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STUDY ON FUNCTIONAL CONNECTIVITY OF HUMAN V5 IN VISUAL CORTEX BASED ON SPATIAL INDEPENDENT COMPONENT ANALYSIS AND TEMPORAL CORRELATION

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Abstract: Functional connectivity of human V5 in different brain activity was investigated by combing spatial independent component analysis with temporal correlation. First, V5 was localized by performing spatial independent component analysis (sICA) on the data from block-design visual motion runs, then low frequency correlations between V5 and other brain regions were calculated in two steady states (resting state and the state with continuous visual motion stimulus) to detect the functional connectivity networks. The experiment indicated that: The functional connectivity network of V5 was more extensive and was consistent with the known anatomical connectivity during rest; when subjects were viewing motion, the network was limited in the visual cortex suggesting that V5 was acting in concert with a network specific to the visual motion processing task.

Key Words: Spatial ICA; Temporal correlation; Functional connectivity; Visual motion

0 Introduction

The brain appears to adhere to two fundamental principles of functional organization: functional integration and functional specialization, where the integration within and among specialized areas describes how functionally specialized areas interact and how these interactions depend on changes of context [1]. More recently the study of functional integration is based on functional connectivity and effective connectivity proposed by Friston et al[2,3].

In the analysis of neuroimaging time-series functional connectivity is defined as the correlations between spatially remote neurophysiological events[2]. This definition provides a simple characterization of functional interactions. While functional connectivity has been studied by means of electrodes placed in the brain [4], by radioisotopes administered intravenously[5], and by EEG[6], functional connectivity can now be studied with functional MR imaging (fMRI)[7]. Functionally related regions of the brain have been identified by means of their synchronous low frequency (＜0.08 Hz) fluctuations on fMRI studies. The highly correlated fluctuations in signal intensity in fMRI reflect synchronous changes in the blood oxygen-level dependent (BOLD) effect.

In this paper, we investigated the functional connectivity of human V5 in visual cortex via an analysis of correlations between regional signal fluctuations recorded in functional MR images obtained in two steady states. First region V5 was localized by performing sICA on the data from block-design visual motion runs; then low frequency correlations between V5 and other brain regions were calculated in resting state and the state with continuous visual motion stimulus to detect the functional connectivity networks.

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1 Materials and Methods

The experiment was composed of two parts: a traditional block-design visual motion processing paradigm and functional connectivity runs in which subjects rested for entire runs or in which subjects viewed moving dots for entire runs. The first part was used to identify a reference visual motion processing region (V5) for the correlations calculated in the second. In the functional connectivity runs, data from the steady state scans were used to create maps of functional connectivity to that reference region in each condition (resting and viewing motion).

1.1 Subjects

Eight healthy right-handed volunteers (five men and three women, aged 24~30) who denied previous history of neurological disorders were scanned with vision corrected to 1.5. All subjects gave informed consent in accordance with a protocol reviewed and approved by the Human Investigations Committee of the Nanjing General Hospital of PLA.

1.2 Experimental paradigm

In the first part, block-design motion localizer stimulus that alternated in time between moving and stationary dot patterns (Figure 1) was used to identify the region V5. Within a 21 deg diameter circular disk, the moving dots traveled towards and away from fixation (6 deg/sec), alternating direction once per second (white dots on a black background, dot diameter=0.25 deg). After 20 sec the moving dot field was replaced by 20 sec of a stationary dot field. This moving/stationary cycle was repeated 10 times in each fMRI scan. Subjects were instructed to maintain fixation on the center of the display.

