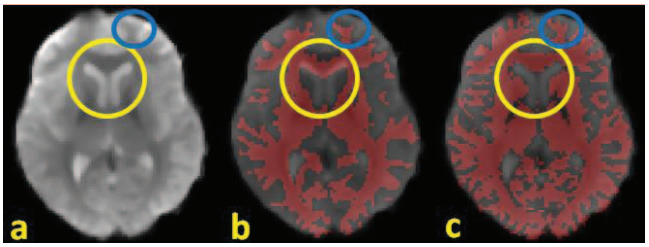

Fig.2. Comparison of misalignments between different modalities. (a): fMRI data; (b): overlapped by WM from T1 segmentation; (c): overlapped by WM from DTI segmentation; the yellow circle and blue circle highlight the severer misalignment of T1 segmentation to fMRI than that of DTI segmentation.

To tackle the distortion problem, we adopted the DTI space as the standard space from which to generate GM segmentation and to report the brain network results on the cortical surface. Since fMRI and DTI sequences are both EPI sequences, misalignments between them are greatly reduced. As can be seen in Fig.2, the misalignment between DTI space and fMRI space is much less than that between T1 space and fMRI space.

2.4. Mapping BOLD signals onto the surface

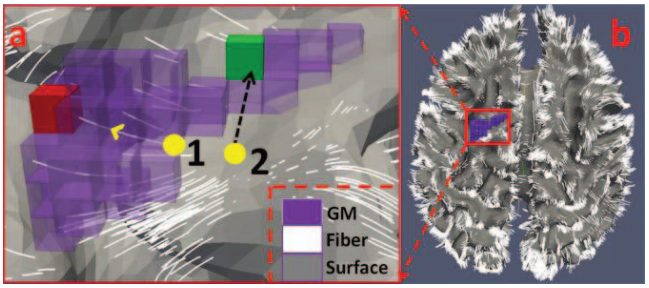

Fig.3. Illustration of BOLD signal mapping for cortical vertices that are *not* in the GM (two yellow bubbles). In (a), Vertex 1 uses fiber guidance to find the GM (highlighted in red) target; Vertex 2 uses normal direction to find the GM target (highlighted in green).

Correctly mapping BOLD signals onto the surface is critical for this framework, as the vertices on the reconstructed cortical surface are not necessarily located in the GM [5, 6]. To ensure a good mapping, we introduce anatomical constraints to the process in two ways: 1) vertices on the surface will represent the BOLD signals from GM. For a vertex that has fibers passing through its neighborhood, the signal that it represents is that of the GM where these fibers end. Since fiber tractography has difficulty in tracking inside GM, there are some fibers that cannot end in the GM. For

these cases, we prolong the fibers along their orientations to the GM; for a vertex that has no fibers around, we use its normal direction to find the GM correspondence. 2) The BOLD signals are geodetically smoothed (Gaussian kernel; sigma: 4mm) around the cortical surface to enhance SNR. This step uses a geodesic neighborhood rather than a Euclidian one, which should make smoothing in a more reasonable way. Fig.3. shows the fiber guidance in signal mapping.

2.5. Data-driven clustering for network identification

After mapping of the BOLD signals onto the surface, each vertex of the surface has a corresponding time course. We perform a vertex-wise clustering analysis using Affinity Propagation clustering [7] to identify the functional networks. This analysis will group similar vertices into networks by maximizing within-network similarity and minimizing across-network similarity. The similarity definition we adopt is the classic Pearson Correlation. Similarities lower than 0.2 are discarded to speed up the clustering process.

The preference, p, for each data point is the initial probability of being a cluster center; it has a significant influence on the number of cluster centers. Generally, the larger the preference, the more clusters we have. In this study the preferences for all data points were set to be equal.

