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Cortical mechanisms involved in selective interactions of negative emotion with spatial and verbal working memory: An fMRI study

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ABSTRACT

Background: Negative emotional state might selectively modulate spatial cognitive activities but not verbal cognitive activities, since both negative mood and spatial cognition are right hemisphere dominant. To test the hypothesis, we used functional magnetic resonance imaging (fMRI) to assess the influence of negative emotion on brain activities associated with spatial and verbal working memory (WM). **Results:** With a modified n-back task, fMRI data showed as compared with neutral emotion, negative emotion elicited increased activities in right insula, right medial frontal gyrus and right anterior cingulate. The contrast between spatial WM and verbal WM showed a right-sided dominance in the superior occipital gyrus for spatial WM, and a left-sided dominance in the middle frontal cortex for verbal WM. Furthermore, ROI analysis suggested that the region relevant to spatial WM task was affected by negative emotion. The same emotion effect was not observed in the region relevant to verbal WM task. **Conclusion:** The main findings from this study indicate significant right hemisphere lateralization of negative emotion and a right-sided dominance in spatial WM, which suggests the neural resource competition on the same dominant hemisphere as the neural basis of the selective influence of negative emotion on spatial WM.

KEYWORDS

Emotion;
Working memory;
Hemispheric asymmetry;
Functional MRI.

BACKGROUND

A large number of studies of the impact of various emotional states on attention, decision-making, and implicit/explicit memory have shown that some of these interactions are diffuse or nonspecific. For example, the cognitive resource model suggests that emotional states, regardless of type, take up resources that would be no longer available for other cognitive activities, and, as a result, most cognitive processes are impacted by negative or positive emotional state in the same way[14-17]. Other studies revealed more specific and selective interactions. For instance, positive mood can improve performance of creative tasks and decision-making[1,21,22] and reduces performance of deductive tasks and planning[35,42]. These inconsistent findings suggest that the emotion-cognition interaction is task dependent.

According to the "hemispheric asymmetry" view on emotion-cognition interaction, impact of emotional states on cognitive functions could be largely affected by the hemispheric dominance of the corresponding emotional and cognitive neural activations[18,19,43,44,48]. Specifically, the left cerebral hemisphere may be specialized for processing positive or approach-related emotions while the right hemisphere may be specialized for processing negative or withdrawal-related emotions[12,51], cognitive functions could be either interfered (because of neural resource competition) or facilitated (because of increased arousal) by an emotional state of the same hemispheric dominance[13,19,20,41].

Working memory tasks are often used in studies examining cognition-emotion interaction. This is because, on one hand, processing efficiency theory suggests that effects of negative emotion (i.e. anxiety) on cognitive performance may be mediated by effects on WM[15]; on the other hand, verbal and spatial WM networks are relatively hemisphere biased with the former extending more into the left prefrontal cortices (PFC) (e.g. Broca's area, supplementary motor and premotor areas) and the latter depending more on right PFC (e.g. premotor areas)[45-47]. As both spatial WM and negative emotion have right hemisphere dominance, spatial WM is more likely to interact with negative emotion than verbal WM.

There are several behavioral studies that have reported evidence supporting the hemispheric asymmetry view of emotion-cognition interaction. For example, Gray[18] used short videos to induce emotional states of approach, neutral, or withdrawal in experiment participants and asked them to perform a spatial or verbal 2-back task afterwards. The results showed that spatial task performance was enhanced by the withdrawal state and impaired by an approach state and the opposite pattern held for verbal task performance. Later, Lavric et al.[28] and Shackman et al.[43] used electric shock to induce anticipated anxiety and examined the interaction of this induced anxiety and the two types WM. They found the anticipated anxiety disrupted selectively the performance of spatial WM, but not that of verbal WM.

Besides hemisphere asymmetry, attentional resource competition is another possible explanation for the selective modulation of emotion on WM. Lavric and colleagues[28] discussed that threat-evoked anxiety and spatial WM may rely on a common visuospatial attention mechanism. Because negative affects usually draw visuospatial attention (e.g. attending to potential threat), which is also essential to spatial WM[2,3,38], there could be an attentional resource competition between negative affects and spatial WM[28,31]. In contrast, verbal WM may be less affected by this competition it primarily depends on phonological processes[5,40].

