2019

Fusion Analysis of Resting-State Networks and Its Application to Alzheimer’s Disease

Shengbing Pei  
the Department of Computer Science and Technology, Tongji University, Shanghai 201800, China.

Jihong Guan  
the Department of Computer Science and Technology, Tongji University, Shanghai 201800, China.

Shuigeng Zhou  
Shanghai Key Lab of Intelligent Information Processing, School of Computer Science, Fudan University, Shanghai 200433, China.

Follow this and additional works at: https://tsinghuauniversitypress.researchcommons.org/tsinghua-science-and-technology

Part of the Computer Sciences Commons, and the Electrical and Computer Engineering Commons

Recommended Citation


This Research Article is brought to you for free and open access by Tsinghua University Press: Journals Publishing. It has been accepted for inclusion in Tsinghua Science and Technology by an authorized editor of Tsinghua University Press: Journals Publishing.
Fusion Analysis of Resting-State Networks and Its Application to Alzheimer’s Disease

Shengbing Pei, Jihong Guan*, and Shuigeng Zhou

Abstract: Functional networks are extracted from resting-state functional magnetic resonance imaging data to explore the biomarkers for distinguishing brain disorders in disease diagnosis. Previous works have primarily focused on using a single Resting-State Network (RSN) with various techniques. Here, we apply fusion analysis of RSNs to capturing biomarkers that can combine the complementary information among the RSNs. Experiments are carried out on three groups of subjects, i.e., Cognition Normal (CN), Early Mild Cognitive Impairment (EMCI), and Alzheimer’s Disease (AD) groups, which correspond to the three progressing stages of AD; each group contains 18 subjects. First, we apply group Independent Component Analysis (ICA) to extracting the Default Mode Network (DMN) and Dorsal Attention Network (DAN) for each subject group. Then, by obtaining the common DMN and DAN as templates for each group, we employ the individual ICA to extract the DMN and DAN for each subject. Finally, we fuse the DMNs and DANs to explore the biomarkers. The results show that (1) the templates generated by group ICA can extract the RSN for each subject by individual ICA effectively; (2) the RSNs combined with the fusion analysis can obtain more informative biomarkers than without fusion analysis; (3) the most different regions of DMN and DAN are found between CN and EMCI and between EMCI and AD, which show differences. For the DMN, the difference in the medial prefrontal cortex between the EMCI and AD is smaller than that between CN and EMCI, whereas that in the posterior cingulate between EMCI and AD is larger. As for the DAN, the difference in the intraparietal sulcus is smaller than that between CN and EMCI; (4) extracting DMN and DAN for each subject via the back reconstruction of group ICA is invalid.

Key words: Independent Component Analysis (ICA); group analysis; fusion analysis; Alzheimer’s Disease (AD)

1 Introduction

Functional Magnetic Resonance Imaging (fMRI) is increasingly used in disease diagnosis owing to its noninvasiveness and high resolution in both space and time[1,2]. Along with the basic task-based fMRI[3,4] studies, the resting-state fMRI (rsfMRI)[5-7] receives wide attention, as rsfMRI requires no subjects to perform cognitive tasks and can be used to study the inner spontaneous functions of human beings. The rsfMRI scan needs the subject to be relaxed without specific focus and be awake; thus, data acquisition can be achieved relatively easily compared with the task-based fMRI scan, especially for individuals who cannot carry out cognitive tasks, such as Alzheimer’s Disease (AD)[8-12].

Certain spontaneous functions still occur in the
human brain even at relaxed state without cognitive tasks. To perform such functions, the anatomically separated brain regions that share the same neuronal pattern in time constitute a functional network[13], i.e., the Resting-State Network (RSN). The RSNs comprise a Default Mode Network (DMN)[14,15], a Dorsal Attention Network (DAN)[16,17], and a FrontoParietal Control Network (FPCN)[18]. Among these networks, DMN is the main functional network in resting state. Affected by diseases, the RSNs are believed to show certain stable changes, which can be biomarkers for disease diagnosis.

The approaches to identify RSNs include seeding-based connectivity analysis[19,20], hierarchical clustering[21], and Independent Component Analysis (ICA)[22–25]. The ICA is widely used in medical image processing as it is data driven, and its independence hypothesis matches the neural signals to a certain extent. As the fMRI data contain both temporal and spatial information, the temporal ICA[26] and spatial ICA[27] are employed. In this paper, we use the spatial ICA, which aims at identifying spatial independent components (also referred to as functional networks, i.e., RSNs).