3. EXPERIMENTAL RESULTS

3.1. Functional networks explored

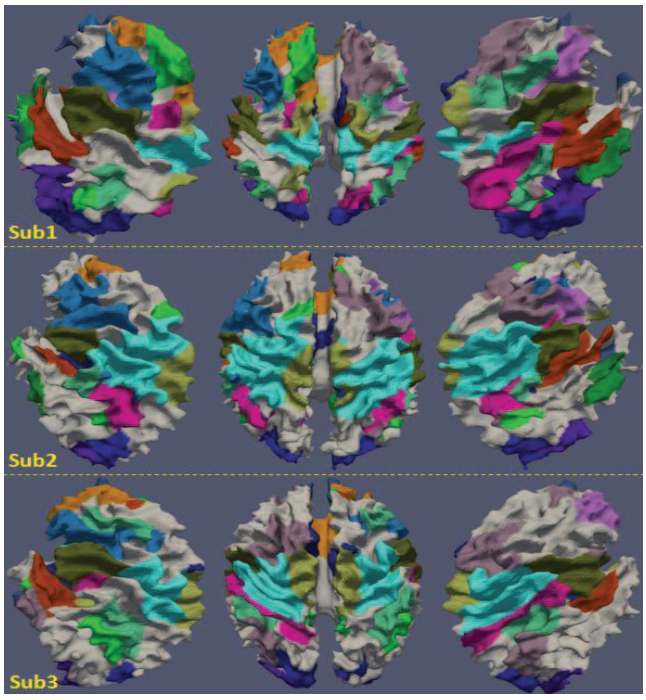

Fig.4. Three examples of consistent functional networks. Each color represents the same network; each row shows a result from a subject; within the row, three views of the networks are presented (left hemisphere, dorsal view, and right hemisphere).

We applied the proposed framework to the datasets described in the section 2.2. By assigning same preference parameter (we use -30 empirically), the whole cerebral cortex can be clustered into 30~40 functional networks. These networks include commonly reported works, such as the default mode network, visual network, motor network, attention network, and memory network [8]. The following figure shows examples of the functional networks from three subjects.

3.2. Sensitivity to clustering parameters

A concern with data-driven exploration of functional networks is determining whether the number of generated clusters represent biologically meaningful functional networks. To test the reproducibility and stability of the method, we changed the parameter p in the Affinity Propagation clustering algorithm, and generated different numbers of functional networks under different clustering environments. Fig.5 shows the comparison of some common functional networks using different clustering parameters. The top row is generated using a small preference (p =-30, which generates 30~40 clusters), whereas the bottom row is generated by s larger preference (p =-15, which generates 70~80clusters).

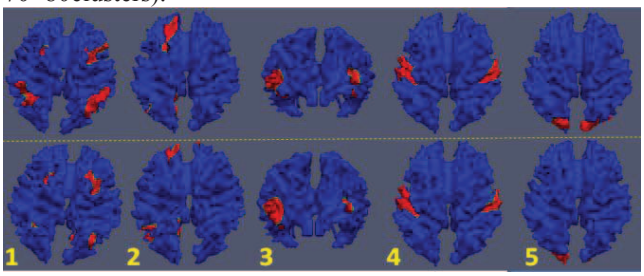

Fig. 5. 1) dorsal attention network; 2) default mode network; (3) language comprehension network; 4) motor network; (5) visual network;

As we can see from Fig.5, despite some changes in size, these functional networks retained similar spatial patterns. This means the proposed framework can generate robust and consistent functional networks under different clustering environments.

3.3. Reproducibility and Consistency study

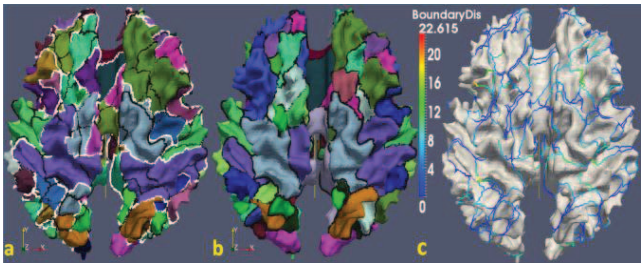

Fig. 6. a) functional networks from the 1st run. White lines are boundaries among the networks, and black ones are those from the

2nd run; b) functional networks from the 2nd run; c) the distance between two boundaries (4.3±3.5mm). The color bar is on the left.

