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EXPLORING INTRINSIC NETWORKS AND THEIR INTERACTIONS USING GROUP WISE TEMPORAL SPARSE CODING

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ABSTRACT

Recent resting state fMRI (rsfMRI) studies have shown that analysis of spontaneous activities may reveal intrinsic functional organization of the human brain. Increasing evidence has demonstrated that the human brain is organized as networks which dynamically interact with each other to realize brain functions. However, it is still challenging to model intrinsic networks and their dynamic interactions simultaneously. In this paper, we propose a novel group-wise temporal sparse coding (GTSC) method on rsfMRI data to address the challenge. Specifically, brain volume at each time point of rsfMRI is rearranged into a sample vector. After pooling all these sample vectors from multiple time points and multiple subjects as a training set, the dictionary learning and sparse coding method is employed to learn a set of spatial networks. Coded in the associated coefficient matrix, these networks are sparsely integrated at each time point while dynamically interacting along the time line. Experiment results have shown that our method is capable of detecting well-recognized intrinsic brain networks, and revealing their dynamic interactions simultaneously.

Index Terms— rsfMRI, group-wise, temporal sparse coding, intrinsic networks, dynamic interactions

1. INTRODUCTION

Recently resting state fMRI (rsfMRI) has been increasingly used in analyzing spontaneous activity in the human brain [1]. The basic premise is that brain function is organized into intrinsic networks, and these networks dynamically cooperate and interact with each other to realize complex brain functions [1, 2]. Many data-driven methods have been proposed to explore the network architecture of spontaneous functional brain activities, such as ICA and clustering based method [3]. However, it is still challenging to analyze brain networks and their network-level interactions simultaneously. Recent research has shown that the brain function involves multiple complex processes with population codes of neuronal activities [4] and it has been reported that when determining neural activity, sparse population coding is more effective than independent exploration [5]. Thus, dictionary learning and sparse coding has been recently explored for brain network analysis [6-9]. However, previous research has merely explored how the networks are organized along the time line, but how these networks interact with each other dynamically has been underexplored. Therefore, new methods are widely called for to simultaneously model brain networks organization and their dynamic interactions.

In this paper, we propose a novel group-wise temporal sparse coding (GTSC) method to learn intrinsic networks from rsfMRI data. Specifically, the brain volume at each time point of fMRI data is treated as a learning sample. The voxels located inside a brain mask are re-arranged into a vector. Pooling vectors from all time points will then construct a training set for dictionary learning and sparse coding [10]. Note that in comparison with the voxel number in a brain volume, the time point number is not sufficiently large for dictionary learning. Therefore, we propose to enlarge the training set by including multiple subjects, i.e., learning dictionary in a group-wise way. Here, voxel correspondence is roughly established by linear image registration and common brain masking. Eventually, a dictionary of spatial network maps will be learned from multi-subjects and the associated sparse coefficient matrices linearly and sparsely combine these networks to realize dynamic brain state at each time point. By analyzing the coefficient matrices along the time dimension, networks are also found to dynamically interact with each other.

2. MATERIALS AND METHODS

2.1 Overview

The framework of our proposed GSTC method is illustrated in Fig.1. First, brain volumes of rsfMRI of a group of subjects are linearly registered into the MNI space and they are unified by a common mask (Fig.1a). Then, all volumes from a group of subjects are pooled together as a training set (Fig.1b). Using the group-wise temporal sparse coding method, the training set is decomposed into a dictionary matrix (D) and a coefficient matrix (A). Thus, we can get several RSNs (resting state networks) from D matrix, meanwhile, the A matrix stores the temporal coding information of the corresponding networks (Fig.1c). It turns out that our group-wise analysis not only detected well-recognized intrinsic brain networks [11], but also revealed dynamic interactions of RSNs at the same time.

