Abnormal Spontaneous Brain Activity in Acute Low-Back Pain Revealed by Resting-State Functional MRI

Shan-shan Zhang, MD, Wen Wu, MD, Jian-ming Yang, PhD, and Chu-huai Wang, MD, PhD

Objective: Neuroimaging studies have revealed that low-back pain (LBP) alters spatiotemporal dynamics of the blood oxygen level–dependent signal in response to persistent noxious stimuli. This study aimed to investigate changes in spontaneous neural activity of various brain regions in acute LBP using resting-state functional magnetic resonance imaging and amplitude of low-frequency fluctuation (ALFF).

Design: Twelve healthy subjects underwent two separate resting-state functional magnetic resonance imaging scans at health status as baseline and after intramuscular injection of hypertonic saline (0.5 mL, 5%) into the back muscles to induce acute LBP.

Results: Compared with baseline, acute LBP showed decreased ALFF in the right posterior cingulate cortex/precuneus and left primary somatosensory cortex (S1) but increased ALFF in the right medial prefrontal cortex, right middle temporal gyrus, bilateral inferior temporal gyrus, bilateral insula, right anterior cingulate cortex, and left cerebellum. In addition, significant negative correlations were observed between visual analog scale scores and ALFF of the bilateral medial prefrontal cortex, left inferior frontal gyrus, left S1, right anterior cingulate cortex, and left middle temporal gyrus.

Conclusions: These findings suggest that abnormally spontaneous neural activity involving some brain regions are responsible for sensory, affective, and cognitive functions, which may be implicated in the underlying pathophysiology of acute LBP.

Key Words: Low-Back Pain, Functional Magnetic Resonance Imaging, Resting State, Amplitude of Low-Frequency Fluctuation

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Low back pain (LBP) is one of the most common forms of chronic pain, and its increased severity and duration causes cognitive and emotional impairments, with accumulating evidences supporting the idea that chronic pain-induced brain reorganization is associated with morphological and functional plasticity.1–3 Previous structural magnetic resonance imaging (MRI) studies found that chronic pain subjects exhibited decreased gray matter density decreases in the bilateral dorsolateral prefrontal cortex (PFC) and right thalamus.4 Recent progress of neuroimaging studies suggest that chronic back pain alters whole-brain gray matter volume and decreases gray matter density in a sex-independent manner that is distinct from the changes associated with human aging.1 The results of functional MRI (fMRI) studies suggest that LBP affects neural activity and alters spatiotemporal dynamics of the blood oxygen level–dependent (BOLD) signal in response to persistent nociceptive stimuli.2 Abnormalities have been revealed in specific regions of the brain, including the PFC, posterior cingulate cortex (PCC), insular cortex (IC), and cerebellum.5,6 Mounting evidence supports the association of LBP with metabolic and chemical changes within the large-scale signal distribution networks central to sensory, motor, cognitive, and affective functions.7

Among human fMRI studies, the most consistent observations depict that the default mode network (DMN) is the primary network involved in LBP.5,6 In contrast to other resting-state networks, the DMN comprising the PCC/precuneus, medial prefrontal cortex (mPFC), inferior parietal lobule, and medial temporal gyrus is functionally identified as being more active at rest. Multiple functional imaging studies have demonstrated that DMN activity is disrupted in response to painful stimulation caused by different acute conditions.8–10 The DMN also participates in episodic memory, monitoring the internal environment to detect salient events and maintaining a baseline level of attention.11 Thus, alterations of spontaneous BOLD activity in these regions probably contribute to the memory, attention, and executive processing of acute LBP. Current evidences from brain fMRI and positron emission tomography studies have confirmed that DMN functional connectivity is closely related to metabolic activity.12 Moreover, DMN can modulate the perception of acute noxious stimuli through other antinociceptive descending modulation networks,13 indicating that the development of LBP may be initiated by the functional alterations of DMN. Furthermore, LBP can induce pain unpleasantness and other negative affective responses, which in turn induce the pronounced activation of the pain matrix.14 Models of experimentally induced LBP have been advocated as powerful tools for investigating mechanisms of muscle pain and pain control that provide insight into the potential pathophysiology of acute pain.15 Within chronic LBP, the brain...
is continuously processing signals originating from spontaneous back pain. Increasing phases of chronic pain are characterized by transient activity in the brain regions that are most commonly activated in acute pain. Therefore, neural activity in acute LBP seems to mimic the properties of nociceptive elicitor and interferences associated with conscious or subconscious processing. Previous studies have explored pain perception after injection of hypertonic saline into low-back muscles. According to those studies, the location, depth, and intensity of experimentally induced pain is distinct for different back muscles (ie, the lumbar interspinous ligament, erector spinae muscle, and superficial/deep multifidus muscles). A previous resting-state fMRI study also found that experimentally induced LBP was associated with abnormally regional homogeneity of resting-state brain activity.