In this section, we did a reproducibility study of the proposed framework using two runs of rsfMRI datasets from the same subject. The parameters for the two runs are identical. As shown in Fig.6, the two runs generate roughly similar functional networks. However, there is also considerable difference in some boundaries, indicating that the functional networks dynamically change over time.

3.4. Correlation between structural connectivity

The relationship between functional and structural connectivity is an open question. To study their relationship, we used the detected functional networks as regions of interest (ROIs), and count the fibers connecting the functional networks. The connection matrix was normalized so that each element (x, y) reflects the ratio between the fibers passing through both ROIs (ROI x and ROI y), and all fibers passing through only ROI y.

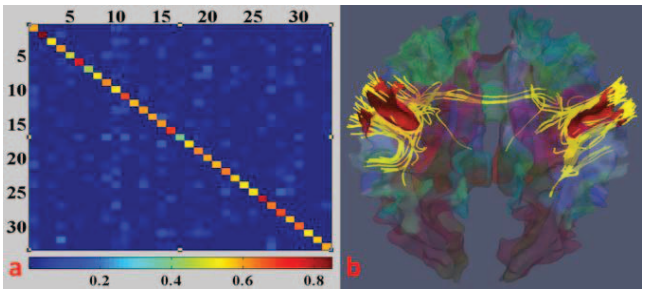

Fig.7. a) structural connection matrix of networks from a subject; bottom: color bar, red means high self-structural connection. b) the fibers connecting the motor network of the subject.

As we can see from the Fig.7a, in general, the diagonal elements have the highest intensities among each row/column. This means most of the functional networks have very strong structural connections within themselves. In Fig. 7b, we show an example of one functional network (motor network) and the fibers connecting this network. As we can see, the functional network has strong structural connections. This observation may indicate consistency between functional and structural connectivity of the cerebral cortex.

It should be noted that some off-diagonal elements in the connection matrix also have strong intensities. This indicates that functionally different brain networks can be connected by strong structures.

3.5. Sub-network exploration

Currently, there have been few reports on whole brain functional networks using high resolution resting state fMRI datasets. Limited by the spatial resolution of rsfMRI data, the exploration of sub-networks might be difficult.

In this study, with the high resolution rsfMRI dataset, our framework was able to explore the sub-networks of a cognitive network. Fig.8 shows the sub-networks of the visual network. As we can see, the primary visual cortices (V1) of the left and right hemisphere are clustered as one network, the superior prestriate cortexes (V2) as another network, and the inferior V2 as yet another network. This result demonstrates the potential ability of the proposed framework in exploring cognitive sub-networks of the human cerebral cortex.

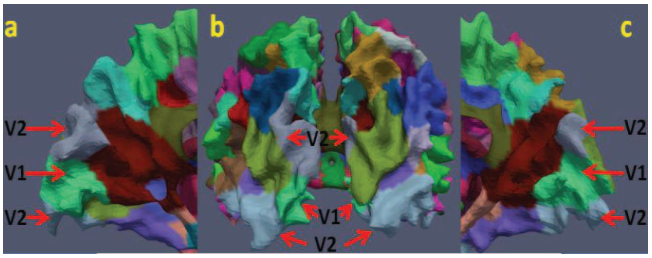

Fig.8. a) medial view of the left visual network; b) posterior view of the visual network; c) medial view of right visual network.

4. DISCUSSION AND CONCLUSION

In this paper, we proposed a novel surface-based data-driven framework to explore functional networks using high resolution rsfMRI data. This framework uses anatomical constraints to map the BOLD signals from rsfMRI data to the cortical surface, reconstructed from DTI data, and adapts the data-driven clustering method to explore the functional networks. In essence, it transfers the study of functional connectivity from an image volume to a cortical surface.

The experimental results show that the framework is able to detect known human functional networks reliably. The results also demonstrate the potential to detect sub-networks within these networks. Considering the extreme variability among individuals, development of algorithms for individualized localization and recognition of those functionally parcellated regions is important for our future work.

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