Published in final edited form as:

Brain Imaging Behav. 2018 June ; 12(3): 758–770. doi:10.1007/s11682-017-9737-4.

Functional Brain Networks Reconstruction Using Group Sparsity-Regularized Learning

Qinghua Zhao^{1,3}, Will X. Y. Li¹, Xi Jiang³, Jinglei Lv^{2,3}, Jianfeng Lu^{1,*}, and Tianming Liu^{3,*,#}

¹School of Computer Science and Engineering, Nanjing University of Science and Technology, Nanjing, China

²Automation Department, Northwestern Polytechnic University, Xian, China

³Cortical Architecture Imaging and Discovery Lab, Department of Computer Science and Bioimaging Research Center, The University of Georgia, Athens, GA, USA

Abstract

Investigating functional brain networks and patterns using sparse representation of fMRI data has received significant interests in the neuroimaging community. It has been reported that sparse representation is effective in reconstructing concurrent and interactive functional brain networks. To date, most of data-driven network reconstruction approaches rarely take consideration of anatomical structures, which are the substrate of brain function. Furthermore, it has been rarely explored whether structured sparse representation with anatomical guidance could facilitate functional networks reconstruction. To address this problem, in this paper, we propose to reconstruct brain networks utilizing the structure guided group sparse regression (S2GSR) in which 116 anatomical regions from the AAL template, as prior knowledge, are employed to guide the network reconstruction when performing sparse representation of whole-brain fMRI data. Specifically, we extract fMRI signals from standard space aligned with the AAL template. Then by learning a global over-complete dictionary, with the learned dictionary as a set of features (regressors), the group structured regression employs anatomical structures as group information to regress whole brain signals. Finally, the decomposition coefficients matrix is mapped back to the brain volume to represent functional brain networks and patterns. We use the publicly available Human Connectome Project (HCP) Q1 dataset as the test bed, and the experimental results indicate that the proposed anatomically guided structure sparse representation is effective in reconstructing concurrent functional brain networks.

Keywords

Sparse representation; Dictionary learning; Group sparsity; AAL template; Functional networks

[#]Correspondence: Tel: 1-706-542-3478; Fax: 1-706-542-2996; tliu@cs.uga.edu.

^{*}Joint corresponding authors.

Compliance with Ethical Standards:

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

1. INTRODUCTION

Sparse representation has been successfully applied to many areas such as signal/image processing, computer vision, machine learning, and bioinformatics (Candès and Wakin 2008; Elad et al. 2010; Mairal et al. 2009; Wright et al. 2010; Wright et al. 2009). Analyzing functional magnetic resonance imaging (fMRI) data based on sparse representation has drawn increasing attention. The key assumption in sparse representation is that an observed signal can be written as a linear combination of a few atoms and a given dictionary. Sparse representation is introduced to study fMRI data analysis by M. Alexander (Alexander and Baumgartner 2001). Subsequently, this data-driven strategy of dictionary learning and sparse coding has been reported efficient and effective in reconstructing concurrent and interactive functional networks from both resting state fMRI (rsfMRI) and task based fMRI (tfMRI) data (Lee et al. 2011; Yamashita et al. 2008; Lv et al. 2015b). However, these pure data-driven sparse representation approaches do not take the advantage of anatomical prior knowledge when reconstructing functional brain networks. In the neuroscience field, it is widely believed that brain anatomy and structure play crucial roles in determining brain function, and anatomical structure is the substrate of brain function. Thus, integrating anatomical structure information into brain network representation is a critical prerequisite for identifying functional brain networks and interactions between the cortical regions of the human brain.

For fMRI data analysis, conventional analysis methods have primarily focused on voxel-by-voxel functional mapping using the general linear model (GLM) in which stimuli or behavioral parameters are used as regressors to account for the BOLD response and finding regions of highly correlated activity (Friston et al. 1994; Worsley et al. 2002; Biswal et al. 1995). In contrast to the widely used GLM, independent component analysis (ICA) relying upon a general assumption of independence, allows the user to be agnostic regarding the exact form of the response. Therefore, ICA has become the popular tool for data-driven fMRI analysis (Smith et al. 2009). However, the popularity of ICA has been challenged recently by a number of studies that show independence is not adaptive for blind source separation in fMRI (Donoho 2006; Smith et al. 2009). Also, it was shown that the most influential factor for the success rate of the ICA algorithm is the sparsity of the components, rather than independence (Daubechies et al. 2009). Actually, the fact that fMRI signal sparsity is more effective than independency in determining neural activity is supported by biological finding of sparse coding in the brain. The sparse property is a general assumption as previously mentioned, and many researchers have performed studies on the sparsity of the fMRI signal to help decode the functional networks and interactions between the cortical regions of the human brain. For example, Georgiev proposed the sparse component analysis (SCA) method (Georgiev et al. 2007), which reveals that the brain responses of sparse (and may be dependent) stimuli could be more successful by SCA than by ICA. Lee (Lee et al. 2011) proposed a novel statistical analysis method of fMRI data to overcome the drawbacks of conventional data-driven methods such as the ICA. Li (Li et al. 2009) introduced an iterative sparse-representation-based algorithm for detecting of brain regions from fMRI data. These studies have demonstrated that the sparsity of the fMRI signal is a useful feature for fMRI signal separation, the sparsity is also very powerful and could significantly