For a group of subjects, two approaches are available for applying the spatial ICA to extracting RSNs for each subject. One approach applies the spatial ICA for each subject (denoted by individual ICA) and extract RSNs separately. The other concatenates the rsfMRI data of all subjects in the temporal dimension first, performs the spatial ICA on the concatenated group data (denoted by group ICA), and finally extracts RSNs for each subject by back reconstruction. However, selecting the suitable templates to extract RSNs by individual ICA presents difficulty, whereas extracting the RSNs for each subject by back reconstruction in group ICA may lose the specificity of RSNs of each subject. In this paper, we present a new method to extract RSNs; this method considers the common RSNs of subject groups by group ICA as templates and uses the templates to extract the corresponding RSNs of subjects by individual ICA.

AD is a neurological, progressive disease that slowly destroys brain cells, leading to loss of memory and thinking skills and ultimately the ability to live. This condition is irreversible, and almost no action can be performed in the late stage. However, in the early stage, certain treatment can be used to delay the process. Thus, several biomarkers must be urgently identified to help early diagnosis. Previous works aimed at exploring effective biomarkers using a number of tools, such as the structured MRI[28], electroencephalograph[29], cerebrospinal fluid protein level[30], gene[31], and positron emission tomography[32]. Given the difficulty in finding structural changes in the early stage, the change of function is another direction. Recently, the fMRI has attracted substantial attention in AD diagnosis, providing a way to explore AD biomarkers from functional analysis. Either exploring biomarkers or classifying subjects via the rsfMRI data analysis for AD, extracting RSNs consistently serves as the starting point.

The DMN receives more attention as it is the major functional network in resting state. Previous research has shown some promising results. Koch et al.[33] applied both the ICA and region of interest functional-connectivity techniques to AD rsfMRI data and observed that the DMN connectivity between healthy controls and MCI subjects shows minimal difference but is less prominent in the AD subjects than in the controls, especially in the posterior cingulate and superior frontal cortex. The DAN features an antagonistic relationship with the DMN and exhibits notable changes in the progression of AD subjects.

Most existing research[34,35] focused on finding biomarkers using a single RSN with individual analysis or group analysis but excluded the interactions between RSNs, which might provide useful information. The techniques utilizing complementary information are useful in multiple modalities[36] and multi-task fMRI[37,38] studies. Calhoun et al.[39] applied the joint ICA to schizophrenia with two tasks, and discovered that schizophrenia patients demonstrate decreased connectivity in a joint network and respond more similarly to two tasks. Remezani et al.[37] performed multi-task fMRI data combination to improve the classification accuracy.

The premise of multi-modality and multi-task approaches is that each modality or task can provide complementary information for the other. Notably, the information can be effectively combined, but the signals should be acquired either simultaneously or on the same subject. As the RSNs are usually extracted from rsfMRI data acquired at the same time and on the same subject, combining them for fusion analysis becomes more possible.

In this study, we apply the joint ICA based on fusion analysis to Cognition Normal (CN), Early Mild Cognitive Impairment (EMCI), and AD subjects. First,
we extract the common DMN and DAN from the rsfMRI data by group ICA. Then, the common DMNs and DANs are used as templates to extract the DMN and DAN by individual ICA. Concretely, we apply the individual ICA to each subject and use the templates from group ICA to sort the components for extraction. Our results show that group ICA can decompose the DMN into two subnetworks, and the extraction of DMN by individual ICA combines the results of using the subnetworks as templates. Finally, we fuse the DMN and DAN from the individual ICA to identify biomarkers in the two transition phases of AD: from CN to EMCI and from EMCI to AD.

The contributions of this paper include the following: (1) With fusion analysis, we effectively use the complementary information among RSNs to detect biomarkers, and experimental results show the effectivity of extracting RSNs by individual ICA based on the templates generated by group ICA. (2) By comparing the group differences in the two transition phases, from CN to EMCI and from EMCI to AD, we observe the differing major regions in the two phases. Thus, we hypothesize that the different regions in the second phase may be the key factors leading to AD.

The paper is organized as follows. Section 2 presents the techniques used in this paper; these techniques include the ICA, group analysis, and fusion analysis. Section 3 introduces the datasets used in this work, which are downloaded from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database. Section 4 describes the experimental pipeline. Section 5 gives the experimental results. Section 6 discusses the results and concludes the paper.