Resting-state fMRI has revealed that spontaneous neural activity at rest highly correlates with low-frequency (\(<0.08\) Hz) fluctuations in BOLD signals that are synchronized between brain regions. In the present study, the amplitude of low-frequency fluctuation (ALFF), a newly developed fMRI marker, was used to investigate abnormalities in regional spontaneous neural activity associated with acute LBP. Unlike the functional connectivity and regional homogeneity methods that are typically used in most resting-state fMRI studies and that mainly focus on the similarities of intraregional and inter-regional time series, ALFF is a promising method for detecting the regional intensity of spontaneous fluctuations in BOLD signal.

Recent studies have demonstrated that ALFF abnormalities occur in attention-deficit hyperactivity disorder, early Alzheimer disease, depressive disorders, and subcortical infarction. In addition, Yang et al. reported the first evidence supporting that the state dependence (eyes open vs eyes closed) of distinct ALFF difference.

Although resting-state fMRI research has advanced the understanding of brain function in experimental LBP and clinical disorders, its underlying neurophysiological mechanisms and regional neuronal activity abnormalities are not completely understood. The aim of the present study was to use fMRI and ALFF methods to investigate changes of regional spontaneous brain activity in acute LBP during resting state. It was hypothesized that the brain regions involved in sensory, affective, and cognitive functions would show ALFF changes associated with acute LBP. To explore whether ALFF measurements vary with pain intensity, correlation analyses were performed to evaluate possible associations between ALFF values and visual analog scale (VAS) scores in LBP.

**Study Design and Ethical Approval**

A self-controlled trial study was conducted to investigate changes in spontaneous neural activity of some brain regions in acute LBP. This study was approved by the Institutional Medical Research Ethics Committee of the First Affiliated Hospital of Sun Yat-sen University. Written informed consent was obtained from each subject after detailed instructions on the experimental procedures and the potential risks of the study had been completely explained.

**Subjects**

Twelve healthy volunteers (7 men and 5 women) who had been pain-free for the past month participated in this study. The mean age was 23.83 ± 3.51 years, with a range of 20 to 28 years. Subjects had 16.50 ± 2.54 years of education, with a range of 14 to 20 years. All subjects were right-handed, had no history of chronic pain or activity-limiting LBP, reported no neurologic or psychiatric conditions, and currently were not taking antipyretics or sleeping pills.

**Stimulus and Data Acquisition**

With subjects in a prone position, a fine plastic cannula (24 gauge) attached to a 1-mL syringe containing sterile hypertonic saline (5%) was inserted 2 cm deep into the right erector spinae muscle at the level of the fourth lumbar vertebra (L4), before scanning for 10 minutes. The pain caused by the needle subsided to preinjection levels within approximately 20 seconds without anesthesia. Each subject underwent 2 separate resting-state fMRI scans at health status as baseline and after injection of hypertonic saline into back muscles to induce acute LBP. After the collection of baseline data for 318 seconds, each subject received an intramuscular injection of 5% hypertonic saline (0.5 mL) via the fine plastic cannula inserted at the L4 level, and the same fMRI scans were repeated 20 seconds after the injection.

All imaging data were acquired at Zhuijiang Hospital using a Philips Achieva 3.0-T MRI scanner (Royal Philips Electronics, Eindhoven, the Netherlands) equipped with a standard 8-channel radio-frequency head coil. Each subject lay supine with their head snugly fixed with pillows and foam pads to reduce head motion. Subjects were asked to close their eyes and rest comfortably throughout the scans without moving or falling asleep. T2*-weighted functional images were acquired in a single-shot gradient echo echo-planar imaging sequence (24 axial slices, repetition time/echo time, 3000/40 milliseconds (ms); flip angle, 90 degrees; matrix, 64 × 64; field of view, 220 mm × 220 mm; slice thickness/gap, 5/0.5 mm). Before obtaining the functional measurements, high-resolution T1-weighted structural images were collected using a fast spin echo sequence (repetition time/echo time, 500/14 ms; matrix, 256 × 256; and flip angle, 90 degrees).