improve the signal separation accuracy compared with ICA algorithms. In addition to the aforementioned analysis methods, recently, Lv *et al.* (Lv et al. 2015a) presented a promising framework based on sparse representations of whole-brain fMRI signals. The basic idea of the computational framework is to aggregate multiple tfMRI or rsfMRI signals within the whole brain of one subject into a big data matrix, which is subsequently factorized into an over-complete dictionary basis matrix and a reference weight matrix via an effective online dictionary learning algorithm (Mairal et al. 2010). Then, the time series of each over-complete basis dictionary represents the functional BOLD (blood-oxygen-level dependent) activities of a brain network and its corresponding reference weight vector stands for the spatial map of this brain network. Furthermore, N. Wang *et al.* (Wang et al. 2013) presented an effective fMRI data analysis method SACICA, which is composed of a wavelet packet decomposition procedure, a sparse approximation coefficients set formation procedure and an ICA decomposition and reconstruction procedure. Because of the effective sparse approximation coefficients set of the mixing fMRI data, the SACICA method exhibits stronger signal reconstruction ability than the classical FastICA method. Lee *et al.* (Lee et al. 2011) presented a novel data-driven sparse GLM framework that combines statistical parametric mapping with sparse dictionary learning for a data-driven brain fMRI analysis. The results showed that a maximum likelihood estimation framework with sparsity constraint can provide spatially adaptive matrices as a subset of learned dictionary acquired from sparse dictionary learning algorithm. This method overcomes the limitations of ICA by exploiting sparsity of the components instead of independence. In addition to, this approach extracts individually adaptive activation patterns more accurately than spatial and temporal ICA, by a simulation and task-evoked experiment. These studies have demonstrated that the sparsity of the fMRI signal is a useful feature for source separation. Besides fMRI signal separation field, other field studies have also demonstrated that the assumption of sparseness is very powerful and could significantly improve the signal separation accuracy and the computation efficiency compared with existing ICA algorithms (Zibulevsky and Pearlmutter 2001; Khan and Kim 2008).

However, despite recent successes of using sparse representation for fMRI signal analysis, it has been rarely explored if/how structured sparse representation of fMRI signals can be utilized to infer functional networks for the whole brain. Recently, more elaborate structured sparse models have been developed, in which non-zero elements are no more unrelated, but appear in groups or hierarchies of groups (Kim and Xing 2010; Yuan and Lin 2006; Jacob et al. 2009; Zhao et al. 2009; Jenatton et al. 2011; Sprechmann et al. 2011). These models have shown they are useful in the analysis of fMRI and genetic data (Sprechmann et al. 2015). The underlying assumption of sparse models are that the input vectors can be reconstructed accurately as a linear combination of the dictionary atoms with a small number of non-zero coefficients. And structured sparse models further assume that the pattern of the non-zero coefficients exhibits a specific structure known a priori. Sparse methods, like the Lasso (Tibshirani 1996) or the Elastic Net (Zou and Hastie 2005), are able to estimate solutions for which only a few voxels are deemed relevant, therefore aiding interpretation. However, these models provide overly sparse solutions, or activation patterns, where the non-zero coefficients are assigned to disparate regions across the brain, without exploiting any spatial or temporal prior information (Michel et al. 2011; Grosenick et al. 2013; Rasmussen et al.

2012). Instead, structured sparsity models (Bach et al. 2012) have been proposed to extend the well-known methods of Lasso and Elastic Net by enforcing more structured constraints on the solution. These include constancy or closeness of the regression coefficients over neighboring or connected regions or graph structures. Although, sparsity models can be easier to estimate and interpret. These new structured sparsity models promise an even greater ease for interpretation of the activation patterns. This is owing to the fact that the active voxels are grouped together in possibly fewer clusters, which coincides well with our knowledge about the brain's specialized regions and networks. Therefore, sparsity alone is not sufficient for making reasonable inferences from these models, because single sparse model could be unstable under resampling or slight changes of the experimental conditions. Hence, In (Jenatton et al. 2012), R Jenatton *et al* consider a sparse hierarchical structured regularization called Multi-scale Mining of fMRI Data. Specifically, the penalization they used is constructed from a tree that is obtained by spatially-constrained agglomerative clustering. This approach encodes the spatial structure of the data at different scales into the regularization, which makes the overall prediction procedure more robust to inter-subject variability. That algorithm is used on real data acquired to study the mental representation of objects. It is shown that the proposed algorithm not only delineates meaningful brain regions but yields better prediction accuracy than reference methods. In (Baldassarre et al. 2012), Baldassarre *et al* presented an extension of the Total Variation method and assessed several other structured sparsity models on accuracy, sparsity and investigated the stability effect of using structured sparsity methods on a dataset of fMRI scans with very high dimensionality. In (Chen and Huang 2012), Chen and Huang *et al* presented a fast convex optimization algorithm to improve CS-MRI. Wavelet sparsity, gradient sparsity and tree sparsity are all considered in their model for real MR images. Real MR images not only tend to be tree structured sparse, but also are sparse in wavelet and gradient domains. And all of experiments demonstrate that the proposed algorithm outperforms the state-of-the-art ones. In summary, structure sparse models could be easier for fMRI signals inference, interpret of activation patterns.

In this work, we proposed a novel structure guided group sparse regression (S2GSR) method for functional network reconstruction by employing anatomical group structures to guide sparse representation of fMRI data, which can incorporate prior knowledge. In general, we separated the whole brain voxels into different groups based on AAL template, and used the joint ℓ_1 and ℓ_2 norms to learn both inter-group sparsity and intra-group homogeneity (Kim and Xing 2012; Simon et al. 2013; Liu and Zhang 2009). Employing 116 brain regions from the AAL template (Tzourio-Mazoyer et al. 2002) as anatomical group information could effectively improve the network representation by constraining both homogeneity within anatomical structure and sparsity across anatomical structures. The experiments were executed on the high quality HCP fMRI data. The results show that the identified functional brain networks have been substantially improved, which also provides anatomical clues for understanding the detected brain networks.

The rest of the paper is organized as follows. Section 2 presents our S2GSR approach and implementation. Specially, it presents the whole brain fMRI signals dictionary learning, anatomically guided group structure regression and mapping of selected feature to brain identified functional networks and patterns. Section 3 focuses on model parameter selection,

identification of group-wise consistent meaningful activation patterns and functional brain networks, reproductively of our approach and comparison between our approach with state-of-the-art methods. Section 4 provides conclusion and possible future extensions.

2. METHODS

2.1. Overview

In this section, we will introduce our computational framework of the proposed algorithm, which is summarized in Figure 1. fMRI images from individual brains are first registered into a standard space in order to align with the AAL template. Then by extracting fMRI signals from a whole brain mask, a global over-complete signal dictionary is learned via online dictionary algorithm (Mairal et al. 2009). By using the learned dictionary as a set of features (regressors), the group structured regression employs anatomical structures as group information to regress whole brain signals. Afterwards, the coefficient matrices are mapped back to the brain volume to represent functional brain networks.

