


RESEARCH ARTICLE

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Dynamic interpersonal neural synchronization underlying pain-induced cooperation in females

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Funding information

China Postdoctoral Science Foundation, Grant/Award Number: 2018T110363; National Natural Science Foundation of China, Grant/Award Number: 31600890; Shanghai Municipal Commission of Health and Family Planning, Grant/Award Numbers: 201540114, ZK2015B01

Abstract

Individuals in pain are motivated to be cooperative in social interaction. Yet, there has been little research on how pain dynamically affects cooperation at a neural level. The present study investigated the cooperative behavior under acute physical pain by asking dyads to complete three blocks of button-press cooperative task, while neural activities were recorded simultaneously on each subject by the fNIRS-based hyperscanning. Results showed that individuals in pain improved their cooperation rate across task blocks. Accordingly, increased interpersonal neural synchronization (INS) was found at the left prefrontal cortex in second block, whereas increased INS was found at the right prefrontal cortex and the right parietal cortex in third block compared to the first block. Moreover, the change of INS in right parietal cortex was positively correlated with subjective pain rating in the pain treatment group. In addition, dynamic interpersonal neural networks were identified in painful condition with increasing frontoparietal networks across time. By uncovering dissociative neural processes involved in how pain affects cooperation in social interaction, the present work provides the first interbrain evidence to highlight the sociality of pain on social interaction in perspective of motivational aspect of pain.

KEYWORDS

cooperation, functional near-infrared spectroscopy, hyperscanning, interpersonal neural synchronization, pain

1 | INTRODUCTION

Pain is a distressing experience that affects sensory, emotional, cognitive, and social components of mind and behavior (Williams & Craig, 2016). In particular, it is highlighted in recent years that pain exerts significant impact on social cognition and behaviors. This has been supported by a number of behavioral studies (Bastian, Jetten, & Ferris, 2014; Langford et al., 2010; Wang, Gao, Ma, Zhu, & Dong, 2018). Humans who shared transient pain experience promoted cooperation by increasing social bonding among a group of strangers (Bastian et al., 2014). Besides, individuals who suffered from acute pain alone also exhibited greater interpersonal trust in monetary decision-making tasks (Wang et al., 2018). In animals, mice chose to approach a familiar same-sex conspecific in pain,

indicating that pain behavior served a function of soliciting social approach (Langford et al., 2010). These findings indicate that acute physical pain promotes cooperative behavior in social interaction. To date, it is unclear about the dynamic influence of pain on cooperative behavior across time. Moreover, the underlying neural basis awaits to be elucidated in a higher ecological validity, which could give us a deep understanding of modulation of pain on cooperation.

Three potential hypotheses may predict how pain modulates cooperation in social interaction. (a) In a perspective of social aspect of pain, acute pain could encourage individuals to cooperate with others in an attempt to seek out social support, as social support is expected to be helpful in coping with pain (Eisenberger et al., 2011; Leknes & Bastian, 2014; Wang et al., 2018). (b) In a perspective of

cognitive aspect of pain, pain might undermine the performance of a cooperative task, as acute pain distracts individuals from a task and makes them in cognitive deficit (Eccleston & Crombez, 1999; Gatchel, Peng, Peters, Fuchs, & Turk, 2007; Moriarty, McGuire, & Finn, 2011). (c) In a perspective of motivational aspect of pain, acute pain could motivate individuals to adjust their behaviors quickly and to gradually improve the cooperation task performance across time, given that pain as an aversive primary reinforcer fundamentally facilitates (social) learning processes (Roy et al., 2014; Seymour et al., 2005; Wiech & Tracey, 2013). In summary, it is expected that pain would either increase (social perspective) or decrease (cognitive perspective) cooperation rate according to the first two hypotheses; whereas pain may change cooperation rate across time in a positive way according to the third hypothesis (motivational perspective).

Previous studies have revealed that many brain regions are involved in cooperative behavior. For example, using fMRI technique, neural activation in the orbitofrontal cortex was selectively observed when two individuals played a specially designed computer game in a cooperative way but not in competition (Decety et al., 2004). Moreover, the right dorsolateral prefrontal cortex was strongly activated when participants confronted with noncooperative opponents in prisoner's dilemma games (Suzuki, Niki, Fujisaki, & Akiyama, 2010). However, one of the limitations of these conventional (or single-brain) studies is that they have mainly focused on aspects of off-line social cognition, whereas most of our social behavior is characterized by on-line mutual interaction, forming a "two-in-one" system (Konvalinka & Roepstorff, 2012; Schilbach et al., 2013). This system is a complex nonlinear system (Beer, 2000; Froese, Iizuka, & Ikegami, 2013) that cannot be reduced to the summation of effects in single isolated brains (Hari & Kujala, 2009; Konvalinka & Roepstorff, 2012). Therefore, it seems logical to simultaneously record two-brain activity during social interactions with a focus on dyads rather than on individuals. Such "two-person neuroscience" (2PN) or hyperscanning has been proposed as a suitable conceptual and methodological framework to study the neural basis of social interaction (Hari, Henriksson, Malinen, & Parkkonen, 2016). Using functional near-infrared spectroscopy (fNIRS)-based hyperscanning, increased synchronous brain activity between two interacting persons has been observed in superior frontal cortex and dorsolateral prefrontal cortex when they performed a cooperation task (Cheng, Li, & Hu, 2015; Cui, Bryant, & Reiss, 2012; Pan, Cheng, Zhang, Li, & Hu, 2017). In addition, in EEG-based hyperscanning studies, alpha interbrain synchrony over centroparietal region is observed in social coordination task (Dumas, Nadel, Soussignan, Martinerie, & Garero, 2010; Mu, Guo, & Han, 2016). Taking together, evidences from single brain activations and interbrain synchrony in dyads indicate that the prefrontal-parietal networks over large scale may serve as neural underpinnings of cooperation in social interaction.