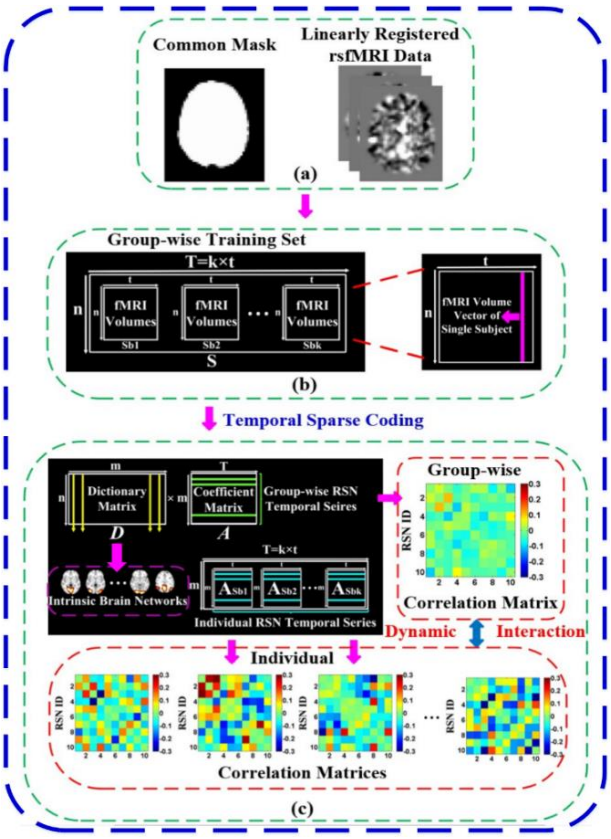

Fig.1. The flowchart of the GTSC method. Fig.1a: Linearly registered brain volumes of rsfMRI data and a common mask used to guide the group-wise voxel extraction. Fig.1b: Each brain volume is reorganized into a column vector and then brain volumes of all subjects are pooled together along the time dimension to get a group-wise training set which is then used for dictionary learning. Fig.1c: The group-wise training set can be decomposed into a dictionary matrix (*D*) and a coefficient matrix (*A*) via temporal sparse coding method. In the *D* matrix, each column could be mapped back to the brain volume that exhibits a certain spatial pattern, which we call a resting state network (RSN). Meanwhile, the *A* matrix stores the temporal coding information of the networks. Here, group-wise RSNs' temporal coefficients are represented by light green row vector in *A*, while individual RSNs' temporal coefficients are represented by light blue row vector in A_{Sb_i} (top-left panel in Fig.1c). Both group-wise and individual dynamic interaction of RSNs can then be derived by analyzing the group-wise coefficient matrix *A* and individual coefficient matrix A_{Sb_i} respectively along the time dimension. Here, dynamic interaction is reflected from correlation matrix calculated by the Pearson's correlation of the RSNs' temporal coefficients (top-right and bottom panel in Fig.1c).

2.2 Data Acquisition and Preprocessing

A group of 20 healthy subjects are randomly selected from the publicly available dataset of the 1000 functional connectome project acquired in the NYU Child Center (http://fcon_1000.projects.nitrc.org/indi/adhd200/). The parameters for fMRI acquisition are as follows: 47 axial slices, matrix size 49×58, 4mm slice thickness, 0mm spacing, 240mm FOV, TR=2s, TE=15ms, flip angle=90, voxel size 3×3×4mm. The preprocessing of fMRI data includes skull removal, motion correction, slice timing correction, temporal pre-whitening, global drift removal and spatial normalization. Then the preprocessed resting state fMRI data are registered into MNI space with nuisance variance removed and spatial smoothing blurred with a 6-mm FWHM Gaussian filter. In addition, we generate a common mask from intersection of brain regions of all subjects. In this way, the same number of voxels is established with correspondence across subjects (Fig.1a).

2.3 Dictionary Learning Theory

Online learning and sparse coding method [10] has been recently applied on fMRI analysis. These approaches learn the signal composition of fMRI, and a representative dictionary of signal basis is learned to represent major network responses in the brain [6-9]. However, it has been rarely explored whether brain networks could be modeled in the spatial domain and how spatial networks dynamically interact. In our approach here, we aim to learn a common dictionary of spatial networks and the associated sparse coefficient matrices from the training set of fMRI volumes of all the subjects. Each brain network mapped from the column of the common dictionary is composed of spatially concurrent regions which can be learned as a dictionary atom, meanwhile, the dynamic interaction of these brain networks can be assessed by the sparse coefficient matrices.

In this paper, we reshape each volume in the fMRI scan into a high dimensional intensity vector as a training sample $\boldsymbol{s}_i$. By pooling the samples from all time points of all subjects, we built the training set $\boldsymbol{S} = [\boldsymbol{s}_1, \boldsymbol{s}_2, \cdots \boldsymbol{s}_T] \in \mathbb{R}^{n \times T}$ (Fig.1b), where n is the voxel number inside the common brain mask. Specifically, sparse representation via temporal sparse coding can be formulated as:

$$\boldsymbol{s} = \boldsymbol{D}\boldsymbol{\alpha}_i = \alpha_i^1 \boldsymbol{d}_1 + \alpha_i^2 \boldsymbol{d}_2 + \cdots + \alpha_i^m \boldsymbol{d}_m \quad (1)$$

where $\boldsymbol{D} = [\boldsymbol{d}_1, \boldsymbol{d}_1, \cdots, \boldsymbol{d}_m]$ is a spatial map dictionary, the column of which can be mapped into brain volumes corresponding to brain networks (Fig.1c left-top panel). $\boldsymbol{\alpha}_i = [\alpha_i^1, \alpha_i^2, \cdots, \alpha_i^m,]^T$ is a sparse coefficient vector, which linearly and sparsely combines dictionary atoms together to reconstruct each sample volume $\boldsymbol{s}_i$. The effective online dictionary learning algorithm [10] is employed in our approach. The empirical cost function is summarized in Eq. (2) by considering the average loss of representation of the training sample.