2 Methods

We aim to detect biomarkers by fusing the RSNs extracted from the rsfMRI data. To this end, we first generate RSN templates by performing group analysis for each group of subjects and then extract the RSNs from rsfMRI data for each subject separately by individual ICA based on the templates. Then, we apply fusion analysis to the extracted RSNs and identify the joint functional brain networks that can distinguish different subject groups. Figure 1 illustrates the flowchart used in this work. In the following section, we present the major techniques, including individual ICA, group ICA for group analysis, and joint ICA for fusion analysis, used in this work.

2.1 ICA

ICA is a generative method that is widely used for fMRI data. This analysis is data driven; its input includes the observed fMRI data or processed data from fMRI data, and its outputs include the independent components and mixing coefficients. The model is presented as follows:

\[ X = AS \]  

(1)

where \( X \) refers to the observation matrix, \( S \) denotes the independent component matrix, and \( A \) represents the matrix of the mixing coefficients.

Solving this model is to find a matrix \( W \) that can maximize the independence of \( Z \) as follows:

\[ Z = WX \]  

(2)

First, we identify a \( W (W^{-1}) \) is the approximation of \( A \) and then obtain \( S \) by letting \( Z \) approximate \( S \). In the fMRI analysis, the infomax algorithm\(^{[40]} \) is a popular approach used to solve the ICA by minimizing the mutual information of components in \( Z \). The result of the infomax algorithm features sparse property, which is highly suitable for spatial analysis.

One problem with ICA is the manner of determining the number of independent components. Several works set the number by experience or use several numbers and select the best one. Minimum Description Length (MDL)\(^{[41]} \) is an effective algorithm for estimating the number used in this paper.

2.2 Group analysis

To extract the RSNs from rsfMRI data for a group of subjects, we can perform extraction for each subject
separately. In such a manner, the different subjects may provide varying components, whereas the predefined templates for extracting RSNs maybe unsuitable. Here, we apply the group analysis to a group of subjects to generate adaptive templates for the group. We also use the ICA for group analysis, i.e., group ICA, as illustrated in Fig. 2.

First, we concatenate the rsfMRI data of all subjects of a group according to the temporal dimension. Let

$$X_{\text{group}} = [X_1^T, X_2^T, \ldots, X_M^T]^T \in \mathbb{R}^{N \times V}$$  \hspace{1cm} (3)

where $$X_i \in \mathbb{R}^{T \times V}$$ denotes the rsfMRI data of subject $$i$$; $$N$$, $$T$$, and $$V$$ refer to the number of subjects, time points for each subject, and voxels of each subject, respectively. Then, we perform the ICA on the group data $$X_{\text{group}}$$, where the results are a matrix of common independent components $$S_{\text{group}} \in \mathbb{R}^{K \times V}$$ and a matrix of mixing coefficients:

$$A_{\text{group}} = [A_1^T, A_2^T, \ldots, A_N^T]^T \in \mathbb{R}^{N \times K}$$  \hspace{1cm} (4)

where $$A_i \in \mathbb{R}^{T \times K}$$ corresponds to subject $$i$$ and $$K$$ is the number of independent components. $$S_{\text{group}}$$ is shared by the group of subjects and usually used to make inference for the group. The group ICA can be implemented using the GIFT software for Matlab (http://mialab.mrn.org/software/gift/index.html).

Meanwhile, we conduct back reconstruction to obtain the independent components for each subject and achieve the following for subject $$i$$:

$$S_i = A_i^{-1}X_i$$  \hspace{1cm} (5)

The RSN in $$S_i$$ is used as the template to sort components in individual ICA for subject $$i$$. Notably, using the RSNs from back reconstruction of group ICA for each subject instead of performing individual ICA for each subject separately leads to distortion of results, as will be discussed in detail in Section 6.

2.3 Fusion analysis

We aim to fuse the RSNs and obtain informative biomarkers. This goal is achieved by combining the RSNs and then decomposing the combined matrix to obtain a smaller set of joint components. We still use the ICA for fusion analysis, i.e., joint ICA. Figure 3 shows the framework.

