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Adolescent earthquake survivors' show increased prefrontal cortex activation to masked earthquake images as adults

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ABSTRACT

The great Sichuan earthquake in China on May 12, 2008 was a traumatic event to many who live near the earthquake area. However, at present, there are few studies that explore the long-term impact of the adolescent trauma exposure on adults' brain function. In the present study, we used functional magnetic resonance imaging (fMRI) to investigate the brain activation evoked by masked trauma-related stimuli (earthquake versus neutral images) in 14 adults who lived near the epicenter of the great Sichuan earthquake when they were adolescents (trauma-exposed group) and 14 adults who lived farther from the epicenter of the earthquake when they were adolescents (control group). Compared with the control group, the trauma-exposed group showed significant elevation of activation in the right anterior cingulate cortex (ACC) and the medial prefrontal cortex (MPFC) in response to masked earthquake-related images. In the trauma-exposed group, the right ACC activation was negatively correlated with the frequency of symptoms of post-traumatic stress disorder (PTSD). These findings differ markedly from the long-term effects of trauma exposure in adults. This suggests that trauma exposure during adolescence may have a unique long-term impact on ACC/MPFC function, top-down modulation of trauma-related information, and subsequent symptoms of PTSD.

1. Introduction

Earthquakes can cause widespread devastation, including loss of property, personal injury, and homelessness (Ursano and McCaughey, 1995). After the great Sichuan earthquake in China on May 12, 2008, more than 69,000 people were dead and more than 37,000 were injured. To date, at least 17,000 people still remain missing. In total, more than 46 million people were affected in the 30,000 km^2 area that was impacted by this disaster.

Events such as this one can have a profound impact on mental health (Bremner et al., 1993; Copeland et al., 2007; Wang et al., 2011) and there is an intensive international effort to understand the role of the brain in the association between psychological trauma and ensuing morbidity (Patel et al., 2012). Previous research has focused on samples of adults and children with posttraumatic stress disorder (PTSD) (Andersen et al., 2008; De Bellis et al., 1999). However, the majority of the trauma-exposed individuals without clinical diagnosis of PTSD (which we will refer as trauma-exposed sample) received little attention. Although there is an emerging effort to understand the neural impact of adulthood exposure to psychological trauma in nonclinical individuals (Ganzel et al., 2007; Gianaros et al., 2007; Liston et al., 2009), less attention has been paid to the long-term effects of adolescence trauma exposure in nonclinical sample. This is of particular interest, as adolescence is a critical period in brain development. This study aims to help to fill this gap.

1.1. Background

Trauma exposure is relatively common in the general population, so that the study of trauma sequelae in nonclinical samples is an important public health issue. For example, epidemiological studies in the United States report that more than half of adults and children experience at least one psychological trauma in their lifetime (Cohen et al., 2006; Copeland et al., 2007; Kessler et al., 1995). Only a small percentage of trauma-exposed people (7%–12%) develop PTSD and rates are lower for children (Copeland et al., 2007). However, after exposure to severe earthquakes, many of these children and adolescents are at risk for sub-clinical posttraumatic stress and depressive reactions (Goenjian et al., 1995; Roussos et al., 2005). If left untreated, these conditions can become chronic in young survivors who at first appear resilient (Bremner et al., 1993; Goenjian et al., 2005). Regrettably, less is known about the long-term consequences of severe life events for

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youth who do not initially develop clinical-level psychiatric symptoms (Copeland et al., 2007).

1.2. Neuroimaging

A growing body of research on the neural and behavioral sequelae of the great Sichuan earthquake suggests that this event had a long-term impact on brain function in both clinical and nonclinical adults. Approximately two months after the earthquake, one of our authors (J.Q.) conducted studies examining event-related potential (ERP) response to the classic and modified Stroop task in a nonclinical sample of adults who were near the epicenter of the earthquake and who had close personal experience of this disaster, relative to a comparison group that was much farther from the epicenter (Qiu et al., 2009, 2010; Wei et al., 2011). The earthquake exposed group demonstrated decreased cognitive monitor and control (Qiu et al., 2009). In addition, the trauma-exposed nonclinical adults showed absence of the typical N400-600 Stroop interference effect, indicating the abnormal functions of the right prefrontal cortex (Brodmann area [BA] 10) (Qiu et al., 2010). Atypical PFC function was also observed in a functional magnetic resonance imaging (fMRI) study of nonclinical adults that was conducted within 25 days of the earthquake. This study found higher resting-state activity in frontolimbic and striatal brain regions, reduced neural connectivity between the two regions, as well as increased anxiety and depression symptoms in nonclinical adults who were close to the earthquake epicenter relative to a comparison group that was farther away (Lui et al., 2009).

Researches of fMRI in nonclinical trauma-exposed individuals reported aberrant neural function in frontolimbic regions (Ganzel et al., 2007; New et al., 2009; Phan et al., 2006). A longitudinal fMRI study of the effects of combat exposure on military paramedics found increased activation in the amygdala, hippocampus, and ventromedial PFC in response to masked trauma-related stimuli (Admon et al., 2009). New et al. (2009) found that the female rape survivors with PTSD and without PTSD both showed impaired ability to diminish response to the emotional imagery, accompanied by attenuated signal in PFC compared to controls during down-regulation of emotional response to overtly presented rape-related imagery. It is argued that trauma exposure impairs MPFC control on the amygdala, which can lead to PTSD symptoms (Williams et al., 2006). Thus, the PFC structure and functions for cognitive and emotional controls are particularly vulnerable to trauma exposure in both clinical and nonclinical adults.

