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Spatial Correlations of Brain fMRI data

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Abstract

In this study we suggest that the spatial correlation structure of the brain fMRI data be used to characterize the functional connectivity of the brain. For some concussion and recovery data, we examine how the correlation structure changes from one step to another in the data analyses, which will allow us to see the effect of each analysis to the spatial correlation or the functional connectivity of the brain. This will lead us to spot the processes which cause significant changes in the spatial correlation structure of the brain. We discuss whether or not we can decompose correlation matrices in terms of its causes of variations in the data.

Keywords : fMRI, functional connectivity, spatial correlation

I. Introduction

The brain functional Magnetic Resonance Imaging (fMRI) data and geological data share some similar properties because both are depicted in the space and data at different locations are often spatially correlated. On the other hand, they are also quite different because of their distinctive correlation structures. To be more specific, let us call a voxel the unit of the data at a location. When a voxel in the brain is functionally active, voxels in its neighbor tend to be active too. This implies that the voxels in close proximity are highly correlated. In addition, some voxels far apart can be active at the same time, which implies that significantly active voxels tend to form clusters regardless of their distances.

In this study we explore the correlation structure of the brain fMRI data at each data analysis step to characterize the functional connectivity of the brain. Also we examine how the correlation structures change from one step to another step during the data analyses, so that we can see how each analysis affects the correlation structure or the functional connectivity of the brain. This will lead us to spot any processes which cause significant changes in the correlation structure of the brain, and finally map the functional connectivity of

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the brain. Also we will discuss whether or not we can decompose correlation matrices in terms of its causes of variations in the data.

Recently, Logan and Rowe (2004) tried to model the spatial correlation of the brain. They adopted the simplest spatial correlation model $f(\rho)=\rho^{d}$, for $0<\rho<1$, and compared the real correlation matrix and the theoretical one by pictures. However this theoretical model considered only the proximity correlations without being able to fit the high correlations between voxels in remote locations. Also this model ignored the negative correlations even though there are loads of voxels negatively correlated. Bowman(2004) instead formed clusters of brain voxels based on the conventional clustering algorithms using correlates of rCBF (regional Cerebral Blood Flow) with PET(Positron Emission Tomography) and fMRI data. Those clusters revealed the brain anatomy and its functional connectivity quite well even though the spatial correlation itself was not used or modeled.

Section 2 will define a spatial correlation matrix for the brain fMRI data and will present the visual image of spatial correlation matrix for a piece of real data. Section 3 adopts an analog of Visual Analysis of Variance (Eddy and McNamee, 2001) to examine whether the correlation or the covariance of the fMRI data can be decomposed orthogonally in terms of its data processing steps.

II. Visualization of Spatial Correlation

Before define the spatial correlation matrix for the brain fMRI data, let us take a look at the data structure. All subjects used in this study were concussed and then recovered. Their Brain fMRI was taken while they were performing the given task which is called nBack. The observations were sampled in the reverse spiral format in k-space or Fourier space. Then they were interpolated to construct a 64×64 matrix, which later on was inverse Fourier transformed into i-space or image space. Meanwhile, their physiological data were collected : Blood Oxygen Level and respiration signal along the fMRI data in k-space. The task variable nBack has three experimental levels : 0back, 1back and 2back. Each of them was repeated 4 times in the random order. For each condition, there are 34 replications along with the time to result in a set of gigantic temporal data. Fig. 1 shows 34 replications of one slice for a condition.

To perform the task, the subject is watching the screen inside the MRI machine, and on the screen a series of letters are coming out. Whenever the target letter comes out, the subject is supposed to press the button with his or her index finger to mean "Yes, it's a target letter". Otherwise he or she press the other button with his or her middle finger. Those buttons are fixed with bandage into his or her fingers beforehand. For 0Back the target letter is ''x", for 1Back the target letter is the one which repeats the previous one without skipping, and for 2Back the target letter is the one which repeats after one skip.

