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Altered Superficial Amygdala–Cortical Functional Link in Resting State After 36 Hours of Total Sleep Deprivation

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The superficial amygdala (SFA) is important in human emotion/affective processing via its strong connection with other limbic and cerebral cortex for receptive and expressive emotion processing. Few studies have investigated the functional connectivity changes of the SFA under extreme conditions, such as prolonged sleep loss, although the SFA showed a distinct functional connectivity pattern throughout the brain. In this study, resting-state functional magnetic resonance imaging (rs-fMRI) was employed to investigate the changes of SFA–cortical functional connectivity after 36 hr of total sleep deprivation (TSD). Fourteen healthy male volunteers aged 25.9 ± 2.3 years (range 18–28 years) enrolled in this within-subject crossover study. We found that the right SFA showed increased functional connectivity with the right medial prefrontal cortex (mPFC) and decreased functional connectivity with the right dorsal posterior cingulate cortex (dPCC) in the resting brain after TSD compared with that during rested wakefulness. For the left SFA, decreased connectivity with the right dorsal anterior cingulate cortex (dACC) and right dPCC was found. Further regression analysis indicated that the functional link between mPFC and SFA significantly correlated with the Profile of Mood State scores. Our results suggest that the amygdala cannot be treated as a single unit in human neuroimaging studies and that TSD may alter the functional connectivity pattern of the SFA, which in turn disrupts emotional regulation.

Key words: sleep deprivation; functional connectivity; fMRI; superficial amygdala; emotion

People are experiencing sleep loss and sleep deprivation (SD) because extended work hours have become a normal state of everyday life (Harrison and Home, 2000; Lockley et al., 2004; Durmer and Dinges, 2005). Except for cognitive deficits, SD can also cause negative emotional and affective reactions, which may adversely impact brain function and result in human errors and accidents (Scott et al., 2006; Franzen et al., 2008; Gujar et al., 2011; Anderson and Platten, 2011). Although several lines of evidence from functional magnetic resonance imaging (fMRI) indicate the impact of SD on emotional functioning, the exact brain mechanisms underlying emotional and affective instability after SD remain largely unknown (Yoo et al., 2007; Van der Helm et al., 2010; Talbot et al., 2010).

Neuroimaging studies with PET and fMRI have investigated the amygdalar activity after SD, which greatly advanced our understanding of the neurophysiological mechanisms of SD (Thomas et al., 2000; Yoo et al., 2007). The amygdala is composed of structurally and functionally distinct nuclei that contribute to the processing of emotion through interactions with other subcortical and cortical structures (Ochsner and Gross, 2005; Phelps and LeDoux, 2005; Frühholz and Grandjean, 2013). The major subregions of the amygdala include the basolateral (BL), superficial (SF), and centromedial (CM) complex on the basis of cytoarchitectonic probability maps (Amunts et al., 2005).

SIGNIFICANCE:

The effects of sleep deprivation (SD) on cognition and motor control are well known, but the impact on emotion is less clear. In the present study, we investigated the effects of 36-hour total SD (TSD) in 14 healthy adults using functional magnetic resonance imaging (fMRI). Our results indicate that TSD was associated with significant decreases in functional connectivity between the superficial amygdala and executive control regions. In addition, increased amygdala functional connectivity was found in medial PFC. Furthermore, the distinct functional connectivity pattern of SFA implicates that amygdala can not be treated as a single unit in human neuroimaging study.

Y. Lei and Y. Shao contributed equally to this work.

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The BL group is believed to play a crucial role in assigning emotional value to sensory stimuli. The CM group receives convergent information from several other amygdaloid regions and sends efferents to various subcortical structures, generating behavioral responses such as modulation of autonomic activity. In our latest study, decreased BL and CM amygdala functional couplings with DLPFC and dorsal ACC were found after 36 hr of TSD (Shao et al., 2014). As a neighboring structure of the BL group, the superficial (cortical) part of the amygdala has been investigated less thoroughly. Traditionally, the SF amygdala (SFA) was believed to be related to the olfactory system (Heimer and Van Hoesen, 2006). However, emerging evidence shows that the SFA is highly related to mood behavior because olfactory signals can unconsciously influence the individual's mood state (Bzdok et al., 2013). Several further studies suggest that the SFA is regulated by social information from human environments, indicating a crucial role of the SFA in social interaction (Dulac and Torello, 2003; Bzdok et al., 2013). According to previous studies suggesting functional differences in the human amygdalar region, further work is needed to elucidate the neural correlates between SFA and other cerebral regions under sleep restriction.