2.2. Whole Brain fMRI Signals Dictionary Learning

Sparse representation assumes that sparse signal recovery is an observed signal can be written as a linear combination of a few atoms of a given dictionary. Most of recent algorithms for dictionary learning (Abolghasemi et al. 2015; Aharon et al. 2006; Lee et al. 2011; Olshausen and Field 1997) are iterative batch procedures, accessing the whole training set at each iteration in order to minimize a cost function under some constraints, and cannot efficiently deal with the large training sets, or dynamic training data changing over time, such as video sequences (Bousquet and Bottou 2008). In our proposed method, a global over-complete dictionary $D = [d_1, d_2, \dots, d_n] \in R^{t \times m}$ (t is the fMRI signal time points and m is the number of dictionary atoms) is first learned from the fMRI signals $X = [x_1, x_2, \dots, x_n] \in R^{t \times n}$ (n is the voxel number) of the whole brain using online dictionary learning method (Mairal et al. 2009). Here, “over-complete” means that the number of basis (dictionary elements) is greater than that of the fMRI signal time points. We reformulate the observation matrix $\tilde{X} = Da$, where $a \in R^{m \times n}$ refers to the coefficient matrix. In this paper we assume that the whole brain fMRI signals could be represented by sparse linear combination of a set of signal basis using dictionary atoms and the empirical cost function can be optimized in Eq. (1).

$$f_n(D) = \frac{1}{n} \sum_{i=1}^n \ell(x_i, D) \quad (1)$$

where $D \in R^{t \times m}$ is the dictionary ($t > m$, making the dictionary over-complete), each column representing a basis vector, and ℓ is a loss function such that $\ell(x, D)$ should be small if D is “good” at representing the signal X . We define the optimal value of the ℓ_1 sparse coding problem in Eq. (2):

$$\ell(x_i, D) = \min_{\alpha \in R^m} \frac{1}{2} \|x_i - D\alpha_i\|_2^2 + \lambda \|\alpha_i\|_1 \quad (2)$$

With sparsity as constraint, the dictionary is learned and optimized, where λ is a regularization parameter, and α is the sparse codes of input signals X . This problem is also known as basis pursuit (Chen et al. 2001), or the Lasso (Tibshirani 1996). It is well known that regularization yields a sparse solution. In this paper, we adopt structure guided group sparse regression to solve this problem.

2.3. Anatomically Guided Group Structure Regression

In conventional approaches, once the features are defined, the learning of coefficient matrix could be summarized into the typical LASSO (Tibshirani 1996) problem in Eq. (3).

$$\alpha = \operatorname{argmin} \ell(\alpha) + \lambda \phi(\alpha) \quad (3)$$

where $\ell(\alpha)$ is the loss function, and $\phi(\alpha)$ is the regularization term, which could regularize feature selection while achieving sparse regularization, and $\lambda > 0$ is the regularization parameter. Once we learned the dictionary $D = [d_1, d_2, \dots, d_n] \in R^{t \times m}$, the conventional LASSO to perform regression of brain fMRI signals $X = [x_1, x_2, \dots, x_n] \in R^{t \times n}$ to obtain a sparse coefficient matrix $\alpha = [\alpha_1, \alpha_2, \dots, \alpha_n] \in R^{m \times n}$ is defined as:

$$\alpha = \operatorname{argmin} \sum_{i=1}^n \|x_i - D\alpha_i\|_2^2 + \lambda \sum_{i=1}^n \sum_{j=1}^m |\alpha_i^j| \quad (4)$$

where $\ell(\alpha)$ is defined as the least square loss, and $\Omega(\alpha)$ is the ℓ_1 norm regularization term to induce sparsity, α_i^j is the coefficient element at the i -th column and j -th row, m is the dictionary size. Eq. (4) can be viewed as the LASSO penalized least squares problem. Conventional LASSO in Eq. (4) is a pure data-driven approach, however, the ℓ_1 regularization model does not consider the structure information of the α . In many real-world applications, in addition to sparsity, the variables in α are often highly correlated and exhibit structured relations such as group structure, so considering the sparsity and group prior simultaneously becomes more important. Besides, according to the previous studies (Kim and Xing 2012; Ye and Liu 2012; Liu et al. 2009a) that have shown that the priori structure information such as disjoint/overlapping groups, trees, and graphs may significantly improve the classification/regression performance and help identify the important features (Ye and Liu 2012).

In this paper, we adopt group guided structured regression of fMRI signals. Specifically, the group information of fMRI signals are defined by the anatomical structure information according to AAL template (Tzourio-Mazoyer et al. 2002). 116 brain regions are employed in our method as shown in Figure 1. Since before signal extraction, each subject has been

registered into the standard space and alignment is established with the AAL template, each voxel in brain mask is associated with a template label. Adjacent voxels with same anatomical AAL label are grouped together. Thus, in each brain, voxels of fMRI signals could be categorized and labeled as 116 AAL groups. This anatomical group information will be used to guide the coefficient learning in this section. The conventional LASSO adopts the ℓ_1 norm regularization term to induce sparsity (Eq. (4)), and the group sparsity to the problem of variable selection is achieved by introducing the regularization function Ω as:

$$\Omega(\alpha) = \sum_{j=1}^m \lambda_j \|\alpha_{G_j}\|_2 \quad (5)$$

where $G_1, G_2, \dots, G_m$ are m disjoint groups such that $\cup_{j=1}^m G_j = \{1, 2, \dots, n\}$ and $G_i \cap G_j = \emptyset$ when $i \neq j$, α_{G_j} denotes the variables of α indexed by the j th G_j , λ_j is a positive weight, and $\|\cdot\|_2$ represents the ℓ_2 norm.