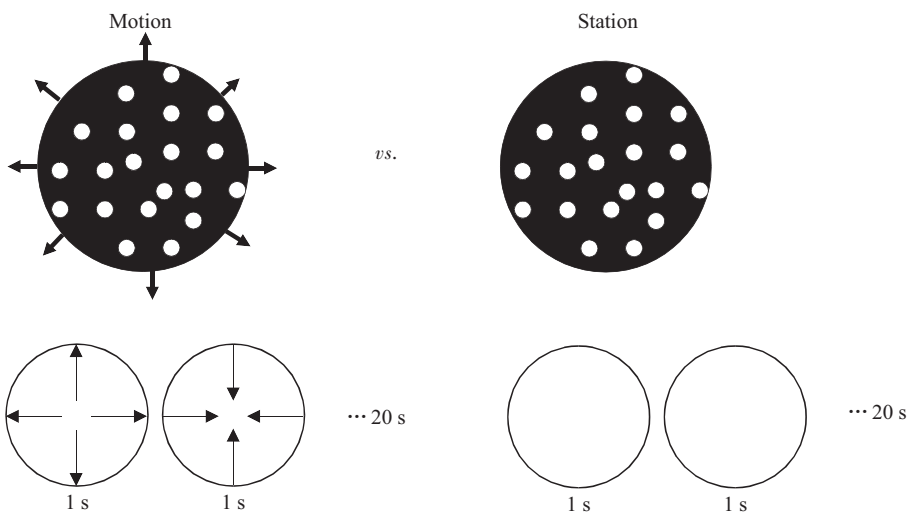

Fig.1 Block design visual motion stimulus

In the second part, in which correlation maps were defined, the time course of signal from the localized V5 region was used as a reference signal to determine which brain areas showed correlated patterns of activity during rest (with eyes closed) and in the motion condition (viewing outwardly expanding and inwardly contracting moving dots, fixating on center). These expanding and contracting moving dots were presented at the same frequency as used for the localizer. Subjects were also instructed to keep their eyes focused on the center of the display.

1.3 Data acquisition

Subjects were scanned in a GE 1.5T Signa LX scanner. T1-weighted images were acquired for anatomical identification (TR=2 000 ms, TE=50 ms, 512×512 acquisition matrix, slice thickness=4 mm, slice=23). Each functional run involved the acquisition of 200 (block-design) or 100 (steady

state) volumes. A T2*-sensitive gradient-recalled, single shot echo-planar pulse sequence was used for acquisition of these functional images (TR=2000ms, TE=50ms, 64×64 acquisition matrix, FOV=24 cm, slice thickness=4 mm , flip angle=90°).

1.4 Data analysis

Figure 2 is the flow chart of functional connectivity analysis. The specific steps are described in detail below.

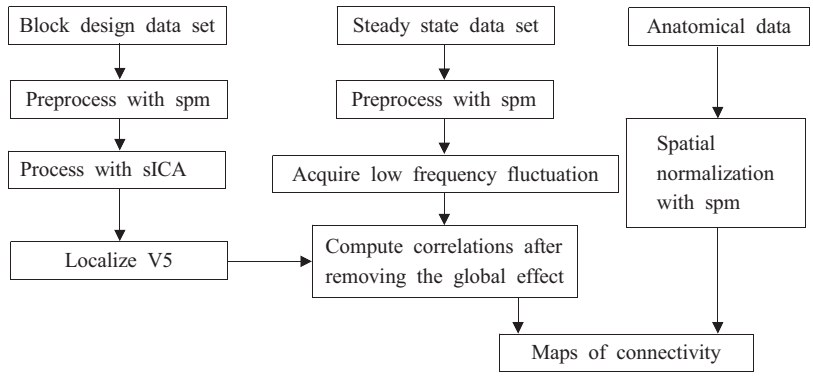

Fig.2 The flow chart of functional connectivity analysis

1.4.1 Preprocessing

Functional images were preprocessed using SPM algorithm: Images were realigned using INRIalign; data were spatially normalized into the standard Talairach space, spatially smoothed with a 6×6×6 (mm^3) full width at half-maximum Gaussian kernel. Anatomical images were also spatially normalized into the same space.

1.4.2 Localization of V5

ICA is a data-driven approach that has been used to extract linearly mixed maximally independent components and their dual time courses from fMRI data. The majority of ICA of fMRI proceeds by extracting spatially independent sources, although temporal ICA is also used. Specifically, for spatial ICA, we assume the fMRI data contains a set of sources (images) that have been linearly mixed by their fMRI time courses. Suppose X is an M-by-N matrix representing the fMRI signals (where M is the number of time points and N is the number of voxels in each scan), then it can be modeled as formula (1):

$$X_{i,j}=\sum_{k=1}^{K} A_{i,k}S_{k,j}+E_{i,j} \quad (1)$$

where i=1,2,⋯,M, j=1,2,⋯,N, S is a $K\times N$ matrix whose rows represent spatially independent components, A is a $M\times K$ mixing matrix whose columns represent the time course of the corresponding component. E is the temporal and spatial white noise. In general, the noise is also considered as an independent component[8].