When the scans were completed and subjects remained inside the scanner, they were asked to rate the maximal pain intensity and unpleasantness after the intramuscular injection of hypertonic saline. Pain intensity was assessed on a 10-cm VAS anchored with “no pain” (0) and “worst pain imaginable” (10). Pain unpleasantness (ie, distressing and horrible) was measured with a 10-cm in-house mood scale anchored with “infinitely small” (0) and “excruciating” (10). Moreover, subjects were asked to estimate the size of the painful area using a standardized diagram depicting a series of 10 circles with diameters ranging from 1 to 10 cm.

**Data Processing**

Resting-state functional images preprocessing and ALFF analysis were performed using Data Processing Assistant for Resting-State fMRI (DPARSF) software (http://rfmri.org/DPARSF). Preprocessing steps included removal of the first 10 volumes, slice timing correction, motion correction, normalization

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to the Montreal Neurological Institute templates, spatial smoothing with a Gaussian kernel of full-width half-maximum of 6 mm. During motion correction, subjects’ head movements of less than 2 mm in translation and 2 degrees in rotation were used for further analysis (no subjects were excluded). Subsequent analyses included linear trend removal and band pass filtering (0.01–0.08 Hz) to reduce the effects of very low–frequency drift and high-frequency noise.

The following ALFF calculation procedure was based on a previous report. The filtered time series were converted into frequency domains with a fast Fourier transform, and the square root of the power spectrum was then calculated at each frequency. The averaged square root was obtained across a 0.01- to 0.08-Hz range at each voxel, which was taken as the ALFF. For standardization purposes, ALFF of each voxel was divided by the mean ALFF value within a brain mask.

**Statistical Analysis**

Statistical analysis was performed using SPSS 13.0 (SPSS, Inc, Chicago, IL). Descriptive statistics (mean ± SD) were calculated for age, education, pain intensity, and pain unpleasantness. Linear correlation was used to determine potential correlations between pain unpleasantness (including distressing and horrible) and VAS score rated for pain intensity.

Random effects analysis was used to create within-group Statistical Parametric Mapping (SPM8, http://www.fil.ion.ucl.ac.uk/spm) and Xjview (http://www.alivelearn.net/xjview) for each network and to explore the ALFF differences between 2 conditions. To extract ALFF values across the subjects that were higher than the global mean, one sample t test was performed against 1 (the global mean ALFF) within each condition. Two-tailed paired t test was used to compare the ALFF difference between LBP and baseline. To explore whether ALFF measurements varied with pain intensity, REST software (http://rfmri.org/rest) was used to compare ALFF at each voxel of the whole brain in pain status versus VAS score. The resulting statistical maps were corrected for multiple comparisons using the false discovery rate (FDR) with a significance level of \( P < 0.05 \) and cluster size of 10 or greater.

**RESULTS**

Twelve subjects completed the study. For all subjects, the rotations of head movements were within 2 mm in translation and 2 degrees in rotation. For the muscle pain series, maximum pain scores of 4 or greater were used for further analysis. The average maximum pain score after intramuscular injection of hypertonic saline was 6.58 ± 2.06 (range, 4–8). Therefore, data for each subject were included in all analyses.

Muscle pain was also described as rostral progressed to a region surrounding the injection site with a 2–to 3-cm diameter. In addition, all subjects experienced mild anxiety (3.12 ± 1.56) and fear (1.97 ± 0.78) related to induced pain. There was no significant linear correlation between anxiety or fear and VAS scores (\( r = 0.06 \) and \( r = 0.12 \), respectively; \( P > 0.05 \) for both).

**Within-Group ALFF Analyses**

The mean ALFF maps within each condition are shown in Figure 1. Upon visual inspection, the PFC showed significantly higher ALFF than the global mean but with different strength between 2 conditions (\( P < 0.05 \), FDR, cluster size ≥10). In addition, other brain regions, including the cingulate cortex and occipital cortex, had higher ALFF values within each condition. The ALFF values in the parietal cortex, temporal cortex, and cerebellum were significantly lower than the mean ALFF within the mask.

