

Can self-pain sensitivity quantify empathy for others' pain?

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Abstract

Empathy is essential for the survival of social species. In many studies, especially those with animal models, empathy for pain was evaluated by the modulation of pain sensitivity. However, the relationship between pain sensitivity and empathy for pain is not well established. Here, by performing two experiments, we aimed to investigate their relationship at both behavioral and electrophysiological levels. In Experiment 1, we characterized individual pain sensitivity using pain threshold and tolerance in a cold pressor test, self-report empathy using Interpersonal Reactivity Index, and pain-related psychological factors, including pain-related anxiety, depression, pain catastrophizing, and pain-related fear, using well-validated questionnaires. We observed that pain sensitivity was positively correlated with emotional empathy, and their relationship was mediated by pain-related anxiety, pain catastrophizing, and pain-related fear. In Experiment 2, we quantified empathy for pain using pain intensity and unpleasantness as well as event-related potentials (ERPs) in an empathy for pain task. Positive correlations were observed between pain sensitivity and psychophysiological empathic responses (i.e., the P3 component and the late positive potential in ERPs), and their relationship was mediated by pain-related fear. These results suggested that being influenced by some pain-related psychological factors, individuals with higher pain sensitivity tended to have stronger empathy for pain, manifested as stronger emotional reactions to others' pain. Our results indicated that the conventional strategy of using pain sensitivity to quantify empathy should be treated with caution, as their relationship could be disturbed by experimental manipulations or pathological modulations that could influence individual emotional states or cognitive processes.

KEYWORDS

empathy | event-related potentials | pain catastrophizing | pain sensitivity | pain-related anxiety | pain-related fear,

1 | INTRODUCTION

Empathy plays a crucial role in social interaction, allowing us to understand and share other's feelings, thus, providing a vital emotional and cognitive bridge to promote prosocial behaviors (Baron-Cohen & Wheelwright, 2004; de Waal & Preston, 2017). Since empathy is essential for the survival of social species (Chen, 2017;

Sivaselvachandran, Acland, Abdallah, & Martin, 2018), numerous human and animal studies have been performed to deepen our understanding of empathic behaviors and their neural mechanisms, for example, the discovery of mirror neurons in macaques (di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992) and humans patients (Keysers & Gazzola, 2010; Mukamel, Ekstrom, Kaplan, Iacoboni, & Fried, 2010).

It is worth noting that, regardless of species, the assessment of empathy in most studies has relied on the investigation of empathy for pain due to the ease of induction and high repeatability (Bernhardt & Singer, 2012; Lamm, Decety, & Singer, 2011; Langford et al., 2006; Li et al., 2014; Rütgen, Seidel, Riečanský, & Lamm, 2015; Zaki, Wager, Singer, Keyser, & Gazzola, 2016). In human studies, empathy questionnaires, such as Interpersonal Reactivity Index (IRI; Davis, 1983) and Empathy for Pain Scale (Giummarra et al., 2014), are widely used to investigate empathy for pain (Fusaro, Tieri, & Aglioti, 2016; Nazarewicz, Verdejo-Garcia, & Giummarra, 2015; Zhao, Ren, Sun, Wan, & Hu, 2020). These self-report questionnaires provide ones' subjective evaluation of their empathy. Alternatively, empathy for pain could also be evaluated using subjective ratings and brain responses to visual stimuli depicting or indicating that another person is in pain (Cui, Zhu, & Luo, 2017; Decety, Yang, & Cheng, 2010; Fan & Han, 2008; Peng et al., 2019). With higher subjective ratings of pain intensity and unpleasantness (Cheng et al., 2007; Peng et al., 2019; Wang, Wang, Hu, & Li, 2014), observing pictures showing others' injuries could evoke larger amplitudes in certain components in event-related potentials (ERPs), such as early frontal-central N1 and N2 components, the central-parietal P3 component, and the late positive potential (LPP; Cui, Zhu, Duan, & Luo, 2016; Cui et al., 2017; Fan, Chen, Chen, Decety, & Cheng, 2013; Meng et al., 2013; Peng et al., 2019).