In our experiment, brain regions activated by visual motion processing task were detected as follows:

1) Spatial ICA based on the FastICA algorithm, was applied to the preprocessed block-design fMRI data set, resulting in independent components whose number was priorly estimated by the Bayesian information criterion (BIC)[9].

2) The time course of each independent component was subjected to cross correlation analysis using a reference function reflecting the sequential epoch patterns of the experiment paradigm. For our data set the reference function was a standard boxcar consisting of ten alternate motion task and station control blocks, each with ten time points. The independent component which shows the largest correlation is the consistently task-related (CTR) component[10,11].

3) The CTR component was extracted and mapped onto each of the subject's own high resolution anatomical images with the same Talairach coordinates as the functional images to obtain

anatomical identification of activated areas. Voxels whose absolute z-value was greater than the threshold 2 (i.e., $|z|>2$)[11] were considered to be activated by the task.

1.4.3 Detection of the functional connectivity networks

Low-frequency (<0.08 Hz) temporal correlations with the signal from V5 were computed in the steady state following these procedures: First, the data were low-pass filtered using wavelet analysis to remove all frequencies above 0.08 Hz. Second, the global time course of the data within the imaging run was found by averaging the time course across all voxels. Third, the average time course of all voxels in V5 was found. Finally, the partial correlation between the time course of each voxel and that of V5 was found, after removing the effect of the global time course. The correlation coefficients for all voxels in the acquired volume were calculated according to formula (2):

$$cc_i=\frac{\sum[g_i(t)-\bar{g}_i][r(t)-\bar{r}]}{\sqrt{\sum[g_i(t)-\bar{g}_i]^2\sum[r(t)-\bar{r}]^2}} \quad (2)$$

where cc_i is the correlation coefficient, $r(t)$ is the reference time course from V5, $g_i(t)$ is the signal for the ith voxel, and $\bar{g}_i$, $\bar{r}$ are the average values of $g_i(t)$ and $r(t)$.

It is considered that there exists synchronous low frequency fluctuations between the ith voxel and V5 if cc_i is larger than a given threshold T. The maps of correlation i.e. the functional connectivity networks of V5 were obtained by mapping these correlative voxels onto the preprocessed anatomical images.

2 Results and Discussion

All subjects showed consistent findings as illustrated in the representative figures described below (the typical subject Xxm, female, 25), each figure shows four different slices separately (Z= –4, –2, 0, 2 mm, Talaraich coordinates).

2.1 Activation maps

Visual motion processing activated a set of brain regions. A region in the temporo-parieto-occipital junction corresponding to V5 was strongly activated as expected, allowing functional definition of a region that could be used as the reference region in the correlation analyses. The middle occipital gyrus just posterior to V5 was also significantly activated by the motion processing task (Figure 3).

2.2 Correlation maps

In the resting state, the connectivity network not only included the visual areas but also included the thalamus (Figure 4). In the state with continuous visual motion stimulus correlation to thalamus decreased significantly in magnitude, with the same threshold as resting state the thalamus couldn't be detected; however, correlations to the visual areas could be both increased and decreased. The increase can be thought as some new visual connective areas were created during this period while the decrease was due to the under-detection of some visual areas in the resting state network (Figure 5).

Under the visual stimulus of continuous motion, the functional connectivity network of region V5 is more limited as compare with the resting state. That may be explained as this: when viewing continuous visual motion, the network devotes itself in processing visual information, so it is only restricted to the visual cortex. There are two hierarchically, functionally specialized, processing pathways in human visual system: the M pathway for spatial vision and visually guided actions and the P pathway for object recognition. With continuous visual motion stimulus, the low frequency oscillations within the other visual areas in M pathway may get tuned that of the region V5, and thus creating new visual areas in the network. Otherwise, the connectivity between V5 and the areas reside outside the M pathway will be suppressed, and thus fading the visual areas in the network. The major difference between resting state and the state with continuous visual motion stimulus lies not only in motion itself, but also in the extra attention drawn by the motion. Friston et al[12] has found that the attention could enhance the effective connectivity between V1/V2 and V5. Under continuous visual motion stimulus, the new

additional visual areas in the network can also be brought forward by attentional modulation of the connectivity between V1/V2 and V5.