The group lasso (5) does not perform feature selection within each feature group. For certain applications, it is desirable to perform simultaneous group selection and feature selection. To overcome this problem, achieved the inter-group sparsity and intra-group homogeneity simultaneous. Here the ℓ_2 norm penalty is introduced into the penalty term as shown in Eq. (5), which will improve the intra-group homogeneity. At the same time, we also combine the ℓ_1 norm and ℓ_2 penalty which will induce both intra-group homogeneity and inter-group sparsity, as shown in Eq. (6).

$$\alpha = \operatorname{argmin} \sum_{i=1}^n \|x_i - D\alpha_i\|_2^2 + \lambda_1 \sum_{i=1}^n \sum_{j=1}^m |\alpha_i^j| + \lambda_2 \sum_{j=1}^m \sum_{s=1}^s \omega_s \|\alpha_{G_s}^j\|_2 \quad (6)$$

Thus, Eq. (6) can be also viewed as the structured sparse penalized least squares problem. The solution of this structured LASSO penalized least squares problem by utilization of joint ℓ_1 and ℓ_2 norms has been discussed in (Liu et al. 2009a) and (Liu et al. 2009b). Our final learning problem is summarized in Eq. (6) and the detailed algorithm is shown in the Algorithm 1. From brain science perspective, each learned dictionary element can be viewed as a functional network component and each row of learned α is mapped back to brain volume to identify and quantitatively characterize those meaningful functional networks.

Algorithm 1

Structured Guided Group Sparse Regression

Input: Dictionary $D \in \mathbb{R}^{n \times m}$, The whole brain signals $y \in \mathbb{R}^{n \times n}$, group $G = \{G_1, \dots, G_m\}$, parameter λ

Output: Coefficient Matrix α_i

Initialize: $T, \lambda, k=116$ ($m < n$), $t=0, T$

$$y = \sum_{j=1}^m \sum_{i=1}^n \|x_i^{(j)} - c_j\|^2$$

$$\alpha_0 = \arg \min_{\alpha} \frac{1}{2} \|y - D\alpha\|_2^2 + \lambda \sum_{k=1}^m |x_k|$$

For $t = 1$ to T do

$$\alpha_t = \arg \min_{\alpha} \frac{1}{2} \|x_t - D_{t-1}\alpha\|_2^2 + \lambda \|\alpha\|_1$$

Update the dictionary D_t

Calculate the next iteration α_{t+1}

$$\gamma(\alpha) = \{\ell(\alpha) + \lambda_1 \|\alpha\|_1 + \lambda_2 \sum_{s=1}^S \omega_s \|\alpha_{G_s}\|_2\}$$

End for

2.4. Mapping Activated Patterns

In our proposed framework, the whole brain signals X is a t -by- n matrix (where t is the number of time points and n is the number of voxels). The “signals” are the n spatial voxels, and signals can be sparsely represented as $X = D\alpha$, where D is the t -by- m estimated linear mixing matrix obtained by dictionary learning algorithm, and α is an m -by- n matrix containing the m independent atoms. We can achieve α via our proposed approach group structured regression, where the spatial independent components (images) are located in the rows of α and the associated spatially independent time courses are found in the columns of D . To decode the spatial information, we mapped the sparse matrix to the whole brain, and checked the whole brain activation areas and functional networks.

This process is similar with spatial ICA decomposition, in the spatial ICA model $X = AS$, the fMRI signal is represented by a $T \times V$ data matrix X , where T is the number of time points and V is the number of voxels in the volumes. This means that each row of S contains an independent spatial pattern and the corresponding column of A holds its time-course. Since the whole mixing model is transposed, the statistical constraint applies to the spatial domain. ICA is essentially blind source separation, the solving process is a dimension reduction problem, the number of components is a free parameter, which has been either determined empirically or estimated by method in (Calhoun et al. 2009). Therefore, a large number of approaches are proposed to discuss this problem for estimating the number of components. However, the number of components selection is still a challenging problem. In our proposed framework, to avoid this problem, we utilize data-driven approach to select atoms and parameters.

3. RESULTS AND DISCUSSION

3.1. Experiment Materials

Our experiment was performed on the publicly released WU-Minn HCP data (Q1). The high-quality tfMRI data (Q1 release) was acquired from 68 subjects and it includes 7 tasks (motor, emotion, gambling, language, rationale, social, and working memory). The acquisition parameters of tfMRI data were as follows: 90×104 matrix, 220mm FOV, 72 slices, TR=0.72s, TE=33.1ms, flip angle = 52°, BW=2290 Hz/Px, in-plane FOV = 208×180 mm, 2.0mm isotropic voxels. The time length of each task and resting state were shown here: working memory (405 time points), gambling (253 time points), motor (284 time points), language (316 time points), social cognition (274 time points), relational processing (232 time points), and emotion processing (176 time points). More detailed data acquisition and preprocessing protocols could be referred to (Glasser et al. 2013; Van Essen et al. 2013).

3.2. Imaging Protocol and Preprocessing

Data preprocessing was carried out with FSL tools. The HCP unprocessed images from MRI scanners invariably contain several types of spatial distortion. They were not in a standard anatomical space, and were misaligned across modalities. They also contain various types of modality-specific noise, artifacts, and biases (Van Essen et al. 2013). To make best use of the high-resolution HCP datasets, it was critical to compensate as much as possible for these distortions, biases, and artifacts, and also to acknowledge the potential impact of residual confounds. The preprocessing pipelines included motion correction, spatial smoothing, temporal pre-whitening, slice time correction, and global drift removal. The detailed processing was applied to each subject: head motion correction by using MCFLIRT, non-brain removal by using BET. Spatial smoothing by using a Gaussian kernel of FWHM 5 mm, registration of each subject's fMRI data to its high-resolution structural image was carried out by using FLIRT. Registration from the high-resolution structural to MNI152 standard space was achieved by using FLIRT affine registration. More details about preprocessing were referred to (Van Essen et al. 2013; Glasser et al. 2013).

3.3. Model Parameter Selection

The proposed model learning relates to the following parameter selection issues: reference dictionary atom size, coefficient matrices sparsity level and regularization term parameters selection. To tune the parameters of the proposed model, we calculated the different values of sparsity level and dictionary sizes. In ideal case, the dictionary sizes should be larger than the fMRI subject's acquisition time points, in order to guarantee dictionary was over-complete. In this paper, we adopt the effective online dictionary learning algorithm. This method gradually updates the dictionary as new data becomes available for sparse representation learning and significantly reduces the amount of memory needed to store the dataset. It updates dictionary using block-coordinate approach, so as to guarantee each of dictionary atoms will be updated twice at least. Here, the minimum number of iterations was 1000. The regularization parameter can be used to control the sparsity levels. When we choose very small sparsity level, we would fail to identify networks. As a trade-off between estimation performance and the number of atoms and coefficients, we chose a dictionary

size of 500 atoms with sparsity level of 1.5, which serves as the parameter for the proposed model estimation procedure.