Suppose that $$M$$ subjects are present, and each subject contains $$L$$ RSNs. These RSNs are concatenated one by one in terms of subjects. That is,

$$X_{\text{fusion}} = [X_{11}, X_{12}, \ldots, X_{1L}; X_{21}, X_{22}, \ldots, X_{2L}; \ldots; X_{M1}, X_{M2}, \ldots, X_{ML}] \in \mathbb{R}^{M \times LV}$$  \hspace{1cm} (6)

where $$X_{ij}$$ is the $$j$$-th RSN of subject $$i$$. The results constitute a set of joint independent components and the associated mixing coefficients. The coefficients are shared by different parts of the joint components, which can be used to capture group difference by $$t$$-test and reflect the strength of functional connectivity. The joint ICA can be implemented by FIT software for Matlab (http://mialab.mrn.org/software/fit/index.html).

3 Materials

All data used in this paper are obtained from the ADNI database (http://adni.loni.usc.edu). The ADNI study started in 2004 and involved three phases: ADNI1, ADNI GO, and ADNI2. The fMRI scans were added to ADNI GO and ADNI2.

3.1 Participants

In total, 54 subjects belonging to three groups are

![Fig. 2 Framework of group ICA and back reconstruction.](image)

![Fig. 3 Framework of joint ICA.](image)
collected for this study, with each group including 18 subjects. The first group consists of CN controls (Female-over-Male ratio (F/M) = 5/4, age mean = 75.5 years and standard deviation (s.d.) = 6.1477 years, Mini Mental State Examination (MMSE) score mean and s.d. are 29.2222 and 1.2154, respectively). The second group comprises the EMCI subjects (F/M = 11/7, age mean = 72.1667 years, and s.d. = 5.0904; MMSE mean and s.d. are 27.3333 and 1.7150, respectively). The AD patients constitute the third group (F/M = 1/1, age mean = 70.7222 years, and s.d. = 7.7140, MMSE mean and s.d. are 21.4444 and 2.7056, respectively). All details are provided in Table 1.

3.2 Image acquisition

Magnetic resonance images were acquired using a 3.0T Philips Medical Systems. In the functional image acquisition process, the subjects are required to keep their eyes open. Each functional image consists of 48 contiguous slices, and the AD patients constitute the third group (F/M = 1/1, age mean = 70.7222 years, and s.d. = 7.7140, MMSE mean and s.d. are 21.4444 and 2.7056, respectively). All details are provided in Table 1.

3.3 Data preprocessing

All subject data are preprocessed using Matlab 2015a and SPM8. First, for each subject, the DICOM images are converted to 140 3D functional images by preprocessed using Matlab 2015a and SPM8. First, for each subject, the DICOM images are converted to 140 3D functional images and a 3D structural image of NIFTI format and are further preprocessed by slice timing, realignment, coregistering, segmentation, normalization, and smoothing. Notably, the first 10 functional images are removed for reliability consideration, and the slice order in slice timing is interleaved. Furthermore, the subjects with translation greater than 2 mm or rotation greater than 2 degree are discarded. All 3D images are normalized to a 61 × 73 × 61 template, and smoothing is performed with an 8 mm Gaussian kernel.

4 Experiments

We combine the ICA, group analysis, and fusion analysis for three groups of subjects, i.e., CN, EMCI, and AD. First, we use the group ICA to generate templates of the DMN and DAN, and then extract the DMN and DAN by individual ICA based on the generated templates. Finally, we fuse the extracted DMN and DAN to detect informative biomarkers.

4.1 Template generation by group ICA

This paper first aims to test the effect of fusing RSNs on finding biomarkers. Before RSN fusion, we need to extract the RSNs for each subject. The group ICA was used to provide templates for DMN and DAN extraction by individual ICA. We conduct the group ICA for CN, EMCI, and AD. The ICASSO [42] is used for group analysis, and the number of independent components for each group is estimated by the MDL algorithm. The number of independent components is set to 27 for CN, 29 for EMCI, and 28 for AD.

In group analysis, the orders of components for each subject are identical and the same as those for the group. The group components are common for the group. Thus, if we want to generate specific templates of DMN and DAN for each subject through back reconstruction, we can obtain them in the same order as in the common components by group ICA.