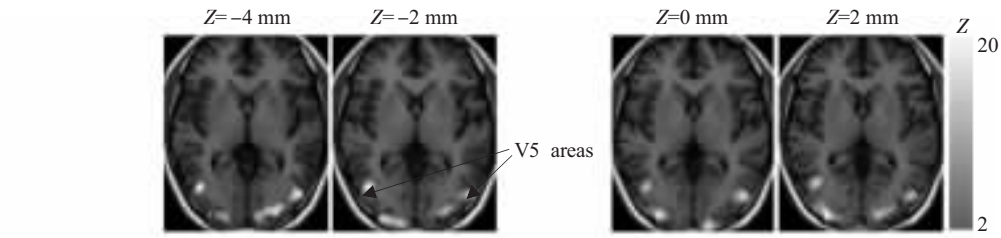

Fig.3 Activation maps of visual motion stimulus. Results are shown in Talairach space, *Z*-coordinates are shown up each slice. The color bar denotes the *z*-value of sICA, threshold is: $|z|>2$

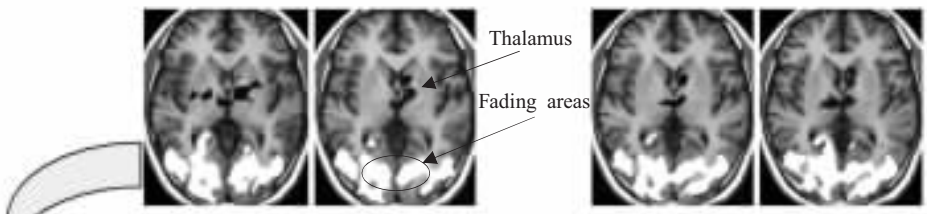

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Fig.4 Correlation maps in resting state. Results shown in Talairach space at a threshold of 0.55. White is positive correlation and black is negative. *Z*-coordinates are the same as in the activation maps

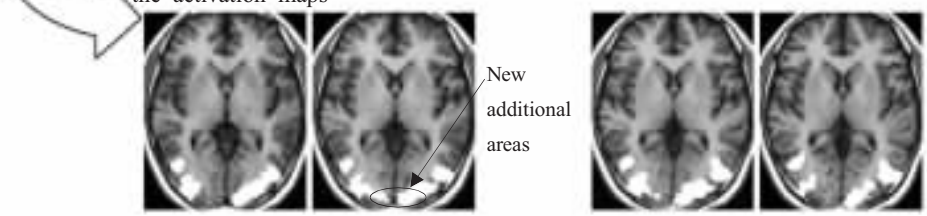

Fig.5 Correlation maps in the state with continuous visual motion stimulus. Results of positive correlation shown in Talairach space at a threshold of 0.55. *Z*-coordinates are the same as in the activation maps

3 Conclusion

Based on the synchronous low frequency fluctuation in fMRI signals, functional connectivity of the human V5 in resting state and the state with continuous visual motion stimulus was studied by combing sICA with temporal correlation. It provides a simple and efficient method for the detection of brain functional connectivity. Such scheme can be also used in the research of amblyopia. With the retinotopic mapping information of visual cortex, through the detection of abnormity of V5 functional connectivity networks for the amblyopia patients, the position of defect within the M pathway can be accurately located, and thus gives us a deeper insight into the amblyopia from the pathophysiologic point of view.

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基于空间 ICA 和时间相关方法的人脑视觉皮层 V5 区的功能连通性研究

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摘要：利用功能磁共振成像技术，将空间 ICA 和时间相关方法相结合来研究不同活动状态下人脑视觉皮层 V5 区的功能连通性。首先利用空间 ICA 处理组块视觉运动刺激的数据，定位 V5 区；然后分别计算静息和连续视觉运动刺激两种稳态下 V5 区与其它脑区低频振荡的时间相关，检测出该区的功能连通网络。实验结果表明，静息时 V5 区的功能连通网络更广泛，且与已知的解剖连通一致；当被试接受连续视觉运动刺激时，与 V5 区连通的脑区网络局限在视觉皮层，此时的网络特定于处理视觉运动这一任务。

关键词：空间 ICA；时间相关；功能连通；视觉运动

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