$$f_T(\boldsymbol{D}) \triangleq \frac{1}{T}\sum_{i=1}^{T} \ell(s_i, \boldsymbol{D}) \quad (2)$$

where $\ell(s_i, \boldsymbol{D})$ is defined in Eq.(3) and λ is a regularization parameter to trade off the regression residual and sparsity level.

$$\ell(\boldsymbol{s}_i, \boldsymbol{D}) \triangleq \min_{\boldsymbol{\alpha}_i \in \mathbb{R}^m} \frac{1}{2}\|x - \boldsymbol{D}\boldsymbol{\alpha}_i\|_2^2 + \lambda\|\boldsymbol{\alpha}_i\|_1 \quad (3)$$

To prevent $\boldsymbol{D}$ from being arbitrarily large, the columns $\boldsymbol{d}_1, \boldsymbol{d}_1, \cdots, \boldsymbol{d}_m$ are constrained with Eq. (4).

$$C \triangleq \{\boldsymbol{D} \in \mathbb{R}^{n \times m} s.t. \forall j = 1, \cdots, m, d_j^T d_j \leq 1\} \quad (4)$$

Finally, the whole problem can be rewritten as a matrix factorization problem in Eq. (5), here, $\boldsymbol{A} = [\boldsymbol{\alpha}_1, \boldsymbol{\alpha}_2, \cdots \boldsymbol{\alpha}_T]$.

$$\min_{\boldsymbol{D}\in C,\boldsymbol{A}\in\mathbb{R}^{m\times T}} \frac{1}{2}\|\boldsymbol{S}-\boldsymbol{D}\boldsymbol{A}\|_F^2 + \lambda\|\boldsymbol{A}\|_{1,1} \quad (5)$$

Here, the dictionary and the coefficient matrix are learned with the online dictionary algorithm in SPAMS package [10].

In our temporal sparse coding scheme, the dictionary size K and λ are empirically and experimentally set to be 400 and 0.15 [6-9]. In addition, we have added non-negative constraints on the elements of the dictionary.

3. RESULTS

3.1 Detection of Intrinsic Brain Networks

In this section, we demonstrate detected intrinsic brain networks RSN1-RSN10 mentioned in section 2.4.