Resting-state fMRI is a powerful way to assess intrinsic connections between brain regions (Damoiseaux et al., 2006; Fox and Raichle, 2007). In rest, spontaneous low-frequency fluctuations can be used to identify correlations between remote brain areas, commonly referred to as *functional connectivity* (Biswal et al., 1995; Fox and Greicius, 2010). Seed-based functional connectivity analysis provides a clear view of regions that are functionally connected with a seed region, making it easy to investigate functional connectivity change in the human brain. For example, clinical studies have revealed that the amygdalar functional connectivity was altered in individuals with generalized anxiety disorder, social phobia, and major depressive disorder (Greicius et al., 2007; Hahn et al., 2011; Demenescu et al., 2013). Moreover, reduced resting-state functional connectivity of the main DMN and anticorrelation network (ACN) nodes has been found with increased sleep pressure (Sämann et al., 2010; De Havas et al., 2012).

In this study, given the crucial role of the SFA in affective processing, especially social interaction, we assumed that the SFA's functional connectivity pattern is disrupted after TSD. We validated this hypothesis by selecting the SFA as the seed region and comparing the whole-brain functional connectivity pattern before and after 36 hr of TSD.

MATERIALS AND METHODS

Subjects

The present study was part of a large fMRI study investigating the neural correlates of working memory after 36 hr of TSD (Shao et al., 2013). In the current report, only subjects with complete resting-state fMRI data are described. Fourteen healthy male participants (mean ± SD age 25.9 ± 2.3 years) were recruited from Beijing Normal University as paid subjects. All subjects were right-handed and had normal or corrected-to-normal vision. None of them had participated in psychophysiological experiments ever before. The exclusion criteria were as follows: diseases of the central and peripheral nervous systems, head trauma, cardiovascular diseases and/or hypertension, cataracts and/or glaucoma, pulmonary problems, and alcohol or drug abuse. None of the subjects showed evidence of clinical symptom levels as assessed by the Symptom Chechlist-90 (SCL-90) with T scores <60 on the General Symptom Index, and all the participants had normal intelligence scores (Raven test IQ >100; Derogatis et al., 1976; Carlson and Heinz Wiedl, 1979). All participants were required to maintain a regular sleep schedule to establish a typical sleep pattern, defined as 8 hr of sleep, and to refrain from alcohol, caffeine, and chocolate intake and napping for 1 week before the study and during it. The subjects gave written informed consent to participate in this study, which was approved by the Research Ethics Committee of Beijing Institute of Basic Medical Sciences and the Fourth Military Medical University (Xi'an, China).

Experiment Paradigm

The experiment was carried out in the Basic Aerospace Institute with nursing staff present at all times. To help with keeping each other awake in the night, each subject was assigned a partner and was under continuous behavior monitoring during the study. Subjects were not allowed to leave the laboratory during the TSD period until they were escorted to the fMRI facility. Two scanning sessions were conducted on each subject, once during rested wakefulness (RW) and once after 36 hr of TSD. The two scanning sessions were conducted 3 week apart to minimize the possibility of residual effects of SD affecting the cognition of volunteers who underwent an SD scan before a RW scan. After each scan session, the Profile of Mood States (POMS) scale was established to record the emotional state of each subject. Both of the scan sessions were performed at the same time (8:00 PM), and the scanning orders were counterbalanced across subjects to reduce the potential influence of order effects.

Resting-State Paradigm

As part of a large fMRI study, participants experienced not only structural MRI and resting-state fMRI scanning but also working memory tasks and a Go/NoGo task. Resting-state scans always occurred before task scans. Foam padding was used to limit head movements within the coil. Earplugs were used to attenuate scanner noise. During the resting-state scans, subjects were instructed to simply keep their eyes closed, to remain as motionless as possible, and not to think of anything in particular. Heart rate and respiration measurements were acquired for removal of physiological noise in the imaging process.