1.3. Developmental trauma exposure

In children and youth, the neural and behavioral sequelae of trauma differ from that observed in adults (De Bellis et al., 1999, 2002). The development of a brain and behavior creates periods of sensitivity to experience that vary in their neural and behavioral impact, depending on the developmental timing of each experience (Ganzel and Morris, 2011). So if psychological trauma occurs during a period of rapid development in a given brain region, that trauma is more likely to affect neural function, structure, and/or connectivity in that region, with parallel specific effects on behavior. Unfortunately, very little is known about the long-term effects of trauma on the nonclinical adolescent brain. One existing study suggests that a sample of nonclinical young adolescents (10 to 15 years of age) who experienced a greater number of traumas in lifetime had decreased structure (regional gray matter volume) in PFC and amygdala, relative to adolescents with fewer traumas in lifetime (Ganzel et al., 2013).

To date, no studies examining the neural functions after trauma exposure in adolescence, a critical period in neurodevelopment, exist. Therefore, we used the great Sichuan earthquake in China on May 12, 2008, as a unique window into this question. Subjects were all nonclinical adults who were high school students (17 to 19 years of age) at the time of the earthquake. This study design gave us good control over a number of key factors in this investigation, including the type of trauma, the intensity of trauma exposure, the age of the study subjects at the time of trauma exposure, and the time elapsed between trauma exposure and neuroimaging data collection. All earthquake-related stimuli were subliminally presented to avoid overt traumatic reminders and possible traumatization in subjects. Additionally, it is now widely accepted that cognitive processes and states can be non-conscious (occurring below awareness). Previous studies have shown that stimuli presented below awareness can elicit an effective reaction that is itself consciously felt (Winkielman and Berridge, 2004).

In summary, we speculated that the ACC/MPFC might play an important role in the regulation and processing of earthquake-related images, even when these stimuli were subliminally presented. We hypothesized that the nonclinical earthquake-exposed individuals would show significantly decreased activity in ACC and MPFC relative to the comparison group, along with heightened activity in the amygdala and associated limbic regions in response to masked trauma-related images.

2. Materials and methods

2.1. Subjects

Thirty volunteers from Southwest University participated in the study. The earthquake survivors were all enrolled in high school on May 12, 2008, the date of the great Sichuan earthquake, and were living in the most serious disaster areas (e.g., Mianyang city, 140 km away from the epicenter of the earthquake, and Deyang city, 101 km away from the epicenter). The control group consisted of volunteers who were also enrolled in high school on May 12, 2008, but were living far from the epicenter of the earthquake and did not have family or close friends harmed in the disaster (e.g., in Beijing city, 1933 km away from the epicenter of the earthquake, and Jinan city, 1593 km away from the epicenter). Data were collected in November, 2010, thirty months after the earthquake on May 12, 2008.

According to this scale, subjects whose total score over 60 are considered to have serious PTSD symptoms. Considering the purpose of our study so the exclusion criteria: (1) had clinical-level PTSD symptoms (PTSD-SS total score over 60); (2) history of past or present psychiatric care, or the presence of acute or chronic medical illness after the Sichuan earthquake; or (3) had undergone any psychotic illness as recorded in the documents of the mental health education department; and (4) undergone any form of psychotherapy or taken psychotropic medications after the Sichuan earthquake were excluded. In total, two subjects were excluded from the current study: one has a PTSD-SS score over 60, and the other one has excessive head motion in the scanner. Informed consent was obtained from all subjects. They were all right-handed and had normal or corrected-to-normal vision. This study was approved by the Southwest University Brain Imaging Center Institutional Review Board and complies with the Helsinki Declaration. Therefore, there were 14 survivors of the Sichuan earthquake (trauma-exposed group, age mean $= 20.64 \pm .74$ years, 6 males, 8 females) and 14 control subjects (control group, age mean $= 20.57 \pm 0.85$ years, 7 males, 7 females).

2.2. Behavioral assessments

The post-traumatic stress disorder self-rating scale (PTSD-SS) was based on the definition and diagnostic criteria of PTSD described in the Diagnostic and Statistical Manual of Mental Disorders: Fourth Edition (DSM-IV: American Psychiatric Association, 1994) and the Chinese Classification of Mental Disorders, Second Edition, Revised (CCMD-II-R). In China, it has been widely applied to evaluate the degree of PTSD symptoms of earthquake survivors (Fan et al., 2009; Liu et al., 2010). There are three factors of the PTSD-SS (re-experiencing/avoidance symptoms, psychological disorders/functional impairment, and emotional numbing/hypervigilance). Five subscales including 24 items make up the PTSD-SS, respectively divided into the subjective assessment for trauma (1 item), re-experience symptom (7 items), avoidance behaviors (7 items), emotional numbing and hyperarousal (6 items), and social dysfunction (2 items) symptom. Items are rated on a 5-point scale from "no symptom" (1) to "most severe with symptom" (5) with higher scores representing the PTSD symptoms were more severe. Total score indicates the degree of PTSD symptoms by combining together all the subscale. The initial psychometric evaluation of this scale revealed adequate internal consistency (0.92), high split-half reliability (0.95) and a good test–retest reliability after two weeks (0.87), which confirmed the validity of the PTSD-SS as a good measurement (Liu et al., 1998). In our study, the Cronbach's alpha coefficient for internal consistency was satisfactory, $\alpha = 0.94$.

