Research Report

Alterations in the cortical thickness and the amplitude of low-frequency fluctuation in patients with post-traumatic stress disorder

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\textbf{ABSTRACT}

The core neuropsychological processes underlying post-traumatic stress disorder (PTSD) have yet to be elucidated, and the association between anatomical and functional deficits in PTSD remains largely unknown. The aim of our study was to investigate the alterations in cortical thickness and amplitude of low-frequency fluctuation (ALFF) in PTSD patients resulting from motor vehicle accidents (MVCs), and to explore the association of cortical thickness and ALFF with the severity of PTSD symptoms. A total of 20 PTSD patients and 20 healthy controls were recruited and examined by high-resolution structural MRI combined with resting-state fMRI. The results showed significant decrease in cortical thickness in the left BA10, BA32 and BA45 and the right superior temporal gyrus in PTSD patients. The ALFF value in PTSD patients increased significantly in the left BA10 and BA32 and the right cerebellum. Linear regression revealed that decreased cortical thickness and increased ALFF in the BA10 were associated with the increased PTSD scores. These findings suggest that the structural integrity and resting-state function in the BA10 play an important role in the pathogenesis of PTSD.

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1. Introduction

Post-traumatic stress disorder (PTSD) is characterized by unique symptoms resulting from exposure to a traumatic event, such as combats, violent crimes, motor vehicle accidents or childhood abuses. The motor vehicle accidents are the leading cause of PTSD in the general population, and it has been found that, of those who were in an accident where medical attention was needed, almost 50% developed PTSD (Blanchard et al., 1994; Blanchard and Hickling, 2004). The symptoms of PTSD include persistent re-experiencing of the traumatic event, avoidance of stimuli associated with the trauma, numbing of general responsiveness, and increased arousal (DSM-IV-TR) (Blake et al., 1995). In recent years,
findings from functional and structural neuroimaging studies have yielded tremendous advances in understanding the neural mechanisms underlying PTSD (Hughes and Shin, 2011). The most consistent finding in patients with PTSD from structural neuroimaging studies is abnormal medial prefrontal cortex (mPFC), including the abnormal anterior cingulate and hippocampal volume (Bremner et al., 2008). Some researches on abnormalities in the PFC of PTSD patients suggest decreased volume in the PFC (Carrion et al., 2001; De Bellis et al., 2002; Hakamata et al., 2007; Richert et al., 2006) or anterior cingulate cortex (ACC) (Abe et al., 2006; Chen et al., 2006; Monson et al., 2006; Villarreal et al., 2004), while some suggest increased volume in some sub-areas of the PFC (Richert et al., 2006). Although some findings show regional changes in the volume in brain areas, most of these findings were obtained based on manual tracing of the regions of interest. The brain structural areas need to be drawn artificially in advance and other important brain areas may be neglected during the process. Recent advances in computational analysis provide new opportunities to use imaging data to derive more knowledge on cortical thickness. The semi-automatic technique used to determine cortical thickness is a relatively new technique, and has become the tool for disease study. Some studies have found that the cortical thickness serves as an index of brain development and aging, and is associated with neurologic degeneration (Landre et al., 2010; Pereira et al., 2012). Some cortical thickness-based studies found that PTSD patients had significantly thinner prefrontal cortices and superior temporal gyrus than age-matched healthy controls (Geuze et al., 2008a; Mollica et al., 2009; Woodward et al., 2009). However, Landrè found normal cortical thickness in a sample of female survivors of sexual abuse with chronic PTSD (Landre et al., 2010). Additionally, Lyoo et al. (2011) found that trauma-exposed PTSD individuals recovering from a South Korean subway disaster had greater dorsolateral prefrontal cortical (DLPFC) thickness 1.42 years after trauma than controls, and the greater DLPFC thickness was associated with greater PTSD symptom reductions and better recovery.