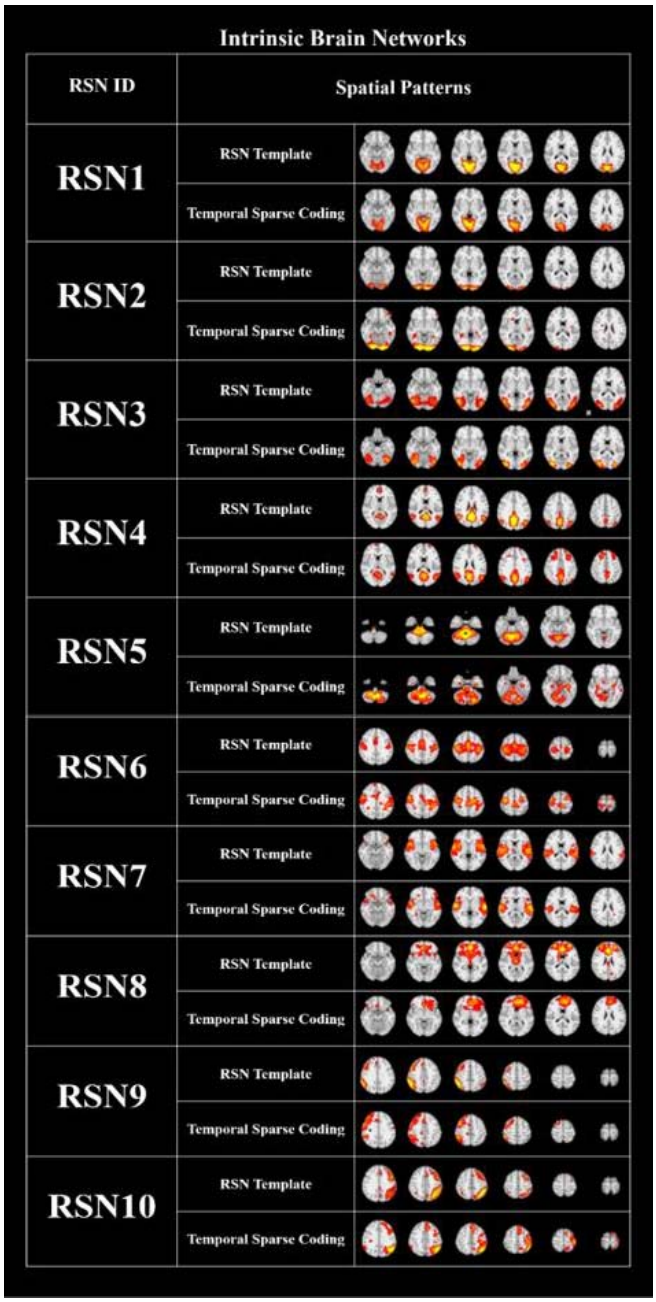

Fig.4. Meaningful intrinsic brain networks consistent with the RSN templates. The index is from #1-#10.

Our group-wise temporal sparse coding scheme discover a common set of intrinsic brain networks across a group of individuals under the resting state. All the RSNs can be visualized in Fig.4 with a corresponding template guidance above. Among these brain networks, RSN1, 2 and 3 correspond to ventral, dorsal and lateral visual areas respectively. Specifically, RSN1 is the primary visual cortex, RSN2 is associated with higher order processing, and RSN3 is related to visual motion. RSN4 is default mode work which is the most widely studied RSN in the resting statefMRI. RSN5 covers the area of cerebellum. RSN6 corresponds to sensorimotor area about touch and movement. RSN7 is auditory area. RSN8 covers several medial-frontal areas corresponding to executive control area. RSN9 and 10 correspond to left and right lateralized networks consisting of superior parietal and superior frontal regions [11].

Moreover, the overlap rate of the detected brain networks of 10 RSNs compared with that of the template is shown in Table 1. Here, the overlap rate is computed by calculating the proportion of shared voxels in both our detected network and its corresponding template. It can be seen that the constructed brain networks by our method are quite similar to the templates.

Table1: The overlap rate of the brain networks of 10 RSNs detected by GTSC method compared with that of the template.

RSN ID	Overlap Rate	RSN ID	Overlap Rate
RSN1	52.43%	RSN6	48.75%
RSN2	34.43%	RSN7	48.13%
RSN3	49.04%	RSN8	49.07%
RSN4	54.27%	RSN9	59.07%
RSN5	44.44%	RSN10	57.77%

3.2 Dynamic Interactions of RSNs

In our temporal sparse coding scheme, intrinsic brain networks are mapped from the columns of the common dictionary $\boldsymbol{D}$ and their temporal series can be achieved from the corresponding rows of the coefficient matrices $\boldsymbol{A}$. Group-wise coefficient matrix can be separated to obtain individual coefficient matrix of each subjects. By calculating the Pearson's correlations of the temporal seires of the 10 RSNs, we obtained a group-wise correlation matrix and presented individual representative correlation matrices of 4 subjects at the same time, the dynamic interactions of which are highly consistent with the group-wise result as shown in Fig.5.

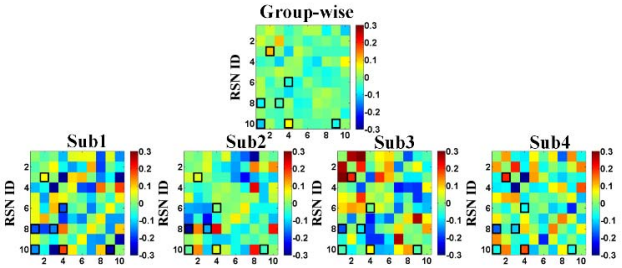

Fig.5 Group-wise and individual correlation matrices.

Fig.5 shows the correlation matrices that reflect the correlation of the temporal series of 10 RSNs. Moreover, we find out 7 prominent RSN pairs among which the positive and negative characteristic of the correlation coefficient keep consistent in at least 16 subjects. Especially, in RSN pair 2-3, the positive characteristic of the correlation coefficient can be detected in 19 subjects. All of the 7 RSN pairs are highlighted by black rectangular boxes. In addition, we select 4 representative RSN pairs of one subject to show more intuitive situation of their dynamic interactions, among which, temporal series of RSN pair 2-3 and RSN pair 4-10 presents a positive correlation relationship whereas the time series of RSN pair 4-6 and RSN pair 9-10 presents a negative correlation relationship. The dynamic interactions of 4 RSN pairs are shown in Fig.6. We can see that, the two visual areas RSN2 and RSN3 mostly exist at the same time period, the condition of which is also the same with the default mode network (RSN4) and right lateralized network (RSN10). In contrast, the existence of default mode network (RSN4) and sensorimotor area (RSN6) are opponent, if one exists, the other mostly not, so is the situation with left (RSN9) and right lateralized network (RSN10).