In this study, we investigated how pain would dynamically influence cooperative behavior. Participants were asked to perform a cooperative task after the induction of acute pain by Capsaicin cream. In the cooperative task, two partners in a dyad devoted themselves to simultaneously make quick responses to a stimulus (Baker et al., 2016; Cheng et al., 2015; Cui et al., 2012). During such a button-press

cooperative task, we speculated that pain would dynamically improve cooperation across time from the perspective of motivational hypothesis. Accordingly, it was expected that dynamic interpersonal neural synchronization (INS) within frontal-parietal network was associated with the cooperative behavior. During the cooperative task in the experiment, neural activities of each dyad were recorded simultaneously by the fNIRS-based hyperscanning technique. We are particularly interested in how synchronous brain activity in prefrontal and parietal regions change as the performance of cooperative task improves. On the one hand, the left prefrontal cortex (LPFC) brain synchrony might be observed when participants adjust their act of button press in accordance with the partners. The LPFC plays important roles in cognitive control (Fregni et al., 2005; MacDonald, Cohen, Stenger, & Carter, 2000; Miller & Cohen, 2001) and executive function (Decety, Jackson, Somerville, Chaminade, & Meltzoff, 2004; Richeson et al., 2003). On the other hand, the synchrony in the parietal region might also occur when participants need to infer the thoughts of their partners. It has been found that the parietal cortex plays an important role in mental imagery of hand movements (Sirigu et al., 1996). In summary, we postulated that dynamic interpersonal fronto-parietal network is involved in the modulation of pain on cooperation in social interaction.

2 | MATERIALS AND METHODS

2.1 | Participants

A total of 66 female university students (age: 20.9 ± 2.1 years) participated in the study. All participants were right handed, with normal or corrected-to-normal vision. Female participants were recruited due to two reasons: first, gender differences in pain perception and prosocial behavior was well-documented (Berkley, 1997; Feingold, 1994; Robinson et al., 2001); second, an increased effect of pain on cooperative behavior was observed only in females but not in males (Wang et al., 2018). Each time, two participants who had never meet before came together and were assigned as a pair. All pairs were divided randomly into pain-treatment (PT) group (16 pairs) and control-treatment (CT) group (17 pairs). This study was approved by the University Committee on Human Research Protection at East China Normal University and was carried out in accordance with the approved guidelines. Informed consent was obtained from each participant prior to experiment. Participants would be paid based on their task performance (ranged from 50 to 70 yuan).

2.2 | Pain/control treatment and assessment

The procedure of pain induction was the same as what we reported in our previous study (Wang et al., 2018). It was a safe and noninvasive paradigm based on the heat/capsaicin sensitization model (Modir & Wallace, 2010). In brief, to generate stable, long-lasting pain sensation, Capzasin-HP cream (Capsaicin 0.1%) was brushed to a $2 \text{ cm} \times 2 \text{ cm}$ area on the volar side of the dominant forearm in the painful treatment. In the nonpainful treatment, hand cream was administrated

to the same area. Participants were asked to have a rest due to that pain intensity caused by the capsaicin increased gradually until 25 min later when it ensured a moderate and sustained painful state. During the rest, recording probes were placed on the head in accordance with the NIRS system. Thus, pain manipulation check was performed both before and 25 min after pain/control treatment. The subjective numerical pain rating was applied with visual analog scale (VAS; scale of 0–10, with 0 corresponding to “no pain at all” and 10 corresponding to the “worst imaginable pain”; Carlsson, 1983; Huang et al., 2013).

2.3 | Tasks and procedures

After filling out a few questionnaires, each pair was randomly assigned to the pain or the control condition. Each participant in a dyad had no idea about the treatment on his/her partner, which could avoid the effects of shared painful experience or empathic responses to others' pain on social interaction. After pain induction, each pair of participants in PT or CT group sat face-to-face in front of two separate computer screens (Figure 1a). Sitting face-to-face ensured a real social interaction that they performed the task in each other's presence, while the separate computer screens prevented the participants from imitating the action of the other people. Thereafter, they were asked to complete a cooperation task and a competition task (as a control task) in which the order of tasks was counterbalanced across pairs of participants. There were three blocks (totally 60 trials) in each task (Figure 1c). There was a 30-s rest period between blocks. All points they gained in the two tasks would be added up and finally became part of their payments. This gave the

participants an incentive to earn as many points as possible, so that they would be actively engaged in the experiment.

2.3.1 | Cooperation task

Each trial began with a hollow gray circle at the center of the screen for 0.6–1.5 s randomly, followed with a “green” signal, by which the participants were instructed to press keys simultaneously by using index or middle finger of the right hand (Figure 1d). The “1” key was assigned to participant #1 (the left one) and the “0” key to participant #2 (the right one). If the difference of their response times was smaller than a threshold, both of them would get one point; otherwise, each of them would lose one point. The threshold (T) was defined by the following formula: $T = (RT1 + RT2)/8$, where RT1 and RT2 represent the response times of the two participants, respectively (Cui et al., 2012; Pan et al., 2017). The parameter 1/8 was chosen to maintain a moderate level of difficulty of the cooperation task in consideration that the average cooperation rates were around 50–70% in the present study. During performing tasks, two participants were not allowed to communicate with each other verbally or physically. After they responded, the feedback screen was present in a duration of 4 s. The feedback consisted of the following information: (a) win or lose; (b) cumulative points; (c) who was faster (“+”) or slower (“-”). This information aided participants in adjusting their responses to maximize their gain points. After the feedback, there was a blank screen (i.e., the intertrial interval) lasting 3.6–4.5 s. In sum, each trial lasted for about 9.6 s and each block consisted of 20 trials for 192 s.