In the aspect of animal studies, empathy for pain has been innovatively evaluated by the modulation of pain sensitivity (e.g., pain threshold or pain tolerance), when the animals were exposed to their painful cagemates (Langford et al., 2006; Li et al., 2014). The underlying premise of this strategy is that the variability of empathy for pain could be perfectly captured by the change of pain sensitivity; in other words, the two variables are highly correlated. Some existing evidence in human studies indeed implied a strong link between pain sensitivity and empathy for pain (Danziger, Faillenot, & Peyron, 2009; Danziger, Prkachin, & Willer, 2006; Liu et al., 2019). For instance, patients with congenital insensitivity to pain showed less negative emotional responses to video clips depicting others in painful situations (Danziger et al., 2006, 2009), which suggested that empathizing with others' pain should be grounded in pain experience of one's own. Besides, in healthy volunteers, individual pain sensitivity to electrical stimuli was highly correlated with amplitudes of some ERP components (e.g., the central-parietal P3 and LPP components) evoked by sounds of others' pain (Liu et al., 2019). This result indicated that participants' sensitivity to physical pain was positively correlated with amplitudes of ERP responses to others' suffering. The close relationship between pain sensitivity and empathy for pain was further supported by the finding that subjective ratings and neurophysiological responses to others' pain changed along with

the modulation of self-pain through various pharmacological or nonpharmacological manipulations (Mischkowski, Crocker, & Way, 2016; Rütgen, Seidel, Riečanský, et al., 2015; Rütgen, Seidel, Silani, et al., 2015).

However, it is still unclear how pain sensitivity and empathy for pain are connected. Considering that pain is an aversive sensory and emotional experience (Loeser & Treede, 2008; Lu, Thompson, Zhang, & Hu, 2019) and empathy for pain is a source of emotional feelings (Gu, Liu, & Cui, 2019), both of them could be influenced by various emotional and cognitive factors (Craig, Versloot, Goubert, Vervoort, & Crombez, 2010; Wiech, Ploner, & Tracey, 2008), such as pain-related anxiety (Terry, Moeschler, Hoelzer, & Hooten, 2016), depression (Piñerua-Shuhaibar, Villalobos, Delgado, Rubio, & Suarez-Roca, 2011), pain catastrophizing (Kjogx et al., 2016), and pain-related fear (Hirsh, George, Bialosky, & Robinson, 2008). In other words, the relationship between pain sensitivity and empathy for pain should not be considered as a simple bivariate correlation, and this relationship is likely to be mediated by other emotional and cognitive processes associated with pain (Craig et al., 2010; Leeuw et al., 2007). Therefore, we hypothesized that (a) pain sensitivity would be positively correlated with empathy for pain, and (b) the relationship between pain sensitivity and empathy for pain would be mediated by pain-related psychological factors, such as pain-related anxiety, depression, pain-related fear, and pain catastrophizing. In addition, given that significant gender differences were reported in previous studies investigating pain sensitivity (Edwards, Haythornthwaite, Sullivan, & Fillingim, 2004; Hirsh et al., 2008), empathy (Birkett, 2014; Han, Fan, & Mao, 2008; Zhao et al., 2018), and pain-related psychological factors (Edwards et al., 2004; Osman, Barrios, Osman, Schneekloth, & Troutman, 1994; Roelofs, Peters, Deutz, Spijker, & Vlaeyen, 2005), we took gender into account when examining the relationship among pain sensitivity, empathy for pain, and pain-related psychological factors.

To test the aforementioned research hypotheses, we performed two experiments. In Experiment 1, we investigated the relationship among pain sensitivity (indexed by cold pain threshold and pain tolerance), self-report empathy (measured by the IRI), and pain-related emotion/cognition (evaluated using well-established questionnaires) at the behavioral level. In Experiment 2, combined with electroencephalography (EEG) recordings, we adopted a classic empathy for pain task to evaluate psychophysiological empathic responses to others' pain (i.e., subjective ratings of pain intensity and unpleasantness as well as amplitudes of empathy-related ERP components, including P3 and LPP components), which enabled us to assess their relationship at the electrophysiological level. It should be noted that, whereas IRI used in Experiment 1 measured self-report empathy (Giummarra et al., 2014), psychophysiological

empathic responses to others' pain collected in Experiment 2 served as neural indices to objectively quantify empathy for pain, which could deepen our understanding of the detailed relationship between pain sensitivity and empathy for pain.

2 | METHOD

2.1 | Experiment 1: The relationship between pain sensitivity and self-report empathy

2.1.1 | Participants

Two hundred right-handed healthy participants aged from 18 to 24 years were recruited in this experiment. Four participants did not complete this experiment, leaving a final sample of 196 participants (123 females, Mean age = 21.14 ± 0.16 years). Based on self-report, all participants have declared no neurological diseases, psychiatric disorders, pain-related diseases, nor current use of any medication, and none of them have been previously exposed to experimentally induced pain. All participants gave their written informed consent and received monetary compensation for their participation. This experiment was approved by the local ethics committee.