Data Acquisition

All MRI data were acquired at the General Hospital of the PLA of China. Structural and fMRI data were acquired on a GE 3.0T Signa scanner with a birdcage RF imaging coil. After participants had been positioned in the scanner, whole-brain anatomical images were acquired with a high-resolution SPGR sequence. Functional images were obtained at rest using an echo-planar imaging (EPI) sequence (TE = 30 msec, TR = 2,000 msec, field of view = 256 × 256 mm, slice thickness = 5 mm, slice gap = 1 mm, flip angle = 90°, matrix = 64 × 64, 20 oblique

slices). To ensure that the subjects did not fall asleep during the scan, subjects were reminded to keep awake through a microphone before each session. After each run, subjects were asked whether they were awake in the previous run, and all the subjects confirmed that they were awake.

fMRI Preprocessing Procedures

Processing of the fMRI data was completed with Analysis of Functional NeuroImages (AFNI) software (AFNI, http://afni.nimh.nih.gov/afni) and FSL 5.0 (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/). For preprocessing of fMRI images, the first 10 data points of resting-state data sets were discarded because of instability of the initial MRI signal and adaption of subjects to the circumstances. Cardiac and respiratory noise was regressed out by 3dretroicor (AFNI). This was followed by despiking (squashing of extreme time series outliers with a hyperbolic tangent function), volume registration, motion correction, and spatial smoothing (Gaussian kernel of full-width half maximum = 6 mm). A set of regressors, including signal averaged over the white matter mask, cerebrospinal fluid mask, and six motion vectors and their first derivatives, were regressed out of the EPI time series. Then, a bandpass filter was applied to keep only low-frequency fluctuations between 0.015 and 0.1 Hz.

Functional Connectivity Analysis

The SFA was used as the seed region to investigate the impact of SD on the emotions, especially affect-related functional connectivity networks (Krain et al., 2009; Qin et al., 2012). Regions of interest (ROIs) were determined by using stereotaxic, probabilistic maps of cytoarchitectonic boundaries developed by Amunts and implemented in FSL's Juelich histological atlas, consistent with Roy's study (Amunts et al., 2005; Krain et al., 2009). Only voxels with a probability of at least 50% of belonging to the SFA subdivision were included in the ROIs in standard space. 3dmaskave (AFNI) was used to extract the mean time series of all voxels within the ROI.

Then, the time courses of all brain voxels were correlated separately with the mean time course generated from the ROI by Pearson cross-correlation. Next, Fisher's z-transform analysis was applied to the Pearson correlation coefficients to obtain an approximately normal distribution [$z = 0.5\ln(1 + r)/(1 - r)$].

Group statistical analyses were conducted separately for amygdalar connectivity maps from the right and left SFA seeds. One-sample *t*-test was first applied to assess the whole-brain functional connectivity of the left and right SFA. Then, a paired *t*-test was conducted to compare functional connectivity differences between the RW and TSD scans. Cluster size was determined in AlphaSim (AFNI) to correspond to a false-positive rate of $P < 0.05$, corrected for multiple comparisons within the ROIs.

RESULTS

Physiological Data

The respiration and heart rates of all subjects were monitored throughout fMRI scanning. The average values of individual respiration and heart rates before and after SD were compared by paired *t*-tests. No differences were found in heart or respiratory rate between the RW and TSD conditions (heart rate: RW, 68.42 ± 7.26; TSD, 72.00 ± 6.61; $t(1,13) = -1.500$; $P = 0.161$; respiratory rate: RW, 19.01 ± 2.42; TSD, 18.42 ± 2.62; $t(1,13) = -1.084$; $P = 0.300$). No one was excluded for head movement, exceeding more than 1 mm translational movement or more than 1° rotational movement. No differences were found in head movement between the RW and the TSD conditions (paired two-sample *t*-test, $P = 0.05$).

Functional Connectivity of the SFA

The whole-brain functional connectivity patterns of the left and right SFA are shown in Figure 1. The right amygdala seed showed positive connectivity with a number of regions, including the bilateral parahippocampal gyri, bilateral middle temporal gyri (MTG), bilateral superior temporal cortex, and bilateral insula, and negative correlation with the left precuneus, right thalamus, right lingual gyrus, and left superior frontal gyrus. The left amygdala seed showed positive connectivity with the bilateral parahippocampal gyri, bilateral insula, and bilateral inferior frontal gyri and negative correlation with the left thalamus, right anterior cingulate cortex (ACC), bilateral medial frontal gyri, and bilateral middle temporal gyri (Table I, Fig. 1).

Altered SFA Connectivity After TSD

Compared with RW, participants after TSD showed reduced left amygdala functional connectivity with the right dorsal PCC/left thalamus (Talairach coordinates x = –1.5, y = 28.5, z = 38.5; k = 564; T score = –5.01) and right dorsal ACC (Talairach coordinates x = –7.5, y = –31.5, z = 26.5; k = 284; T score = –6.03) and reduced right amygdala functional connectivity with right dorsal PCC (Talairach coordinates x = –13.5, y = 28.5, z = 38.5; k = 301; T score = –6.67). After TSD, increased right amygdalar functional connectivity was found with right medial prefrontal cortex (mPFC; Talairach coordinates x = –1.5, y = –43.5, z = 23.5; k = 324; T score = 4.46; Table II, Fig. 2).