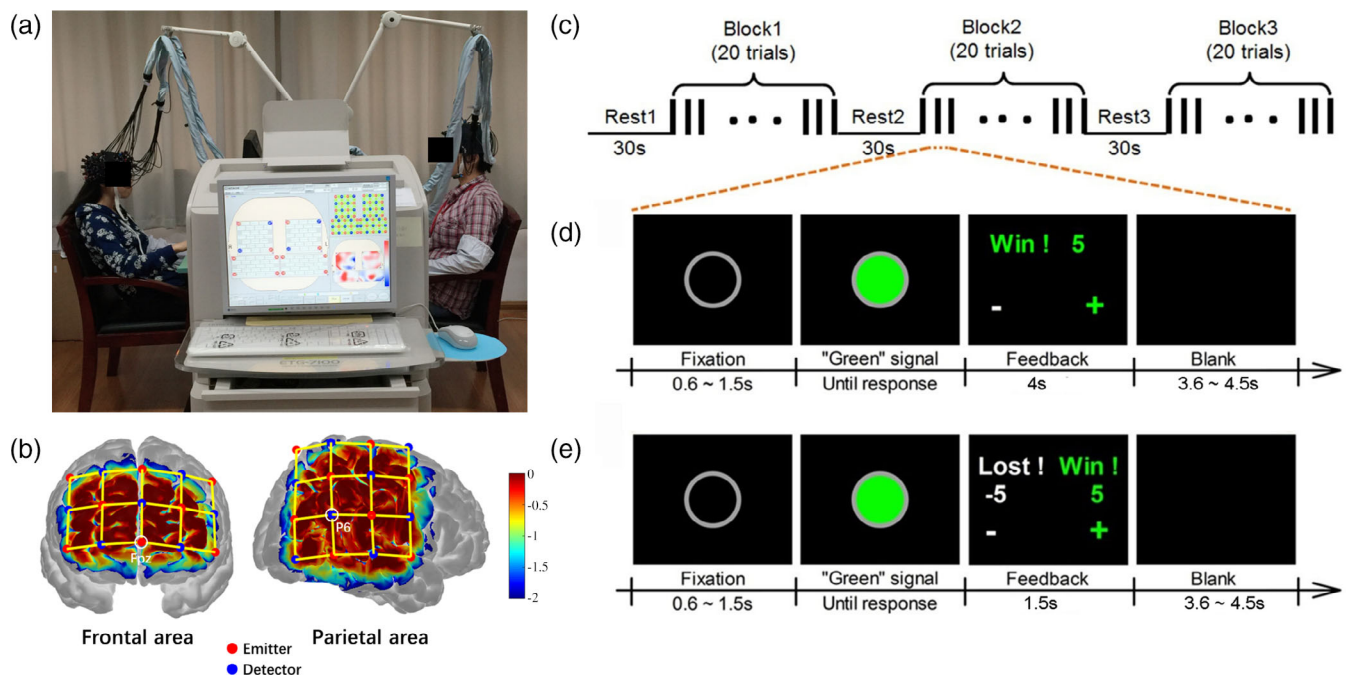


FIGURE 1 Experimental settings and the procedure of tasks. (a) Each participant of a pair sat face-to-face in front of two separate computer screens. (b) The optode probes were placed over the frontal and right parietal cortices with sensitivity profile. Red dots indicate the sources, blue dots indicate the detectors, and yellow lines indicate the formed channels. The color scale depicts the sensitivity profile from -2 (low sensitivity) to 0 (high sensitivity). (c) Three blocks of cooperation tasks and three blocks of competition tasks were included in the experiment. Each block consisted of 20 trials. (d) The events of each trial of cooperation task. (e) The events of each trial of competition task [Color figure can be viewed at wileyonlinelibrary.com]

2.3.2 | Competition task

INS observed in the cooperative task might be a mixture of two components, cooperative mind and synchronous action. To rule out the possibility that the observed INS was determined merely by synchronous action but without any involvement of cooperative mind, we employed the competition task as a control (Figure 1e). The procedure of competition task was similar to that of cooperation task, except that the participant was encouraged to respond to stimulus ("green" signal) as faster as possible and no need to cooperate with the partner. In the task, the one who responded faster would get one point while the other one would lose one point. After responses, a 1.5 s feedback screen was presented, with the signs of "Win!" shown to the winner and "Lost!" shown to the loser, along with their accumulative points.

2.4 | fNIRS data collection

The concentration changes of oxygenated hemoglobin (Hbo) and deoxygenated hemoglobin (Hbr) during performing tasks were measured by NIRS system (ETG-7100, Hitachi Medical Corporation, Japan). A 3×5 probe patch with a 3 cm distance between the emitter probe and the detector probe was put over frontal area for each participant (Figure 1b). The placement of the patch followed the International 10–20 system (see the MNI coordinate of each channel in Table S1). The middle optode of lowest row of the probe was placed on the frontal pole midline point (FPz as the reference site) and the middle column of probe was aligned exactly along the sagittal reference curve. Another 4×4 probe patch was put over the right central-parietal area for each participant. The middle optode was placed on the P6 site in the 10–20 system, and the row of probe was aligned along with the sagittal reference curve. The sampling rate was 10 Hz. The correspondence between the NIRS channels and the measurement points on the cerebral cortex was displayed on the basis of the results of the virtual registration method (Lancaster et al., 2000; Singh, Okamoto, Dan, Jurcak, & Dan, 2005; Tsuzuki et al., 2007; Tzourio-Mazoyer et al., 2002), which was confirmed by a multi-subject study of anatomical craniocerebral correlation (Okamoto et al., 2004). A spatial sensitivity profile (Figure 1b) was calculated based on the Monte Carlo photon migration modeling by an open-source software AtlasViewer, a part of the fNIRS analysis package Homer2 (Aasted et al., 2015; Cooper et al., 2012; Custo et al., 2010). This proved that the selected probe setup was positioned to primarily measure brain activity over the prefrontal and right parietal cortices.

2.5 | Data analysis

2.5.1 | Behavioral performance

To compare the influence of pain on cooperation task, we calculated (a) cooperation rate: the percentage of the win trials in all three blocks of cooperation task within each dyad; (b) valid response rate: the percentage of the trials in which response time differences were within

three standard deviations of the mean in all blocks of both cooperation task and competition task within each dyad.

2.5.2 | The fNIRS data analysis

Two categories of signals, namely Hbo time series and Hbr time series, were collected from the NIRS channels. As Hbo signal was more sensitive to the changes in cerebral blood flow than Hbr signal (Hoshi, 2003; Lindenberger, Li, Gruber, & Müller, 2009), only Hbo time series were analyzed as our previous studies did (Cheng et al., 2015; Hu, Hu, Li, Pan, & Cheng, 2017; Pan et al., 2017).