2.1.2 | Questionnaires

Pain-related anxiety (Terry et al., 2016), depression (Piñerua-Shuhaibar et al., 2011), pain catastrophizing (Kjogx et al., 2016), and pain-related fear (Hirsh et al., 2008) have potential effects on the relationship between pain sensitivity and empathy for pain. For this reason, these pain-related emotional and cognitive factors were considered in the present study. Details of the questionnaires to measure these psychological characteristics were provided as follows.

Pain Anxiety Symptoms Scale (PASS) is a 40-item scale that measures the level of anxiety under daily pain events (McCracken & Dhingra, 2002). *Beck Depression Inventory (BDI)* is a 21-item scale that measures the existence and severity of depression symptoms (Beck, Steer, & Carbin, 1988). *Pain Catastrophizing Scale (PCS)* is a 13-item scale used to measure one's tendency to exaggerate the threat and severity of pain (Sullivan, Bishop, & Pivik, 1995). *Fear of Pain Questionnaire (FPQ)* is a 30-item scale that measures the fear under specific pain-producing situations (McNeil & Rainwater, 1998). The reliability and validity of these questionnaires have been well established in Chinese populations (PASS: Wong, McCracken, & Fielding, 2012; BDI: Shek, 1990; PCS: Xu, Wei, Wang, Liu, & Chen, 2015; FPQ:

Yang, Jackson, Gao, & Chen, 2012). The total score of each questionnaire was used in the present study.

To evaluate the self-report empathy for each participant, we adopted the IRI (Davis, 1983), which is one of the most widely used multidimensional measures of empathy (Ren, Sun, Lu, Huang, & Hu, 2019). The Chinese version of IRI was well validated in Chinese populations (Wang et al., 2013; Zhao et al., 2018). It includes 22 items divided into four sub-scales: perspective taking (PT, 5 items), fantasy (FS, 6 items), empathic concern (EC, 6 items), and personal distress (PD, 5 items). PT assesses the tendency to adopt another's perspective; FS reflects the ability to appreciate the emotion of fictional characters of books, movies, and plays; EC describes a person's tendency to share the feelings of others or concern for others; PD measures the extent of feeling uneasiness as a result of witnessing another's distress or suffering. In general, PT reflects cognitive empathy, and EC and PD are two measures of emotional empathy focusing on the other- and self-oriented feelings, respectively (Dziobek et al., 2008). FS is considered not to measure empathy *per se* (Baron-Cohen & Wheelwright, 2004).

2.1.3 | Experimental procedures

Ten minutes after completing the above questionnaires following standardized instructions, participants were instructed to take a cold pressor test (CPT), which has good reliability and validity for examining individuals' pain sensitivity (Hirsh et al., 2008; Koenig et al., 2014). Cold pain was induced by immersing participants' hands into the cold pressor, a circulating water bath (DX-208 water bath, Beijing Changliu Scientific Instruments Co., China) with the water temperature maintained at $2 \pm 0.1^\circ\text{C}$ and flow speed at 15 L/min.

To ensure that the skin temperature before the CPT was consistent across participants, all participants were required to put their left hands into the water at the temperature of $\sim 22^\circ\text{C}$ for 60 s. Subsequently, participants were instructed to place their left hands into the cold water at a depth of about 8 cm above the wrist. Participants were required to report their pain once they began to feel it and keep their hands immersed until the pain became unbearable, and only then, they could immediately remove their hands from the cold water. An uninformed ceiling (i.e., participants were not told about the maximal duration that they could keep their hands in the cold water) of 300 s was enforced for participants' safety. Seven participants were asked to withdraw their hands at the 300th s. *Pain threshold* was defined as the duration of immersion (in seconds) from the time the hand was placed in the water to the time that the participant began to feel pain. *Pain tolerance* was defined as the duration of immersion (in seconds) from the time the hand was placed in the water to

the time that the participant actively or passively withdrew the hand from the cold water. The time was recorded by an experimenter using a stopwatch. After finishing the test, all participants were instructed to immerse their hands in the water at the temperature of $\sim 22^{\circ}\text{C}$ to reduce their suffering and were provided with a towel to dry their hands.