Connectivity Strength and POMS

The POMS indices cover six broad scales (tension–anxiety, depression–dejection, anger–hostility, fatigue, confusion, and vigor). A total mood disturbance score is obtained by summing the scores across all six factors, with vigor weighted negatively. In this study, the POMS sum scores were significantly greater after TSD ($P < 0.001$) compared with the RW state. Regression analysis for the mPFC showing group connectivity differences revealed a significant positive correlation between the resting-state functional connectivity strength and the POMS scores ($r = 0.415$, $P = 0.035$; Fig. 3). No significant correlation between POMS score and any other regions showed group connectivity differences.

DISCUSSION

This study shows that SFA functional connectivity with right mPFC was increased after TSD compared with that

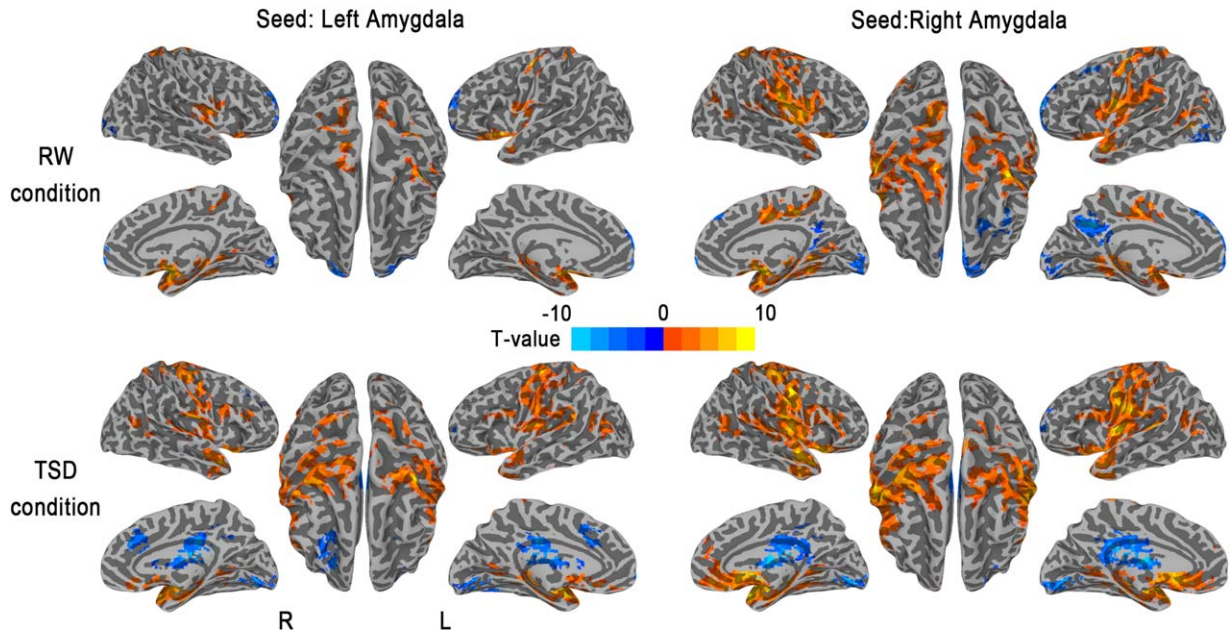

Fig. 1. Whole-brain functional connectivity patterns of the left and right SFA before and after 36 hr of TSD. Brain regions with positive correlations are displayed in warm colors, whereas negative correlations are displayed in cool colors. SFA, superficial amygdala; TSD, total sleep deprivation. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

after normal sleep. Moreover, the strength of functional coupling between SFA and mPFC also showed significantly positive correlation with POMS sum scores. In addition, participants showed decreased SFA functional connectivity with right dorsal ACC and right dorsal PCC after TSD compared with that in the RW scan. These findings indicate that altered functional connectivity in the emotional brain network may be attributed to the neural basis of emotional instability during long-term sleep loss.