2.3. Stimuli

Prospective stimuli consisted of 400 images of the Sichuan earthquake that were collected from the Internet. Each image contained a scene of the earthquake as it was happening or it depicted the consequences of the earthquake, including rescue scenes, fallen buildings, and/or earthquake casualties. These images were screened by three independent raters to ensure that the content of each image was clear and directly reflected the nature of the earthquake event or its consequences. Forty images were removed as not meeting these criteria. The 360 remaining images were normalized for brightness, contrast ratio, and color using Adobe Photoshop (Adobe Systems, Inc., San Jose, CA) and resolution was adjusted to 100 pixel/in., with a final image size of 10×7.5 cm^2.

Next, sixty four healthy undergraduates (23 males, 41 females; mean age $= 21.55 \pm 1.46$ years, range 18 to 26 years) participated in validation of the image rating scales. Subjects who took part in the validation study were not enrolled in the imaging portion of the study and were not from any of the disaster areas associated with the Sichuan earthquake. Subjects rated the images according to three criteria: "happiness", "arousal" and "familiar". "happiness" was rated on a scale from 1 (very unhappy) to 9 (very happy); "arousal" was rated on a scale from 1 (very calm and relaxed) to 9 (very excited and stressed); "familiar" was rated on a scale of from 1 (very unfamiliar, completely strange) to 9 (know well).

Finally, among these images, 30 earthquake-related images with low happiness (mean $= 2.69 \pm .53$) and high arousal (mean $= 6.07 \pm .73$) scores were selected as stimuli for the neuroimaging task. Additional 30 earthquake-unrelated neutral images that were selected from the native Chinese Affective Picture System (CAPS; (Bai et al., 2005)) were included. The two groups of pictures were significantly different in valence and arousal. All of the images were matched by physical characteristics such as color, size, and complexity.

2.4. Experimental design

Each subject took part in one imaging session. Subjects who were selected to take part in our scanning (all the 28 samples) were unaware of the intent of the study or that there would be exposed to earthquake-related imagery. The stimulus set consisted of one four-minute run containing six alternating blocks, including three blocks of masked earthquake-related images and three blocks of masked neutral (control) images. Each block lasted 40 s and consisted of a 20 s fixation interval and a 20 s set of masked stimulus trials (two per second). Each 500 ms trial consisted of a 33 ms target, which was either an earthquake-related or neutral image; this was immediately followed by a 467 ms neutral image (mask). There were 40 trials per block (Fig. 1). Order of presentation was counterbalanced across masked earthquake-related (E) and masked neutral (N) blocks (either EN or NN), randomly determined by equal probabilities.

To test whether subjects had never seen the mask trauma pictures objectively and performed the task adequately, we asked all subjects to concentrate on the screen during the scanning and informed them that there would be a recognition task after the scan (Whalen et al., 1998). We used three kinds of pictures during the post-imaging recognition task. Subjects were asked to respond whether the pictures had been seen before. The pictures included "old" which selected from the fMRI stimulus set (earthquake-related and earthquake-unrelated images) and "new" which had never appeared in experiment.

2.5. Neuroimaging data acquisition and analysis

Data of fMRI were gathered while subjects viewed the stimuli as described above. Imaging was conducted using a Siemens Symphony/Sonata 3 Tesla whole body scanner (Siemens Medical Systems, Iselin, NJ) equipped with an eight-channel phased array coil. T2*-weighted echo planar images were obtained for this study (32 slices, 3.4 mm $\times$ 3.4 mm $\times$ 3 mm voxels, TR $=$ 2 s, TE $=$ 30 ms, flip $= 90°$, FOV $=$ 192 mm $\times$ 192 mm, slice gap $=$ 1 mm).

Imaging data analysis was performed using SPM8 (Wellcome Trust Centre for Neuroimaging, University College, London, UK) implemented on MatLab 7.10.0 R2010a (MathWorks, Natick, MA). During preprocessing, scans were first slice time corrected, then realigned, normalized into standard Montreal Neurological Institute (MNI) space via 12-parameter affine transformation, smoothed with an 8 mm full width at half maximum (FWHM) Gaussian kernel, and finally filtered (high-pass filter set at 128 s, low-pass filter achieved by convolution with the hemodynamic response function).

At the individual (first) level, the design was modeled by convolving with a canonical hemodynamic response function (HRF). Statistical analyses for each individual subject were based on the fixed-effects general linear models (GLM) and analyses on the level of the group were

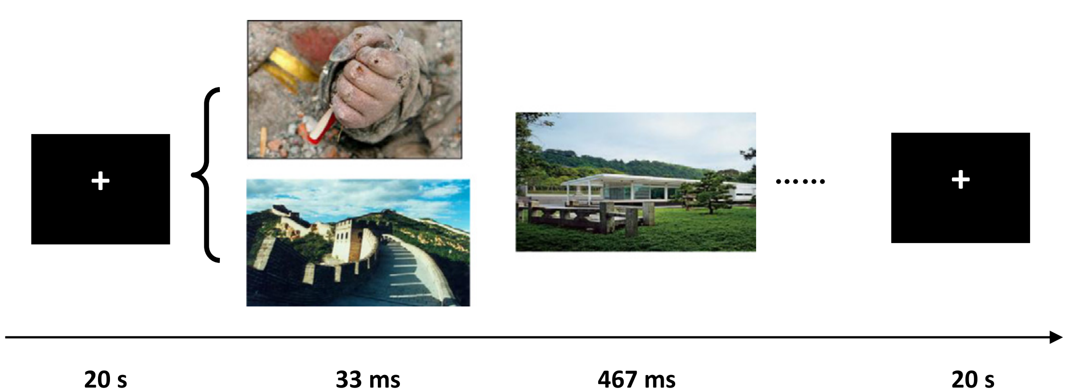

Fig. 1. Outline of the experiment. Every block contained a 20 s fixation and a 20 s task. There were 40 stimulus trials, and each stimulus trial consisted of two stimuli: target and mask.

based on random-effects models (Friston et al., 1999). Comparison contrasts (t-tests) were performed on earthquake-related versus neutral images and the reverse (neutral versus earthquake). Both conditions (earthquake-related, neutral) were included in the SPM model. In addition, the six motion parameters produced during realignment were entered into a regression analysis against the fMRI data for each individual subject in order to account for residual effects of movement.