Meanwhile, functional neuroimaging studies have also identified a number of brain areas with altered activity in patients with PTSD, including the PFC, temporal cortex, insula, amygdala, and hippocampus (Francati et al., 2007; Nemeroff et al., 2006). However, most functional neuroimaging studies of PTSD have involved the examination of brain activation during symptom provocation tests or cognitive tasks (Etkin et al., 2004; Frewen et al., 2008), and some results are not consistent. For example, some studies have reported increased activation of the mPFC in PTSD (Bremner et al., 2008; Villarreal et al., 2004), while some have found decreased (Hakamata et al., 2007; Herry and Mons, 2004) or even no activation in the mPFC (Stein et al., 2007). The complex patterns of findings may be due to the different cognitive tasks, or the nature of the comparison groups used. Recently, the spontaneous low-frequency (0.01–0.08 Hz) blood oxygenation level-dependent (BOLD) fluctuation in resting state fMRI has been measured to investigate intrinsic functional baseline activity of the brain (Mohamed et al., 2004; Raichle and Mintun, 2006). During a resting state scan, the absence of demanding cognitive activities and instructions makes it more straightforward to compare brain activity across groups that may differ in motivation or cognitive abilities. Thus, resting fMRI may be helpful for further understanding of abnormalities in brain activity in participants with brain disorders. Up to now, fewer studies have examined resting brain activity in PTSD (Bluhm et al., 2009; Lanius et al., 2010). Lanius et al. (2010) examined the relationship between resting-state coordinated activity and PTSD symptoms using an acutely traumatized sample, and found that resting state connectivity of the posterior cingulate cortex (PCC) with the perigenual anterior cingulate and the right amygdala was associated with current PTSD symptoms, and that correlation with the right amygdala predicted the future PTSD symptoms. Bluhm et al. (2009) have compared women with early-life trauma to healthy women, and also found that spontaneous low-frequency activity in the default network during rest was altered in patients with PTSD, and that spontaneous activity in the PCC/precuneus was more strongly correlated with activity in other areas of the default network in healthy controls than in patients with PTSD. However, previous resting-state studies of PTSD have measured correlated activity of the default mode using a seed-point method. This method may be biased by the choosing of particular seed regions and focuses on long-distance patterns of connectivity. Zang et al. (2007) reported that the regional activities during resting state can be examined by the amplitude of low-frequency fluctuation (ALFF) of the BOLD signal, which serves as an alternative way of measuring intrinsic brain responses. The ALFF is associated with field potential activity in local brain regions (Logothetis et al., 2001), and the amplitude of activation can be used as an index to evaluate changes in brain function (Mohamed et al., 2004). It has been reported that abnormality in ALFF existed under resting conditions in PTSD patients exposed to a major earthquake, and that the ALFF value in the right medial frontal gyrus was positively correlated with severity of the disorder (Yin et al., 2011b). However, the mechanism of alterations in the ALFF and the relationship between the regional brain ALFF and the local cortical thickness in PTSD patients are still unclear and need further exploration.

The core neuropsychological processes underlying PTSD have yet to be elucidated (Liberzon et al., 2007; Shin et al., 2005), and the association between the anatomical and functional deficits in PTSD is largely unknown. Additionally, to our knowledge, the relationship between cortical thickness and ALFF has not been studied in the PTSD population. The aim of our study was to investigate the changes in cortical thickness and ALFF in PTSD patients by combining high-resolution structural MRI with resting fMRI, and to explore the association between cortical thickness and ALFF in PTSD resulting from motor vehicle accidents. The relationship of these two factors with the PTSD symptom severity is another key point we intend to elucidate. We hypothesized that (1) PTSD patients may show different cortical thickness and ALFF in some brain areas compared with control subjects, (2) cortical thickness and ALFF in some brain areas may be correlated to PTSD symptom severity, and (3) correlation may exist between the different cortical thickness and ALFF in some brain areas.
2. Results

PTSD patients and the control group were matched for age, gender and years of education, and there was no significant difference in IQ between the two groups. Patients with PTSD had significantly higher CAPS (Clinician-Administered PTSD Scale) scores than the controls (Table 1). According to the Structured Clinical Interview for DSM-IV (SCID), three subjects in the PTSD group met DSM-IV diagnostic criteria for the depressive disorder. After examining the PTSD patients who had been involved in motor vehicle accidents (MVAs) without any brain injury, we found that 12 subjects had lower leg amputation and 8 had paralysis of the lower limbs resulting from spinal cord injury. The range for time since trauma was 7.2 ± 1.6 months. Among the controls, the SCID did not reveal any psychiatric disorder.

The visualization of difference maps of the cortical thickness clearly showed the focal cortical thinning areas (Fig. 1). In the left hemisphere, a significant decrease in cortical thickness was observed in the medial prefrontal cortex (BA10), the triangular part of the inferior frontal gyrus (BA45) and the anterior cingulate cortex (BA32) of PTSD patients (P < 0.05, FDR-corrected) (Fig. 1, Table 2). In the right hemisphere, a significant decrease in cortical thickness was also found in the superior temporal gyrus of PTSD patients compared with the control group (P < 0.05, FDR-corrected) (Table 2).