INS analysis

Firstly, we applied a robust principle component analysis (PCA) approach to remove signal contamination that was caused by spontaneous blood flow oscillations or other global systematic (Zhang, Noah, & Hirsch, 2016). Then we used wavelet coherence (WTC) MatLab package to calculate the synchronous activity between two brains (i.e., INS), by computing the wavelet coherence of two time series of the same channels from two brains (Grinsted, Moore, & Jevrejeva, 2004; Murphy, Birn, Handwerker, Jones, & Bandettini, 2009). The wavelet coherence software was provided by Grinsted et al. (2004) accessible online (<http://noc.ac.uk/using-science/crosswavelet-wavelet-coherence>). A frequency band between 0.16 Hz (period 6.4 s) and 0.08 Hz (period 12.8 s) was identified, corresponding to the duration of a trial in each task. We then calculated the average INS for each task-block and baseline. The task-related INS was defined as the INS difference of each task-block relative to its baseline (i.e., task-rest). Then, the values of task-related INS were converted into z-scores by a Fisher z-statistics before any statistical tests were performed (Chang & Glover, 2010; Cui et al., 2012). Finally, we performed one-sample t-test with false discovery rate (FDR) correction for each channel to identify the channels showing significant task-related INS ($p < 0.05$). For FDR correction, calculate p -values for each channel, order the p -values from smallest to largest, and then for the i th ordered p -value check if the following is satisfied: $p(i) \leq \alpha \times i/m$. At the same time, we also generated a t-map of INS and smoothed it using the spline method.

Statistical analyses were applied to INS of significant channels in two ways. First, two-way analyses of variance (ANOVAs) of Treatment (Pain, Control, between-subject) and Time (Block1, Block2, Block3, within-subject) was conducted. Second, as it was hypothesized that pain would dynamically improve cooperation across time, paired sample t-tests were performed between INS of different blocks (Block2 vs. Block1, Block3 vs. Block1, Block3 vs. Block2) separately for each group.

Interbrain synchronization network analysis

We attempted to explore the dynamic changes of synchronous activities between different channels of two brains, which could be associated with modulation of pain on neural network synchronization during interpersonal social interaction. Similar WTC analysis was performed in this section. We first identified the "More-pain" participant with a higher subjective pain rating and the "Less-pain" participant with a lower subjective pain rating in each dyad. This identification

was to test whether information flow between the two participants was directional, as we assumed that the “More-pain” participant was much highly motivated to cooperate and might play a leading role during the interaction. Then, we calculated the task-related INS between each channel of the ‘More-pain’ participant and all channels of the “Less-pain” participant. Therefore a 46×46 array of INS was generated for each dyad. Last, circular graphs were plotted to represent interbrain synchronization networks consisted of significant task-related INS ($p < 0.001$, uncorrected).

2.5.3 | The subjective pain rating-INS correlation analysis

To measure the relationship between the changes of task-related INS in cooperation task and pain, a bivariate Pearson correlation analyses were performed between the differences of INS within two blocks (i.e., Block2-Block1, Block3-Block1) and the mean subjective pain ratings for each dyad in both PT and CT groups.

3 | RESULTS

3.1 | Behavioral performance

Pain manipulation check was performed. Before Capzasin or hand cream induction, subjective pain intensities were near zero (pain condition: 0.03 ± 0.18 ; control condition: 0.03 ± 0.17) and did not differ between two groups, $t(64) = 0.04$, $p = 0.97$. Twenty-five minutes after induction, pain rating was significantly higher in the pain condition (5.59 ± 2.00) than in the control condition (0.21 ± 0.40), $t(64) = 15.43$, $p < 0.001$. It demonstrated a successful induction on individuals applied with Capzasin.

Mean cooperation rate in PT group was not significantly different from that in CT group (0.69 ± 0.14 vs. 0.75 ± 0.13), $t(31) = 1.22$, $p = 0.230$ (Figure 2A). However, valid response rate in PT group was higher than that in CT group in the cooperation task ($96.0\% \pm 2.8\%$ vs. $92.9\% \pm 4.9\%$), $t(31) = 2.20$, $p = 0.035$ (Figure 2b). The finding indicated that individuals in physical pain may devote themselves more to the cooperation task than those in control group. In contrast, valid response rate was not distinguished between the PT and CT groups in the competition task ($97.5\% \pm 1.2\%$ vs. $97.7\% \pm 1.2\%$), $t(31) = 0.59$, $p = 0.56$.

To further test change of behavioral performance induced by pain across blocks, block cooperation rates were calculated and then entered into a two-way analysis of variance (ANOVA) of Treatment (pain, control) and Block (Block1, Block2, Block3). The main effect of Block was significant ($F [1, 30] = 5.57$, $p = 0.009$), suggesting that the cooperation rate increased when the participants adjusted to the task across time. However, when separated by group, the enhancement of block cooperation rate was only evident in PT group (Figure 2c, Block2 vs. Block1: $t(15) = 3.38$, $p = 0.004$; Block3 vs. Block1: $t(15) = 3.10$, $p = 0.007$), but not in the control group (Figure 2c, Block2 vs. Block1: $t(16) < 1$, $p > 0.05$; Block3 vs. Block1: $t(16) = 1.33$, $p > 0.05$). The interaction of Treatment by Block did not reach