In the group random effects (second-level) analysis, subject-specific linear contrasts of these parameter estimates were entered in a series of one-sample t-tests, each constituting a group-level statistical map. Our main contrasts of interest were BOLD signal in response to masked earthquake-related versus neutral stimuli and its reverse (neutral versus earthquake-related stimuli). We generated a cluster-level significance threshold using the AlphaSim program in the REST software (http://www.restfmri.net/forum/RESTV1.7). This Monte Carlo procedure (1000 simulations, Gaussian filter width = 8 mm, cluster connection radius = 5 mm) estimated that whole-brain cluster-level correction for multiple comparisons at $p < 0.01$ was achieved for our data by combining a voxel-level threshold of $p < 0.005$ with a minimum cluster size of 68 contiguous voxels. If significant activation was found in our a priori regions of interest (ACC, medial frontal gyrus, amygdala), we analyzed the fMRI raw data using the Marseille Region of Interest Toolbox software package (MarsBaR 1.86, http://www.sourceforge.net/projects/marsbar). Using an 8 mm radius sphere at a peak activation voxel, we extracted the BOLD signal data from those significant coordinates. Finally, we did a correlation analysis by using the extracted percent change of the BOLD signal data with the PTSD symptoms (PTSD-SS).

3. Results

Post-scan subject debriefing indicated that no subject had seen earthquake related material. On the post-scan recognition test, the recognition rate was 31% (i.e., below 50%, which was regarded as below chance), providing evidence that earthquake-related images were masked successfully. The mean scores of PTSD-SS in the trauma-exposed group were 57.27 ± 4.76, while the control group's was 34.75 ± 5.13: $t(26) = 11.99$, $p < .001$.

Collapsing across groups, significant BOLD signal was observed in PFC (including right ACC, MPFC), as well as medial and parietal lobes in the earthquake-related versus neutral condition (Table 1). There were no whole-group or between-group differences in the amygdala activation in earthquake-related versus neutral condition or in the reverse contrast.

Independent sample t-tests of the difference scores of the extracted data revealed significantly greater right ACC/MPFC activation in the trauma-exposed group compared with the control group during presentation of masked earthquake-related images (Figs. 2, 3). In the trauma-exposed group, elevated PTSD symptoms were associated with decreased signal in ACC (earthquake versus neutral images): $r(14) = -.31$, $p = .04$ (Fig. 4). Such correlation was not observed in the MPFC.

Table 1
Regions display a significant effect in the contrast of earthquake-related vs. earthquake-unrelated image conditions.
All regions are significant at $p < .01$ after whole brain cluster correction with a voxel-level threshold of $p < .005$ and cluster size (k) of 68 voxels.

Brain region	MNI coordinates			Peak t-value	Size (# of voxels)
	x	y	z		
Medial frontal gyrus	−7	−24	55	4.68	257
Right anterior cingulate cortex	4	44	16	4.12	259
Right inferior parietal lobule	51	−54	52	3.95	82
Left superior medial frontal cortex	−7	44	52	3.76	81

4. Discussion

We investigated differences in brain function and behavior in response to masked earthquake-related images in adults who, as adolescents, had been at different distances from the epicenter of the great Sichuan earthquake on May 12, 2008. In this study, we anticipated that masked earthquake-related stimuli (compared to masked neutral stimuli) would induce intrusive recollections of the earthquake in the trauma-exposed group, together with increased amygdala activation. We hypothesized that this increased limbic response would be accompanied by a decrease in PFC function in regions associated with attention and ability to concentrate, similar to findings in adult patients with PTSD (Rauch et al., 2000; Williams et al., 2006).

Contrary to these expectations, we saw up-regulation of ACC and MPFC activation in the trauma-exposed group during their viewing of masked trauma-related images, along with no group differences in the amygdala activation. In addition, only the earthquake-exposed subjects showed a significant negative association between PTSD symptoms and degree of activation in the ACC in response to masked trauma-related images, such that signal in ACC increased as PTSD symptoms decreased. This is the first study to examine automatic (non-conscious) neural processing of trauma-related stimuli in adults who were known to have trauma exposure specifically during late adolescence.

The current findings of the increased ACC and MPFC activation in the sample of adults who experienced trauma in their adolescence contrast with the results of existing neuroimaging studies of trauma-exposed adults, whether or not they have PTSD. In adults, trauma exposure is associated with characteristic dysregulation in the corticolimbic system, including increased amygdala response to masked and nonmasked threat-related stimuli (Ganzel et al., 2008; Rauch et al., 2000; Williams et al., 2006), which is accompanied by decreased signal in dorsal ACC, and MPFC (Rauch et al., 2000; Shin et al., 2001, 2004; Williams et al., 2006). The increased ACC and MPFC activations among the trauma-exposed individuals in our study may be associated with the timing of the trauma exposure in adolescence. During adolescence, the ACC and PFC are still immature. Adolescents recruit greater ACC and PFC activation for emotion processing and regulation compared to adults (Blakemore, 2008; Pfeifer and Blakemore, 2012; Steinberg, 2005). Although the exact reason is unclear, we speculate that exposure to trauma during adolescence may have disrupted a normal development, so that the individuals exposed to trauma during adolescence may require elevated levels of the ACC and PFC activity to process emotional information in adulthood compared to individuals who were not exposed to trauma in adolescence even when the emotional stimuli were presented subliminally.

