Chinese Science Bulletin

ARTICLES

The task dependent interaction of the deactivation regions

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Although deactivation has been found frequently in former functional brain imaging researches, only recently has it become a focus of systematic study because of its not well understood physiological mechanism. However, most of the researches concentrated on the brain areas that would present deactivation, and, to our knowledge, the deactivation connectivity between these brain areas during the cognitive tasks has rarely been reported in literature. In this work, using the functional connectivity method WICA (within-condition interregional covariance analysis), we analyzed the deactivations in two different cognitive tasks——symbol orientation and number comparison. The results revealed deactivations in the posterior cingulate, precuneus, anterior cingulate and prefrontal cortex in both tasks. However, the interaction between the deactivated regions shows many differences. Our result further indicates that the potential implication of special deactivation connectivity may be related to the different task or attention resource. Further research is needed to clarify the exact reason.

deactivation, fMRI, WICA

NEUROBIOLOGY

Deactivation has been found frequently in previous functional brain imaging researches, which refers to the decrease in the regional brain activity during the cognitive task condition in comparison with the resting state. There is no universally accepted explanation of deactivation because its physiological mechanism is not well understood, and it is only recently that it has become a focus of systematic studies.

In the research of deactivations, it has been found that certain brain regions, including dorsomedial frontal cortex, orbital frontal cortex, anterior cingulate gyrus, posterior cingulate gyrus, and angular gyrus etc.[1−4], routinely exhibit activity decreases. Because the decreases in these regions were not associated with specific cognitive tasks, they were named task-independent deactivations[3,4]. To explain this phenomenon, McKiernan and colleagues[6] advanced processing resources reallocation theory. This theory points out that decreases in cerebral blood flow are caused by interruption of ongoing internal processing that occurs in the passive or "rest" state. This model assumes that "rest" is a state of organized, functional brain activity. When the brain performs an exogenously generated task, these organized processes are suspended or interrupted, and the processing resource would be reallocated to process of the exogenous task, thus the regions that lose processing resource will show deactivations[5]. This hypothesis is supported by the current researches. Raichle et al.[5] proposed the concept of the default mode network, and the correlative researches have indicated the existence of the default mode network of the brain[4,5]. Greicius et al.[7] and Fransson[8] confirmed this hypothesis through their studies on the resting state using the functional connectivity method. This default mode network is composed

Received September 14, 2007; accepted March 2, 2008
doi: 10.1007/s11434-008-0222-8
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Supported by the National Natural Science Foundation of China (Grant Nos. 60472017 and 30670699), Ministry of Education of China (Grant No. NCET-06-0277) and the Research Fund for the Doctoral Program of Higher Education (RFDP) (Grant No. 021010)

of the brain regions that show deactivations during the cognitive tasks. These brain regions are not only active, but also cooperative with each other to sustain the various cognitive activities during the resting state. Using the functional connectivity method and ICA (interregional covariance analysis), Fransson[9] have found that the default mode network not only exists in the resting state, but also in the task state. However, the correlation is stronger in the task state than in the resting state because of the infection of the cognitive task.

However, this definition of task-independent deactivation is based on the traditional General Linear Model statistic method and the voxel Cluster Analysis method. At present, the deactivation researches mostly aim at confirming the brain regions that present the decrease of the brain blood flow, but the response mode and space-time relation from overall and dynamic angle are left untouched. Although Greicius et al.[7] and Fransson[8] has analyzed the interaction of several regions that show deactivation during the resting state, and Fransson[9] have compared the differences in the default mode network of the brain between the resting state and the task state, they neglected the interaction of deactivations under different tasks, especially the interaction of the brain regions that show deactivation during the task state.

ROI-based functional connectivity analyses[10] was employed to investigate the interaction and the law of activity of the brain regions that show deactivation during task state, and the interaction during symbol orientation task and number comparison task was analyzed. ROI-based functional connectivity analyses is a kind of functional modulation model of brain circuitry through cross-correlation analysis of BOLD signal or activation index, and with it the relation between these ROIs has been found out through comparing different ROIs in the task state with themselves in the resting state[10,11]. This method could distinctly notify the interactions between different regions in the same task and directly reflects the functional modulation in the brain circuitry[12]. In this paper, one of the ROI-based functional connectivity analyses, within-condition interregional covariance analysis (WICA), is employed to analyze the interaction of the brain regions that show deactivation during different task states.

