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Deactivations during the numerical processing

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Deactivation has been encountered frequently in functional brain imaging researches. However, the deactivations during the numerical processing have not been reported yet. In this study, the functional magnetic resonance imaging (fMRI) was employed to investigate the pattern of the deactivation in the brain of 15 healthy subjects during the numerical addition task. Analyses revealed significant deactivations in several brain regions, including the posterior cingulate, precuneus, anterior cingulate and prefrontal cortex. Especially, we found notable deactivation in bilateral insula. Accounting for the cognitive functions of these regions participating in a combinated way, we discuss their contributions in sustaining the brain activity during conscious resting state, and indicate that the insula is an important area of gathering auditory information from the external world.

fMRI, numerical addition, deactivation, insula, resting state

As a non-invasive imaging method, fMRI has been widely employed in human brain functional imaging researches. A fundamental aspect of fMRI experimentation is the identification of a control or resting state against which the cognitive task condition of interest can be compared. And there are two opposite results of the comparison: the increase of regional brain activity referred to as activation, and the decrease referred to as deactivation. Although deactivation has been encountered frequently in functional brain imaging researches, it is only recently that it became the focus of systematic studies because its physiological mechanism is not well understood[1].

There are several explanations of the deactivation. One is that deactivation arises simply on the basis of how control tasks and tasks of interest are manipulated in the image-analysis strategy. For example, while comparing a visual task and a non-visual task, the change of the blood flow in visual areas will be identified as activation if the non-visual task was taken as the control task, and reversely, the change will be identified as deactivation. Although this explanation does not involve the specific concepts of brain physiology, it cannot be completely denied because sometimes the information of the experiment tasks and operations is insufficient[2]. Another brain haemodynamics related explanation on deactivation was proposed that during the task state regional blood flow diverts from the adjacent areas in which the regional blood flow decreases to the task-related regions to meet the activation issue's need. This phenomenon is named 'vascular-steal'[3]. This explanation could be valid in the level of microvasculature[4], but there seems to be no physiological need to 'steal' because the haemodynamic reserve of the brain is so large that it could accommodate the relatively small blood flow increase (approximately 10% relative to the overall blood flow of the cortex) induced by the brain cognitive activity[5]. During the performance of various kinds of attention-demanding cognitive tasks，certain brain regions, including posterior cingulate gyrus[6−9]

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that often extends dorsally into the cuneus[6,8], dorsomedial frontal cortex in the middle and superior frontal gyri, anterior cingulate gyrus, typically extend ventrally into the gyrus rectus and the orbital frontal cortex, and angular gyrus[6−9], routinely exhibit activity decreases.

Because the decreases in these regions were not associated with specific cognitive tasks, they were named task-independent deactivations[8,9]. Based on this phenomenon, processing resources reallocation theory was proposed that deactivation was induced by the reallocation of those resources during the task state[2,10]. The regions that exhibit task independent deactivations are active in the resting state; and composing a network sustaining some cognitive functions[9] including monitoring the external environment, monitoring the internal sensory state and body image, emotional processes, and ongoing inner ‘thought’, which are usually spontaneous, self-referential, and independent of specific cognitive task[6,9]. When attention-demanding cognitive tasks are performed, those organized processes might be disturbed or interrupted, and the processing resource would be reallocated from internally generated information processing to process of the exogenous task; thus the regions that lose processing resource will show deactivations whereas the regions obtaining the resources will show activations.

McKiernan and colleagues[11] have found that the magnitude of the deactivation changes with the difficulty in the cognitive task. Numerical addition task involving visual processes, episodic memory, numerical operation and other cognitive processes is representative of deactivation researches. Therefore, a numerical addition experiment was employed to explore the deactivation in numerical processes. Here its physical mechanism is preliminarily discussed.

1 Materials and methods

1.1 Subjects

Participants were 15 neurologically normal undergraduates (8 females and 7 males), ages from 18 to 25 years. All subjects were right-handed as measured by a standard Handedness Inventory[12].