![FIGURE 1. Mean ALFF maps in health status and pain status (\( P < 0.05 \), cluster threshold ≥10). Visual examination indicates high ALFF values in the prefrontal cortex and cingulate cortex, and lower ALFF values in parietal cortex, temporal cortex, and cerebellum within each group. The strength of ALFF values is different between 2 conditions. On the color bar (lower section), ALFF values that are regionally higher than the global mean are shown as red-yellow, whereas ALFF values lower than the global mean are shown as blue-green.](http://www.ajpmr.com)
Between-Group ALFF Analyses

The group analysis showed significant ALFF differences between pain status and baseline (Fig. 2, Table 1). Compared with the baseline level, acute LBP showed significant ALFF decreases in the right PCC/precuneus and left primary somatosensory cortex (S1), and increases in the right mPFC, bilateral insula, right anterior cingulate cortex (ACC), right middle temporal gyrus, bilateral inferior temporal gyrus, and left cerebellar tonsil (\(P < 0.05\), FDR, cluster size \(\geq 10\)).

Correlations Between ALFF and VAS Scores

The ALFF of peak voxel showed significant negative correlations with VAS scores in LBP (Fig. 3, Table 2). Correlation analysis revealed that there was a strong negative association between ALFF in the bilateral mPFC and VAS scores. Moreover, significant negative correlations were observed in the left S1, left inferior frontal gyrus, left middle temporal gyrus and right ACC (\(P < 0.05\), FDR, cluster size \(\geq 10\)).

DISCUSSION

In the current study, the ALFF method was used to investigate the mechanisms underlying the changes of spontaneous brain activity in acute LBP induced by intramuscular injection of hypertonic saline and to emphasize the importance of network interactions between brain regions in this response. The results of the study suggest a functional relationship between pain and certain brain regions reflected by ALFF and are

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>BA</th>
<th>Cluster Sizes</th>
<th>Peak t Value</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>R medial prefrontal cortex</td>
<td>10</td>
<td>10</td>
<td>5.27</td>
<td>42</td>
<td>−18</td>
<td>27</td>
</tr>
<tr>
<td>L/R insular cortex</td>
<td>13/13</td>
<td>17/44</td>
<td>9.33/9.26</td>
<td>−33/30</td>
<td>6/6</td>
<td>12/12</td>
</tr>
<tr>
<td>L/R inferior temporal gyrus</td>
<td>20/20</td>
<td>10/15</td>
<td>6.32/6.13</td>
<td>−42/51</td>
<td>−24/−15</td>
<td>−27/−24</td>
</tr>
<tr>
<td>R middle temporal gyrus</td>
<td>21</td>
<td>12</td>
<td>7.03</td>
<td>66</td>
<td>−33</td>
<td>−6</td>
</tr>
<tr>
<td>R anterior cingulate cortex</td>
<td>32</td>
<td>18</td>
<td>6.49</td>
<td>15</td>
<td>42</td>
<td>9</td>
</tr>
<tr>
<td>L cerebellar tonsil</td>
<td>—</td>
<td>16</td>
<td>10.12</td>
<td>−21</td>
<td>−54</td>
<td>−45</td>
</tr>
<tr>
<td>R posterior cingulate cortex</td>
<td>31</td>
<td>10</td>
<td>−7.54</td>
<td>12</td>
<td>−33</td>
<td>42</td>
</tr>
<tr>
<td>L primary somatosensory cortex</td>
<td>2</td>
<td>11</td>
<td>−5.28</td>
<td>−39</td>
<td>−36</td>
<td>42</td>
</tr>
</tbody>
</table>

Paired t-test analysis, \(P < 0.05\) (FDR), \(K \geq 10\).

BA, Brodmann area; L, left; MNI, Montreal Neurological Institute; R, right.
similar to previous reports that used different methodologies. Signals in cortical and subcortical regions, including the DMN, cingulate cortex, somatosensory cortex, IC and cerebellum, displayed significant ALFF differences during resting state under LBP versus baseline. Furthermore, the ALFF value of the bilateral frontal cortex, left temporal cortex, left parietal cortex, and right cingulate cortex showed significant negative correlations with VAS scores.

The ALFF pattern in the default mode network during acute LBP was very similar to the DMN proposed by Raichle et al., which was based on the results of a positron emission tomography study. Specifically, ALFF changes were observed in the PCC/precuneus, mPFC, and middle temporal gyrus, implying that back pain evokes abnormal spontaneous brain activity in the DMN. Posterior cingulate cortex/precuneus as a critical node within the circuitry during resting state showed significant lower ALFF than other brain regions in acute LBP, suggesting that acute painful stimuli may induce decreases in resting-state brain activity. This result is consistent with previous findings indicating altered DMN dynamics and decreased functional connectivity in chronic LBP. In contrast, ALFF in the mPFC and middle temporal gyrus were significantly higher in the presence of acute LBP. The mPFC is usually activated in acute pain, with responses to modulation, expectancy, and emotional processing. Thus, abnormal spontaneous brain activity of mPFC within the DMN may cause the disruption of pain modulation over frontal cortical activity, which is also critical to the perception of negative effects in pain state.