1 Materials and methods

1.1 Subjects

Participants were 15 neurologically normal undergraduates (7 females and 8 males), ages from 21 to 25 years. All subjects were right-handed as measured by a standard Handedness Inventory[13].

1.2 Experiment design

Block design was employed, and two tasks were completed in the same scan. Either task was composed of 6 blocks, and the task block which lasted 16 s and control block which lasted 20 s were presented alternatively. During the control block, the subjects should fixate the '+' located in the centre of the screen.

The first task was symbol orientation task. The stimuli were presented as follows: two symbols (erective or slant to the right) were presented on the screen first, and the third symbol was presented in 0.5 s. Another stimulus would be presented if there were no response in 1.5 s. The subjects were asked to press the button with the left thumb if they found the orientation of the first two was consistent with the third, or press the button with the right thumb. The two buttons were balanced.

The second task was number comparison task. The stimuli were presented as follows: two numbers were presented on the screen first, and the third number was presented in 0.5 s. Another stimulus would be presented if there were no response in 1.5 s. The subjects were asked to press the button with the left thumb if they found either of the first two was bigger than the third, or press the button with the right thumb (the equal situation was excluded). The two buttons were balanced.

During the experiment, the subjects were asked to lie flat on their back with their heads fixed, both hands at their sides, and both thumbs on the buttons. White characters with the black background were presented on the screen using an LCD projector connected to a computer. The subjects responded to the stimuli presented on the screen under the prompt on the screen during the scan. All stimuli were presented and responses were recorded by E-prime software.

1.3 Data acquisition

Scanning was conducted at 1.5 Tesla on a General Electric Signa scanner. Spin-echo sequence was employed to obtain the axial T1-weighted anatomic images with 500 ms repetition time, 14 ms echo time, 7 mm slice thickness, 1 mm scanning interval, 24 cm field-of-view, and matrix size of 256×192 pixels. Functional data were collected via a multi-slice, gradient-echo, echo-planar sequence with a repetition time of 2000 ms and an echo time of 40 ms. Imaging parameters included a field-of-view of 24 cm, flip angle of 90°, slice thickness of 7 mm, scanning interval of 1 mm, and a matrix size of 64×64 pixels. Each EPI series began with four baseline images which were not included in the data analysis to allow equilibrium of the magnetic resonance signal to be reached. High-resolution, T1-weighted anatomic images were collected as a set of 70 contiguous sagittal slices (2.5 mm thick) using a 3-D fast spoiled gradient-echo sequence (FSPGR). The first 8 s of the scan were designed to show black screen, and the images acquired in that time would be taken out.

2 Data analysis and results

2.1 Behavioral results

Due to technical difficulties with the response recording software, behavioral data (accuracy and reaction time) were recorded for 13 subjects (Table 1). No significant differences in the accuracy and reaction time were found between two tasks (P<0.05).

Table 1 Behavioral results

	Accuracy (%)	Reaction time (ms)
Symbol orientation task	97.09±0.87	659.81±43.17
Number comparison task	96.34±1.21	695.57±40.39

2.2 Voxel-based statistic analysis and results

All image analyses were completed using spm99 (statistical parametric mapping, http://www.fil.ion.ucl.ac.uk/spm). All the images were realigned to the first to correct slice acquisition delays and subjects' motion. Different brain image spaces were resampled with a size of 2 mm×2 mm×2 mm. The anatomic differences between subjects were eliminated by normalizing the realigned images to standard stereo-tactic space using an EPI template (SPM99 standard template from the Montreal Neurological Institute). Subsequently, the images were smoothed with an 8 mm (FWHM) isotropic Gaussian kernel to increase the signal-to-noise ratio. After these preprocesses, fMRI model was established for every single subject, and basic model of 10 subjects was established with 5 subjects' data excluded due to too much brain motion (more than 3 mm) or incomplete behavior recorded with P<0.001 (uncorrected). The clusters larger than 10 volumes served as functional areas.