These increased levels of the ACC activity appear to be important for improved psychological outcomes among trauma-exposed individuals. In the current study, an individual-level analysis within the trauma-exposed group showed that more robust ACC response was associated with fewer symptoms of posttraumatic stress. This is consistent with previous findings of a reciprocal relationship between the ACC activity and PTSD symptoms (Liberzon and Sripada, 2007; Shin et al., 2006; Williams et al., 2006) and supports previous conjecture that the ACC plays an important part in the self-control and regulation of amygdala response to trauma-related information. This automatic cognitive control of threat-related stimuli might play an important role in better long-term psychological outcomes.

Notably, in the current study, trauma-exposed group did not show any evidence of amygdala hyperactivity in response to masked trauma-related stimuli, relative to their own responses to masked neutral stimuli or relative to the responses of a comparison group. This is consistent with previous findings that amygdala did not show greater activity neither in PTSD nor in non-PTSD (Bremner et al., 2003; Lanius et al., 2001; Shin et al., 1999). For example, Hendler et al. (2003) reported no increase in the amygdala activation in response to trauma-related stimulus in traumatized subjects without a PTSD diagnosis. We

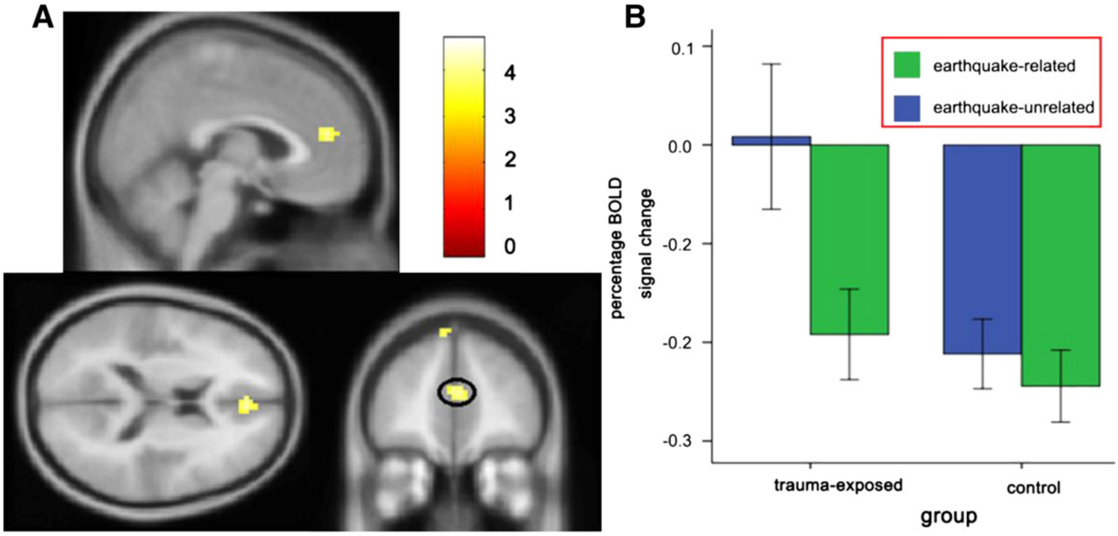

Fig. 2. Anterior cingulate. A. Statistical parametric map (earthquake-related minus earthquake-unrelated trials) showing activity in the right anterior cingulate in the whole group ($p < .01$ cluster-corrected, x, y, z = 4, 44, 16). Activity is represented in T-scores. B. The bar graph shows blood oxygen-level dependent (BOLD) signal change in this region in each condition.

speculate that the increased levels of the PFC and ACC activation among the trauma-exposed group may contribute to effectively regulate the amygdala activation, which can further be associated with nonclinical status of the trauma-exposed group. Additionally, we know that functional imaging studies are largely methodologically demanding so that can vary dramatically regarding paradigms and analytic methods. We employed subliminal presentation of trauma-related information here while the amygdala hyperactivation associated with trauma exposure may be better detected by explicit presentation rather than subliminal presentation. Future studies should examine whether subliminal versus explicit presentation of trauma-related information is associated with differences in the amygdala activation between trauma-exposed and control groups.

There are a few limitations of the present study. First, we did not include a group of patients with PTSD, so that we can only infer a comparison of our results and those of the previous PTSD studies. Thus, future work is needed to compare neural activity among trauma-exposed PTSD patients, trauma-exposed nonclinical group, and no trauma-exposure group. Also, the current study did not conduct a structured clinical interview. Future studies should also use in-depth clinical interview to determine a clinical diagnosis of PTSD among trauma-exposed individuals. Second, the current study examined a prospective association between adolescent trauma exposure and adult brain functions. However, it is still unknown about the concurrent associations between adolescent trauma, neural changes and PTSD symptoms when the trauma occurred. Thus, it is important that future work will reveal the longitudinal effects of adolescent trauma exposure on the neural developmental trajectories by collecting neuroimaging data at multiple time points across ages. Third, the sample size was relatively small, future studies must replicate our findings using larger samples.