The neural mechanism underlying selective impact of emotion on WM has also been investigated by previous psychophysiological and functional neuroimaging studies. With fMRI Gray and colleagues[19] examined the effects of prior emotional mood on a 3-back face and verbal WM function. Their data showed impaired and enhanced WM performance for faces in positive and negative mood, respectively; but WM performance for words exhibited the reverse pattern. In addition, they reported that fMRI signal changes in the bilateral prefrontal cortices (BA9) correlated with these behavioral performances therefore could be responsible for the integration of emotion and cognition. However, this study did not directly examine the role of hemispheric dominance in interactions of emotion and cognition. Possibly, it was because that the prior mood may have relatively indirect modulation on task-related activations, which may not be strong enough to show direct competitive effect[43].

In our prior event-related potential (ERP) study[31], reductions of positive components in memory evoked potentials were observed during negative emotion and this emotion effect was greater in spatial than in verbal WM task. We did not observe hemispheric difference in the emotion effect, possibly because of the lower spatial resolution of ERP technique.

In the current study, we aimed to test the impact of task-irrelevant emotional context on WM and fMRI was used to provide evidence for a specialization or fractionation of this psychological function. In contrast to most previous studies, IAPS pictures as the task-irrelevant distracters were interspersed into the experimental trials, which induced a rather direct modulation of task relevant activation and mild mood could be induced by presenting aversive and neutral pictures respectively in two sessions. Prior ERP study showed that self-reported positive affective and negative affective scale (PANAS) scores between the negative and neutral pictures sessions were changed prominently, which suggested that watching aversive pictures was able to induce the participants' negative emotions[31]. We hypothesized that the selective influence of negative emotion on spatial WM is based on hemisphere asymmetry mechanism, and right hemispheric cortex is mostly involved in emotional effect of spatial WM.

METHODS

Participants

Twelve students (6M6F, 25± 4.1 y.o.) at Emory University participated in the present study. They were all right-handed with normal or corrected-to-normal vision and had no history of neurological/psychiatric disorder. All participants gave informed consent (in accordance with Emory University's Institutional Review Board) and received monetary compensation for their time.

Stimulus

The emotional distracting stimulus set consisted of 84 digitized color pictures selected from the International Affective Picture System (IAPS)[27]. Among these pictures, 42 were emotionally aversive (e.g. criminal assault) and the other 42 were emotionally neutral (e.g. kitchen utensil). The aversive pictures were significantly different from the neutral ones in valence (2.09 vs. 5.00, $p<0.001$) and arousal (6.42 vs. 2.96, $p<0.001$) scores. The memory stimuli were a set of 12 English letters in uppercase. During the presentation, a letter could randomly appear at 1 of 12 positions that concentrically distributed on 2 imaginary circles with a radius of 2 and 6 cm. Stimuli were presented using E-PRIME software (Psychology Software Tools, Pittsburgh, PA) and back-projected onto a screen viewed by the subject via a mirror.

Task

A block-design paradigm was used in the present study with subjects performing either a 2-back verbal or spatial WM task during the fMRI scans. The stimuli for these two tasks were identical and tasks were distinguished only by instructions. All task trials had the following stimulus presenting sequence (see Figure 1): an IAPS picture at the center of screen (1500 ms), a fixation cross (250 ms), a capital letter display (at random locations, 250 ms) and finally another fixation cross (500 ms). In the verbal WM task, participants were instructed to indicate (by pressing one of 2 buttons on MR-compatible response box) whether the letter being presented was the same as ("match") or different from ("non-match") the one shown two letters before (hence, 2-back). In the spatial task, the participants were asked to make the same 2-back decision based on the letter location instead of their identity. Participants were instructed to pay attention only to the relevant attribute of the stimuli (either location or identity of the letters) depending on the task and ignore the distracting pictures. The match and non-match stimuli were pseudo-randomly distributed in the displaying list with equal occurring probability. In the fMRI scans, the spatial and verbal WM task blocks were alternating with control blocks. The control blocks had trials with the same structure as the task ones except that the distracting pictures were scrambled and the letters were displayed upside down at the center of screen. No response was required in the control blocks. Each WM and control block consisted of 17 and 11 trials, respectively.

FMRI data were acquired in a single scan run, with the aversive distracting pictures applied continuously in halve of the scan time and the neutral distracting pictures applied continuously in the other half. The order of the distracting conditions was counter balanced in different participants. This approach was used because a stable emotion-WM interaction requires a relatively constant emotional mood[31]. There were totally 4 task blocks for each of the possible combinations of emotion and WM condition: negative (distraction)-verbal (WM), negative-spatial, neutral-verbal, and neutral-spatial. WM task blocks were pseudo-randomly distributed in the scan with a control block between every two task blocks.