Extensive research on the central mechanisms governing the sensory-discriminative dimensions of pain have revealed a complex network of cortical and subcortical brain regions that is involved in the transmission and integration of pain, the so-called pain matrix. Activity within the pain matrix, which consists of the S1, secondary somatosensory cortex (S2), IC, ACC, frontal lobe, and parietal lobe, shows a strong relationship with pain. The results of this study indicated that the pain matrix exhibited abnormal ALFF in response to acute LBP, including the left S1, bilateral IC, right ACC, and right PFC. Because both the present results and previous findings from functional imaging studies combined with psychophysiological measurements detected pain-related S1 deactivation, this specific region that corresponds to the somatotopic representation may reflect neurovascular mechanisms related to functional inhibition in response to acute LBP. This process is totally different from the pathogenesis of chronic pain that nociceptive afferents become sensitized in a way that the signaling of these nociceptive afferents increases perceived pain disproportionately to the pain stimulus.

### TABLE 2. Correlations between ALFF and VAS scores in acute low-back pain

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>BA</th>
<th>Cluster Sizes</th>
<th>Peak r Value</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>L/R medial prefrontal cortex</td>
<td>10/10</td>
<td>11/34</td>
<td>−0.89/−0.89</td>
<td>−9/15</td>
<td>69/60</td>
<td>9/3</td>
</tr>
<tr>
<td>L inferior frontal gyrus</td>
<td>47</td>
<td>27</td>
<td>−0.88</td>
<td>−24</td>
<td>24</td>
<td>−6</td>
</tr>
<tr>
<td>L middle temporal gyrus</td>
<td>19</td>
<td>19</td>
<td>−0.91</td>
<td>−30</td>
<td>−69</td>
<td>21</td>
</tr>
<tr>
<td>R anterior cingulate cortex</td>
<td>32</td>
<td>30</td>
<td>−0.91</td>
<td>15</td>
<td>33</td>
<td>15</td>
</tr>
<tr>
<td>L primary somatosensory cortex</td>
<td>3</td>
<td>10</td>
<td>−0.91</td>
<td>−60</td>
<td>−21</td>
<td>36</td>
</tr>
</tbody>
</table>

Correlation analysis, $P < 0.05$ (FDR), $K \geq 10$.

BA, Brodmann Area; L, left; MNI, Montreal Neurological Institute; R, right.
previous studies showed that negative BOLD signal changes were observed in the ipsilateral S1, whereas an increased BOLD signal was observed in the contralateral S1. This finding revealed an overlap of negative BOLD signals with the stimulus-induced contralateral (left) S1, which was in contrast with the right back muscle pain induced by hypertonic saline. Painful stimuli evoke opposing stimulus-response functions in the S1 may reflect differences on pain-related potential using unique modes of stimulation.

Recent fMRI studies have shown that the insula is involved in multidimensional conceptualization of pain comprising sensory, affective, cognitive, and behavioral components. The insula is typically activated in neuroimaging studies of acute experimental pain. As the key region in the endogenous pain modulation system, it is likely that spontaneous brain activity in the insula is changed during acute pain sensation. The present study found that ALFF was significantly increased in bilateral IC, indicating that acute LBP may increase insular sensitivity and facilitate the interaction in descending pain modulatory circuits. Multiple lines of evidence have indicated that the anterior insula is activated during anticipation and empathy, and it encodes pain location and quality. Therefore, transient insular activity in LBP may provide a sensory-related nociceptive elicit signal that can be amplified according to pain duration. The insula is functionally connected to the S1, S2, and ACC during resting state, suggesting that pain-related activations were caused by enhanced broad monitoring of the external environment. Moreover, the perceived unpleasantness of muscle stimulation is positively correlated with bilateral insular metabolism. This data implies that bilateral insular activation may be involved in encoding the unpleasantness resulting from tonic muscle pain. Furthermore, a recent study showed generally stronger pain-related activations in male subjects. Sex differences (7 men, 5 women) in neural responses may influence insular activation in acute LBP. However, in contrast to previous reports that have shown a positive correlation between insular connectivity and pain intensity, this study did not reveal any significant correlation between ALFF of insula and VAS scores. These findings highlight the complexity of the neural mechanisms underlying LBP and suggest that acute pain disrupts normal neural activity in the cortical areas of the insula.