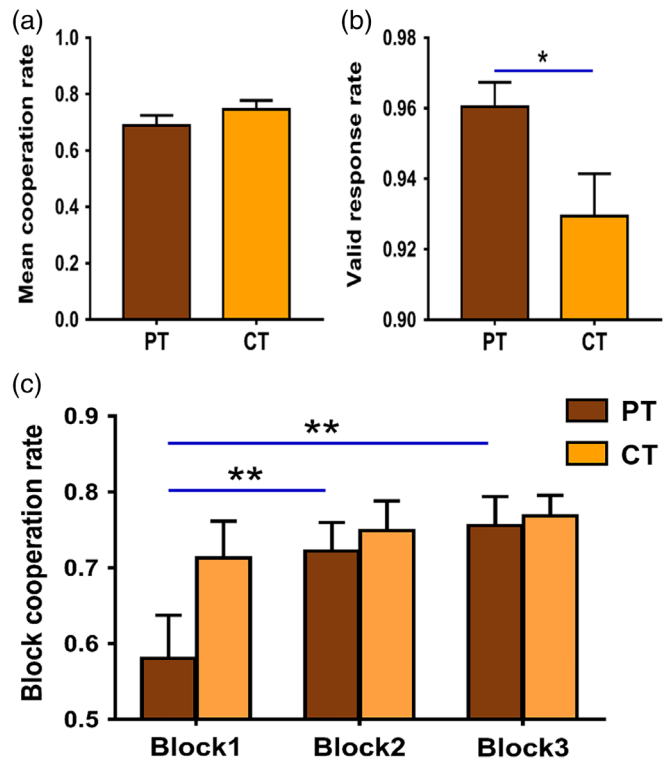


FIGURE 2 Behavioral performance in the cooperation task. (a) Mean cooperation rate. (b) Valid response rate, which defined as the ratio of trials with less than 3 standard deviations of differential reaction times to all trials. (c) The changes of cooperation rate in three blocks of cooperation task. PT represents the group of participants with pain-treatment; CT means the group of participants with placebo-treatment. * $p < 0.05$; ** $p < 0.01$ [Color figure can be viewed at wileyonlinelibrary.com]

significant level ($F [1, 30] = 1.67$, $p = 0.205$). These findings suggested that pain could promote interpersonal social interaction across time.

3.2 | Task-related INS

Significantly enhanced task-related INS was found by one-sample t-test at eight channels in frontal or parietal areas among three blocks of cooperation task (Figure 3, $ps < 0.05$, FDR corrected), but not in competition task (Figure S1, $ps > 0.05$, FDR corrected). Next, we separated these channels into three regions of interest (ROIs) indicated by red dashed ellipses in Figure 3, including the left prefrontal cortex (LPFC, Figure 3b, Ch14 and Ch20), the right prefrontal cortex (RPFPC, Figure 3c, Ch12 and Ch22) and the right parietal cortex (Figure 3f, Ch15, Ch18, Ch 19, and Ch 23).

After averaging INS of all channels in each ROI, we performed a two-way ANOVA of Treatment (pain, control) and Block (Block1, Block2, Block3) on the task-related INS. The main effect of Treatment was marginally significant in LPFC, $F(1, 31) = 2.92$, $p = 0.06$. When separated by group, paired sample t-test showed that the INS in LPFC was higher in Block2 than in Block1 (Figure 4a), $t(15) = 2.44$, $p = 0.03$ in the PT group, but not in the CT group (Figure 4a), $t(16) = 0.89$, $p > 0.05$. There was no significant difference between Block3 and Block1 in either group (Figure 4a, $ps > 0.05$).

