

Resting-State Functional Connectivity Predicts Emotional Conflict Control

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Abstract

Emotional conflict control refers to the ability to select task-relevant emotional information and ignore task-irrelevant emotional distractors. Previous fMRI studies provide some evidence about brain structure and function related to emotional conflict control. Yet, the underlying resting-state functional connectivity was largely unknown. Here, this is the first study to explore the resting-state functional connectivity related to emotional conflict. According to the literature which used the whole-brain analysis to investigate the key brain area associated with emotional conflict, we select the amygdala (AMY) as the seed region. We then investigated the association between emotional conflict and functional connectivity between amygdala (AMY) and another brain region in a large sample. We found the emotional conflict effect was positively correlated with functional connectivity strength between AMY (the seed ROI) and right supplementary motor area (SMA). This finding implied that the functional connectivity between AMY and SMA was linked to emotional conflict and that AMY was the key region which plays a crucial role in emotional conflict.

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Introduction

Conflict control refers to the ability to select task-relevant information and ignore task-irrelevant distractors [1]. In the daily life, many emotionally salient stimuli around us will interfere with our goal behavior. Individuals must inhibit the emotional interference and resolve the "emotional conflict" that stem from cognitive control [2] [3]. Emotion conflict control was the important executive function for both healthy people and some clinical patients such as mood and anxiety disorders [4-6].

Previous studies often used the face-word Stroop task to measure the emotional conflict effect in both healthy people and clinical study [5-8]. During this task, participants need to judge facial expression of target face while ignoring the meaning of superimposed words. Many previous fMRI studies provide some evidence about the important brain regions and neural activity during this paradigm [2, 7, 9-11]. For instance, Etkin et al. found that task activation in amygdala (AMY) reflected the amount of emotional conflict [2]. Egner et al. found AMY and rostral anterior cingulate (rACC) were sensitive to emotional conflict [7]. These two regions were two dissociable neural circuits for resolving emotional conflict or cognitive conflict. Chechko et al. suggest that inferior frontal gyrus (IFG) and supplementary motor area (SMA) also played an important role in emotional conflict resolution besides AMY [11]. These findings focused on functional task activation during specific experimental paradigm and provided some neural evidence of emotional conflict. Besides, Deng et al. found that the regional gray matter volume (rGMV) of orbitofrontal cortex was associated with emotional conflict effect [12]. Xue et al. found that the amplitude of low frequency fluctuations (ALFF) of AMY was also related to emotional conflict control [13]. However, the resting-state functional connectivity related to emotional conflict was largely unknown. The spontaneous fluctuations in the BOLD signal during resting-state reflected the intrinsic functional activity of the brain and relate to extrinsic task performance [14] [15]. Previous study suggests that this intrinsic resting-state activity also could predict brain activation and behavioral performance [16]. Thus, the aim of the present study was to explore the underlying

resting-state functional connectivity related to emotional conflict. In the present study, we used seed-based functional connectivity to investigate the resting-state functional connectivity of emotional conflict control. Previous studies often used the amplitude of low frequency fluctuations (ALFF) as an index of resting-state brain activity to study the association about human cognition [17], emotion [18], and personality [19]. Also, the ALFF provide a potential biomarker for a variety of mental disorders, such as depression [20]; schizophrenia [21]; and mild cognitive impairment [22]. This index was the more stable measure index for resting-state fMRI to reflect regional properties of intrinsic brain dynamics [23]. Specifically, Xue et al. found that was the emotional conflict associated with the ALFF of AMY [13].

On the other hand, functional connectivity was another widely used approach in the resting-state fMRI study [14, 24, 18]. This method examined inter-regional correlations among spontaneous low-frequency fluctuations in the BOLD signal during rest [25]. We investigated the association of emotional conflict with resting-state functional connectivity among different brain regions.

To our knowledge, no study has yet explored the relationship between the functional connectivity and emotional conflict. Here, in the present study, we investigated the functional connectivity of resting-state fMRI signals to elucidate the intrinsic neural basis of emotional conflict. Based to prior studies [2, 7, 13], we selected the AMY as the seed region. We hypothesized that emotional conflict shall be associated with the strength of functional connectivity between AMY and frontal brain region (e.g., SMA).

Materials and Methods

Participants

Two hundred and thirty-four healthy university students (144 females; average age = 19.87 years, standard deviation [SD] = 1.08) with no history of psychiatric or neurological disorders. The present study was a part of an ongoing research project (GBB project) which explored the associations among gene, brain, and behavior [26] [27]. This data set was analysis and some results were reported at our previous study [13]. All participants had normal eyesight or corrected eyesight,

no color blindness, and were right-handed [as indicated on the Edinburgh Handedness Inventory; [28]]. Written informed consent was obtained from all the participants prior to the study. Both behavioral and MRI protocols were approved by the Institutional Review Board of Southwest University.