5. Conclusion

Our study used fMRI to investigate non-conscious processing of earthquake-related versus neutral images in a nonclinical sample of adults who, as adolescents, experienced the great Sichuan earthquake. In this earthquake trauma-exposed group, we found greater ACC/MPFC response to earthquake-related stimuli, relative to a comparison

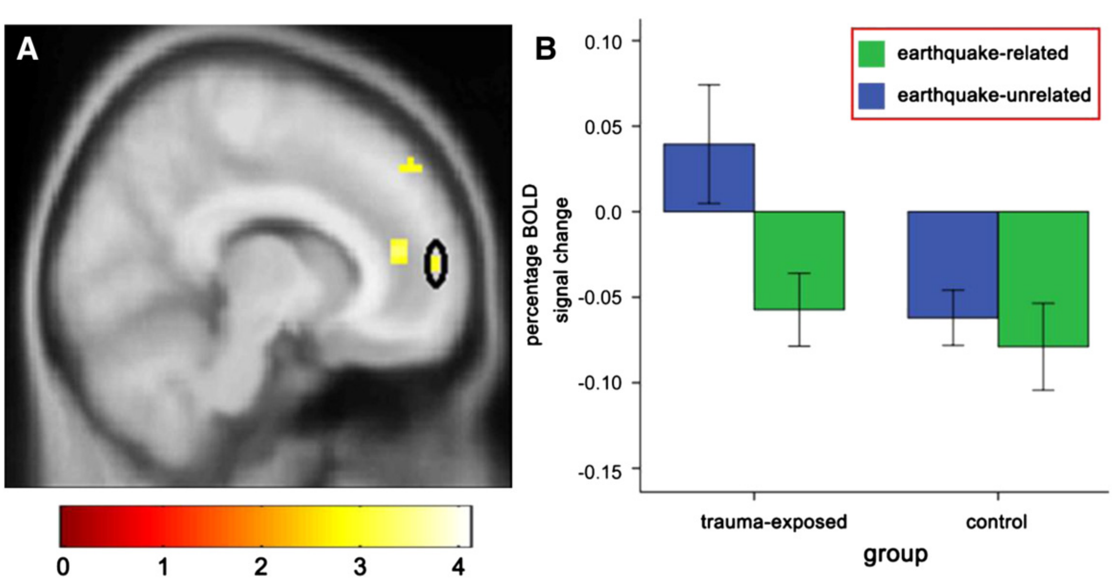

Fig. 3. Medial prefrontal cortex (MPFC). The statistical parametric map on the left displays activity in the MPFC in the earthquake-related minus earthquake-unrelated condition, collapsing across groups ($p < .01$ cluster-corrected, x, y, z = −7, −24, 55). Activity is represented in T-scores. The bar graph on the right shows BOLD signal change in this region in each condition.

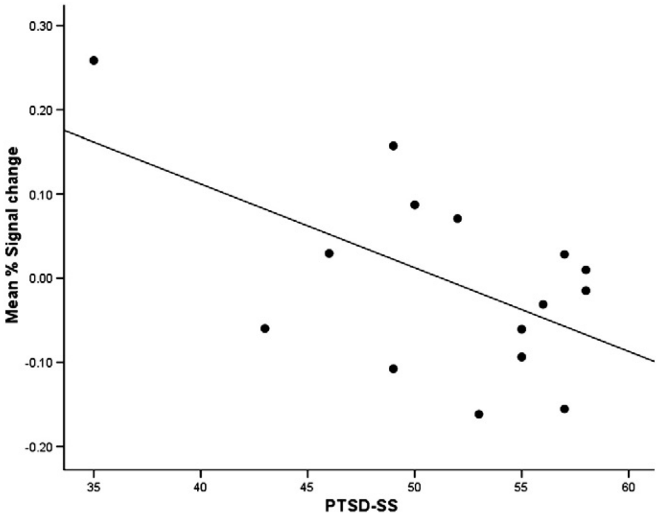

Fig. 4. Correlation between BOLD signal in the anterior cingulate and the PTSD-SS score (r= -0.56, p=0.03, x, y, z = 4, 44, 16) in the earthquake-related condition in the trauma-exposed group only.

group that was farther from the epicenter of the earthquake. This ACC hyperactivity (earthquake versus neutral images) was negatively associated with symptoms of PTSD, with no evidence of heightened amygdala response. Our results suggest that automatic cognitive control of threat-related stimuli might play an important role in long-term psychological health. These results contrast strongly with research findings with trauma-exposed adults with and without PTSD. These differences in findings may shed light on the long-term neural sequelae of trauma exposure that occurs during adolescence, relative to that of trauma exposure that occurs during other points in the lifespan.

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References

Admon, R., Lubin, G., Stern, O., Rosenberg, K., Sela, L., Ben-Ami, H., Hendler, T., 2009. Human vulnerability to stress depends on amygdala's predisposition and hippocampal plasticity. Proc. Natl. Acad. Sci. 106, 14120–14125.

American Psychiatric Association, 1994. Diagnostic and statistical manual of mental disorders (DSM-IV). American Psychiatric Association, Washington, DC.

Andersen, S., Tomada, A., Vincow, E., Valente, E., Polcari, A., Teicher, M., 2008. Preliminary evidence for sensitive periods in the effect of childhood sexual abuse on regional brain development. J. Neuropsychiatry Clin. Neurosci. 20, 292–301.

Bai, L., Ma, H., Huang, Y.-X., 2005. The development of native Chinese affective picture system—a pretest in 46 college students. Chin. Ment. Health J. 19, 719–722.