Our major finding in this study was the increased functional connectivity between SFA and mPFC after TSD. As with many previous studies (Rosen et al., 2006; Selvi et al., 2007), we also found that SD resulted in significantly increased total mood disturbance. Furthermore, the current finding of a strong positive correlation between SFA–mPFC functional link and POMS sum scores suggests that the SFA–mPFC functional link might play an important role in emotional regulation, which is consistent with a recent study indicating that the mPFC is important for emotional regulation (Hermann et al., 2009). Many studies have demonstrated the effect of the mPFC on emotion generation and regulation because the mPFC not only structurally but also functionally associated with the amygdala (Hermann et al., 2009; Stevens et al., 2013). The extent of amygdalar engagement can be influenced by the mPFC and result in contextually appropriate emotional response (Yoo et al., 2007). Previous studies have shown that the functional link between mPFC and amygdala decreased under task-related conditions (Yoo et al., 2007). Because mPFC is a core brain area of the DMN, a functional brain network whose activities are enhanced in the resting state and decreased in the task state, this enhanced functional connectivity is an important supplement to the variation in task-state functional connection, indicating that cognitive demand for emotional control is increased after SD. Moreover, functional connectivity studies have provided additional and potentially more direct information on the regulatory relationships among specific PFC regions (mPFC, DLPFC, and ACC) and the amygdala, known as the *amygdala–frontal circuits* (Banks et al., 2007; Kim et al., 2011; Burghy et al., 2012; Gee et al., 2013). Frontal regions exert a top-down inhibitory influence on the amygdala, and many studies indicate that increased amygdala–frontal coupling could reflect enhanced cognitive effort as a result of failure to downregulate amygdalar activity (Banks et al., 2007). The finding of increased functional connectivity between SFA and mPFC in this study is consistent with this, because more effort is needed to suppress negative emotion induced by sleep loss. In comparison with our previous study (Shao et al., 2014), the altered SFA–mPFC coupling is distinct. The results indicated that, in the amygdala–frontal circuits, the functional link between SFA and mPFC was more sensitive to TSD because it is important in affective processing.

Beyond the increased functional connectivity, we also found decreased functional connectivity between SFA and dACC, consistent with our previous study (Shao et al., 2014). According to our previous analysis, BL and CM amygdala also showed decreased functional connectivity with dACC, which is closely related to the process