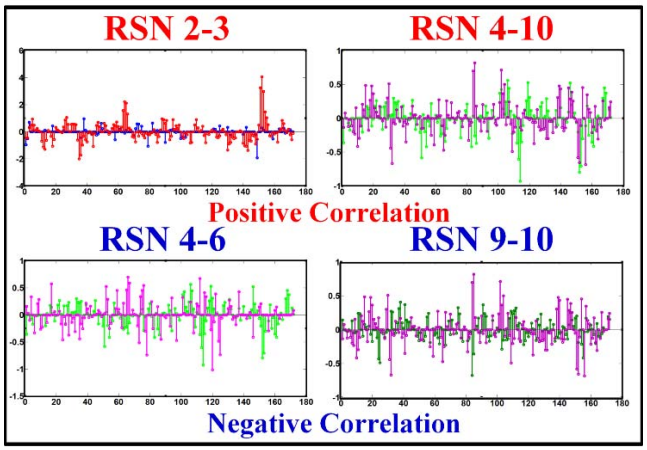

Fig.6 Dynamic interactions of 4 representative RSN pairs, RSN2: blue, RSN3: red, RSN4: magenta, RSN6: light green, RSN9: dark green, RSN10: purple.

4. CONCLUSIONS

In this paper, we present a novel data driven strategy based on group-wise temporal sparse coding (GTSC) scheme to model intrinsic brain networks as well as their dynamic interactions based on rsfMRI data. It turns out that there exists a stable and reproducible dynamical state that characterizes the coherent intrinsic brain networks in multi-subjects. Our proposed approach can serve as a potentially useful tool in analyzing rsfMRI data at network level and study their corresponding temporal characteristics at the same time. Therefore, clinical application of our method based on rsfMRI data to derive more biomarkers of diseases is also desired in the future.

5. ACKNOWLEDGEMENTS

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6. REFERENCES

[1] M. D. Fox, *et al.*, "Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging," *Nature Reviews Neuroscience*, vol. 8, pp. 700-711, September 2007.

[2] M. D. Fox, *et al.*, "The human brain is intrinsically organized into dynamic, anticorrelated functional networks," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 102, pp. 9673-9678, May 2005.

[3] M. P. van den Heuvel, *et al.*, "Exploring the brain network: a review on resting-state fMRI functional connectivity," *Eur Neuropsychopharmacol*, vol. 20, pp. 519-34, Aug 2010.

[4] R. Q. Quiroga, *et al.* "Sparse but not 'grandmother-cell' coding in the medial temporal lobe," *Trends in cognitive sciences*, vol. 12, pp. 87-91, March 2008.

[5] I. Daubechies, *et al.*, "Independent component analysis for brain fMRI does not select for independence," *Proceedings of the National Academy of Sciences,* vol. 106, pp. 10415-10422, April 2009.

[6] J. Lv, X. Jiang *et al.*, "Identifying functional networks via sparse coding of whole brain fMRI signals," in *2013 6th IEEE International Conference on Neural Engineering NER 2013,* San Diego, CA, United States, pp. 778-78, 2013.

[7] Li, *et al.*, "Sparse representation of whole-brain fMRI signals identification of functional networks," *Medical Image Analysis,* vol. 20(1), pp. 112-134, February 2015.

[8] J. Lv, X. Jiang, X. Li, *et al.*, "Holistic atlases of functional networks and interactions reveal reciprocal organizational architecture of cortical function," in press, *IEEE Transactions on Biomedical Engineering*, vol. 62(4), pp. 1120-1131, November 2014.

[9] S. Zhao, J. Han, X. Hu X, et al., "Extendable supervised dictionary learning for exploring diverse and concurrent brain activities in task-based fMRI, " *Brain Imaging & Behavior*, vol. 1, pp. 1-15, June 2017.

[10] J. Mairal, F. Bach, J. Ponce, and G. Sapiro, "Online learning for matrix factorization and sparse coding," *The Journal of Machine Learning Research,* vol. 11, pp. 19-60, January 2010.

[11] S. M. Smith, *et al.*, "Correspondence of the brain's functional architecture during activation and rest," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 106, pp. 13040-5, August 2009.