Emotional Conflict Task and Behavior Analysis

The face-word Stroop task was adopted as the experimental paradigm to measure emotional conflict for this study [12] [13]. In this task, participants need to see a face picture which was superimposed an emotion word, and they were instructed to identify the facial expression of the target face while ignoring the meaning of the words by pressing a button.

The target stimuli consisted of 5 male and 5 female face pictures, with either happy or sad expression, selected from the Chinese affective picture system [29]. Each face picture was superimposed two Chinese characters, “愉快” (which means “happy”) or “悲伤” (which means “sad”). The combinations of facial expressions and superimposed words yielded two conditions: a congruent condition (e.g., character meaning happy superimposed onto a happy face picture) and an incongruent condition (e.g., character meaning happy superimposed onto a sad face picture). The stimuli were programmed by E-Prime 2.0 software.

A total 120 trials consisting of an equal amount of congruent and incongruent trials were included in the formal experiment and another 24 trials was for practice. Stimuli were presented in pseudo-random order for avoiding repetition priming effect [30]. The timing and order of each trial was as follows: a fixation dot was presented for a specific duration (500 ms) followed by a blank screen of variable duration (300–500 ms). Then, the target face appeared for 1000 ms at the center of the screen. Participants had to respond within 1500 ms. The inter-trial interval (ITI) varied randomly between 800 ms and 1200 ms, with a mean of 1000 ms.

All behavior data analysis was implemented in SPSS 18. For each participant, we calculated mean accuracy and reaction time (RT) for each condition. The paired t test was performed on the accuracy and RT

data, respectively. The difference between mean RT of incongruent trials and mean RT of congruent trials was defined as “emotional conflict effect” or “emotional interference effect” [12] [13].

Assessment of General Intelligence

To adequate control for individual differences in emotional conflict control, all participants completed the Combined Raven's Test (CRT, Chinese version). The CRT was widely used for intelligence testing in China, and it has been proved to have good reliability and validity [31]. The CRT comprises 72 nonverbal items and each item consists of a matrix with a missing piece that is to be filled in by selecting the best answer from 6 or 8 alternatives. The number of correct answers while completing the CRT test within 40 minutes was used as an index of general intelligence, and it was served as a covariate in our statistical analyses.

Image Acquisition

MRI scanning was conducted on a Siemens 3T scanner (MAGENTOM Trio, a Tim system) with an eight-channel phased array coil. For each participant, 242 functional images were acquired with a gradient echo type Echo Planar Imaging (EPI) sequence (echo time (TE) = 30 ms; repetition time (TR) = 2000 ms; flip angle = 90 degrees; slices = 32; slice thickness = 3.0 mm; slice gap = 1 mm; field of view (FOV) = 220 × 220 mm²; resolution matrix = 64 × 64; in-plane resolution = 3.4 × 3.4 mm²; interslice skip = 0.99 mm). In addition, a high-resolution T1 weighted magnetization prepared gradient echo sequence (MPRAGE: TR/TE/TI = 1900/2.52/900ms, flip angle = 9 degrees, matrix = 256 × 256) anatomical scan also was acquired for registration purposes and anatomically localizing the functional regions. One hundred and seventy-six contiguous sagittal slices were obtained with 1 × 1 mm in-plane resolution and 1 mm slice thickness. Before the resting-state fMRI scanning, participants were instructed to keep their eyes closed without falling asleep, and to keep their head as still as possible during the scanning.

Image Preprocessing

Image preprocessing was performed using statistical parametric mapping software (SPM8, <http://www.fil.ion.ucl.ac.uk/spm>) and using the data processing assistant for resting state (DPARSF, [\[www.openaccesspub.org\]\(http://www.openaccesspub.org\) | IJPR CC-license DOI: \[10.14302/issn.2574-612X.ijpr-19-3045\]\(https://doi.org/10.14302/issn.2574-612X.ijpr-19-3045\)](http://</p></div><div data-bbox=)