TABLE I. Activation Results From Single-Group, Whole-Brain, Voxelwise Analysis

Brain region	Cluster size	Talairach coordinates			T score
		x	y	z	
Left amygdala connectivity in RW					
Left parahippocampal gyrus	2,235	+16.5	+4.5	−9.5	16.45
Right parahippocampal gyrus		−30.0	+3.0	−10.0	11.6
Left thalamus		+12.0	+27.0	0.0	4.29
Right insula		−34.0	+5.0	+13.0	5.87
Left insula		+31.0	+2.0	+13.0	5.68
Left precentral gyrus		+57.0	+3.0	+15.0	4.54
Right precentral gyrus		−57.0	+2.0	+15.0	4.29
Right inferior frontal gyrus		−35.0	−23.0	−13.0	6.17
Left inferior frontal gyrus		+30.0	−21.0	−13.0	5.59
Left medial frontal gyrus	230	+1.0	−62.0	−4.0	−7.28
Right precentral gyrus	116	−17.0	+19.0	+65.0	6.15
Left superior frontal gyrus	91	+25.0	−56.0	+17.0	−4.85
Right precentral gyrus	86	−56.0	−2.0	+14.0	4.45
Left inferior parietal lobule	76	+37.0	+43.0	+56.0	7.0
Right cuneus	74	−11.0	+91.0	+5.0	−4.36
Left precentral gyrus	74	+43.0	+10.0	+53.0	8.37
Left precentral gyrus	69	+58.0	+4.0	+14.0	4.54
Right superior frontal gyrus	68	−23.0	−56.0	+26.0	−6.25
Left amygdala connectivity in TSD					
Left lentiform nucleus	4,142	+19.0	+4.0	−7.0	17.59
Left parahippocampal gyrus		+26.0	+8.0	−9.0	10.33
Right parahippocampal gyrus		−28.0	+4.0	−9.0	10.11
Right superior temporal gyrus		−38.0	−8.0	−19.0	7.50
Left superior temporal gyrus		+32.0	−4.0	−16.0	8.72
Right insula		−42.0	+2.0	+3.0	3.64
Left insula		+35.0	+9.0	+10.0	5.46
Left inferior frontal gyrus		+54.0	−5.0	+25.0	5.02
Right inferior frontal gyrus		−54.0	−7.0	+25.0	4.40
Right precentral gyrus		−45.0	+14.0	+53.0	6.86
Left precentral gyrus		+47.0	+8.0	+48.0	5.73
Left thalamus	563	+4.0	+10.0	+17.0	−7.29
Right lingual gyrus	281	−5.0	+70.0	−4.0	−6.52
Right anterior cingulate cortex	159	−11.0	−32.0	+29.0	−5.56
Left middle temporal gyrus	97	+40.0	+67.0	+14.0	5.55
Right medial frontal gyrus	85	−20.0	−35.0	+29.0	−5.65
Right middle temporal gyrus	81	−59.0	+52.0	+8.0	4.41
Right parahippocampal gyrus	76	−23.0	+43.0	−1.0	4.93
Right amygdala connectivity in RW					
Right lentiform nucleus	5,423	−26.0	+4.0	−7.0	22.25
Right parahippocampal gyrus		−28.0	+6.0	−9.0	10.76
Left parahippocampal gyrus		+23.0	+4.0	−9.0	10.69
Right insula		−42.0	−1.0	+9.0	7.36
Left insula		+34.0	+4.0	+13.0	5.09
Left precentral gyrus		+56.0	+2.0	+13.0	6.76
Right precentral gyrus		−55.0	−2.0	+13.0	6.67
Right superior temporal gyrus		−33.0	−4.0	−18.0	6.01
Left superior temporal gyrus		45.0	−3.0	−19.0	6.86
Left superior frontal gyrus	520	+22.0	−59.0	+17.0	−9.46
Right lingual gyrus	237	−11.0	+82.0	−4.0	−5.74
Left precuneus	214	+13.0	+52.0	+32.0	−9.05
Left precentral gyrus	107	+28.0	−14.0	+35.0	−5.83
Left middle occipital gyrus	101	+37.0	+61.0	+2.0	7.26
Right middle temporal gyrus	94	−29.0	+67.0	+23.0	4.44
Right amygdala connectivity in TSD					
Right lentiform nucleus	6,969	−26.0	+4.0	−7.0	22.28
Right parahippocampal gyrus		−26.0	+3.0	−13.0	9.83
Left parahippocampal gyrus		+30.0	+2.0	−13.0	9.30
Right middle temporal gyrus		−49.0	+4.0	−13.0	8.83

TABLE I. *Continued*

Brain region	Cluster size	Talairach coordinates			T score
		x	y	z	
Left middle temporal gyrus		+44.0	−6.0	−24.0	5.20
Right insula		−35.0	+10.0	+13.0	5.88
Left insula		+35.0	+9.0	+13.0	6.87
Right precentral gyrus		−54.0	+9.0	+36.0	8.83
Left precentral gyrus		+52.0	+7.0	+36.0	6.92
Right thalamus	747	−5.0	+7.0	+17.0	−8.28
Right lingual gyrus	235	−2.0	+73.0	−4.0	−8.75
Left superior temporal gyrus	94	+40.0	+55.0	+17.0	4.87
Left superior frontal gyrus	64	+10.0	−68.0	+11.0	−4.57