1.2 Experiment design

The intention of this experiment is to explore the deactivations during numerical addition task. Block design was employed and the task block and control block were presented alternatively. The stimuli were presented as follows: two numbers were presented on the screen first, and the third number was presented in 0.5 s. The subjects were asked to press the right button if they found the summation of the first two was bigger than the third, or press the left button (the equal situation was excluded). The two buttons were balanced. During the control block, the subjects should fixate the ‘+’ located in the centre of the screen. All stimuli were presented and responses were recorded by E-prime software (Version 1.1).

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, 1mm scanning interval, 24 cm field-of-view, and matrix size of 256 by 192 pixels. Functional data were collected via a multi-slice, gradient-echo, echo-planar sequence with 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 by 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).

1.4 Data analysis

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. 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 12 subjects was established with 3 subjects’ data excluded either for too much brain motion (the motion was greater than 3 mm in 2 of the 3-D of the SPM standard) or for incomplete behavior recorded with $P<0.001$(uncorrected). The clusters larger than 10 volumes served as functional areas[13].

2 fMRI results

During the numerical addition task, significant activations were found in the left superior frontal gyrus, middle frontal gyrus, parietal lobe, middle occipital gyrus and fusiform gyrus. This is identical to our previous study[14]. The regions exhibiting deactivations were posterior cingulate (BA29/30) extended to adjacent precuneus and cingulate area (BA31), anterior cingulate (BA42), medial prefrontal gyrus (BA9/10) and superior frontal gyrus (BA8), middle temporal gyrus (BA21/39) and superior temporal gyrus (BA22), bilateral insula (BA13) (Figures 1 and 2; Table 1).

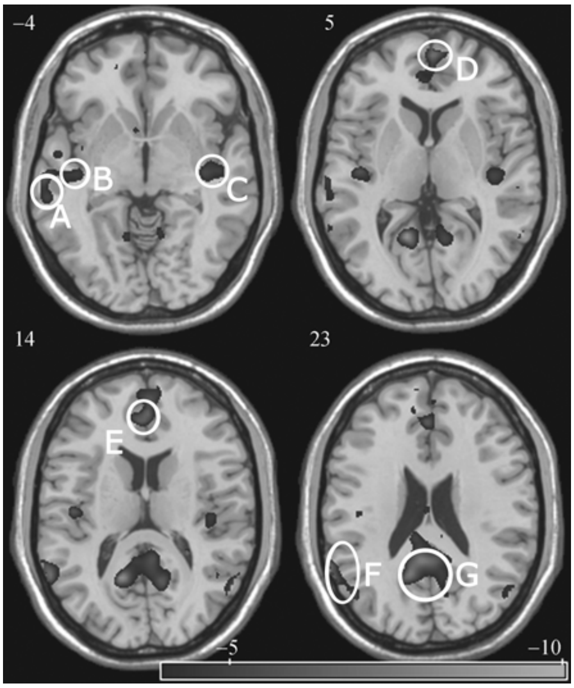

Figure 1 The regions presented significant deactivations. A, Middle temporal gyrus (BA21); B, left insula (BA13); C, right insula (BA13); D, anterior cingulate (BA32/42); E, left medial frontal (BA9/10); F, middle temporal gyrus and superior temporal gyrus; G, posterior cingulate (BA29/30) and adjacent precuneus.

3 Discussion

The deactivation result was consistent with previous studies. Compared with the PET experiment involving 197 subjects who performed different kinds of tasks finished by Shulman and colleagues[6,7] by using large meta-analysis, common deactivations were found in posterior cingulate, precuneus, left frontal and anterior cingulate. Binder et al.'s results[8] reported in the fMRI study of rest were also in remarkable agreement with ours at the level of the posterior cingulate, anterior cingulate and superior frontal gyrus. Compared with Mazoyer et al.'s meta-analysis of 9 tasks experiment[9], common deactivations areas were precuneus and posterior cingulate, angular, middle frontal cortex and anterior cingulate. Although numeric addition experiment employed a different task which included language stimulus, visual motion, mental arithmetic, visual mental imagery and self-paced finger motion from those experiments, common decreases were observed in posterior cingulate, precuneus, anterior cingulate, etc.; therefore, the deactivations in those areas were task independent.