Blakemore, S.-J., 2008. The social brain in adolescence. Nat. Rev. Neurosci. 9, 267–277.

Bremner, J.D., Southwick, S.M., Johnson, D.R., Yehuda, R., Charney, D.S., 1993. Childhood physical abuse and combat-related posttraumatic stress disorder in Vietnam veterans. Am. J. Psychiatr. 150, 235–239.

Bremner, J.D., Vythilingam, M., Vermetten, E., Southwick, S.M., McGlashan, T., Staib, L.H., Soufer, R., Charney, D.S., 2003. Neural correlates of declarative memory for emotionally valenced words in women with posttraumatic stress disorder related to early childhood sexual abuse. Biol. Psychiatry 53, 879–889.

Cohen, R.A., Hitsman, B.L., Paul, R.H., Mccaffery, J., Stroud, L., Sweet, L., Gunstad, J., Niaura, R., MacFarlane, A., Bryant, R.A., 2006. Early life stress and adult emotional experience: an international perspective. Int. J. Psychiatry Med. 36, 35–52.

Copeland, W.E., Keeler, G., Angold, A., Costello, E.J., 2007. Traumatic events and posttraumatic stress in childhood. Arch. Gen. Psychiatry 64, 577.

De Bellis, M.D., Keshavan, M.S., Clark, D.B., Casey, B., Giedd, J.N., Boring, A.M., Frustaci, K., Ryan, N.D., 1999. Developmental traumatology part II: brain development. Biol. Psychiatry 45, 1271–1284.

De Bellis, M.D., Keshavan, M.S., Shifflett, H., Iyengar, S., Beers, S.R., Hall, J., Moritz, G., 2002. Brain structures in pediatric maltreatment-related posttraumatic stress disorder: a sociodemographically matched study. Biol. Psychiatry 52, 1066–1078.

Fan, Y., Sun, Y., Guan, R., 2009. PTSD in primary and secondary school students resume school in another place after the Wenchuan earthquake and its impact on mental health. Adv. Psychol. Sci. 17, 527–531.

Friston, K.J., Holmes, A.P., Price, C., Büchel, C., Worsley, K., 1999. Multisubject fMRI studies and conjunction analyses. Neuroimage 10, 385–396.

Ganzel, B.L., Morris, P.A., 2011. Allostasis and the developing human brain: explicit consideration of implicit models. Dev. Psychopathol. 23, 955.

Ganzel, B., Casey, B., Glover, G., Voss, H.U., Temple, E., 2007. The aftermath of 9/11: effect of intensity and recency of trauma on outcome. Emotion 7, 227.

Ganzel, B.L., Kim, P., Glover, G.H., Temple, E., 2008. Resilience after 9/11: multimodal neuroimaging evidence for stress-related change in the healthy adult brain. NeuroImage 40, 788–795.

Ganzel, B.L., Kim, P., Gilmore, H., Tottenham, N., Temple, E., 2013. Stress and the healthy adolescent brain: evidence for the neural embedding of life events. Dev. Psychopathol. 25, 879–889.

Gianaros, P.J., Jennings, J.R., Sheu, L.K., Greer, P.J., Kuller, L.H., Matthews, K.A., 2007. Prospective reports of chronic life stress predict decreased grey matter volume in the hippocampus. Neuroimage 35, 795–803.

Goenjian, A.K., Pynoos, R.S., Steinberg, A.M., Najarian, L.M., Asarnow, J.R., Karayan, I., Ghurabi, M., Fairbanks, L.A., 1995. Psychiatric comorbidity in children after the 1988: earthquake in Armenia. J. Am. Acad. Child Adolesc. Psychiatry 34, 1174–1184.

Goenjian, A.K., Walling, D., Steinberg, A.M., Karayan, I., Najarian, L.M., Pynoos, R., 2005. A prospective study of posttraumatic stress and depressive reactions among treated and untreated adolescents 5 years after a catastrophic disaster. Am. J. Psychiatr. 162, 2302–2308.

Hendler, T., Rotshtein, P., Yeshurun, Y., Weizmann, T., Kahn, I., Ben-Bashat, D., Malach, R., Bleich, A., 2003. Sensing the invisible: differential sensitivity of visual cortex and amygdala to traumatic context. Neuroimage 19, 587–600.

Kessler, R.C., Sonnega, A., Bromet, E., Hughes, M., Nelson, C.B., 1995. Posttraumatic stress disorder in the National Comorbidity Survey. Arch. Gen. Psychiatry 52, 1048.

Lanius, R.A., Williamson, P.C., Densmore, M., Boksman, K., Gupta, M.A., Neufeld, R., Gati, J.S., Menon, R.S., 2001. Neural correlates of traumatic memories in posttraumatic stress disorder: a functional MRI investigation. Am. J. Psychiatr. 158, 1920–1922.

Liberzon, I., Sripada, C.S., 2007. The functional neuroanatomy of PTSD: a critical review. Prog. Brain Res. 167, 151–169.

Liston, C., McEwen, B., Casey, B., 2009. Psychosocial stress reversibly disrupts prefrontal processing and attentional control. Proc. Natl. Acad. Sci. 106, 912–917.

Liu, X.C., Ma, D.D., Liu, L.Q., Zhao, G.F., Li, C.Q., Yang, J., Shun, L.M., 1998. Development of the post-traumatic stress disorder self-rating scale and its reliability and validity. Chin. J. Behav. Med. Sci. 7, 93–96.