Let V be the $pq \times \tau$ data matrix, where p and q are the numbers of rows and columns on a slice and τ is the length of the time series at each location. In our study both p and q are 64. To measure a spatial correlation the sample correlation matrix R is adopted, and $R = VV^T$. Since pq is usually much greater than the time points τ, often R is not full rank. More precisely, the sample correlation coefficient of two time

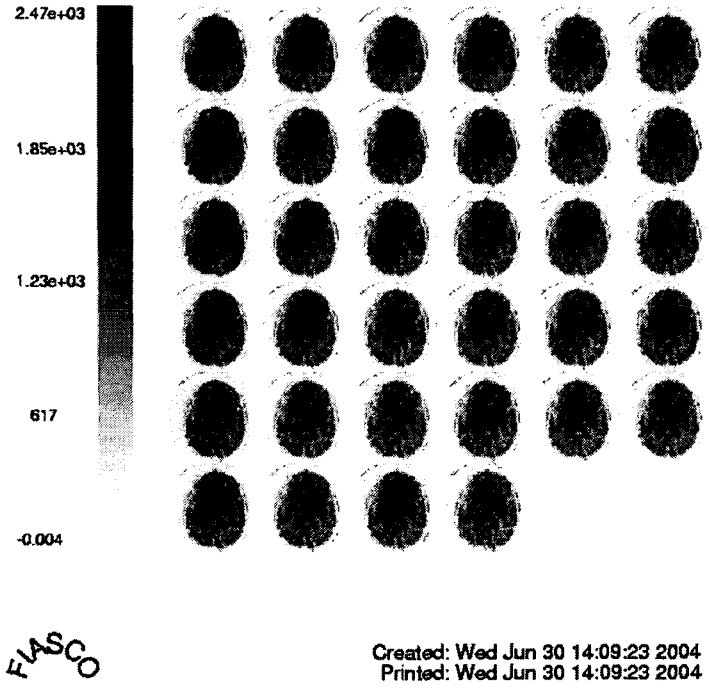

Fig. 1 34 images of brain fMRI data

series data $v_{(x,y)}$ and $v_{(x',y')}$ at two different locations (x, y) and (x', y') in i-space is defined as follows:

$$R_{v_{(x,y)}, v_{(x',y')}} = \frac{\mathrm{Cov}(v_{(x,y)}, v_{(x',y')})}{\sqrt{\mathrm{Var}(v_{(x,y)})\,\mathrm{Var}(v_{(x',y')})}}.$$

To illustrate the spatial correlation, let us use a small piece data, which is a 6×6 matrix. For $p = 6$ and $q = 6$, the following Fig. 2 is a 6×6 matrix of brain voxels which does not include air. In this figure white means weak signal or weak functional activity, and black means strong signal or strong functional activity.

Fig 2. 6×6 matrix of brain voxels

Then Fig. 3 is the corresponding 36×36 correlation matrix R of the 6×6 brain matrix. The first row of the correlation matrix is the correlation coefficients between the voxel (1, 1) and the others. The eighth row of the correlation matrix is the correlation coefficients between the voxel (2, 2) and the others. Every six columns of the correlation matrix in Fig. 3, strong correlation shows up and fades out. This explains the correlation between rows of the brain voxels and reveals the stripes along the diagonal. Also every six rows of the correlation matrix in Fig. 3, another strong correlation shows up and fades out. This explains the correlation between columns of the brain voxels and constructs the mosaic of 6×6 squares. It is very interesting to notice that even a small piece of the brain can create the beautiful spatial pattern like in Fig. 3. It seems that the spatial correlation model $f(\rho) = \rho^d$ for $0 < \rho < 1$ might fit locally this pattern.