2.3 Deactivations in the two different tasks

The regions exhibiting deactivations in the symbol orientation task were posterior cingulate (BA29), medial prefrontal gyrus (BA10) and superior frontal gyrus (BA10), middle temporal gyrus (BA21) and superior temporal gyrus (BA22), cuneus (BA19), angular gyrus (BA39) and precuneus (BA7). The regions exhibiting deactivations in the number comparison task were posterior cingulate (BA29/30) extended to adjacent precuneus (BA7) and cingulate area (BA24), medial prefrontal gyrus (BA9/10) and superior frontal gyrus (BA8), middle temporal gyrus (BA21/39), superior temporal gyrus (BA22/38) and the right insula (BA13) (Figure 1).

It can be seen that in two different tasks, posterior cingulate, precuneus and prefrontal cortex have consistently presented the decrease of the brain blood flow. These results were consistent with those of previous studies[5,7]. WICA method was employed to further examine the deactivation results to see if the correlation of the regions exhibiting deactivations reflects the synchronism of the processing resource reallocation caused by the tasks.

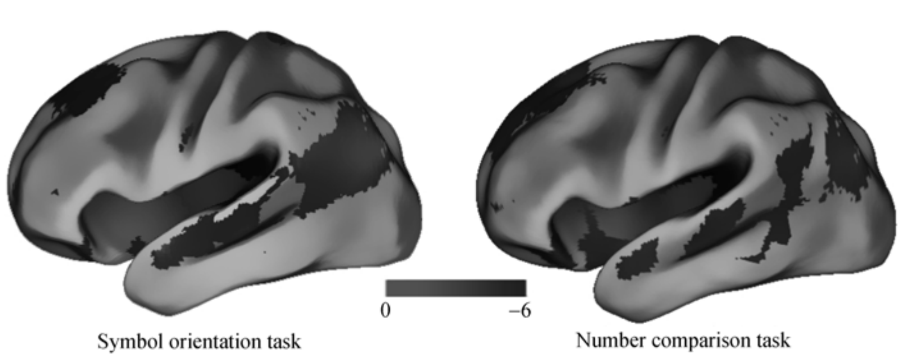

Figure 1 Deactivations in the two tasks. Left is the symbol orientation task and right is the number comparison task.

3 WICA and results

3.1 Specify the region of interest (ROI)

Data preprocessing and modeling were completed using spm99. Based on the processing resources reallocation theory, it was found that the appearance of the deactivations in the brain regions, which were acquired by the analysis of spm99, was closely related to the cognitive function of these regions during the resting state. Evidence indicates that the functions to which the posterior cingulate and precuneus contribute include the visuospatial processing[14] and the orientation of the environment[15]. The posterior precuneus had been repeatedly reported concerning conscious retrieval of episodic memory[16]. Maddock[17] suggested that the posterior cingulate might participate in emotional processing. Castelli and colleagues[18] indicated that the cognitive processes in which the dorsal medial prefrontal cortex (BA 8/9/10) and the adjacent paracingulate sulcus participate fall into two general categories: monitoring or reporting one's own mental state, and attributing mental states to others. Insula is commonly considered as an area involved in the functions of visceral sensory, visceral motor attention and emotion processes[19,20], and it is also considered to participate in sound processing and allocating auditory attention[21,22]. Therefore, five ROI were specified basing on the functions and the distribution of these deactivation regions, including prefrontal cortex, insula, precuneus, posterior cingulate and angular gyrus.