Liu, Z., Yang, Y., Ye, Y., Zeng, Z., Xiang, Y., Yuan, P., 2010. One-year follow-up study of post-traumatic stress disorder among adolescents following the Wen-Chuan earthquake in China. Biosci. Trends 4, 96–102.

Lui, S., Huang, X., Chen, L., Tang, H., Zhang, T., Li, X., Li, D., Kuang, W., Chan, R.C., Mechelli, A., 2009. High-field MRI reveals an acute impact on brain function in survivors of the magnitude 8.0 earthquake in China. Proc. Natl. Acad. Sci. 106, 15412.

New, A.S., Fan, J., Murrough, J.W., Liu, X., Liebman, R.E., Guise, K.G., Tang, C.Y., Charney, D.S., 2009. A functional magnetic resonance imaging study of deliberate emotion regulation in resilience and posttraumatic stress disorder. Biol. Psychiatry 66, 656–664.

Patel, R., Spreng, R.N., Shin, L.M., Girard, T.A., 2012. Neurocircuitry models of posttraumatic stress disorder and beyond: a meta-analysis of functional neuroimaging studies. Neurosci. Biobehav. Rev. 36, 2130–2142.

Pfeifer, J.H., Blakemore, S.-J., 2012. Adolescent social cognitive and affective neuroscience: past, present, and future. Soc. Cogn. Affect. Neurosci. 7, 1–10.

Phan, K.L., Britton, J.C., Taylor, S.F., Fig, L.M., Liberzon, I., 2006. Corticolimbic blood flow during nontraumatic emotional processing in posttraumatic stress disorder. Arch. Gen. Psychiatry 63, 184.

Qiu, J., Li, H., Zhang, Q., Huang, L., Guo, Y., Tu, S., Wang, T., Wei, D., 2009. Electrophysiological evidence of personal experiences in the great Sichuan earthquake impacting on selective attention. Sci. China Ser. C Life Sci. 52, 683–690.

Qiu, J., Su, Y., Li, H., Wei, D., Tu, S., Zhang, Q., 2010. How personal earthquake experience impacts on the Stroop interference effect: an event-related potential study. Psychophysiology 47, 995–1001.

Rauch, S.L., Whalen, P.J., Shin, L.M., McInerney, S.C., Macklin, M.L., Lasko, N.B., Orr, S.P., Pitman, R.K., 2000. Exaggerated amygdala response to masked facial stimuli in posttraumatic stress disorder: a functional MRI study. Biol. Psychiatry 47, 769–776.

Roussos, A., Goenjian, A.K., Steinberg, A.M., Sotiropoulou, C., Kakaki, M., Kabakos, C., Karagianni, S., Manouras, V., 2005. Posttraumatic stress and depressive reactions among children and adolescents after the 1999 earthquake in Ano Liosia, Greece. Am. J. Psychiatr. 162, 530–537.

Shin, L.M., McNally, R.J., Kosslyn, S.M., Thompson, W.L., Rauch, S.L., Alpert, N.M., Metzger, L.J., Lasko, N.B., Orr, S.P., Pitman, R.K., 1999. Regional cerebral blood flow during script-driven imagery in childhood sexual abuse-related PTSD: a PET investigation. Am. J. Psychiatr. 156, 575–584.

Shin, L.M., Whalen, P.J., Pitman, R.K., Bush, G., Macklin, M.L., Lasko, N.B., Orr, S.P., McInerney, S.C., Rauch, S.L., 2001. An fMRI study of anterior cingulate function in posttraumatic stress disorder. Biol. Psychiatry 50, 932–942.

Shin, L.M., Orr, S.P., Carson, M.A., Rauch, S.L., Macklin, M.L., Lasko, N.B., Peters, P.M., Metzger, L.J., Dougherty, D.D., Cannistraro, P.A., 2004. Regional cerebral blood flow in the amygdala and medial prefrontal cortex during traumatic imagery in male and female Vietnam veterans with PTSD. Arch. Gen. Psychiatry 61, 168.

Shin, L.M., Rauch, S.L., Pitman, R.K., 2006. Amygdala, medial prefrontal cortex, and hippocampal function in PTSD. Ann. N. Y. Acad. Sci. 1071, 67–79.

Steinberg, L., 2005. Cognitive and affective development in adolescence. Trends Cogn. Sci. 9, 69–74.

Ursano, R.J., McCaughey, B.G., 1995. Individual and Community Responses to Trauma and Disaster: The Structure of Human Chaos. Cambridge Univ Pr.

Wang, B., Ni, C., Chen, J., Liu, X., Wang, A., Shao, Z., Xiao, D., Cheng, H., Jiang, J., Yan, Y., 2011. Posttraumatic stress disorder 1 month after 2008 earthquake in China: Wenchuan earthquake survey. Psychiatry Res. 187, 392–396.

Wei, D., Qiu, J., Du, X., Luo, Y., 2011. Emotional arousal to negative information after traumatic experiences: an event-related brain potential study. Neuroscience 192, 391–397.

Whalen, P.J., Rauch, S.L., Etcoff, N.L., McInerney, S.C., Lee, M.B., Jenike, M.A., 1998. Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. J. Neurosci. 18, 411–418.

Williams, L.M., Kemp, A.H., Felmingham, K., Barton, M., Olivieri, G., Peduto, A., Gordon, E., Bryant, R.A., 2006. Trauma modulates amygdala and medial prefrontal responses to consciously attended fear. Neuroimage 29, 347–357.

Winkielman, P., Berridge, K.C., 2004. Unconscious emotion. Curr. Dir. Psychol. Sci. 13, 120–123.