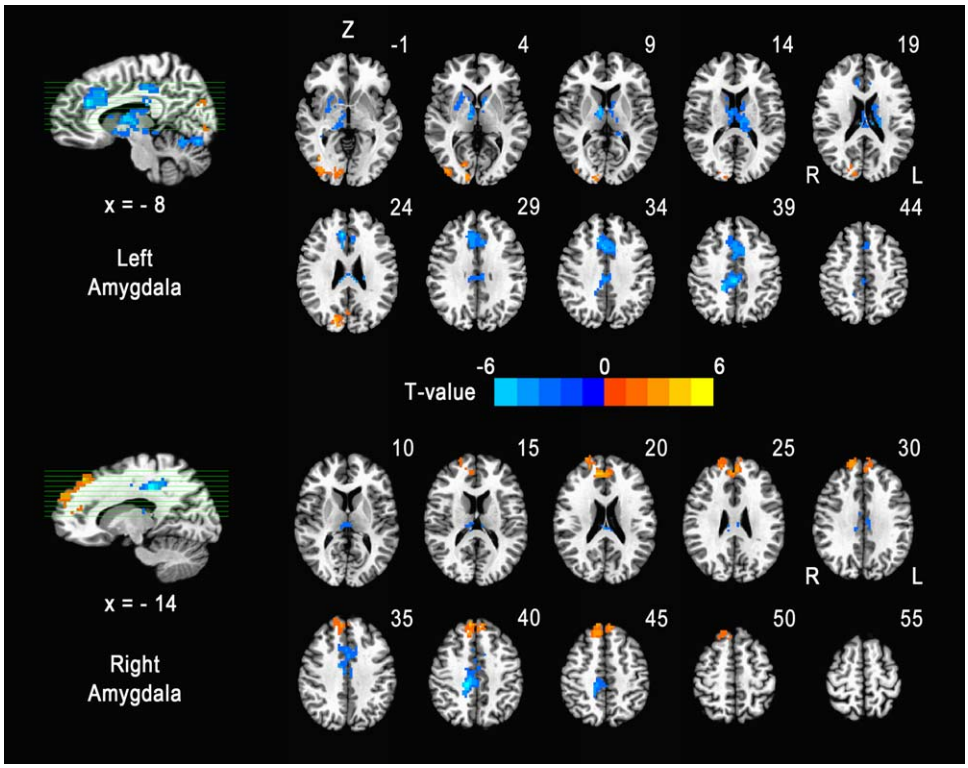

Fig. 2. Functional connectivity analysis results of the between-group comparison. Brain areas that exhibited altered functional connectivity with the left SFA (**top**) and right SFA (**bottom**) after 36 hr of TSD. The left sides of the images in transverse views represent the right hemisphere. SFA, superficial amygdala; TSD, total sleep deprivation. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

of executive control. The dACC has a unique executive attention role in actively maintaining assessment of both stimulus representations and goals in interference-rich contexts and has been identified previously as a region particularly sensitive to TSD (Mohanty et al., 2007; Gujar et al., 2010). Many studies have investigated executive control function with Go/NoGo tasks and found decreased activities of dACC after TSD, indicating the reduced response inhibition after sleep loss (Gujar et al., 2010; Renn and Cote, 2013). Reported effects of TSD on working memory also include the reduced activity of dACC with enhanced working memory load after TSD (Mu et al., 2005; Chee et al., 2006). Because the dACC is part of the executive control network (ECN), which largely manages human brain function, the emotional deficits after TSD may result from altered brain function in this network. Motomura and colleagues (2013) conducted a partial-SD experiment and found that continuous and accumulating sleep debt can downregulate functional suppression of the amygdala by ACC. Our results support

TABLE II. Anatomical Localization, Cluster Size, Talairach Coordinates, and Maximum T Values of TSD-Induced Functional Connectivity Changes

Brain region	Cluster size	Talairach coordinates			T score
		x	y	z	
Seed: Left amygdala (after TSD vs. before TSD)					
Right dorsal PCC	564	−1.5	+28.5	+38.5	−5.01
Left thalamus		+9.0	+19.0	+17.0	−3.05
Right dorsal ACC	284	−7.5	−31.5	+26.5	−6.03
Right middle occipital gyrus	233	−37.5	+64.5	−9.5	5.72
Left culmen	209	+7.5	+67.5	−9.5	−4.17
Seed: Right amygdala (after TSD vs. before TSD)					
Right medial PFC	324	−1.5	−43.5	+23.5	4.46
Right dorsal PCC	301	−13.5	+28.5	+38.5	−6.67

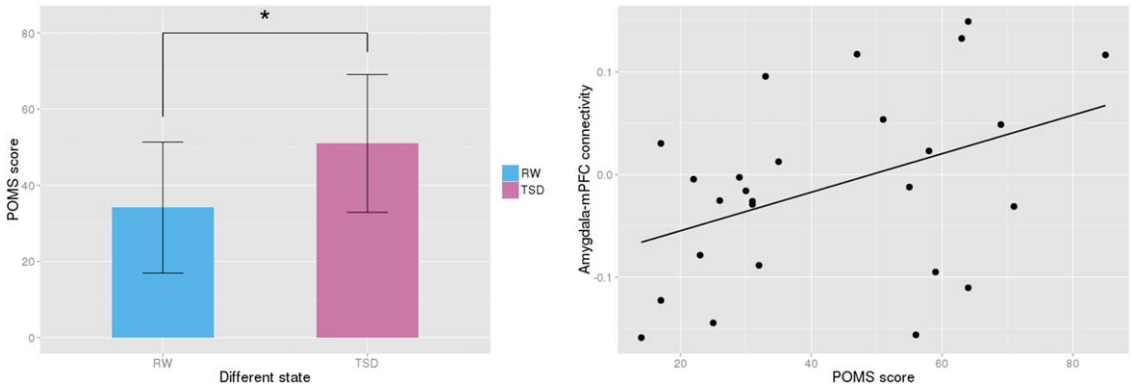

Fig. 3. Significantly increased POMS in subjects after 36 hr of TSD. POMS sum score was significantly correlated with functional connectivity between the SFA and the medial prefrontal cortex. $\star P < 0.05$. POMS, Profile of Mood State; TSD, total sleep deprivation. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

this conclusion and indicate that negative variation of individuals' emotion is closely associated with the decrease of this functional connection.