During the whole fMRI scan, galvanic skin response (GSR) was measured via a "BIOPAC MP-100" GSR recorder (BIOPAC Systems, Inc) with two electrodes attached to the palmar end of the index and middle fingers.

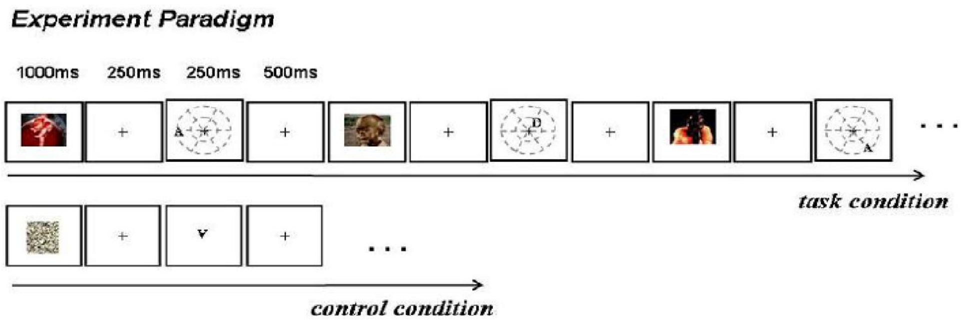

Figure 1 : Schematic diagram of the task trails in WM (top row) and control (bottom row) conditions with stimulus timing depicted. Dash line indicated the two imaginary circles with a radius of 2 and 6 cm and the cross dots where the upper letter presents on.

Imaging data acquisition

Functional and anatomical MRI data were collected with a Siemens 3T Trio scanner (Siemens Medical Solutions, Malvern, PA). For fMRI, T2*-weighted EPI images were acquired (492 volumes, 30 axial slices, slice thickness=4mm, slice gap=0mm, FOV=220mm, matrix=64×64, TR=2500msec, TE=34msec, flip angle=90°). Following the functional scan, a high-resolution, T1-weighted anatomical volume was acquired using an "MPRAGE" sequence.

Data analysis

AFNI (http://afni.nimh.nih.gov) was used for fMRI data analysis. After slice timing correction, volume registration and 5mm FWHM Gaussian smoothing, activation maps were derived for each subject with a multiple regression analysis. The regressors were generated by convolving the 4 conditions' (negative/neutral × verbal/spatial) boxcar stimulation functions with a previously reported hemodynamic response function[8]. The 6 rigid body head motion parameters (X, Y, Z displacements and roll, pitch, yaw rotations) were also included in this multiple regression to account for motion-related signal variation. To obtain group activation maps, a random-effects within-group analysis of variance (ANOVA) was performed with a 2 (emotional state, neutral vs. negative) × 2 (memory type, verbal vs. spatial) design. The activation maps were generated at a threshold of $p<0.001$ (uncorrected).

Based on the voxel-wise ANOVA results, additional analysis was performed using regression coefficients extracted from a set of regions of interest (ROIs) that defined by the main and interaction effects: (i) in clusters with significant task main effect, impact of emotional distractions were examined; (ii) in clusters with significant emotion main effect, task by emotion interactions were examined; (iii) in clusters with significant task-emotion interaction, we examined specifically how the two factors were affecting each other.

The GSR data was analyzed using Acknowledge software. Since the fMRI scan consisted of two separate emotional state sessions, the GSR data was divided into two parts with one negative emotion and the other neutral emotion. The mean amplitude of GSR in each part was measured using the Acknowledge software and paired t-test was conducted on the mean amplitudes of GSR between negative emotion and neutral emotion in eight subjects.

RESULTS

Behavioral data

The 2 (memory type, spatial vs. verbal) × 2 (emotional state, negative vs. neutral) ANOVA showed significant emotion ($F(1, 11) = 6.371$, $p=0.028$) and interaction effect ($F(1, 11) = 7.833$, $p=0.017$) in the data of memory accuracy. As shown in the TABLE 1, accuracy of spatial task was significantly reduced than the verbal task during the negative-emotion condition ($t(11) = -3.364$, $p=0.006$). In order to make sure the normality-assumption of the parametric statistics, the accuracy scores were log-transformed and put into the ANOVA analysis. The significant main effect of emotion ($F(1, 11) = 6.476$, $p=0.027$) and interaction effect ($F(1, 11) = 7.001$, $p=0.023$) were observed again.