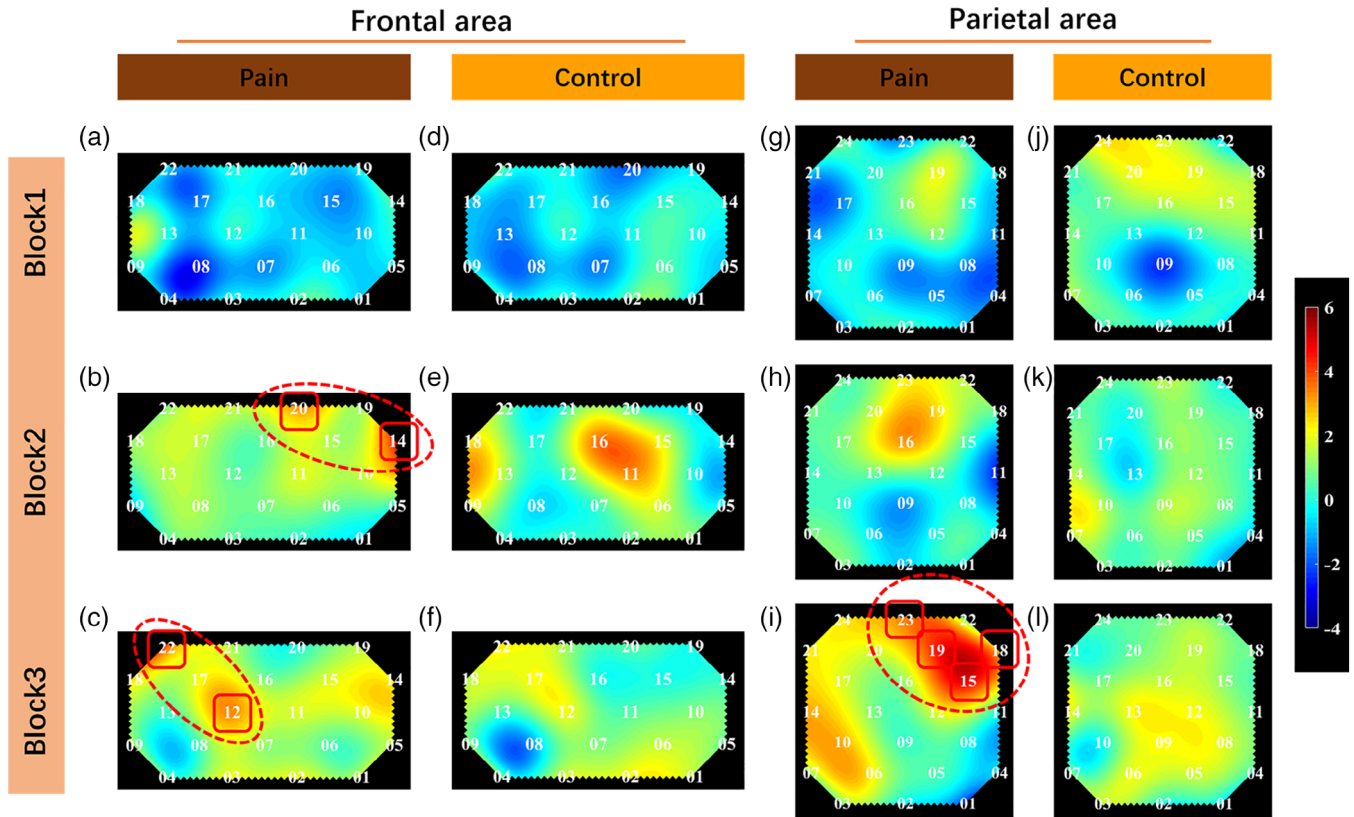


FIGURE 3 Task-related interpersonal neural synchronization (INS) in different blocks of cooperation task. T-maps of INS in frontal area (a–f) and parietal area (g–l) are shown during PT (a–c, g–i) or CT (d–f, j–l) group of participants performing cooperation task. The red squares represent the channels with significant enhancement of INS during the cooperation task compared to baseline (i.e., the mean INS within 20 s just before each block of cooperation task). The red dashed ellipses illustrate the regions of interest (ROIs) to be used in further analyses. All INSs were averaged within each ROI, including the left prefrontal cortex (b, Ch14 and Ch20), the right prefrontal cortex (c, Ch12 and Ch22) and the right parietal cortex (i, Ch15, Ch18, Ch19, and Ch 23) [Color figure can be viewed at wileyonlinelibrary.com]

For the task-related INS in the RPF, the two-way ANOVA of Treatment and Block did not result in any significant main effect or interaction. Paired sample *t*-test showed that the INS was higher in Block3 than in Block1 in the PT group (Figure 4b), $t(15) = 2.54$, $p = 0.02$, but not in the CT group (Figure 4b), $t(16) = 1.37$, $p > 0.05$. Significant difference between Block2 and Block1 was observed in neither group (Figure 4b, $p_s > 0.05$).

The ANOVA of Treatment and Block on the task-related INS in the right parietal cortex did not show any significant effect. Paired sample *t*-test showed that the INS was higher in Block3 than in Block1 in the PT group (Figure 4c), $t(15) = 3.26$, $p = 0.01$, but not in the CT group (Figure 4c), $t(16) = 0.73$, $p > 0.05$. Additionally, INS in Block3 was also higher than that in Block2 in the PT group (Figure 4c), $t(15) = 2.70$, $p = 0.02$.

Neither the main effect nor the interaction effect of INS was found significant in the PT or CT group of participants performing competition task (Figure S2). Paired sample *t*-tests further showed no significant result between blocks for each group.

All these findings indicated that modulation of pain on cooperation task was associated with dynamics of synchronized neural activities in different brain regions. The LPFC was involved in the early stage while the RPF and right parietal cortex were involved in the late stage of such modulation.

3.3 | Interpersonal neural networks induced by pain during social interaction

To investigate how pain dynamically modulated the synchronous activities at the level of neural networks during interpersonal social interaction, all potential task-related INS between different channels of two brains were calculated, therefore a 46×46 array of INS was generated for each of six conditions, 2 (PT group, CT group) \times 3 (Block1, Block2, and Block3). Only three channels in Block1 displayed significant task-related coherence in PT group (Figure 5a). Interestingly, the number of channels which displayed significant task-related INS increased in Block2 (Figure 5b) and continued to increase in Block3 (Figure 5c) in PT group. Moreover, compared to Block1, much more INS in the fronto-parietal networks was obtained in both Block2 and Block3 in the PT group, especially the connections between the parietal area of the “More-pain” participant and the frontal area of the “Less-pain” participant in each dyad (Figure 5b,c, see also in Figure S3), suggesting differential roles of prefrontal area and parietal area in different stages of pain-induced cooperation. However, much fewer channels with significant task-related INS were found in all three blocks of cooperation task in the CT group (Figure 5d–f). In addition, no significant task-related INS was observed in the competition task in

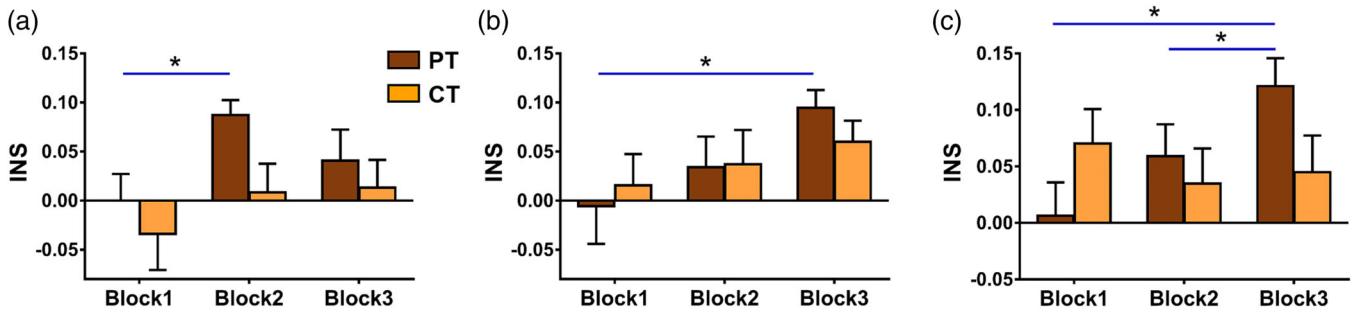


FIGURE 4 Comparisons of interpersonal neural synchronization in different blocks of cooperation task. (a) interpersonal neural synchronization (INS) in the left prefrontal cortex (including Ch14 and Ch20 which shown in Figure 3b); (b) INS in the right prefrontal cortex (including Ch12 and Ch22 which shown in Figure 3c); (c) INS in the right parietal cortex (including Ch15, Ch18, Ch19, and Ch23 which shown in Figure 3l). * $p < 0.05$, paired t -test [Color figure can be viewed at wileyonlinelibrary.com]

PT or CT group. The findings suggested that pain promoted an intensive interpersonal neural network during social interaction.

3.4 | The behavior-neural activities correlation

We conducted a number of correlation analyses to further explore the relationship between subjective pain rating and the enhancement of task-related INS across blocks of cooperation task. A significant positive correlation was found between changes of INS from Block1 to Block3 in right parietal cortex and the mean of subjective pain rating in each dyad in PT group ($r = 0.46, p = 0.04$; Figure 6). Such a correlation was not found in CT group ($r = 0.004, p = 0.49$; Figure 6). The changes of INS in the other two regions (RPFC and LPFC) were not

correlated with subjective pain ratings in PT or CT group ($ps > 0.05$). These results suggested that right parietal cortex, rather than prefrontal cortex, might be critical to the late modulation of pain on the interpersonal social interaction.