By comparing the ALFF values of the PTSD patients with the controls, we found that the PTSD patients exhibited increased ALFF values mainly in the left medial prefrontal

<table>
<thead>
<tr>
<th>Variable</th>
<th>PTSD (n = 20)</th>
<th>Controls (n = 20)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in years (SD)</td>
<td>32.92(8.48)</td>
<td>31.53(7.43)</td>
<td>0.451</td>
</tr>
<tr>
<td>Gender</td>
<td>Male(13), female(7)</td>
<td>Male(14), female(6)</td>
<td>0.736</td>
</tr>
<tr>
<td>Mean education in years (SD)</td>
<td>11.20(3.80)</td>
<td>13.00(2.20)</td>
<td>0.374</td>
</tr>
<tr>
<td>IQ (SD)</td>
<td>98.20(5.50)</td>
<td>103.20(6.30)</td>
<td>0.242</td>
</tr>
<tr>
<td>CAPS total score, mean (SD)</td>
<td>52.33(9.44)</td>
<td>8.26(9.31)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

CAPS, clinician-administered PTSD scale (range, 0–136)

* P values were calculated by χ² statistics for categorical measures and 2-tailed t statistics for continuous measures.

Table 2 – Significant clusters identified by different imaging techniques in PTSD patients compared with controls.

<table>
<thead>
<tr>
<th>Anatomic definition</th>
<th>Imaging technique</th>
<th>Results</th>
<th>Voxels</th>
<th>MNI coordinates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial prefrontal cortex (BA10)</td>
<td>Cortical thickness</td>
<td>Decreased</td>
<td>672</td>
<td>−24 53 10</td>
</tr>
<tr>
<td>Anterior cingulated (BA32)</td>
<td>Cortical thickness</td>
<td>Decreased</td>
<td>324</td>
<td>−1 20 8</td>
</tr>
<tr>
<td>Frontal triangular (BA45)</td>
<td>Cortical thickness</td>
<td>Decreased</td>
<td>362</td>
<td>−23 46 10</td>
</tr>
<tr>
<td>Superior temporal gyrus</td>
<td>Cortical thickness</td>
<td>Decreased</td>
<td>124</td>
<td>−2 60 23</td>
</tr>
<tr>
<td>Medial prefrontal cortex (BA10)</td>
<td>ALFF</td>
<td>Increased</td>
<td>165</td>
<td>−24 54 −11</td>
</tr>
<tr>
<td>Anterior cingulate (BA32)</td>
<td>ALFF</td>
<td>Increased</td>
<td>87</td>
<td>1 21 −9</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>ALFF</td>
<td>Increased</td>
<td>66</td>
<td>12 −93 −27</td>
</tr>
</tbody>
</table>

Fig. 1 – Color maps showing a significant (P < 0.05, FDR-corrected) decrease in the thickness of the grey matter mainly in the ACC and left frontal cortex in PTSD patients compared with the controls. Corresponding t values are color-coded with blue-to-yellow (−6.47 to 6.47). (A) anterior cingulate cortex; (B) MPFC (BA10); (C) Triangular part of the inferior frontal gyrus (BA45). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
cortex (BA10), the anterior cingulated (BA32) and the right cerebellum ($P < 0.05$, FDR-corrected) (Fig. 2; Table 2).

Linear regression revealed a strong linear negative correlation between CAPS scores and cortical thickness in BA10 ($R^2 = 0.351$, $P = 0.021$), and a weaker linear correlation between CAPS scores and cortical thickness in BA32 ($R^2 = 0.243$, $P = 0.046$), indicating that thinner cortex is associated with greater PTSD scores. There was no significant association between CAPS scores and the cortical thickness in BA45 and superior temporal gyrus. Linear regression of CAPS scores with ALFF showed that there was only a linear positive correlation between CAPS scores and ALFF in BA10 ($R^2 = 0.372$, $P = 0.026$), indicating that higher ALFF in BA10 is associated with greater PTSD scores.

The overlapped areas were BA10 and BA32 in cortical thickness and ALFF (Table 2). Linear regression revealed that a linear negative correlation existed between cortical thickness and the ALFF in BA10 ($R^2 = 0.315$, $P = 0.036$), but no significant correlation was found between ALFF and the cortical thickness in BA32 (Table 3).