For the reaction time (RT), no significant main or interaction effects were revealed by the ANOVA. However, there was a tendency of longer RT under the negative-emotion condition in both the spatial and verbal tasks. These behavioral results replicated the previous observations of the impact of anxious emotion on spatial and verbal WM[28,43].

GSR data

GSR was recorded in 10 of the 12 subjects. Because the electrodes fell off during the scans in 2 of the 10 subjects, GSR data of 8 subjects were finally usable. All GSR data was shown in TABLE 2. The mean amplitude of GSR was greater in negative emotion compared to neutral emotion in six of the subjects, the difference reaching a significance level of $p<0.05$ in the eight subjects ($t(7)=2.66$, $p=0.032$).

FMRI data

(a) Main memory effect

The main effect of task type was determined by contrasting regression coefficients of the spatial WM condition with the verbal WM condition. Right superior occipital gyrus (BA19) was more activated in the spatial WM task, as compared with the verbal WM. In contrast, the verbal WM evoked more activation in the left middle frontal gyrus (BA46/45) (see TABLE 3).

In ROI data analysis, the 2 (memory type, spatial vs. verbal) × 2 (emotional state, negative vs. neutral) ANOVA on the right superior occipital gyrus and left middle frontal gyrus revealed significant main effects of memory again ($F(1, 11) = 22.46776$, $p=0.0006$, $F(1, 11) = 31.99$, $p=0.0001$, respectively). In addition, a significant emotion effect was shown in the right superior occipital gyrus during the spatial WM task ($t(11)=2.47$, $p=0.03$). However, the same emotion effect was not observed in the left middle frontal gyrus during the verbal WM task ($t(11)=-0.39$, $p=0.7$). The ROI analysis suggested that the region relevant to spatial information processing, but not relevant to verbal information processing, was affected by negative emotion (see Figure 2).

TABLE 1 : Mean and standard deviation of response time (RT) and accuracy

Emotion state	Task type	RT (ms)	Accuracy
Negative emotion	Spatial WM	475±92	0.824±0.17
	Verbal WM	490±89	0.800±0.16
Neutral emotion	Spatial WM	497±103	0.753±0.20
	Verbal WM	508±87	0.796±0.17

TABLE 2 : The mean amplitude of GSR in negative emotion and neutral emotion in eight subjects

Subject (No.)	GSR (Siemens)	
	Negative emotion	Neutral emotion
3	8.68	6.98
4	4.604	5.17
6	10.87	9.11
7	18.33	15.6
8	13.91	12.74
9	2.06	1.84
10	2.12	2.29
11	6.69	3.81

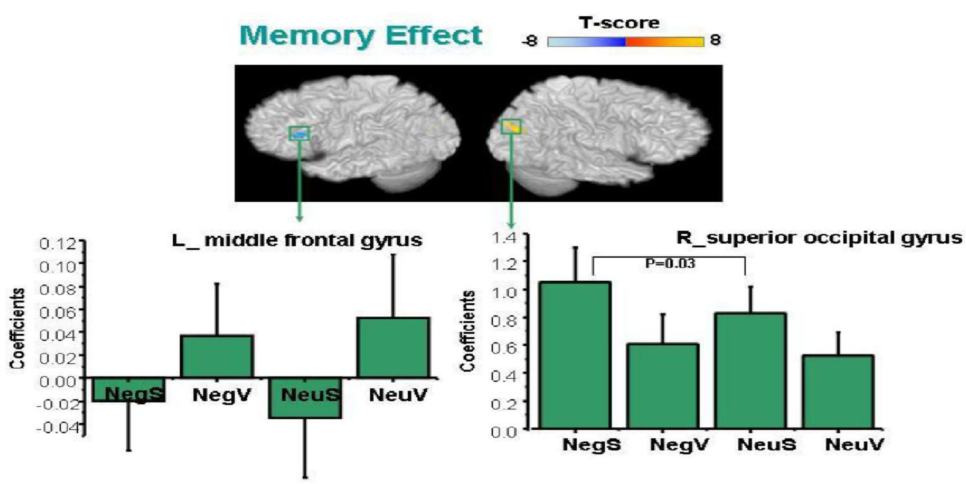

Figure 2 : The brain activation in memory effect (spatial>verbal). The activation maps were made at a threshold p<0.001 (uncorrected).