4 | DISCUSSION

In the present study, we found that dyads of participants in pain improved their cooperative behavior across different blocks of task compared to ones in control. Meanwhile, such modulation involved a series of dynamic interbrain coupling activities in a dyad recorded by the fNIRS-based hyperscanning approach. Specifically, the INS in the left prefrontal cortex (LPFC) arose at an early stage whereas the INS

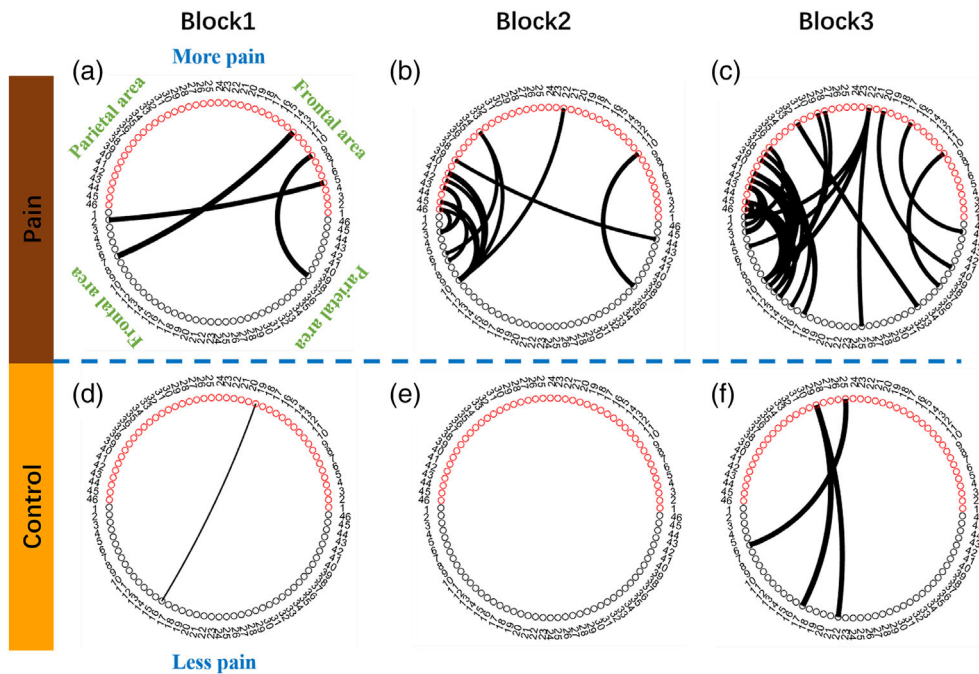


FIGURE 5 Dynamic interpersonal networks during different blocks of cooperation task. (a–c): The enhanced interpersonal neural synchronization during different blocks of cooperation task compared to the baseline ($p < 0.001$) in the pain-treatment (PT) group. (d–f): The enhanced interpersonal neural synchronization in the control-treatment group. The circles represent the channels of the participants with a relatively higher (red circles) and lower (gray circles) subjective pain ratings in each dyad. The weight of each line means the T -value of a comparison of the task and the baseline. The frontal area contains 22 channels (i.e., Ch1 to Ch22) and the parietal area contains 24 channels (i.e., Ch23 to Ch46) for each participant in a dyad [Color figure can be viewed at wileyonlinelibrary.com]

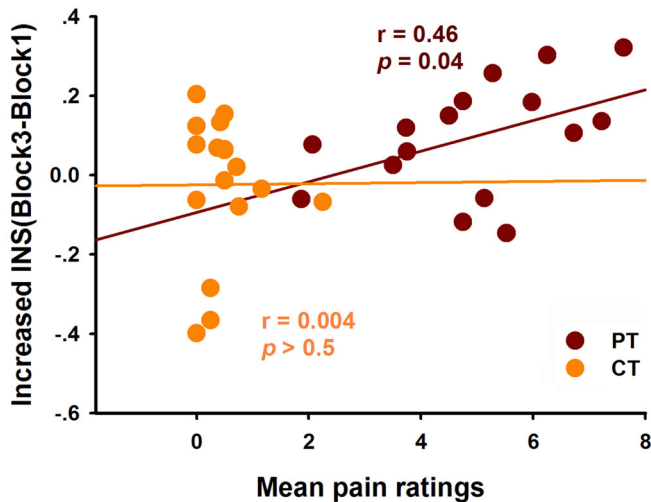


FIGURE 6 The behavior-neural correlation in the cooperation task. Pain-treatment (PT; dark red) represents the group of participants with pain-treatment; control-treatment (CT; orange) means the group of participants with control treatment [Color figure can be viewed at wileyonlinelibrary.com]

in the RPF and right parietal cortex arose at a late stage across the entire cooperation task. Moreover, increased dynamic cross-channel neural networks specified as a fronto-parietal association across time were also observed under pain. Therefore, we provide the first evidence in the framework of 2PN to study dynamic modulation of acute pain on interpersonal cooperation.

According to the hypotheses from a social or a cognitive perspective, it would be expected that pain either increased (social perspective) or decreased (cognitive perspective) cooperation rate compared to control condition. However, the main effect of treatment on overall cooperation rates was not evident in current study. Thus, our findings did not directly support hypotheses based on the social or cognitive aspects of pain. On the other hand, we found dynamic changes of cooperation rates across different blocks of task in PT group, while no changes was observed in CT group. Therefore, pain facilitated a learning process, in which Individuals were motivated to adjust their behaviors and improved task performance across time. This improvement might be guaranteed by a strong motivation of painful individuals to devote themselves to the task, as more valid responses were found in pain group in our study. Therefore, we provided evidence for the hypothesis from a motivational perspective of pain. Nevertheless, we could not totally exclude the possibility of cognitive influence of pain on social interaction, because a lower cooperation rate in the pain condition was observed at the beginning of the task. It was probably due to a negative consequence of pain, as pain was found to distract individuals from a task and make it difficult to coordinate (Moriarty et al., 2011). Meanwhile, increased cooperation at the later blocks of the task may reflect an expectation that cooperating with others can be beneficial to pain relief. Therefore, further investigation is needed to disentangle how the cognitive and social influences of pain may contribute to the motivational influence of pain.