To evaluate the performance of our proposed framework, we defined a similarity index to check the similarity between our identified networks and the RSNs template. Here, we used Jaccard similarity coefficient to calculate the similarity of our identified networks and template networks. Jaccard coefficient was commonly used to measure the overlay of two datasets and was defined as the quotient between the intersection and the union of the pairwise compared variables among two objects, as shown in Eq. (7).

$$Jaccard(X, Y) = \frac{X \cap Y}{X \cup Y} \quad (7)$$

where X was the spatial map of our identified network component and Y was that of the RSNs template network.

3.4. Learned Group-wise Consistent Data-driven Functional Networks

The preprocessed different subjects' task fMRI data are registered to the MNI152 standard space, and then we performed quantitative measurements on the Working Memory (WM) task dataset and the 10 primary functional networks are shown in Figure 2. Spatial characteristics of these networks show example slices for ten spatial patterns, which are overlaid onto the mean subjects high-resolution structural image (1×1×1.5 mm) aligned to the MNI template. The Slice #1, #2, and #3 (visual network) correspond to medial, occipital pole, and lateral visual areas. Slice #4 (default mode network) includes medial parietal (precuneus and posterior cingulate), bilateral inferior-lateral-parietal and ventromedial frontal cortex. It's noted that #4 slice (DMN) shows large variations and this network also is one of the most widely study RSNs in the rsfMRI literatures. However, this network is most commonly seen as deactivating in task fMRI experiments. Hence, it is not surprising that DMN exhibit large variations in our task-evoked datasets. Slice #5 (cerebellum) covers the cerebellum. This region most strongly relates to action-execution and plays an important role in motor control. It may be also involved in some cognitive functions such as attention and language. Slice #6 (sensorimotor) includes supplementary motor area, sensorimotor cortex, and secondary somatosensory cortex. Slice #7 (auditory) includes the superior temporal gyrus, Heschl's gyrus, and posterior insular. It includes primary and association auditory cortices. Slice #8 (executive control) covers several medial-frontal areas, including anterior cingulate and paracingulate. Slice #9 and #10 (frontoparietal) cover several frontoparietal areas, and these areas are corresponding to several cognition/language paradigms (Smith et al. 2009).

Our findings show that the template networks, which with ICA and dual regression method together with our approach have similar results in all subjects. The identified networks are visualized in Figure 2. It is shown that they are quite consistent with the templates, but the corresponding RSNs #4 (DMN) show large variations. The DMN typically consists of the medial prefrontal cortex (MPFC), the posterior cingulate (PCC)/precuneus, inferior parietal

lobe (IPL), lateral temporal cortex (LTC), and hippocampal formation (HF). Recent studies have reported that the DMN shows activation during a wide range of cognitive tasks, including stimulus independent thought, mind wandering, monitoring of the external environment, self-reference, autobiographical, prospective memory, and social cognition (Koshino et al. 2014; Koshino et al. 2011). According to task-evoked stimuli experiments report (Koshino et al. 2014), during the task preparation period, the typical DMN regions, including the MPFC, PCC, lateral IPL, lateral temporal, and HF, showed greater activation for the Dual Task condition than the Single Task condition. No brain region exhibited greater activation for the Single Task than for the Dual Task. Most important, during the task execution period, the same DMN regions, including the MPFC, PCC, lateral IPL, lateral temporal, and HF, showed less activation than single condition (Koshino et al. 2014). In this study, our identified #4 DMN network come from Working Memory dataset and the template network of RSNs #4 derived from resting dataset. Since the DMN regions where greater activation for the preparation(resting-state) than the execution period. Therefore, this conclusion might be suggest that DMN derived from resting state fMRI data exhibits greater activation than from task related execution condition.

3.5. Reproducibility and Spatial Similarities

To validate our approach reproducibility, we test our framework on seven different task datasets and the results are summarized in Figure 3. The visualization of these 10 RSNs on the different datasets are shown in Figure 3(a)–(b). *The visual network, default mode network and cerebellum are shown in Figure 3(a)*, sensorimotor, auditory, executive control, and frontoparietal networks are shown in Figure 3 (b). By observation, we can see that these ten RSNs are similar with those template networks. In addition, we quantitative analysis the spatial similarity between our identified networks and template networks. The similarity index range is between 0 and 1. The higher value indicates higher similarity. As shown in Table 1, the highest similarity value is 0.86 and the average value is 0.72. These relatively high values suggest that the identified networks are more similar with template networks, also indicates that our proposed approach are stable and robust.

The spatial similarity on seven datasets achieved really consistent results, which can be observed from Table 1. *It is evident that the results by our approach are similar with the RSNs templates.* In addition, with quantitative analysis, we found that the similarity values on the seven different datasets are also highly consistent with the RSNs template (Table 1). The first column of Table 1 is task dataset, and the second to the forth column are visual networks. The fifth column to the ninth column are DMN, cerebellum network, sensorimotor network, auditory network, executive control network and the last two columns are frontoparietal networks. Compared with the RSNs the highest similarity is # 1; the lowest is # 8; and the average similarity is 0.63. With regard to the disagreement between our identified networks and template networks, it is still not clear whether they are caused by different tasks, or by the variability in the data acquisition, preprocessing and analysis.

However, as shown in Figure 3(a) and Table 1, the inconsistent functional networks are DMN, Sensorimotor and Executive control network. From our analysis, these networks variability are likely caused by the task-related datasets, because the template networks are

utilized resting-state fMRI data, but our identified networks on task-evoked datasets. In summary, our proposed structured guided group regression algorithm is robust and powerful in identifying group-wise consistent functional networks.

3.6. Comparison between Our Approach and State-of-the-art Methods

To compare our proposed approach and state-of-the-art methods, we choose template networks as the baseline, then utilized Lasso algorithm and our approach computed RSNs similarity respectively. The parameters are selected in a similar way. Firstly, we learned an over-complete dictionary matrix for each subject, then coefficient matrix is solved by the lasso algorithm and our proposed approach. On average, it took 1000 iterations to obtain the over-complete dictionary respectively. However, the coefficient matrices at least took 1500 iterations to reach convergence. The threshold of lasso and our proposed approach were set to 1.5 and the test datasets based on the HCP Q1 Working memory and Gambling respectively.