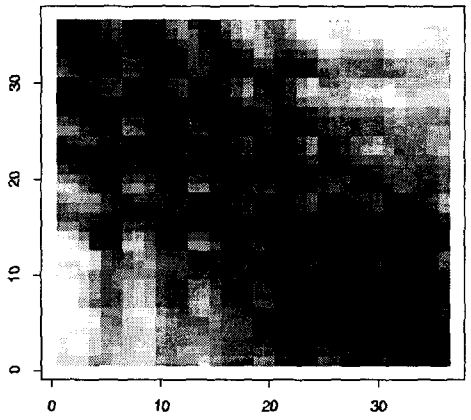

Fig. 3. 36×36 of correlation matrix

However if both $p = 64$ and $q = 64$ are considered, then R is exploded into a gigantic matrix 4096×4096 which contains about half a million numbers in it. This correlation structure is no longer simple enough to fit a single specific function, and illustrating a full correlation matrix requires 3 giga bytes. Therefore it is worthy to decompose the correlation matrix to find out its causes instead, and fit a linear model like analysis of variance.

III. Visual Analysis of Spatial Correlation

Lazar, Genovese, Eddy, and Welling (2001) triggered the idea of visually decomposing the variance in the brain fMRI data as an analog of analysis of variance. Then McNamee and Eddy (2001) further developed it and named it as visual analysis of variance, which assesses statistical changes in data at each data processing step. It provides quantitative and visual information at each processing step, so that it helps determine which data processing step contributes more to the variation in the data.

Decomposing the correlation matrix by its causes is an analog of the analysis of variance. There are two different sources of causes. One is caused by the task-related experimental design such as Subject, Concussion or Recovery, nBack, and the other is caused by the mechanical design. The usual mechanical design factors are often considered as nuisance

variables, so that they are analysed and removed before the main analysis related to the task.

For analysis FIASCO (Functional Image Analysis Software Computational Olio), the locally developed software at Carnegie-Mellon University, provides some data preprocessing analyses which are Despike, Physiological correction, Mean correction, 2D Motion correction, Outlier removal, Spatial filtering. For Physiological correction it uses the algorithm developed by McNamee and Eddy(2004). Despike removes outliers or spikes in Fourier space, Physiological correction regresses out the heart beat effect from the data in Fourier space, Mean correction standardize the whole data over the time, Motion correction corrects and relocates images using the structural images of the brain, Outlier removal removes outliers in image space, and Spatial filtering smoothes the images using Gaussian filter. In this paper we consider the data prepocessing steps as causes of mechanical design, and we will examine the spatial correlation matrices before and after each preprocessing data analysis.

Each data preprocessing analysis involves gigantic amount of data, so that it often fills up the huge memory space instantly and it takes long time to run through the whole processes. For instance running one step of analysis often requires more than 20 giga bytes. As mentioned earlier, the picture of full correlation matrix is too large to be included here, we instead depict 256×256 correlation matrix in Fig. 4 which was obtained from 16×16 brain voxels at each preprocessing data analysis. Red means strong positive signal or functional activity, and blue means strong negative signal or functional activity.

There are big changes right after Physiological correction and Spatial filtering. Definitely the spatial correlation has increased enormously by revealing certain patterns in the correlation matrices. One possible explanation for this phenomena is the inverse Fourier transformation after the Physiological correction in the Fourier Space often introduces some spatial correlation to the data instead of removing them. Also note that Physiological correction was designed and preformed not to reduce the spatial correlation in the data, but to reduce the variation in the data caused by heart beat. On the other hand, the increase of spatial correlation right after Spatial filtering has revealed as was expected. So Spatial filtering has the effect of emphasizing the pattern of the correlation matrix. Since the most data analyses related to the task variable assume that voxels are spatially independent, a series of resultant figures of spatial correlation give a warning that the further analysis should consider the spatial correlation, and from the data collection step to the end of analyses the correlation figures will be an excellent barometer whether spatial correlation has been reduced.

In Fig. 4, we can see the regular pattern in all the correlation matrices. Moreover the blue and red patterns are alternating and showing how the voxels are functionally connected each other. If the correlation is represented as red, the corresponding voxels have positive functional connectivity. Otherwise they have negative functional connectivity. If colors are

darker, there are stronger connectivities. A line along the principal diagonal means the correlation coefficient 1 with itself.