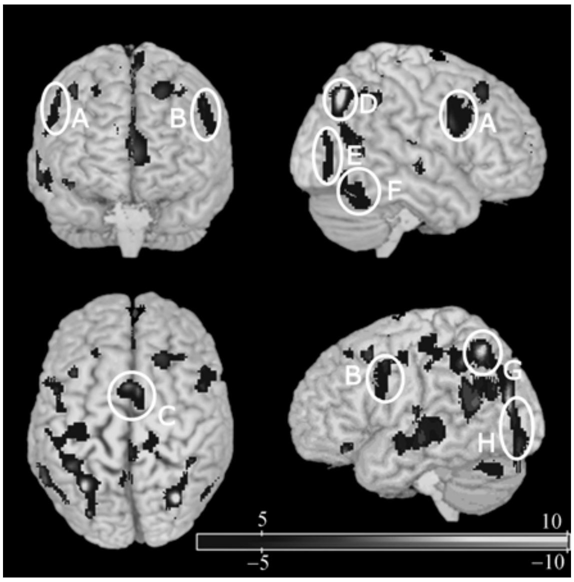

Figure 2 The activations and deactivations over the whole brain. A, Right middle frontal gyrus and inferior frontal gyrus; B, left middle frontal gyrus and inferior frontal gyrus; C, superior frontal gyrus; D, right parietal lobel; E, right middle occipital gyrus; F, right fusiform gyrus; G, left parietal lobel; H, left middle occipital gyrus.

Those areas that present deactivation across various tasks have significant functions during the resting state. Evidence indicates that the functions to which the posterior cingulate and precuneus contribute include the visuospatial processing[2]. Additionally, animal studies indicate that these regions are involved in the orientation within the environment[15]. Therefore, posterior cingulate cortex and adjacent precuneus might be active regions that continuously gather information about the world around and possibly within us. Additionally, the posterior precuneus had been repeatedly reported con-

Table 1 MNI coordinates for areas that show maximal deactivation during numeric addition task

Atlas structure	Brodmann's area	MNI Coordinates			*Z*-score
		MNI coordinates	*Z*-score	atlas structure	
Posterior cingulate (L)	29/30	–12	–58	10	–5.16
Cingulate gyrus (L)	31	–6	–30	28	–4.72
Superior temporal gyrus (L)	22	–58	–58	16	–4.43
Middle temporal gyrus (L)	39	–46	–70	28	–3.98
Medial frontal gyrus (R)	9/10	4	58	6	–4.30
Anterior cingulate (R)	32/42	4	48	10	–4.17
Middle frontal gyrus (L)	8	–38	16	48	–4.23
Middle temporal gyrus (L)	21	–62	–20	–10	–4.06
Insula (L)	13	–44	–16	12	–4.05
Superior frontal gyrus (R)	8	22	28	50	–4.04
Middle frontal gyrus (R)	8	38	28	52	–3.99
Superior temporal gyrus (R)	22/39	62	–56	8	–3.94
Middle temporal gyrus (R)	22	58	–62	12	–3.72
Insula (R)	13	40	–16	4	–3.71
Superior frontal gyrus (L)	8	–22	30	50	–3.38