Increased cooperative behavior within the second block was accompanied with enhanced task-related INS in the left prefrontal cortex. The LPFC is found to play important roles in cognitive control (Fregni et al., 2005; MacDonald et al., 2000; Miller & Cohen, 2001) and executive function (Decety et al., 2004; Richeson et al., 2003). For example, the increased activity in the dorsal part of LPFC was linked to the implementation of executive control in the Stroop color task (MacDonald et al., 2000). Meanwhile, it was reported that the dorsolateral PFC activity was negatively correlated with perceived pain intensity and unpleasantness, suggesting a function of cognitive control of pain experience (Lorenz, Minoshima, & Casey, 2003). Therefore, the increased INS in the second block in our study may serve as cognitive control of coordinating behaviors (e.g., adjusting one's act of button press in accordance with the partner), which may result in the increased cooperation rate. Further investigation may clarify whether the LPFC synchronization in this study involves in a cognitive modulation of pain experience itself.

As task continued to third block, task-related INS appeared at the RPF and right parietal cortex. Previous fNIRS-based hyperscanning studies have raised a theory of mind hypothesis of interpersonal coherence, which is associated with INS at the right superior frontal cortex (Cui et al., 2012; Pan et al., 2017). In our study, dyads with higher pain ratings exhibited stronger INS in the right parietal cortex, suggesting that this component of brain synchrony, but not that in RPF, was subject to the late modulation of pain on interpersonal social interaction. It was found that the mental representation of hand movements was impaired after parietal cortex damage (Sirigu et al., 1996). Thus, stronger INS in the right parietal cortex in our study might be associated with an enhanced mental imagery of the partner's action in the social interaction task.

An alternative explanation suggested that the increased INS by pain we observed was due to physiological noise such as respiration changes induced by pain. Indeed, the observed fNIRS signals originated from brain activity inevitably mixed more or less with blood flow oscillations or other physiological changes like blood pressure or respiration (Caldwell et al., 2016; Scholkmann, Gerber, Wolf, & Wolf, 2013), while pain was found to be especially associated with changes in respiration and with changes in the state of the autonomic nervous system (Holper et al., 2014). However, this alternative explanation may have very limited contribution in this study. Firstly, we employed a novel and robust PCA approach to exclude the signal of physiological processes from the targeted brain activities. Secondly and more importantly, physiological changes were expected to equally influence the INS in both the cooperation task and the competition task; but increased INS was only observed in the cooperation task.

The present work contributes to the understanding of how interpersonal cooperation is developed under pain by providing a perspective of dynamic neural networks. In addition to the INS in bilateral PFC and right parietal cortex, interpersonal neural networks were formed dynamically during social interaction under pain, with increasing number of fronto-parietal associations across time. While the fronto-parietal network is commonly regarded to be associated with selective attention and working memory (Gazzaley & Nobre, 2012; Scolar, Seidl-Rathkopf, & Kastner, 2015), it is found to play a role in

cognitive modulation of pain (Kong et al., 2013). Thus, we claim that the dynamic interpersonal fronto-parietal networks are pain-related neural components involved in cooperation. This may reflect an intentional control over the cooperation task.

This work extends our knowledge about the influence of pain on social cognition and behavior. While being well documented the impact of pain on brain function, emotion and cognition, the social influence of pain has recently been focused on (Williams & Craig, 2016). Rather than chronic pain disturbing to social life and work (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006; Gureje et al., 2008), acute pain, to some extent, promotes social bonding and cooperation (Bastian et al., 2014), and interpersonal trust (Wang et al., 2018). Here we add an empirical piece of hyperscanning work, demonstrating that dissociative neural processes are involved in how pain affects cooperation in social interaction. Further investigation is highly encouraged to critically compare the effect of acute pain with chronic pain on an identical cooperative task, which may figure out why chronic pain undermines social interaction in some circumstances.

It is also worth noting the limitations in our study. First, only females were measured in the current study. Although pain did not affect cooperation behaviorally in males in our previous study (Wang et al., 2018), it was still possible that the cooperation-related synchronous brain activity may somewhat be modulated in males. We admit that having also males measured would then have made it possible to check the measured results if they comply with this previous finding. Second, the causal role of INS in the modulation of pain on social interaction needs to be further clarified by noninvasive stimulation approaches, such as TMS, tDCS/tACS. We believe that the coherence in a dyad reflects specific synchronous mentalization, which is not due to performing the same task, since the increased interbrain coherence was absent in the competition task. Third, we proposed that individuals in pain was "motivated" to cooperate; however, the brain structures including ventral striatum and medial prefrontal cortex in the motivation and reward system (Haber & Knutson, 2010) are mostly subcortical, leaving it hard to be recorded by fNIRS. Future studies could investigate these brain regions by using fMRI-based hyperscanning technique.

In summary, when a dyad performing a cooperation task in pain, the INS in bilateral PFC and right parietal cortex occurred successively, along with increased fronto-parietal associations. The dynamic interpersonal neural activities in fronto-parietal network suggest that pain-induced cooperation demands cognitive control of the coordinating behavior and inference of others' mind. The present work provides the first interbrain evidence to the literature of neural mechanisms underlying the social influences of pain, especially in perspective of motivational aspect of pain.

ACKNOWLEDGMENTS

This work was supported by grants from China Postdoctoral Science Foundation (2018T110363) and National Natural Science Foundation of China (31600890). This work was also supported by the Key Specialist Projects of Shanghai Municipal Commission of Health and Family

Planning (ZK2015B01) and the Programs Foundation of Shanghai Municipal Commission of Health and Family Planning (201540114).

CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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SUPPORTING INFORMATION

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How to cite this article: Wang C, Zhang T, Shan Z, Liu J, Yuan D, Li X. Dynamic interpersonal neural synchronization underlying pain-induced cooperation in females. *Hum Brain Mapp*. 2019;40: 3222–3232. <https://doi.org/10.1002/hbm.24592>