In total, 10 RSNs were obtained on Working memory and Gambling datasets using different approaches respectively. We randomly select four slices of RSNs for comparison. These slices of RSNs are shown in Figure 4(a)–(d). The visualization of results on the first row is template of RSNs, the second row is corresponding network identified by lasso algorithm, and the third row is corresponding network identified by our approach. From Figure 4, we can see that identified functional networks are roughly similar between lasso and our approach. Indeed, these two methods have huge differences. The Lasso algorithm can only guarantee the global sparsity, when regularization parameter was defined as a large value, mapping these features to the whole brain will produce a lot of noise, and these features scattered on the cortex surface, which lead to fail to identify these networks. However, our proposed approach not only considers the sparsity of the inter-group, but also can consider the homogeneity of the intra-groups. Figure 4 shows the results of two methods comparison with the template, in which our method is based on individual subject, while the lasso method uses the group-wise results.

Table 2. Shows statistical results of the two methods compared with templates respectively. Here we assume that the coefficient of the template is 1. Higher values mean that the RSNs are more similar with the template. For these 10 networks, the highest similarity is 0.86 of the Visual network and the lowest is executive control network. The average value is 0.72. And the highest similarity index of the lasso algorithm is 0.83. In Table 2, the results of Lasso algorithm are based on the group-wise, however, the results of our approach are based on individual. It is obvious that our proposed approach is superior to the lasso algorithm. It is evident that compared with the method without utilizing structured information, our approach has substantially improved the identified functional networks. On the other hand, it also indicates that the prior knowledge plays an important role in the reconstruction of the brain functional network.

Finally, to evaluate the influence of the selection of different brain templates on the functional network reconstruction, we also applied the Harvard-Oxford atlas as the template to test our proposed methods. Both qualitative and quantitative results (Figure 5 and Table 3) confirmed that our framework works well on the Harvard-Oxford atlas.

4. CONCLUSIONS

In this paper, a novel structure guided group regression method is proposed for brain network identification. Experiments on 7 different task datasets have demonstrated the effectiveness of our S2GSR method in identifying consistent brain networks. Comparisons have shown that our method is more effective and accurate than the traditional method of LASSO. In general, our approach provides the anatomical substrates for the reconstructed functional networks. In the future, we plan to apply and test this S2GSR method in larger fMRI datasets and compare it with other brain network construction methods. In addition, it will be applied on clinical fMRI datasets to reveal the abnormalities of brain networks in diseased brains.

Acknowledgments

Funding: This study was funded by NSF CAREER Award (IIS-1149260), NIH R01 DA-033393, NIH R01 AG-042599, NSF CBET-1302089, NSF BCS-1439051 and NSF DBI-1564736. J Lu was supported by the Natural Science Foundation of Jiangsu Province under Grant (No. 20131351). Q Zhao was supported by the Chinese scholarship council.

References

- Abolghasemi V, Ferdowsi S, Sanei S. Fast and incoherent dictionary learning algorithms with application to fMRI. *Signal, Image and Video Processing*. 2015; 9(1):147–158.
- Aharon M, Elad M, Bruckstein A. K-SVD: An Algorithm for Designing Overcomplete Dictionaries for Sparse Representation. *IEEE Transactions on Signal Processing*. 2006; 54(11):4311–4322.
- Alexander M, Baumgartner R. The importance of appropriate (sparse) representation of data: application to de-noising fMRI time courses. *NeuroImage*. 2001; 13(6):60.
- Bach F, Jenatton R, Mairal J, Obozinski G. Structured sparsity through convex optimization. *Statistical Science*. 2012:450–468.
- Baldassarre, L., Mourao-Miranda, J., Pontil, M. Structured sparsity models for brain decoding from fMRI data. *Pattern Recognition in NeuroImaging (PRNI), 2012 International Workshop on; IEEE; 2012*. p. 5-8.
- Biswal B, Zerrin Yetkin F, Haughton VM, Hyde JS. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magnetic resonance in medicine*. 1995; 34(4):537–541. [PubMed: 8524021]
- Bousquet O, Bottou L. The tradeoffs of large scale learning. *Advances in neural information processing systems*. 2008:161–168.
- Calhoun VD, Liu J, Adalı T. A review of group ICA for fMRI data and ICA for joint inference of imaging, genetic, and ERP data. *NeuroImage*. 2009; 45(1):S163–S172. [PubMed: 19059344]
- Candès EJ, Wakin MB. An introduction to compressive sampling. *IEEE signal processing magazine*. 2008; 25(2):21–30.
- Chen C, Huang J. Compressive sensing MRI with wavelet tree sparsity. *Advances in neural information processing systems*. 2012:1115–1123.
- Chen SS, Donoho DL, Saunders MA. Atomic decomposition by basis pursuit. *SIAM review*. 2001; 43(1):129–159.
- Daubechies I, Roussos E, Takerkart S, Benharrosh M, Golden C, D'ardenne K, Haxby J. Independent component analysis for brain fMRI does not select for independence. *Proceedings of the National Academy of Sciences*. 2009; 106(26):10415–10422.
- Donoho DL. Compressed sensing. *IEEE Transactions on information theory*. 2006; 52(4):1289–1306.
- Elad M, Figueiredo MA, Ma Y. On the role of sparse and redundant representations in image processing. *Proceedings of the IEEE*. 2010; 98(6):972–982.