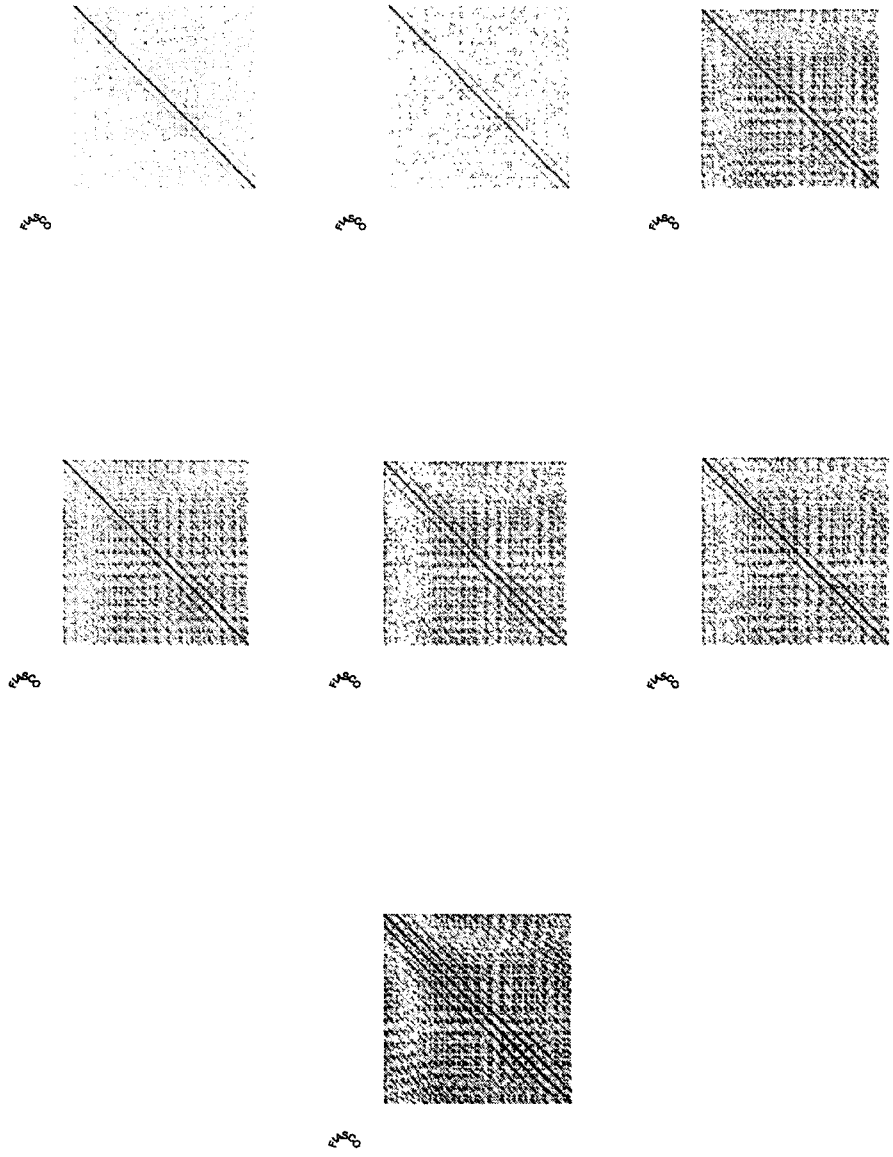

Fig. 4. Spatial Correlation Matrix : The Initial Data, After Despike, After Physiological correction, After Mean correction, After 2D Motion correction, After Outlier removal, After Spatial filtering

In addition to a series of correlation pictures, a summary statistic would help understand the change in correlations from step to step. Table 1 and Table 2 quantify the whole 4096×4096 correlation matrices of 3 Concussion and Recovery data by taking the sum of all correlation coefficients at each data preprocessing step. The reason of using the sum of all correlation coefficients is that this statistic would somehow help understand the total amount of correlations at each step. The theoretical maximum is 4096^2, and the theoretical minimum is 0 when there is no correlation at all between voxels. However this statistic still does not explain enough how the positive and negative correlations have increased or decreased. So in the future study the separate summary statistics should be developed and provided to explain positive and negative correlation coefficients.