4.2 Fusing DMN and DAN

Difficulty arises from extracting the RSNs by applying ICA to each subject, since each result retains individual specificity with different number and order of components. Selecting the effective templates for DMN and DAN presents difficulty, although we test several templates similar to other existing works [16], we observe that the templates exhibit inconsistency with regard to the effectiveness for every subject. However, the DMN and DAN generated by the group ICA for each group could serve as the templates for each group of subjects. The templates of DMN and DAN generated by the group ICA can be obtained in two ways: by using the common DMN and DAN as templates for each group; by using the DMN and DAN obtained by back reconstruction as templates for each group.
subject. Here, we use the common DMN and DAN as templates for each group. Remarkably, the DMN achieved by the group ICA can be decomposed into two subnetworks. Thus, the DMN extracted by individual ICA is the combination of the results obtained using the two subnetworks as templates. The independent components for each subject are still estimated by the MDL algorithm.

With the extracted DMN and DAN for each subject, we perform joint ICA on CN and EMCI, and on EMCI and AD, respectively, and a two-sample t-test is performed to capture the group difference. The results are compared with the findings obtained without using fusion analysis.

5 Results

Fusion analysis is applied to the RSNs extracted from rsfMRI data through individual ICA. Group ICA is used to generate the templates for the DMN and DAN extracted by individual ICA. The DMN and DAN have been studied and shown changes in the progression of AD; they are antagonistic, and this property might be used in fusion analysis. Thus, we use these functional networks as our research targets.

5.1 Group ICA

As the results of group ICA are common components for each group, the DMNs and DANs could be identified for each group (CN, EMCI, and AD), where the DMNs are all decomposed into two subnetworks, denoted by DMN-1 and DMN-2. Figure 4 shows the three networks (i.e., DMN-1, DMN-2, and DAN) for CN, EMCI, and AD. These networks are used as templates to extract the DMNs and DANs by individual ICA.

5.2 Fusion of DMN and DAN

After extracting the DMN and DAN for each subject, we perform the joint ICA for CN and EMCI, and for EMCI and AD. A two-sample t-test is applied to the mixing coefficients to capture the group difference. The number of estimated joint components is 3 for CN and EMCI, and 5 for EMCI and AD. Figures 5a and 5b show the significant joint components of CN and EMCI, and of EMCI and AD, respectively.

No significant difference is observed in the case of CN and EMCI. Figure 5a shows the components with the most difference ($p$-value $= 0.123$). In the case of EMCI and AD, the two components show a significant difference ($p$-value $= 0.000$ and $p$-value $= 0.048$). This result is consistent with actual conditions. No significant difference is observed between CN and EMCI, resulting in difficulty in the early stage diagnosis. However, in the late stage, a significant difference is identified between EMCI and AD.

Meanwhile, we separately use the same method for the DMN and DAN, the results are shown in Figs. 6 and 7, respectively.

Figures 5a and 6a show the minimal difference in the connectivity between CN and EMCI. Meanwhile, Figs. 5b and 6b show the decreased connectivity in the posterior cingulate in AD. These findings are consistent with the results in Ref. [33]. Moreover, comparing the joint components with the most difference in Figs. 5b, 6b, and 7b, the fusion of DMN and DAN captures their antagonistic relationships (the additional negative regions in blue located in inferior parietal lobule and superior parietal lobule), which could not be considered separately. This biomarker provides a larger consistent region for disease diagnosis. Comparing the components with the most difference in Figs. 5a and 5b, differences are noted in the different regions of AD subjects in the early stage (from CN to EMCI) and late stage (from EMCI to AD). In the DMN, the difference in the medial prefrontal cortex is smaller in the late stage than that in the early stage, whereas the difference in the posterior cingulate is larger in the late stage than that in the early stage. In the DAN, the difference in the intraparietal sulcus is smaller in the late stage than that in the early stage. This information might aid in checking the subject condition. For the AD patients, the
Fig. 5 Significant joint sources of DMN and DAN for CN and EMCI, and for EMCI and AD. From left to right, the figures show the distributions of mixing coefficients, and the corresponding maps related to DMN and DAN. The joint components are sorted by group difference.

6 Discussion and Conclusion

In this paper, we apply the ICA combined with group and fusion analyses to the rsfMRI data of CN, EMCI, and AD subjects. First, we use the group ICA to generate the templates of DMN and DAN and then use the individual ICA to extract the DMN and DAN for each subject based on the templates. Finally, we use the joint ICA to fuse the two networks to explore the biomarkers. Our main findings are as follows: (1) the proposed method of generating templates by group ICA is effective; (2) the extracted RSNs can be used for fusion analysis; (3) the most different functional regions in DMN and DAN in the transitions from CN to EMCI and from EMCI to AD differ.