- Friston KJ, Holmes AP, Worsley KJ, Poline JP, Frith CD, Frackowiak RS. Statistical parametric maps in functional imaging: a general linear approach. *Human brain mapping*. 1994; 2(4):189–210.
- Georgiev, P., Theis, F., Cichocki, A., Bakardjian, H. Data mining in biomedicine. Springer; 2007. Sparse component analysis: a new tool for data mining; p. 91–116.
- Glasser MF, Sotiropoulos SN, Wilson JA, Coalson TS, Fischl B, Andersson JL, Polimeni JR. The minimal preprocessing pipelines for the Human Connectome Project. *NeuroImage*. 2013; 80:105–124. [PubMed: 23668970]
- Grosenick L, Klingenberg B, Katovich K, Knutson B, Taylor JE. Interpretable whole-brain prediction analysis with GraphNet. *NeuroImage*. 2013; 72:304–321. [PubMed: 23298747]
- Jacob, L., Obozinski, G., Vert, JP. Group lasso with overlap and graph lasso. *Proceedings of the 26th annual international conference on machine learning; ACM; 2009*. p. 433–440.
- Jenatton R, Gramfort A, Michel V, Obozinski G, Eger E, Bach F, Thirion B. Multiscale mining of fMRI data with hierarchical structured sparsity. *SIAM Journal on Imaging Sciences*. 2012; 5(3): 835–856.
- Jenatton R, Mairal J, Obozinski G, Bach F. Proximal methods for hierarchical sparse coding. *Journal of Machine Learning Research*. 2011; 12(Jul):2297–2334.
- Khan A, Kim IT. Sparse Kernel Independent Component Analysis for Blind Source Separation. *Journal of the Optical Society of Korea*. 2008; 12(3):121–125.
- Kim, S., Xing, EP. Tree-Guided Group Lasso for Multi-Task Regression with Structured Sparsity. *Proceedings of the 27th International Conference on Machine Learning (ICML-10); 2010*. p. 543–550.
- Kim S, Xing EP. Tree-guided group lasso for multi-response regression with structured sparsity, with an application to eQTL mapping. *The Annals of Applied Statistics*. 2012:1095–1117.
- Koshino H, Minamoto T, Ikeda T, Osaka M, Otsuka Y, Osaka N. Anterior medial prefrontal cortex exhibits activation during task preparation but deactivation during task execution. *PLoS One*. 2011; 6(8):e22909. [PubMed: 21829668]
- Koshino H, Minamoto T, Yaoi K, Osaka M, Osaka N. Coactivation of the default mode network regions and working memory network regions during task preparation. *Scientific reports*. 2014; 4:5954. [PubMed: 25092432]
- Lee K, Tak S, Ye JC. A data-driven sparse GLM for fMRI analysis using sparse dictionary learning with MDL criterion. *IEEE Transactions on Medical Imaging*. 2011; 30(5):1076–1089. [PubMed: 21138799]
- Li Y, Namburi P, Yu Z, Guan C, Feng J, Gu Z. Voxel selection in fMRI data analysis based on sparse representation. *IEEE Transactions on Biomedical Engineering*. 2009; 56(10):2439–2451. [PubMed: 19567340]
- Liu H, Zhang J. Estimation Consistency of the Group Lasso and its Applications. *AISTATS*. 2009:376–383.
- Liu, J., Ji, S., Ye, J. *Proceedings of the twenty-fifth conference on uncertainty in artificial intelligence*. AUAI Press; 2009a. Multi-task feature learning via efficient l_2 , l_1 -norm minimization; p. 339–348.
- Liu J, Ji S, Ye J. SLEP: Sparse learning with efficient projections. *Arizona State University*. 2009b; 6:491.
- Lv J, Jiang X, Li X, Zhu D, Chen H, Zhang T, Huang H. Sparse representation of whole-brain fMRI signals for identification of functional networks. *Medical image analysis*. 2015a; 20(1):112–134. [PubMed: 25476415]
- Lv J, Jiang X, Li X, Zhu D, Zhang S, Zhao S, Han J. Holistic atlases of functional networks and interactions reveal reciprocal organizational architecture of cortical function. *IEEE Transactions on Biomedical Engineering*. 2015b; 62(4):1120–1131. [PubMed: 25420254]
- Mairal, J., Bach, F., Ponce, J., Sapiro, G. Online dictionary learning for sparse coding. *Proceedings of the 26th annual international conference on machine learning; ACM; 2009*. p. 689–696.
- Mairal J, Bach F, Ponce J, Sapiro G. Online learning for matrix factorization and sparse coding. *Journal of Machine Learning Research*. 2010; 11(Jan):19–60.
- Michel V, Gramfort A, Varoquaux G, Eger E, Thirion B. Total variation regularization for fMRI-based prediction of behavior. *IEEE Transactions on Medical Imaging*. 2011; 30(7):1328–1340. [PubMed: 21317080]

- Olshausen BA, Field DJ. Sparse coding with an overcomplete basis set: A strategy employed by V1? Vision research. 1997; 37(23):3311–3325. [PubMed: 9425546]
- Rasmussen PM, Hansen LK, Madsen KH, Churchill NW, Strother SC. Model sparsity and brain pattern interpretation of classification models in neuroimaging. Pattern Recognition. 2012; 45(6): 2085–2100.
- Simon N, Friedman J, Hastie T, Tibshirani R. A sparse-group lasso. Journal of Computational and Graphical Statistics. 2013; 22(2):231–245.
- Smith SM, Fox PT, Miller KL, Glahn DC, Fox PM, Mackay CE, Laird AR. Correspondence of the brain's functional architecture during activation and rest. Proceedings of the National Academy of Sciences. 2009; 106(31):13040–13045.
- Sprechmann P, Bronstein AM, Sapiro G. Learning efficient sparse and low rank models. IEEE transactions on pattern analysis and machine intelligence. 2015; 37(9):1821–1833. [PubMed: 26353129]
- Sprechmann P, Ramirez I, Sapiro G, Eldar YC. C-HiLasso: A collaborative hierarchical sparse modeling framework. IEEE Transactions on Signal Processing. 2011; 59(9):4183–4198.
- Tibshirani R. Regression shrinkage and selection via the lasso. Journal of the Royal Statistical Society. Series B (Methodological). 1996:267–288.
- Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Joliot M. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. NeuroImage. 2002; 15(1):273–289. [PubMed: 11771995]
- Van Essen DC, Smith SM, Barch DM, Behrens TE, Yacoub E, Ugurbil K. Consortium WMH. The WU-Minn human connectome project: an overview. NeuroImage. 2013; 80:62–79. [PubMed: 23684880]
- Wang N, Zeng W, Chen L. SACICA: A sparse approximation coefficient-based ICA model for functional magnetic resonance imaging data analysis. Journal of neuroscience methods. 2013; 216(1):49–61. [PubMed: 23563324]
- Worsley KJ, Liao C, Aston J, Petre V, Duncan G, Morales F, Evans A. A general statistical analysis for fMRI data. NeuroImage. 2002; 15(1):1–15. [PubMed: 11771969]
- Wright J, Ma Y, Mairal J, Sapiro G, Huang TS, Yan S. Sparse representation for computer vision and pattern recognition. Proceedings of the IEEE. 2010; 98(6):1031–1044.
- Wright J, Yang AY, Ganesh A, Sastry SS, Ma Y. Robust face recognition via sparse representation. IEEE transactions on pattern analysis and machine intelligence. 2009; 31(2):210–227. [PubMed: 19110489]
- Yamashita O, Sato M-a, Yoshioka T, Tong F, Kamitani Y. Sparse estimation automatically selects voxels relevant for the decoding of fMRI activity patterns. NeuroImage. 2008; 42(4):1414–1429. [PubMed: 18598768]
- Ye J, Liu J. Sparse methods for biomedical data. ACM Sigkdd Explorations Newsletter. 2012; 14(1):4–15.
- Yuan M, Lin Y. Model selection and estimation in regression with grouped variables. Journal of the Royal Statistical Society: Series B (Statistical Methodology). 2006; 68(1):49–67.
- Zhao P, Rocha G, Yu B. The composite absolute penalties family for grouped and hierarchical variable selection. The Annals of Statistics. 2009:3468–3497.
- Zibulevsky M, Pearlmutter BA. Blind source separation by sparse decomposition in a signal dictionary. Neural computation. 2001; 13(4):863–882. [PubMed: 11255573]
- Zou H, Hastie T. Regularization and variable selection via the elastic net. Journal of the Royal Statistical Society: Series B (Statistical Methodology). 2005; 67(2):301–320.