3. Discussion

The former studies have reported ACC and frontal lobe with smaller volume in PTSD patients. For example, Bush et al. (2000) reported that the left dorsal ACC, which was associated with more cognitive functions, was reduced in volume in PTSD patients. Woodward et al. (2009) also reported that the ACC volume was smaller in combat-related PTSD patients. Ehlers et al. (Ehlers and Clark, 2000) suggested that PTSD was accompanied by smaller volume in the left frontal lobe and other brain structures. The thickness of the cerebral cortex is an additional indicator of integrity of cytoarchitecture in the cortex (Luders et al., 2009; Makris et al., 2007; Shaw et al., 2006), and the cortical thickness-based studies found that PTSD veterans had significantly thinner prefrontal cortices and superior temporal gyrus than age-matched healthy controls (Geuze et al., 2008b). Our results showed focal thinning in the left ACC (BA32), MPFC (BA10), BA45 and in the right superior temporal gyrus in PTSD patients, consistent with the previous studies (Araki et al., 2005; Geuze et al., 2008b), and revealed the selective thinning of the cerebral cortex that subserves emotional and memory functions (Buckner et al., 2004; Eldridge et al., 2000). Herry et al. (Herry and Mons, 2004) indicated that the ACC acted to facilitate fear extinction by modulating the amygdala. MFCC has been implicated in the processing of emotional materials generated internally (George et al., 1995), as well as the regulation of arousal (Zubieta et al., 1999). Some researchers have suggested that apparent memory deficits in PTSD patients may be due to frontal lobe dysfunction (Daniels et al., 2010; Geuze et al., 2008a). Vasterling et al. (1998) indicated that deficits in attention and working memory have been interpreted as

![Fig. 2 – Comparison of the ALFF value of PTSD with that of NC subjects in the resting state. ALFF increased in the left BA10, ACC, and the right cerebellum. Corresponding t values are color-coded with yellow-to-red. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)](image-url)
suggesting an involvement of the prefrontal lobes. On the other hand, our results revealed a strong linear negative relationship of CAPS scores with cortical thickness of BA10, and a weaker linear negative correlation of CAPS scores with cortical thickness of BA32, indicating that lower cortical thickness of BA10 and BA32 is associated with higher CAPS scores. Therefore, we suggest that cortical thickness in the left ACC and MFFC is negatively correlated with the severity of the PTSD symptom, and reduced cortical thickness in the left ACC and MFFC could possibly contribute to difficulties in extinguishing fear and deficits in working memory in PTSD patients.

Interestingly, the PTSD patients in the study of Landre et al. (2010) are chronic patients who have had the disease for 10.7 ± 4.7 years and their cortical thickness is not significantly different from that of the control group. The PTSD patients who were recovering from a South Korean subway disaster in the study of Lyoo et al. (2011) have had the PTSD disease for 1.42 years. At this stage, DLPFC thickness is restored and vicariously becomes thicker, and the greater DLPFC thickness is strongly related to successful reductions in PTSD symptoms. In our study, only 7.2 ± 1.6 months have passed since the trauma, and the patients are at the early stage of the disease. Thus, the symptoms are severe, and the cortex becomes thinner. Therefore, we infer that cortical thickness is likely in dynamic change at different recovery stages of PTSD, but the mechanism is unclear and needs further exploration.

Our results also showed increased ALFF values in the left PFC (BA10), ACC (BA32) and cerebellum, which confirms the previously published results and provides further evidence to support that altered resting brain function is involved in the neuropathology of PTSD (Yin et al., 2011a). Overactivity in the ACC and the frontal regions has been reported in PET/SPECT studies in the resting state (Lowe et al., 1998). PTSD subjects exhibited increased regional cerebral blood flow (rCBF) in the mPFC in processing of acoustic traumatic scripts under neutral conditions and during combat-sound stimuli compared with normal subjects (Lanius et al., 2006). Lui et al. (2009) also reported that PTSD survivors of earthquakes showed significantly increased ALFF in the left PFC and the left precentral gyrus. The increased regional activity in the frontolimbic regions in the left hemisphere is known to be important for emotional processing (Drevets, 2000). Some functional neuroimaging studies have provided direct evidence that prefrontal-limbic and striatal systems play a critical role in anxiety disorders, including the recollection of traumatic memories and the processing of fear and pain (Stein et al., 2007). In addition, recruitment of the mPFC may be involved in unconscious fear processing in PTSD patients (Bryant et al., 2008). In the current study, linear regression showed a linear positive relationship between CAPS scores and ALFF of left BA10, suggesting that the abnormally increased spontaneous activities in the mPFC may be associated with the clinical symptoms of PTSD patients. The result is consistent with prior studies, suggesting that increased rCBF in mPFC correlates at trend levels with stress responsiveness in PTSD patients (Phan et al., 2006; Zubieta et al., 1999). In general, the ALFF increase implies that functional and morphologic damages of brain tissue exceed a certain lower limit in PTSD. Thus, by virtue of its non-invasiveness, high spatial and temporal resolution, low cost, and clinical convenience, resting-state ALFF can be an advantageous choice for PTSD pathologic analysis.