Fig. 5 and Fig. 6 depicted the total correlations of Table 1 and Table 2. In both Fig. 5 and 6, we can see that the total correlation has notably increased after both Physiological correction and Spatial filtering. This result coincides with a series of correlation in Fig. 4. However one more thing to notice here is the difference between concussion data and recovery data. While concussion data shows sudden changes after Physiological correction and Filtering, recovery data shows more stable changes. This might be explained by the fact that the concussed brain would require more activity to earn the similar performance compared to the recovered brain. In Fig. 5, one concussion data has been corrupted after Despike, so it shows a big jump after Despike and a big drop after a physiological correction. Also two graphs cross after Despike and before Physiological corrections, which would imply that those two could be confounded. This phenomenon does not occur consistently in the other subjects. Thus as long as there is no confoundedness between Despike and Physiological correction, in view of spatial correlation we can assume that the given data analysis steps are independent and they can be represented as the linear model.

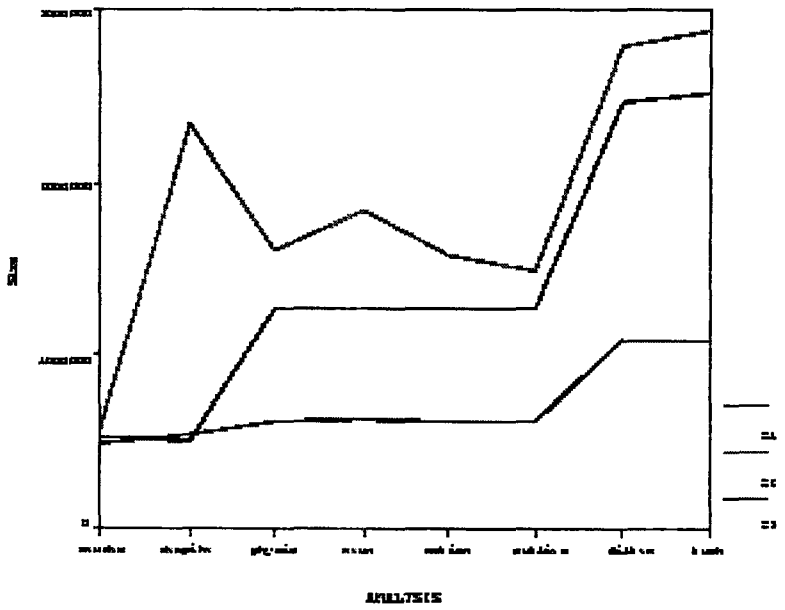

Fig. 5. Sum of absolute values of correlation coefficients after each data analysis step : Concussion
Vertical axis is for sum, and horizontal Axis is for Analyses. The Upper most line is subject 1, the middle line is subject 2, and the bottom most line is subject 3

Data Processing	subject 1	subject 2	subject 3
Initial	496986	589528	535451
Despike	549319	2342976	510373
Physiological	634517	1614893	1288098
Mean	642476	1848489	1287986
Motion	635599	1589015	1281921
Outlier	635382	1498698	1281949
Task	1103930	2875956	2519758