2.1.4 | Statistical analyses

Statistical analyses were performed using SPSS 22.0 and Amos 22.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were provided for pain sensitivity (i.e., pain threshold and pain tolerance), self-report empathy (i.e., IRI subscale scores), and pain-related emotion/cognition (i.e., PASS, BDI, PCS, and FPQ scores). The relationships among pain sensitivity, self-report empathy, and pain-related emotion/cognition were estimated using Pearson correlation analyses. To ensure that the values used in the correlation analyses were normally distributed, the values of pain threshold and pain tolerance were log-transformed (both $p > .05$ after transformation, the Shapiro–Wilk test). To account for multiple comparisons in the correlation analyses, a false discovery rate (FDR) procedure (Benjamini & Hochberg, 1995) was used to correct the significance level (p value). All participants, including the participants who withdrew their hands at the 300th s, remained in the analyses because excluding these participants may bias the statistical results (Birnie, Petter, Boerner, Noel, & Chambers, 2012).

To investigate the potential mediating effects of pain-related emotion/cognition on the relationship between pain sensitivity and self-report empathy, structural equation modeling (SEM) with maximum likelihood estimation was adopted (Byrne, 2016), given that the close relationships among the three variables be confirmed by the correlation analyses. The model fit was assessed using the following criteria: the ratio of chi-square to degrees of freedom (χ^2/df) < 2 (Kline, 2015), root mean square error of approximation (RMSEA) ≤ 0.06 (Hu & Bentler, 1999), both goodness-of-fit index (GFI) and adjusted goodness-of-fit index (AGFI) ≥ 0.90 , both comparative fit index (CFI) and normed fit index (NFI) ≥ 0.95 (Hooper, Coughlan, & Mullen, 2008). Besides, to assess the significance of the indirect and direct effects, bias-corrected 95% confidence intervals (CIs) were calculated using the bootstrapping procedure (Preacher & Hayes, 2008). The estimate was considered statistically significant if the 95% CI (based on 2,000 bootstrap samples) excluded zero. Standardized estimate (b), standard error (SE), 95% CI, and p value were reported for both direct and indirect effects. In accordance with Zhao, Lynch, and Chen (2010), there are three patterns of mediating effect: (a) a complementary mediation exhibits both significant indirect and direct effects, which point to the same direction; (b) a competitive

mediation exhibits both significant indirect and direct effects, which point to opposite directions; and (c) an indirect-only mediation exhibits a significant indirect effect but insignificant direct effect.

To explore the possible influence of gender on the relationship between pain sensitivity and self-report empathy, we performed (a) independent sample t tests between females and males on pain sensitivity (i.e., pain threshold and pain tolerance), self-report empathy (i.e., IRI subscale scores), and pain-related emotion/cognition (i.e., PASS, BDI, PCS, and FPQ scores), and (b) another SEM with gender as a confounder.

2.2 | Experiment 2: The relationship between pain sensitivity and psychophysiological empathic responses

2.2.1 | Participants

Fifty right-handed healthy participants aged from 18 to 24 years were recruited in this experiment (33 females, Mean age = 20.70 ± 0.24 years). The inclusion and exclusion criteria and other experimental requirements were identical to those of Experiment 1.

2.2.2 | Questionnaires and materials

To evaluate the psychological characteristics associated with pain-related emotion and cognition, the four questionnaires (i.e., PASS, BDI, PCS, and FPQ) that were used in Experiment 1 were also adopted in Experiment 2. Besides, to assess pain sensitivity, participants were instructed to take the CPT, which was identical to that of Experiment 1.

To evoke the psychophysiological empathic responses to others' pain, forty pictures from a published empathy ERP study (Meng et al., 2013) were administrated in the present experiment. These pictures describe a body part (i.e., a hand, a forearm, or a foot) under daily scenarios in painful (e.g., using a knife improperly and one hand got cut; 20 pictures) or nonpainful situations (e.g., using a knife properly to cut vegetables; 20 pictures). Painful and nonpainful pictures (see examples in Figure 1) were well matched in terms of luminance, contrast, and color (Meng et al., 2013). All pictures were 7.08×5.32 inch (width $\times$ height) with 100 pixels per inch.