In addition, decreased functional connectivity was found between the SFA and the right dorsal PCC. Although dPCC and dACC have a close relationship to executive brain function, dPCC is engaged mostly in the response inhibition process (Liddle et al., 2001; Menon et al., 2001). Response inhibition is an important function of the human body and plays a significant role in pursuing advantages and avoiding risks. Many clinical studies have shown that individuals with weak abilities for brain processing have some decreased PCC function (Shin et al., 2001; Critchley et al., 2003). The declined resting-state functional connectivity between SFA and dPCC in this study might indicate the decreased response inhibition on emotional control.

Compared with our previous work, this study indicates that the impact of 36 hr TSD on the functional connectivity pattern of the SFA has particular characteristics involving the affective processing during TSD. The finding of a distinct functional connectivity pattern of SFA is consistent with several previous studies demonstrating that the role of amygdaloid subnuclei during the decoding of emotions is not consistent and that the SFA is involved with socially relevant information processing, being associated with thalamus and dACC (Bzdok et al., 2013; Koelsch and Skouras, 2014). Although the SFA showed a distinct functional connectivity pattern after 36 hr of TSD, our results also indicate that each of the amygdaloid subnuclei shares some common features in emotional regulation.

Our previous study showed that not only dACC but also DLPFC had decreased functional connectivity with the BLA after TSD (Shao et al., 2014). Prior neuroimaging studies of emotional regulation have posited that conscious downregulation of emotion appears to have a top-down inhibitory effect on prefrontal brain regions, including the DLPFC (Banks et al., 2007; Kohn et al., 2014). Because the DLPFC, dACC, and dPCC have a very close relationship and belong to the ECN, our results show that TSD might result in decreased executive brain function and cause fragmentation of the ECN–amygdala networks. From the brain network viewpoint, such a lack of inhibition from ECN regions to the amygdala can be interpreted as a deficit in automatic emotional regulation or a lack of cognitive control over emotion. Our findings are an important supplement to previous studies showing

that, during long TSD, the executive brain network attends to emotional regulation beyond the mPFC, with reduced functional linkage with the SFA after TSD.

The findings of reduced functional connectivity between the SFA and emotion-regulation regions suggest plausible mechanisms involved in exaggerated emotional responses and apparent dysfunction of emotional regulation in participants after TSD. These results suggest that the decreased executive control function and SFA functional connectivity after sleep deprivation reflect the decreased emotion regulation abilities, especially emotion management, after SD. In summary, we conclude that, for the resting brain, the connection between SFA and regions involving executive control decreases, whereas the connection between SFA and mPFC increases, after TSD, suggesting that the production of negative emotion increases and the emotion control ability decreases after SD. This phenomenon can be identified by the functional linkage of the SFA, which reflects the differences and changes in individuals' emotional processes after SD. These results reveal the effects of disturbances in sleep and biological rhythm on individuals' emotions and their characteristics.

LIMITATIONS

Several limitations of this study exist. First, all the participants were male, so generalizations to women cannot be made. The experimental conditions and the long time course required prevented us from recruiting female volunteers, limiting the clinical utility of our findings. In the future, it would be interesting to investigate sex differences in functional connectivity changes after TSD. Second, our findings are based on the assumption that participants under both RW and TSD states respond similarly to the scanning environment. However, it is possible that the participants experienced higher anxiety levels during the scan after TSD, and this could potentially contribute to the different connectivity patterns that we observed. Third, verbal report of subjects' in-scanner sleeping behavior is not an adequate measure. In future experiments, we will consider using real-time EEG to monitor subjects' state in the scanner.

CONCLUSIONS

Our results suggest that TSD altered functional connectivity in the emotional brain network, which in turn disrupts emotional regulation. Such alterations of functional links in emotion control might in part be the neural basis for emotional instability during SD. Furthermore, the distinct functional connectivity pattern of the SFA implies that the amygdala cannot be treated as a single unit in human neuroimaging studies.

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