A previous work\cite{43} performed subject classification in the context of back reconstruction of group analysis. Here, we implement a linear Support Vector Machine (SVM) classifier\cite{44} in the context of back reconstruction of group analysis to check whether using back reconstruction to obtain RSNs for each subject is effective in subject classification. Concretely, we first extract two RSNs for each subject by back reconstruction of the group ICA and then fuse the two RSNs. Finally, we use the mixing coefficients as lower dimensional features for each subject to train an SVM classifier to distinguish different subjects.

As discussed in Section 5, the DMNs of the three groups can all be decomposed into two subnetworks. As they originate from the same functional network, the DMNs may share similar complementary information. Thus, we conduct joint ICA of the two subnetworks for CN and EMCI, and for EMCI and AD. In each of the two cases, the number of independent components is 2, as estimated by the MDL algorithm.

The results of joint ICA yield a mixing coefficient matrix that provides a 2D feature for each subject. With a low dimensional feature, we construct a linear
Fig. 6 Sources corresponding to those in the joint ICA of DMN for CN and EMCI, and for EMCI and AD. From left to right the figures show the distributions of mixing coefficients, the corresponding map related to DMN. The two components in Fig. 6b are sorted corresponding to the results in Fig. 5b.

SVM classifier to classify the subjects to CN, EMCI, and AD groups. The SVM classifier is implemented by the Statistical Pattern Recognition Toolbox (STPRtool) software for Matlab (http://cmp.felk.cvut.cz/cmp/software/stprtool/). In classification, we use a leave-one-out cross-validation. In training, we perform the joint ICA with the following:

\[ X_{(\text{test})} = A_{(\text{test})}S_{(\text{train})} \]  

where \( X_{(\text{train})} \) is the training set, \( S_{(\text{train})} \) indicates joint components, and \( A_{(\text{train})} \) denotes the mixing coefficients. In testing, the input for validation is determined by least-square solution:

\[ X_{(\text{test})} = A_{(\text{test})}S_{(\text{train})} \]

Figures 8a and 8b show the results of joint ICA. The right two columns show the joint components and the left column shows the distributions of the mixing coefficients for each joint component.

From these results, the mixing coefficients provide a measure of functional connectivity under the three conditions (CN, EMCI, and AD), but the distributions of mixing coefficients exhibit a slight fluctuation in each group, implying that the functional network obtained by back reconstruction is non-discriminative for each group. This finding is inconsistent with the actual conditions, leading to distorted classification performance in the context of back reconstruction as shown below.

The two-dimensional coefficients are used to perform classification, and the results are compared with those obtained when DMN is decomposed without fusion. The results are shown in Table 2.

Table 2 Classification accuracy for CN and EMCI and for EMCI and AD. Classification is performed using DMN-1, DMN-2, and DMN-1+DMN-2.

<table>
<thead>
<tr>
<th></th>
<th>DMN-1 (%)</th>
<th>DMN-2 (%)</th>
<th>DMN-1+DMN-2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CN vs EMCI</td>
<td>100</td>
<td>88.89</td>
<td>100</td>
</tr>
<tr>
<td>EMCI vs AD</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
We estimated the $p$-values of the results in Fig. 8, which indicates the significant difference for both joint components in CN and EMCI and in EMCI and AD, thus presenting inconsistency with the actual conditions. The results of classification show that either classifying CN and EMCI or classifying EMCI and AD in the context of back reconstruction, the classifiers in the cases with and without fusion are almost linearly separable, which is also inconsistent with the results in Ref. [45]. Thus, using group ICA and back reconstruction to obtain the RSNs for subjects, the individual results are compiled to the common group components in each group, leading to unreasonable $p$ values and classification performance.

The following presents the solution for the group ICA:

$$X_{\text{group}} \approx A_{\text{group}}S_{\text{group}}$$  \hspace{1cm} (9)

which implies that

$$X_i \approx A_iS_{\text{group}}$$  \hspace{1cm} (10)

Back reconstruction applies $A_i^{-1}X_i$ to representing $S_i$. All $A_i^{-1}X_i$ approximate $S_{\text{group}}$. This condition might be the reason why all $S_i$ “gathered to” $S_{\text{group}}$. And we can obtain a relatively high accuracy in classification through back reconstruction when the common group components differ among groups.