cerning conscious retrieval of episodic memory[16]. In a review of 51 emotion-related studies, Maddock[17] suggested that the posterior cingulate and retrosplenial cortex might participate in emotional processing, which is also supported by observations in the fields of psychology and communication[18]. Donaldson et al.[19] suggested the left superior temporal gyrus (BA19) and the middle temporal gyrus (BA39) might be engaged in the retrieval of episodic memory information, and they made the specific point that this process need not be controlled or driven by current task demands of the resting state. Castelli and colleagues[20] indicated that the cognitive processes in which the dorsal medial prefrontal cortex (BA 8—10) and the adjacent paracingulate sulcus participate fall into two general categories. The first involves monitoring or reporting one's own mental state, such as self-generated thoughts, intended speech and emotions. The second category of functions which this region involves is attributing mental states to others. Furthermore, Friths[21] have postulated that these regions are concerned with explicit representations of states of oneself. Anterior cingulate cortex is involved in many functions such as cognitive and emotional processing, receiving a range of sensory information from the external environment, and monitoring one's own mental state[22].

Especially, notable deactivation was found in bilateral insula. Insula is commonly considered as an area involved in the functions of visceral sensory, visceral motor attention and emotion processes[23,24]. Engelien et al.[25] indicated that the insula of the normal subjects are obviously activated by passively listening to sounds and maybe thus participate in sound processing. There is converging evidence that the insula, as an integral component of the central auditory nervous system, whose bilateral damage may result in total agnosia, is not only involved in sound detection and entry of the sound into awareness, but also in allocating auditory attention[26]. Therefore, by combining the functions in which insula participates, including auditory information processing, monitoring/gathering auditory information from the external, and inverting the sound into consciousness, we suggest that insula, the same as the PCC, precuneus, and ACC, is an active area during the resting state. In the state without any task, insula is responsible for monitoring/gathering auditory information from the external (such as the sounds in the outside environment, the noise of the MRI instruments), and monitoring the self state and the outside world with the adjacent ACC and dorsolateral prefrontal cortex. During the numerical addition task (without auditory stimuli), because of the various functions with which the task is concerned, such as visual processes, episodic memory, numerical operation and other cognitive processes, the processing resources in the brain were reallocated from the insula to the exogenous task-related areas, thus the insula area presented deactivation. Although no similar report was found in the previous studies of deactivation made by Binder et al.[8], Mazoyer et al.[9], McKiernan et al.[11], it may arise from the difference in the task, because auditory stimuli were included in their experiments. During the small-field optokinetic stimulation experiment, consisting with our results, Dieterich et al.[27] found significant deactivation in the insula area, which may be attributable to their pure visual stimuli. Because of the variety of the functions the insula is involved in, more studies of the cause for the deactivation in insula will be required.

In brief, deactivation areas mainly participate in monitoring the external environment, the internal sensory state and emotional processes which are incognizant, and default activities that sustain the cognitive activity during the resting state. The reallocation of resources processing is automatic for its persistent use, but not the instant result of task performance. Only when performing task attentively, will the activity of gathering broad information curtail[10]. McKiernan et al.[28] found out the task difficulty level is positively correlated with task induced deactivation (TID) magnitude whereas it correlated with task unrelated thoughts (TUTs) negatively. TUTs refers to the ongoing, internally generated, task independent processing during the resting state, such as monitoring of the external environment and us, working memory retrieval, etc. TUTs will decrease when there is processing resources reallocation induced by the external task. As the task difficulty increases, more resources would be needed and TUTs decrease, and correspondingly, more significant deactivations would be found. Therefore, there is a close relationship between the deactivations and the cognitive activities during the resting state. And the researches on deactivations provide a quantitative way to investigate the cognitive activities during the resting state and clinical evidence[29,30].

4 Conclusion

During the numerical processing, we found significant deactivations in several regions, including the posterior cingulate, precuneus, anterior cingulate and prefrontal cortex, by which the cognitive activities during the conscious resting state in human brain is sustained. Significant deactivation in bilateral insula is also found. Accounting for the cognitive functions in which insula participates, such as visceral sensory, visceral motor, attention, and emotion processes, especially the significant functions in the auditory cognition in a combinated way, we suggest that the insula is an important area of gathering auditory information from the external during the resting state. These results add to a growing understanding of the function of insula and the deactivations.

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