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(b) Main emotion effect

The main effect of emotion was determined by contrasting the negative condition with the neutral condition. Comparing with neutral emotion, negative emotion increased fMRI signal in the right insula, right medial frontal gyrus (BA 6), right postcentral gyrus, right anterior cingulate (BA24) and left posterior cingulate (BA31) (see TABLE 3).

The two-way ANOVA on those activated regions showed significant main emotion effects (see Figure3). Most of these regions showed hypoactivities under the neutral emotion condition and hyperactivities under the negative emotion condition, which are consistent with most of studies about emotion processing. But ROI analysis didn't find significant interaction effects on any of these regions.

(c) Interaction effect

Significant interaction effect was found in the bilateral cuneus (BA17/18) (see TABLE 3).

The two-way ANOVA in this region also revealed significant interaction effect ($F(1,11)=30.23$, $p=0.0002$). To clarify the nature of the interaction effect, paired t-test showed more activations for negative emotion than neutral emotion in the spatial WM ($t(11)=2.13$, $p=0.057$), and also more activations for verbal WM than spatial WM under the neutral emotion condition ($t(11)=-3.65$, $p=0.004$). Thus, the interaction effect is possibly due to the contrast (negative spatial –neutral spatial > negative verbal – neutral verbal) or the contrast (neutral verbal –neutral spatial >negative verbal –negative spatial) (see Figure 4).

TABLE 3 : FMRI results

Region	X	Y	Z	T-score	Volume
Emotion effect					
R_medial frontal gyrus (BA6)	-18	9	54	7.547	335
R_insula	-55	20	16	6.125	135
L_posterior cingulated	7	64	19	6.006	127
R_postcentral gyrus	-42	20	28	5.944	109
R_anterior cingulate (BA24)	-6	-3	32	7.258	99
Memory effect					
R_superior occipital gyrus (BA19)	-40	77	26	5.758	146
L_middle frontal gyrus (BA45/46)	43	-23	20	-5.509	97
				F-score	
Interaction effect					
L/R_cuneus (BA18)	2	79	9	43.86	149

All areas p<0.001/voxel (uncorrected).