3.2 Connectivity analysis

We assume that $A_{i,j}$ is the value of the jth ROI of the ith subject in the task state in comparison with the resting state

$$A_{i,j}=\left(\frac{\sum\limits_{k\in\text{Task}} S_{i,j,k}}{T\times L}-\frac{\sum\limits_{k\in\text{Control}} S_{i,j,k}}{C\times L}\right)\Bigg/\frac{\sum\limits_{k\in\text{Control}} S_{i,j,k}}{C\times L}$$

$$(i=1, 2, \ldots, P;\ j=1, 2, \ldots, M;\ k=1, 2, \ldots, N),$$

$S_{i,j,k}$ is the signal value of the kth image of the ith subject in the jth ROI, where T and C are the numbers of the images in task duration and control during every period, and L is the number of the periods in the experiment design.

If the number of the subjects is P, then

$$A=\begin{bmatrix} A_{1,1} & A_{1,2} & \cdots & A_{1,M} \\ A_{2,1} & A_{2,2} & \cdots & A_{2,M} \\ \cdots & \cdots & \cdots & \cdots \\ A_{P,1} & A_{P,2} & \cdots & A_{P,M} \end{bmatrix}.$$

Set every rank in the matrix as a sample. M samples compare with each other by twos. Then the connection extent of the validity will be acquired, and correlation coefficient is

$$r(A_{\bullet,x}, A_{\bullet,y}) = \frac{\langle V(A_{\bullet,x},t)V(A_{\bullet,y},t)\rangle - \langle V(A_{\bullet,x},t)\rangle\langle V(A_{\bullet,y},t)\rangle}{\sigma(V(A_{\bullet,x}))\sigma(V(A_{\bullet,y}))},$$

where $V(A_{\bullet,x},t)$ is the average value of the xth ROI. $\sigma^2(V(A_{\bullet,x},t)) = \langle V(A_{\bullet,x},t)^2\rangle - \langle V(A_{\bullet,x},t)\rangle^2$, $\langle\bullet\rangle$ being the average of time. As the correlation coefficient between these two regions tends toward one, the relativity of them will be stronger; if the correlation coefficient tends toward zero, meaning that there is no modulation on their connectivity even though these two regions could be anatomically connected[10−12].

3.3 Results of the WICA method

The results indicated that: in the symbol orientation task, posterior cingulate, angular gyrus and precuneus showed comparatively strong relativity (Table 2); in the number comparison task, prefrontal cortex, insula, precuneus and angular gyrus showed comparatively strong relativity, especially the relativity between the insula and prefrontal cortex was the strongest (0.698) (Table 3).

In the symbol orientation task, the adjacent regions including posterior cingulate, angular gyrus and precuneus, constituted a cycle with relativity; and in the number comparison task, the relativity between prefrontal cortex, insula, precuneus and angular gyrus were stronger than between posterior cingulate, angular gyrus and precuneus. Thus these regions also constituted a cycle (Figure 2).

Table 2 Correlation coefficient between the ROIs in the symbol orientation task

	Prefrontal cortex	Insula	Precuneus	Posterior cingulate	Angular gyrus
Prefrontal cortex	1				
Insula	0.107788	1			
Precuneus	0.083483	0.049131	1		
Posterior cingulate	–0.13037	0.179851	0.428231	1	
Angular gyrus	0.172896	0.070828	0.852324	0.35589	1

Table 3 Correlation coefficient between the ROIs in the number comparison task

	Prefrontal cortex	Insula	Precuneus	Posterior cingulate	Angular gyrus
Prefrontal cortex	1				
Insula	0.698243	1			
Precuneus	0.62416	0.539097	1		
Posterior cingulate	0.206472	0.155001	0.357328	1	
Angular gyrus	0.483952	0.458169	0.247996	–0.20335	1