Table 1. Sum of absolute values of correlation coefficients : Concussion

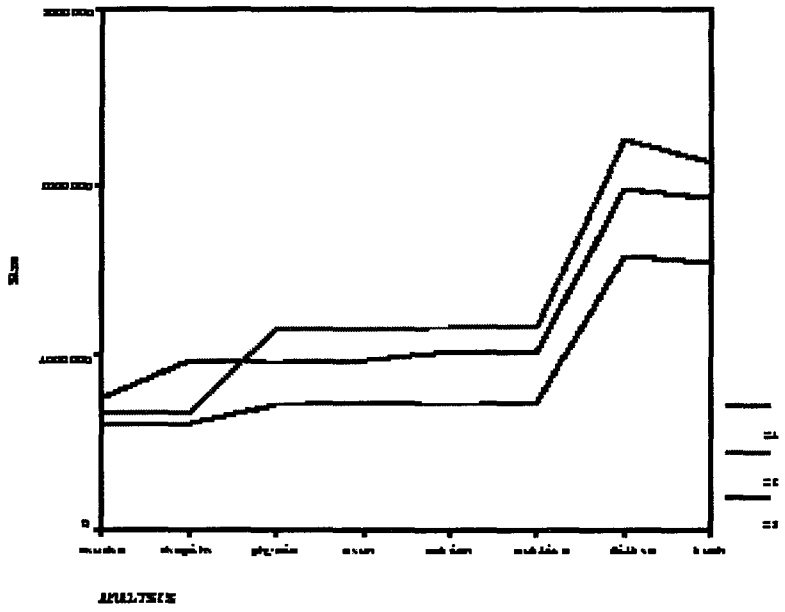

Fig. 6. Sums of absolute values of correlation coefficients after each data analysis step : Concussion
Vertical axis is for sum, and horizontal Axis is for Analyses. The Upper most line is subject 1, the middle line is subject 2, and the bottom most line is subject 3

Data Processing	subject 1	subject 2	subject 3
Initial	615989	666770	753221
Despike	618857	667157	974525
Physiological	710046	1157271	967328
Mean	716956	1150431	974936
Motion	716311	1170017	1022896
Outlier	716580	1170143	1022832
Filter	1586560	2244734	1964733

Table 2. Sum of absolute values of correlation coefficients : Recovery

Summary statistic and its graph are often necessary and they provide an useful additional information about the spatial correlations through the analyses. Therefore from the data collection step to the end of analyses this summary statistic can be used as another excellent barometer to decide whether there has been an increase or decrease of correlations.

IV. Conclusion

The functional connectivity of the human brain is very complicated, and so there have been lots of approaches to reveal it. For this purpose, we visualized and examined the spatial correlation matrix of the brain. From each correlation matrix, we could see how the voxels are functionally connected. It is obvious that each process reveals more negative correlations.

Also we found out that Physiological correction and Spatial filtering adds more spatial correlations to the data, so that more caution is needed at these steps. However after the motion correction the spatial correlation has not been removed as much as we expected from the data. Also Despike and Physiological correction were sometimes confounded. It means that removing spikes in Fourier space often introduces the strong pattern of the spatial correlation in the image space and Physiological correction removes some. Sometimes Despike reduces the spatial pattern and then Physiological correction increases it.

Ignoring the confoundedness between Despkie and Physiological correction, we can assume that all the given data processing analysis are independent. Let us those effects have been removed. Since the task variables are independent from the data preprocessing analyses and they are independent each other, the total covariance between voxels can be represented as an analog of Analysis of Variance:

$$\text{Total Covariane} = \sum_{S}\sum_{CR}\sum_{nBack}\sum_{MD}\text{Covariane}_{S,\ CR,\ nBack,\ MD} + \text{Unexplained part}$$

where S is subject, CR is Concussion or Recovery, and $nBack$ is the task variable, and MD is the mechanical design factors. This means that the total covariance can be decomposed into independent effects. Therefore except for the confounded Despike and Physiological correction, we can assume the independence among preprocessing data analyses.

There are another way of decomposing the correlation matrix, that is using Singular Value Decomposition (SVD). SVD of the correlation matrix follows right away from mathematics. The correlation matrix R is then expressed as a weighted sum of products of orthogonal matrices. Then we can also obtain the un-correlated data from the previous SVD result. Interestingly, the un-correlated data can be expressed as the sum of product of both orthogonal image and orthogonal temporal series. However the equality does not hold because the eigenvectors and eigenvalues of R are not unique. Yet, we still can have a good approximation. This decomposition always provides orthogonality.

As a future study, more useful summary statistics should be developed to quantify the

results in pictures. Also more concussion and recovery data will be included and analyzed to confirm the results in this study.

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