www.restfmri.net/forum/DPARSF). For each subject, the first 10 images were discarded due to instability of the initial MRI signal and adaptation of participants to the circumstance. The remaining 232 images were preprocessed, which included slice timing, head motion correction, spatial normalization, and smooth. Briefly, the 232 images were slice acquisition corrected, aligned to the middle images for head-motion correction. The various covariates including white matter, cerebrospinal fluid, and Friston 24-parameter were regressed out in order to reduce potential impact of physiological artifacts [32]. Prior study has proved that regressing out Friston 24-parameter is more effective than other movement correction methods [33]. None of the subjects had more than 2.5 mm maximum displacement in x, y, or z translation and 2.5° of angular motion during the whole fMRI scan. Then, the corrected images were spatially normalized to the Montreal Neurological Institute (MNI) EPI template in SPM8 and resampled to 3×3×3 mm³ voxels. The images then were spatially smoothed with a Gaussian kernel (full-width at half-maximum [FWHM] = 6 mm). In order to be consistent with previous, we selected 6 mm isotropic Gaussian kernel [13]. Finally, the smoothed data was linearly detrended, and was filtered using a typical bandpass (0.01–0.08 Hz) to reduce the influences of high-frequency noise and low-frequency drift.

Functional Connectivity Analysis and Connectivity-Behavior Analysis

To explore whether the key region we identified in the ALFF-behavior analysis interacted with other brain regions to predict the emotional conflict, a seed-based whole-brain functional connectivity approach was conducted. We selected the AMY (MNI: 2, 14, 50) as the seed region according to previous study [13]. The region which was associated with emotional conflict in ALFF was as seed region of interest. We created spherical ROI (radius = 8 mm) according to the peak of seed region identified in the ALFF-behavior analysis. For each participant, the correlation coefficients, between mean time series of all voxels with the seed region and the time series of each voxel of other brain regions, were calculated. The correlation coefficients were converted into Z scores using Fisher's

r-to-z transformation, which formed a z-functional connectivity map for each participant.

Then, we performed a partial correlation analysis to explore the functional connectivity that was related to emotional conflict. The gender, age, and IQ were treated as the confounding covariates, and the interference effect of emotional conflict was treated as the covariate of the interest. The corrected cluster threshold was set at $p < 0.05$ (AlphaSim corrected for multiple comparisons, with a combined individual voxel p value < 0.01 with cluster size > 75 voxels).

Results

Behavior Analysis

The demographic information of the sample (age, gender, and Raven's score) and detailed behavior data were reported in our previous study [13]. The paired t test was performed on the accuracy and RT data to detect the emotional conflict effect, respectively. The emotional conflict effect was 21 + 2 ms (RT of congruent trials minus RT of incongruent trials). The emotional conflict effect was not influenced by gender and IQ.

Functional Connectivity-Behavior Analysis

To explore whether the AMY identified in prior ALFF-behavior analysis interacted with other brain regions to predict the emotional conflict, we performed a seed-based whole-brain functional connectivity analysis. The AMY (MNI: 2, 14, 50) was defined as the seed region of interest (ROI). We found that after controlling age, gender, and Raven's scores, emotional conflict was positively correlated with functional connectivity strength between the AMY (the seed ROI) and right supplementary motor area (SMA) (MNI: 21, -33, 51; $t = 3.70$; cluster size = 130 voxels; $p < 0.05$ corrected) (Fig 1, Table 1).

Discussion

To our knowledge, the present study was the first to explore the resting-state functional connectivity related to emotional conflict. We used face-word task to measure the emotional conflict [12] [13]. At the behavior level, the RT results showed significant emotional conflict effect. At the neural level, we firstly investigated the association between emotional conflict