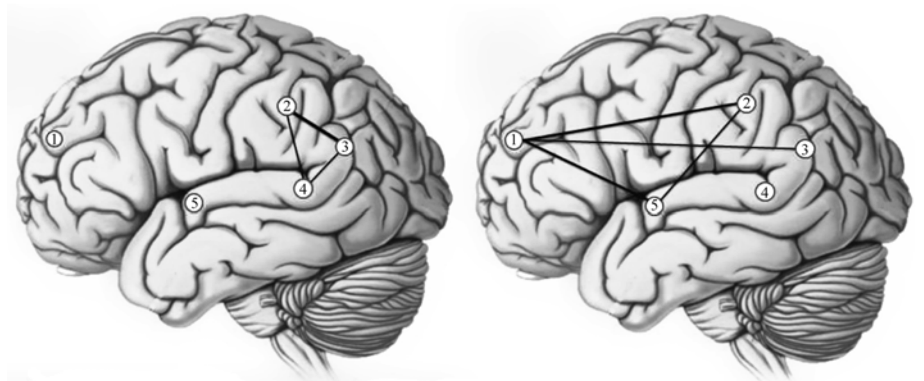

Figure 2 Sketch map of the WICA results (just the linked regions that had the strongest relativity). (a) The symbol orientation task; (b) the number comparison task. 1, Prefrontal cortex; 2, precuneus; 3, angular gyrus; 4, posterior cingulate; 5, insula.

4 Discussion

Consistent decreases had been found in the regions including posterior cingulate, precuneus, prefrontal cortex, etc. during two different tasks, suggesting that the deactivations in those areas were task independent. Previous studies have shown that deactivation areas mainly occurred in the process of monitoring the external environment, the internal sensory state and emotional processes that are incognizant, and default activities that sustain the cognitive activity during the resting state. During the experiment, these organized processes are suspended or interrupted, and the processing resource would be reallocated to process the exogenous task; thus the regions that lose processing resource will show deactivations[14,22].

WICA method was employed to further explore the deactivation regions. The results showed that although prefrontal cortex, precuneus, angular gyrus, posterior cingulate and insula presented significant deactivation during the two tasks—symbol orientation and number comparison, the interaction mode between the deactivated regions shows many differences: in the symbol orientation task, posterior cingulate, angular gyrus and precuneus showed comparatively strong relativity; but in the number comparison task, prefrontal cortex, insula, precuneus and angular gyrus showed comparatively strong relativity, especially the relativity between the insula and prefrontal cortex was the strongest. Thus we suggested that the interaction between the deactivation regions may be related to the difference in the tasks. In the research of activity, the relativity of the different regions reflects their ability to work together during the exogenous task, while in the situation of deactivation, the relativity reflects the synchronism of the processing resource reallocation caused by the tasks in these regions. The symbol orientation task is only concerned with the orientation and the judgment of the direction, and needs little processing resource. Previous studies have indicated that posterior cingulate and adjacent precuneus are the core regions in the resting state[23]; thus the processing resource would be easily reallocated from there to process of the exogenous task. Therefore, in such a simple cognitive task, only posterior cingulate and adjacent precuneus synchronously presented deactivation. Numerical processing is one of the foremost thought forms to the humans, and involves more advanced cognitive functions than the symbol orientation task. Dehaene and Cohen[24] has proposed a triple code model of the processing that distinguishes between an auditory verbal code, a visual code for Arabic digits, and an analog magnitude code that represents numerical quantities as variable distributions of brain activation.

These functions need frontal lobe and parietal-temporal-occipital association area to work together. The researches of the brain imaging indicated that there is a neural network participating in the numerical processing, including prefrontal cortex, parietal lobe, occipital lobe and cerebellum. When these regions worked together to accomplish the number comparison task, more processing resource reallocation in these areas was induced than that of the symbol orientation task. Especially, the great demand of processing resource in the frontal lobe and parietal lobe cortex resulted in the synchronous deactivation in the precuneus, insula, posterior cingulate gyrus and frontal lobe, and the notable strong relativity between these regions. Therefore, although deactivations presented consistency during different tasks, the interaction between the deactivated regions showed many differences according to different cognitive tasks. However, further research is needed to clarify the exact reason of these interactions.

5 Conclusion

In this paper, WICA method was employed to analyze the deactivations in two different cognitive tasks. Although the results revealed task independent deactivations, the interaction between the deactivated regions showed many differences. The relativity of the deactivation regions reflected the synchronism of the processing resource reallocation caused by the tasks in these regions. Our result further indicates that the potential implication of special deactivation connectivity may be related to the different tasks or attention resource, whereas further research is needed to clarify the exact reason. These results open up a new perspective and are of great significance in the research of the deactivations in the future.

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