Notably, the results of our research indicate that the brain areas which showed increased ALFF in the resting state partly overlapped the areas which showed decreased cortical thickness in BA10 and BA32. This demonstrates the association between the brain function and structure to a certain extent. Linear regression revealed a linear negative association between cortical thickness and the ALFF of BA10, suggesting that the increased ALFF in the resting state may be a compensatory mechanism to overcome the cortical thinning of BA10 in PTSD patients. Moreover, the ALFF is considered to be the reflection of regional spontaneous neuronal activity (Kiviniemi et al., 2000) and physiological state of the brain (Yang et al., 2007). Therefore, ALFF of BA10 may objectively reflect the abnormal regional brain activation in resting state, thus facilitating the further exploration of PTSD pathogenesis.

To avoid repeating previous research in this small sample, we only used thickness and ALFF as factors for our analysis. The approach to combining structural and functional data in PTSD derived from resting-state FMRI and cortical thickness is indeed a very interesting and promising method. However, the thinning in the cortical regions identified in this study should be interpreted cautiously because of some limitations. First, the healthy controls were selected from the community rather than from MVA victims, and the PTSD group were at increased risk of experiencing head trauma, which may affect the results, though we had tried to exclude the head injury. The individuals who experienced MVAs, but were not PTSD patients should be chosen as controls in our future studies to minimize the interference of the factors resulting from the trauma. Other limitations of this study are listed as follows: the small sample size, and the fully automated method used in FreeSurfer software. The technique of three-D parametric surface modeling of FreeSurfer overcomes the limitations of volumetric segmentation and represents complex sulcal structures. However, errors in the cortical surface model still exist in folded regions because of the limit of resolution in volume images, which may occasionally obscure subtle neuroanatomic effects (Devlin and Poldrack, 2007). Some of the group differences may be chance findings due to the lack of full correction for multiple comparisons. We still have much to learn about the relationship between the brain structure and function in PTSD patients, and our findings need to be replicated to validate these initial observations.

4. Experimental procedure

4.1. Subjects

A total of 20 PTSD patients (age, 18–40 years; mean, 32.92 years) who had been involved in motor vehicle accidents (MVAs) were recruited from Southwest Hospital, Third Military Medical University. Diagnosis of PTSD was established using the Clinician-Administered PTSD Scale for DSM-IV (CAPS-DX) (Blake et al., 1995). All the subjects met criterion
A for PTSD, as assessed by CAPS, i.e., a threat of death or serious injury, or a threat to the subject’s physical integrity. Three main kinds of symptoms were rated for both frequency and intensity, including re-experiencing symptoms, avoidant symptoms and symptoms of increased arousal. A severity score for each symptom was calculated by summing up the frequency and intensity scores, which were then summed up for all 17 symptom questions and/or for the three symptom clusters. Twenty healthy controls (age, 20–38 years; mean, 31.53 years) individually matched for age, gender and years of education were consecutively recruited from the community. Inclusion criteria for all the subjects were right-handedness and an IQ>80, as assessed with the Wechsler Adult Intelligence Scale (WAIS). Patients had no history of Axis I psychiatric diagnoses other than depression on the Structured Clinical Interview for DSM-IV (SCID) Axis I Disorders, whereas controls were free from Axis I diagnoses on the SCID (First, 1997). Exclusion criteria for both groups were contraindications for MRI and other neuropsychiatric disorders, such as schizophrenia, mental retardation, epilepsy, and head injury (i.e., abnormalities on CT or MRI, neurological abnormality during emergency department evaluation, or loss of consciousness for more than 5 min during the accident). All PTSD patients had not taken psychotropic medication for at least two months.