All the data-driven methods for rsfMRI analysis, including ICA, are confronted with the difficulty of
identifying RSNs. Several samples may be easy to identify, but others present difficulty. Performing the individual ICA for a group, prior templates might be useful for portion of the group but usually could be ineffective for all, but they still relatively easily used to identify the RSNs in group ICA. In this paper, we use the RSNs extracted from group ICA as templates to identify the RSNs by individual ICA. This method could improve the effectiveness of the templates, because the extracted templates originate from the group and are more suitable for RSN extraction. Moreover, using back reconstruction can obtain specific group and are more suitable for RSN extraction. because the extracted templates originate from the group and could improve the effectiveness of the templates, which is more informative for AD stage prediction.

The estimated numbers of joint components for RSNs in this paper are smaller compared with those of fusion analysis for task fMRI. Such finding is understandable, as RSNs are spontaneous and more integrated, whereas the subtracted images corresponding to tasks are cooperated among more subfunctions.

Fusion of DMN and DAN indicates the changes in the most different regions between the early stage (from CN to EMCI) and the late stage (from EMCI to AD), and it could be used to predict the state of an AD patient. On the other hand, the joint component provides a consistent region, which is more informative for AD stage prediction.

In summary, this study demonstrates the effectiveness of fusing the RSNs of rsfMRI to provide more informative biomarkers. A method for template generation is proposed to conquer the difficulty of extracting RSNs. In addition, we observe that extracting the RSNs for each subject through back reconstruction of group ICA can gather individual components to the common group components in each group, which is actually invalid. As classifying AD patients in early stage is difficult but meaningful, our ongoing work will focus on the extraction of features from rsfMRI data for high accuracy classification.

Acknowledgment

This work was supported by the National Natural Science Foundation of China (NSFC) (No. 61772367) and the Program of Shanghai Subject Chief Scientist (No. 15XD1503600). Shuigeng Zhou was supported by the National Key Research and Development Program of China (No. 2016YFC0901704).

References

[15] G. B. Chand and M. Dhamala, Interactions among the


Shengbing Pei et al.: Fusion Analysis of Resting-State Networks and Its Application to Alzheimer’s Disease


Shengbing Pei received the BA degree from Nanjing Agricultural University in 2011, and the MS degree from University of Shanghai for Science and Technology in 2014. He is currently a PhD candidate at the Department of Computer Science and Technology, Tongji University. His research interests include machine learning, functional neuroimaging, and precision medicine.

Jihong Guan received the bachelor degree from Huazhong Normal University in 1991, the master degree from the Wuhan Technical University of Surveying and Mapping (merged into Wuhan University in 2000) in 1991, and the PhD degree from Wuhan University in 2002. She is currently a professor in the Department of Computer Science and Technology, Tongji University, Shanghai, China. Before joining Tongji University, she served in the Department of Computer, Wuhan Technical University of Surveying and Mapping, from 1991 to 1997 as an assistant professor and an associate professor since 2000. She was an associate professor (2000–2003) and a professor (since 2003) in the School of Computer, Wuhan University. She has extensively published in domestic and international journals and conferences. Her research interests include databases, data mining, and bioinformatics.

Shuigeng Zhou received the bachelor degree from Huazhong University of Science and Technology in 1988, the master degree from the University of Electronic Science and Technology of China in 1991, and the PhD degree in Computer Science from Fudan University in 2000. He is currently a professor in the School of Computer Science, Fudan University. He served in Shanghai Academy of Space-flight Technology from 1991 to 1997, as an engineer and a senior engineer (since 1995), respectively. He was a post-doctoral researcher in the State Key Lab of Software Engineering, Wuhan University, from 2000 to 2002. He has extensively published in domestic and international journals (including VLDB Journal, IEEE Transactions on Knowledge and Data Engineering, IEEE Transactions on Parallel and Distributed Systems, IEEE/ACM Transactions on Computational Biology and Bioinformatics, IEEE Transactions on Geoscience and Remote Sensing, Nature Communications, Nucleic Acids Research, and Bioinformatics) and conferences (including SIGMOD, SIGKDD, VLDB, ICDE, AAAI, IJCAI, ICCV, SODA, ISMB, and RECOMB). His research interests include data management, data mining, machine learning, and bioinformatics.