Figure 1.

The flowchart of proposed S2GSR method pipeline: Step1: Data acquisition, preprocessing and extracting the whole brain signals. Step2: Using the whole signals for learning dictionary D . Step3: Labelling the whole signals via the AAL template. Step4: Feature selection based on S2GSR method. Step5: Mapping the selected feature (coefficient matrix) in the whole brain to identify these meaningful functional networks.

Figure 2.

Comparison 10 our identified networks with template networks on working memory dataset. The (RSN#1---RSN#10) represents 10 template networks, (#1--#10) represents our method identified networks.

(a)

(b)

Figure 3.

Our approach identified networks on 7 different datasets. (a) and (b) shows 10 random selected subject's RSNs. The first row represents 7 different tasks, the first column to the seventh column are corresponding identified networks. The last column shows the template networks.

Figure 4. Comparisons of our method with LASSO on Working Memory and Gambling datasets. (a), (b), (c) and (d) show the results from two task datasets.

Figure 5.
The results of using Harvard-Oxford atlas as the guidance in 10 networks reconstruction. The first row annotates 7 different tasks and the first to the seventh columns are corresponding identified networks. The last column shows the template networks.

Table 1

Similarity index between our results and the templates on 7 different task datasets. The first column represents 7 task datasets. The first row (#1–#10) represents 10 networks. The average similarity on 7 tasks achieves 0.623.

Datasets	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10
WM	0.84	0.66	0.72	0.61	0.67	0.74	0.68	0.45	0.63	0.69
Emotion	0.82	0.65	0.61	0.46	0.54	0.84	0.62	0.42	0.65	0.70
Gambling	0.86	0.65	0.61	0.53	0.54	0.57	0.55	0.43	0.66	0.73
Language	0.86	0.66	0.62	0.57	0.74	0.56	0.62	0.45	0.67	0.72
Motor	0.83	0.66	0.62	0.47	0.47	0.53	0.51	0.41	0.60	0.79
Relational	0.81	0.68	0.62	0.47	0.47	0.53	0.51	0.41	0.60	0.79
Social	0.82	0.66	0.67	0.48	0.54	0.56	0.63	0.42	0.71	0.71

Table 2

The similarity comparison results of two methods with the templates. The first row represents 10 resting state networks (#1–#10). The first column represents two different methods. The second column represents two datasets (working memory and Gambling).

Method	Datasets	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10
Lasso	Working Memory	0.79	0.64	0.71	0.62	0.50	0.48	0.53	0.44	0.58	0.68
	Gambling	0.83	0.64	0.55	0.49	0.52	0.56	0.47	0.43	0.52	0.62
S2GSR	Working Memory	0.84	0.66	0.73	0.61	0.71	0.74	0.68	0.45	0.63	0.69
	Gambling	0.86	0.65	0.61	0.53	0.54	0.57	0.55	0.43	0.66	0.73

Table 3

The similarity results by utilizing the Harvard-Oxford atlas to guide the network reconstruction on 7 different datasets. The first column represents 7 tasks. The first row (RSN#1--RSN#10) represents 10 networks. The second row to the eighth row represent similarity comparisons with the templates.

Datasets	RSN#1	RSN#2	RSN#3	RSN#4	RSN#5	RSN#6	RSN#7	RSN#8	RSN#9	RSN#10
<i>WM</i>	0.9478	0.6937	0.8818	0.8630	0.7674	0.8906	0.7684	0.6510	0.7317	0.8065
<i>Emotion</i>	0.9026	0.6691	0.8591	0.7051	0.7198	0.8821	0.7184	0.5533	0.6683	0.7193
<i>Gambling</i>	0.9309	0.6866	0.8155	0.7033	0.7046	0.8718	0.7348	0.5869	0.6982	0.7658
<i>Language</i>	0.6712	0.6712	0.8231	0.8170	0.7852	0.8823	0.7093	0.5723	0.7024	0.7530
<i>Motor</i>	0.8938	0.6954	0.8388	0.7808	0.8653	0.8739	0.7680	0.6051	0.7003	0.7643
<i>Relational</i>	0.9119	0.7135	0.8286	0.7553	0.7282	0.8778	0.7387	0.5297	0.7094	0.7538
<i>Social</i>	0.9043	0.6834	0.9030	0.7183	0.7374	0.8806	0.7587	0.4611	0.7375	0.7507