4.2. Ethical statement

This research was conducted in accordance with international ethical guidelines, and had been approved by the Ethics Committee of the Third Military Medical University. All the participants have signed the informed consent after receiving a complete description of the study.

4.3. Image acquisition

All the experiments were performed on a 3.0 T Siemens MRI scanner (Trio; Siemens Medical, Erlangen, Germany). Foam padding was used to minimize the head motion of the subjects. T1-weighted images on the sagittal plane of the subjects were acquired using a 3D MPRAGE sequence (TR, 2000 ms; TE, 2.34 ms; flip angle, 7°; FOV, 256 × 256; and slice thickness, 1 mm). The resting-state fMRI data were acquired using the following parameters: TR/TE/FA, 2000 ms/30 ms/90°; 36 transverse slices; thickness, 3.0 mm; FOV, 220 × 220; and alignment along the anterior commissure–posterior commissure (AC–PC) line. Each session lasted 360 s. During the resting state, the subjects were told not to concentrate on any particular object, but just to relax with their eyes closed.

4.4. Image processing and analysis

The cortical thickness of the brain was analyzed by FreeSurfer (http://surfer.nmr.mgh.harvard.edu/), a new method by which automated surface reconstruction yielded measure ment of the cortical thickness for each subject’s entire brain and computed cross-subject statistics based on the cortical anatomy. Brain surfaces were reconstructed and inflated, and the cortical thickness was estimated as described previously (Fischl, 2012). Briefly, the procedure included segmentation of the white matter, tessellation of the gray/white matter junction, automatic correction of topologic defects, inflation of the folded surface tessellation patterns, and registration into an average spherical surface template. Next, a deformable surface algorithm was used to detect the gray/white boundary and surfaces with sub-millimeter precision. Finally, the data for cortical thickness were smoothed with a 10-mm full width at one-half height Gaussian kernel to improve the signal-to-noise ratio. Statistical thickness difference maps were generated by performing t-tests between PTSD patients and the healthy controls. A statistical threshold of P<0.05 (FDR corrected) was used for an exploratory whole-brain analysis. Individual cortical thickness values from these significantly different areas were calculated and exported to SPSS 12.0 for regression analysis.

The resting-state fMRI data were spatially normalized to a standard template (Montreal Neurological Institute) and re-sampled to 3 × 3 × 3 mm. Subsequently, the functional scans were spatially smoothed with a 8 × 8 × 8 mm full width one-half maximum Gaussian kernel to decrease spatial noise. The REST1.5 software program (http://www.restfmri.net/) was used to calculate the ALFF. After the data were linearly detrended and temporally band-pass filtered (0.01–0.08 Hz) [3], the filtered time series were transformed into a frequency domain with a fast Fourier transform (FFT) (parameters: taper percent=0; FFT length=shortest), and the power spectrum was obtained. Since the power of a given frequency is proportional to the square of the amplitude of this frequency component of the original time series in the time domain, the power spectrum obtained by FFT was square-rooted, and then averaged across 0.01–0.08 Hz at each voxel. This averaged square root was taken as the ALFF. For standardization purposes, the ALFF of each voxel was divided by the global mean ALFF value. The standardized ALFF of each voxel should have a value of approximately 1 and this standardization procedure is analogous to that used in PET studies (Zou et al., 2009). The noise components from head motion, white matter and cerebrospinal fluid controlled in ALFF analyses, and the global mean ALFF were calculated only within the brain, with the background and tissues outside the brain removed. At last, ALFF maps of the PTSD patients and the controls were compared on a voxel-wise basis by a two-sample t-test in SPM5 (http://www.fil.ion.ucl.ac.uk/spm). A threshold of P<0.05 (FDR corrected) was considered statistically significant. Individual ALFF values from these significantly different areas were calculated and exported to SPSS 12.0 for regression analysis.

4.5. Statistical analysis

Simple linear regression analyses were performed to investigate the relationship between cortical thickness and ALFF in each of those significantly different areas (independent variable) with clinical CAPS scores (dependent variable). Linear regression was then conducted to determine a possible association of cortical thickness with ALFF in the corresponding (overlapping) significantly different areas. All the results are quoted as two-sided P values. P<0.05 was considered statistically significant. All the statistical analyses were performed using SPSS 12.0 (SPSS Inc, Chicago, Illinois, USA).
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