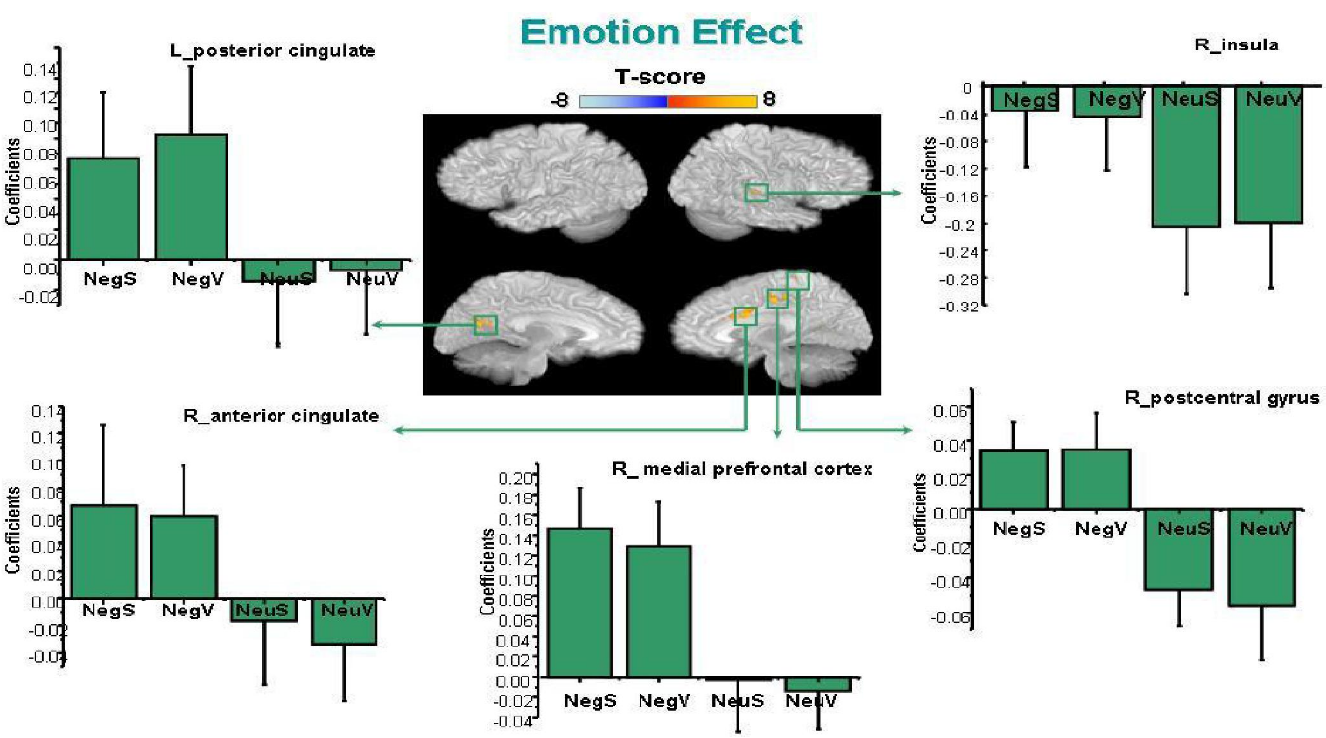

Figure 3 : The brain activation in emotion effect (negative>neutral). The activation maps were made at a threshold p<0.001 (uncorrected).

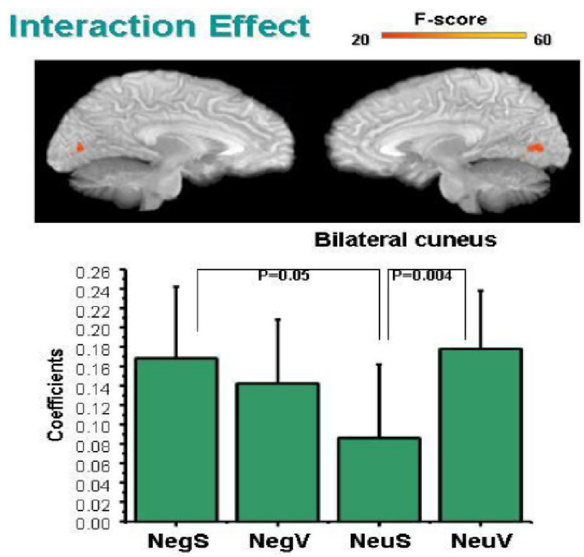

Figure 4 : The brain activation in interaction effect [(spatial-negative > spatial-neutral) > (verbal-negative > verbal-neutral)]. The activation maps were made at a threshold p<0.001 (uncorrected).

DISCUSSION

The present study was designed to investigate the neural basis of the effect of negative emotion on verbal and spatial WM. The GSR responses measured in the scan pointed to a successful induction of negative emotional state. Behavioral results indicated the induced negative emotion selectively interrupted with the accuracy of spatial WM but not with the verbal WM, which is consisting with our prediction and also confirmed by activation results.

The underlying mechanism of the behavioral results could be revealed by memory and emotion effects. As noted in the introduction, spatial and verbal WM should have significant hemispheric specializations. Left prefrontal cortex has been tied to the rehearsal of verbal information[8,45]. Using positron emission tomography, Awh and colleagues revealed activations in the verbal recognition task, mostly in the left hemisphere, including Broca's area (BA44), left premotor area (BA6), left SMA (BA6) and left posterior parietal cortex (BA40). The left prefrontal cortices were tentatively assigned the role of mediating a subvocal, rehearsal process and the posterior parietal area was thought to underlie a storage process. Subsequently, Cohen et al.[8] conducted 2-back WM study and also found identical activation patterns of frontal speech regions (BA44/45). In contrast, for the spatial WM, previous neuroimaging studies assigned right superior parietal area (BA7) and premotor (BA6) with responsibility for the rehearsal of spatial information and right inferior parietal area (BA40) and superior occipital area (BA19) with responsibility for the storage of spatial information[8,46]. In the present study, the results of memory effect confirmed the typical finding. As predicted, a left-sided dominance was found in the left middle frontal cortex (BA45/46) for the verbal WM, and a right-sided dominance was found in the superior occipital cortex (BA19) for the spatial WM. These results confirm that the left middle frontal cortex play a key role in verbal WM and right parietal-occipital cortex plays a key role in spatial WM as the previous studies underlined[32,50]. Further ROIs analyses indicated that only the region associated with spatial WM had significant emotion effect, but not the region specific to verbal WM, which gave more evidence for the selective effect of negative emotion on spatial WM on the right-sided hemisphere.