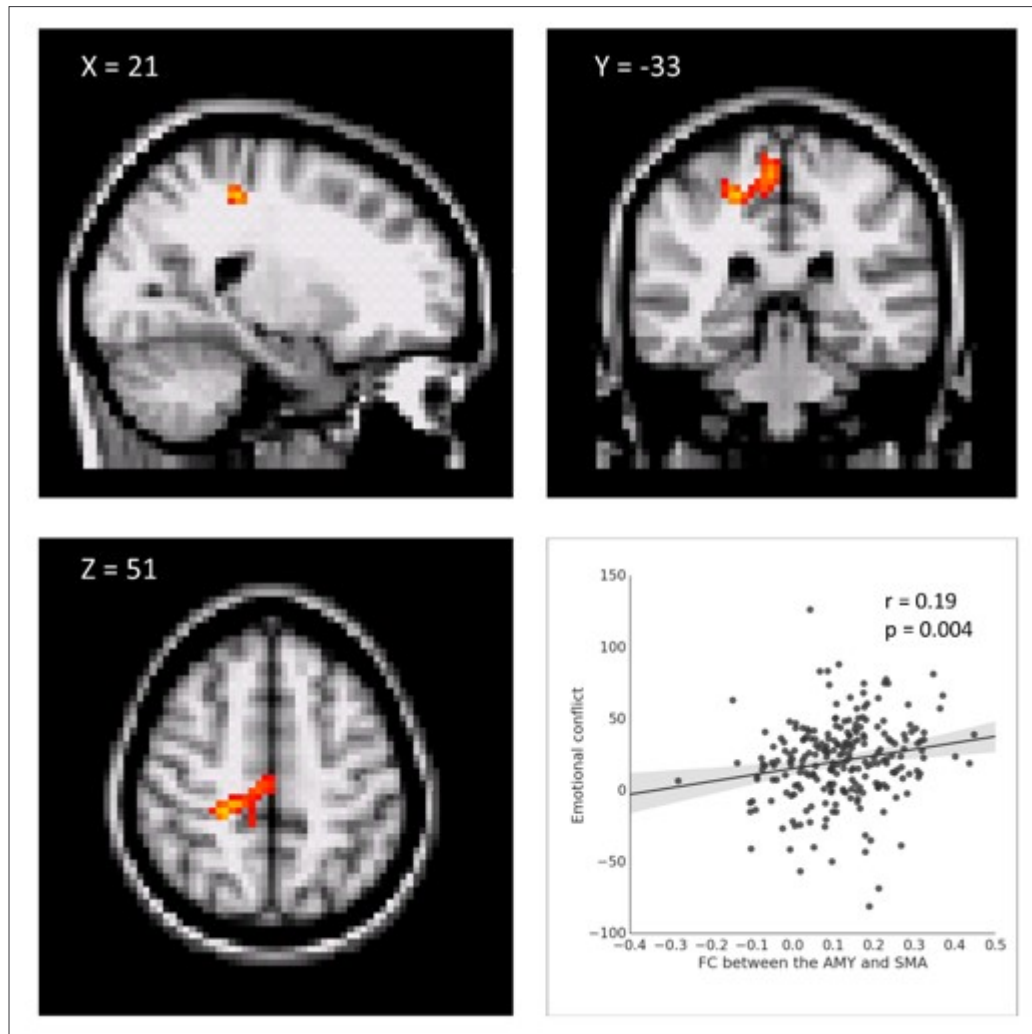


Figure 1. Correlation between seed-based functional connectivity (FC) and emotional conflict. The FC between the AMY and the right supplementary motor area (SMA) was positively correlated with emotional conflict. Scatter plot between the AMY-SMA FC and emotional conflict is shown for illustration purposes.

Table 1. Brain regions showing significant correlations between the strength of resting-state functional connectivity with Amygdala and emotion conflict effect.

Anatomical region	Side	Cluster size (#voxels)	Peak voxel			
			T	x	y	z
Supplementary motor area	R	130	3.70	21	-33	51

All the clusters survived $p < 0.05$, Alphasim corrected (individual voxel threshold $p < 0.01$ and a minimum cluster size of 75).

and functional connectivity. Specifically, we did a seed-based (AMY as the seed region) functional connectivity analysis, and we found that functional connectivity between AMY and right supplementary motor area (SMA) was associated with emotional conflict.

Consistent with prior hypotheses, we found that emotional conflict was positively correlated with the strength of functional connectivity between AMY and SMA, and that increased AMY-SMA connectivity was associated with worse face-word Stroop performance. The SMA played a key role in cognitive control, motor control, and movement [34]. During the emotional conflict task, Chechko et al. found that SMA was activated in the incongruent condition compared to congruent condition, which might be linked to premotor planning [10]. Moreover, previous studies demonstrated that the SMA and AMY were coactivated during the perception of emotional expressions [35, 36, 37], and that the SMA and AMY functionally connected during both the positive and negative emotional stimuli processing [38]. In addition, a recent study provided evidence of a structural connection between AMY and motor-related areas by using diffusion-weighted magnetic resonance imaging method [39]. Taken together, we thought that, during the present face-word Stroop task, AMY-SMA connectivity might be associated with the perception of emotional expressions and motor control, which might contribute to the emotional conflict resolution. In some recent studies, researchers use machine learning method to investigate networks [40] [41]. We might study the association between brain network and emotional conflict in the future.

To examine the robustness of the ALFF-behavior correlation results and functional connectivity-behavior correlation results, we performed the prediction analysis in both results. The prediction analysis results showed that the correlation between AMY-SMA connectivity and behavior were steady. Therefore, we verified the results that AMY-SMA functional connectivity were associated with emotional conflict resolution. These findings provided a better understanding of the neural mechanism underlying emotional conflict control.

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