The ACC is specifically involved in pain perception and responds directly to noxious stimuli. Increased ALFF in the right ACC suggested that acute muscular pain induced an increase in nociceptive signaling and disrupted ACC activity. It is important to note that ACC represents a major region responsible for encoding the affective dimensions of pain perception that can regulate how one initiates behavior and inhibits certain responses. Thus, spontaneous neural activity changes in this region during pain-related stimulations most likely reflect a negative emotional state and serve to modulate mesocorticolimbic activity. Moreover, several lines of evidence have shown that efficient pain processing and compensatory damage are functionally associated with PFC. Therefore, significant ALFF increases in the ACC may be related to compensatory responses caused by PFC decreases. This relationship may explain acute pain affecting brain activity related to pain effects away from ACC to PFC. Furthermore, this study demonstrated that all subjects suffered mild anxiety and fear while they were experiencing pain, which further supports the hypothesis that ACC is mainly involved with negative affective responses to painful stimuli.

It should be noted that in the bilateral inferior temporal gyrus, ALFF in acute LBP under resting-state condition was significantly higher than that at baseline. The inferior temporal gyrus is associated with recognition memory and behavioral responses and is known to receive information from the ventral stream. The present results showing that the inferior temporal gyrus exhibits regional cerebral blood flow increases according to acute pain. Thus, ALFF changes in this brain region may be due to increased recognition of somatotopic organization and alteration of behavioral responses to noxious stimuli. In addition, ALFF of the cerebellum significantly increased with induced acute pain. Cerebellar function is important in LBP because the pain-specific region directly receives afferent input from peripheral nociceptive pathways and has been regularly shown to be involved in cognitive processing. In particular, the highest ALFF detected in this region may reflect painful stimuli disrupting various cognitive processes that mediate the attenuation of pain perception and cognitive control mechanisms. Moreover, high activation of the cerebellum during pain provides further evidence for increased stimulus-evoked activity and abnormal brain chemistry within the cerebellum in response to diverse states of pain.

Since spontaneous brain activity and pain intensity are highly correlated, this study investigated the potential association between ALFF values and VAS scores in induced LBP. Correlation analysis revealed significant negative correlations during LBP in the left S1, left inferior frontal gyrus, left middle temporal gyrus, and right ACC, suggesting that inhibitory systems contribute to the pathogenic mechanism of LBP. In this study, changes of spontaneous neural activity in S1 showed a significant negative correlation with pain intensity. Thus, it seems reasonable to suggest that the persistent afferent nociceptive input to S1 degrades functional organization of somatosensory cortex and attenuates responses to peripheral nociceptive stimuli. Similarly, ALFF changes in the inferior frontal gyrus correlated with changes in VAS scores. The painful stimuli processed within the frontal cortex may result in dysfunctional pain perception, altering stimulus intensity and quality. Interestingly, negative correlations were found for the resting-state fMRI data within the middle temporal gyrus and ACC. Although DMN is strongly interconnected with the limbic system, high consistency among the regional brain areas located between the middle temporal gyrus and ACC have rarely been reported. This finding demonstrated that increased pain intensity over time was associated with a decrease ALFF in the right ACC. Thus, the increasing phase of spontaneous brain activity in ACC was most likely caused by the emotional components of pain and also for ongoing pain increasing by emotional salience.

CONCLUSIONS

In conclusion, the findings of this study have demonstrated that acute LBP is associated with abnormal regional spontaneous neural activity in various cortical and subcortical brain regions. Resting-state spontaneous brain activity changes associated with functional modulation during pain processing
evoked with acute LBP differ from chronic LBP. Cerebral BOLD signal changes within the somatosensory system, limbic system, prefrontal cortex, and temporal cortex suggest the pathophysiology of acute LBP involves sensory, affective, and cognitive processing. The results of correlation analyses evaluating the relationship between the amplitude of low-frequency fluctuation and VAS scores in pain status provide insight into the mechanisms underlying the perception of pain in response to noxious stimulation of low-back muscles. To gain additional insight into the origins of brain activity in LBP, future studies should evaluate larger cohorts, consider other functional network modeling methods to investigate the complex mechanisms governing the interplay among multiple brain regions and investigate potential sex-related difference in the cerebral BOLD signal. Besides, whether intramuscular injection of hypertonic saline sheds light on anything other than dominant pain sensation of muscular origin needs more research.

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