Furthermore, the results of emotion effect revealed significant right-lateralized activations mainly in medial frontal gyrus, insula, anterior cingulated gyrus, and post-central gyrus. In addiction, left posterior cingulated gyrus was also activated by negative emotion. These results implied that the emotion effect on right-sided was greater than left-sided hemisphere. It is well known that paralimbic system (e.g. amygdala, hippocampus and cingulated gyrus) has a general role in the evaluation and experience of affection[33,37,49]. A very recent meta-analysis of affective neuroimaging studies found consistent activations in medial and lateral frontal gyrus, temporal gyrus and anterior insula[25] and those regions have implicated in emotional regulation[4,36]. The insula has been directly implicated in PET studies of emotion and anxiety[7,26]. In particular, Chua et al.[7] induced normal people' anticipatory anxiety and found significant increase in the rCBF in the insula and anterior cingulate. They suggested that the insula connecting with anterior cingulate mediated in anticipatory anxiety. Anterior cingulated cortex is likely to play a role both in the generation (rostral or perigenual "affective" anterior cingulate) and the regulation of emotion (dorsal or supragenual "cognitive" anterior cingulate)[6,25]. The medial prefrontal cortex seems to be involved almost exclusively in the cognitive aspects of emotional processing, and it could serve (together with anterior cingulate and other brain regions) as a top-down modulator of intense emotional responses[24,26,37]. In the current study, as predicted, negative emotion elicited widespread activities in the regions associated with emotion processing and demonstrated a critical role of the right hemisphere in the processing of highly arousal, unpleasant emotions. Hereby, spatial WM not verbal WM had been interfered by negative emotional state of the same hemispheric dominance.

The interaction effect in the present study revealed additional activities in bilateral cuneus, which could be explained on account of more engagements of visual attention processes in the negative spatial condition than that in the neutral spatial condition. Since the occipital cortex works as the primary visual processing cortex and the important part of the bottom-up attention network, it is activated when visual attention processes is involved. In the negative spatial condition, both aversive pictures and spatial WM task require more attention than did neutral spatial condition. In addiction, according to ROI analysis, the interaction effect could be regarded as more activities of bilateral cucues for verbal WM than spatial WM under the neutral emotion, which is proved by previous neuroimaging studies for the contrast between the spatial WM and verbal WM. A number of studies showed the verbal working memory tasks were accompanied by additional rCBF in the inferior temporal-occipital areas, such as fusiform gyrus, lingual gyrus and cuneus as comparing with spatial or objective tasks. Therefore the interaction effect in the present study could be due to both reasons mentioned above. The interaction effect didn't activate more right-sided regions as expected, which is not clear whether this is due to reduced statistical power in the present block-design due to the lack of randomization of emotion factor or fewer blocks in each experimental conditions.

Besides the hemispheric asymmetry, the selective effect of negative emotion on spatial WM could be explained by different hypothesis. Previous research also revealed a possible attentional resource competition between negative emotion and spatial WM[28,30,31]. Because negative affects commonly draw visuospatial attention (e.g. attention to threat), which is also essential to spatial WM[2,3,23,38]. In contrast, this competition is less pronounced when it comes to verbal WM due to its primary dependence on phonological processes[5,40]. Therefore, visuospatial attention might be an overlapping area between negative emotion and spatial WM, which leads to affects induced selective impairment of spatial WM. In the present study, aversive pictures as a powerful exogenous cue can produce a transient involuntary capture of spatial attention and trigger reflexive shifts in spatial attention toward its location. Therefore, it is another alternative explanation for the selective effect in the performance.

Also, eye-movement could also be the reason which caused the spatial WM was affected by negative emotion. Previous studies have shown disruptive effects of eye movements on spatial WM, because eye movements are often associated with movement of attentional focus[29,39]. In our study, eye movements from pictures to targets could probably disrupt the spatial WM. Since eye-movements were not recorded, it is uncertain whether they contributed to any differences in BOLD signal between experimental conditions, which would be the limitation of the present study.

CONCLUSION

Nonetheless, the main findings from this study indicate significant right hemisphere lateralization for negative emotion processing and a right-sided dominance in spatial WM, which to some extent suggests the neural resource competition on the same dominant hemisphere as the neural basis of the selective influence of negative emotion on spatial WM.

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