2.2.3 | Experimental procedures

Participants were instructed to sit in a comfortable chair in a silent, temperature-controlled room (25°C). To get familiar

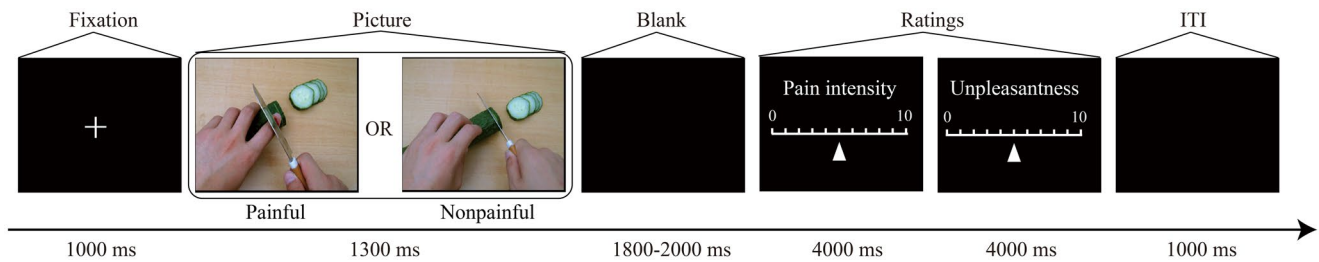


FIGURE 1 ERP experimental design (Experiment 2). Each trial started with a fixation cross presented for 1,000 ms, followed by a picture (painful or nonpainful) presented for 1,300 ms. After a blank interval of 1,800–2,000 ms, participants were instructed to rate the subjective pain intensity (4,000 ms) and unpleasantness (4,000 ms) of the picture on the 11-point numerical rating scale. The intertrial interval (ITI) was 1,000 ms

with the procedure, participants were instructed to complete a 6-trial task in a training session, in which all pictures were different from those of the test session.

In the test session, painful and nonpainful pictures were presented at the center of a computer screen with a black background. Each picture subtended a visual angle of $12.68^\circ \times 9.59^\circ$ at a viewing distance of about 80 cm. All pictures were pseudo-randomly presented in such a way that painful or nonpainful pictures never showed in three consecutive trials. As illustrated in Figure 1, each trial began with a fixation cross presented for 1,000 ms, and then, there was a picture presented for 1,300 ms, followed by a blank screen for 1,800–2,000 ms. Subsequently, participants were required to successively rate pain intensity (0 = *no pain*, 10 = *unbearable pain*) and unpleasantness (0 = *not unpleasant*, 10 = *extremely unpleasant*) within 8,000 ms on the 11-point numerical rating scale. Specifically, participants were asked to move the pointer on the screen to the corresponding rating using two buttons on the keyboard. It should be noted that ratings of pain intensity and unpleasantness refer to participants' own experience when observing the pictures, instead of the experience of the observed subject in the pictures. The intertrial interval was 1,000 ms, and there were 40 trials in total.

2.2.4 | EEG recording

EEG data were continuously recorded from DC to 155 Hz with a 1,024 Hz sampling rate via a 64-electrode BioSemi ActiveTwo system (BioSemi Inc., Netherlands). The BioSemi system works with a “zero-ref” setup, replacing the conventional ground and reference electrodes with a Common Mode Sense/Driven Right Leg circuit (please refer to www.biosemi.com/faq/cms&drl.htm for further information). Electrode impedances were kept below 10 k Ω .

2.2.5 | EEG data preprocessing

EEG data were preprocessed using EEGLAB (Delorme & Makeig, 2004), an open-source toolbox running in the

MATLAB environment (R2016a; MathWorks, USA). Continuous EEG data were down-sampled to 1,000 Hz, and band-pass filtered between 0.01 and 30 Hz. Then, EEG epochs were extracted using a window analysis time of 1,200 ms (200 ms before and 1,000 ms after the onset of the stimulus), and baseline corrected using the prestimulus interval. Epochs contaminated by gross artifacts (e.g., large muscle activity) were removed (the removed trials in the painful and nonpainful conditions were 0.3% and 0.6% of all trials, respectively). Besides, epochs contaminated by eyeblinks and movements were corrected using an independent component analysis algorithm (Delorme & Makeig, 2004). After preprocessing, EEG data were re-referenced to the common average.

2.2.6 | EEG data analyses

Epochs belonging to the same condition were averaged, thus, yielding two average waveforms for each participant. Single-participant average waveforms were subsequently averaged across participants to obtain group-level waveforms. Consistent with previous studies (Coll, 2018; Cui et al., 2017; Cui, Zhu, Gu, & Luo, 2016), four salient ERP components were identified, that is, N1, N2, P3, and LPP components (see Figure). Specifically, N1 and N2 components were, respectively, defined as the most negative deflections within 100–200 ms and 200–300 ms after stimulus onset with a maximal distribution over the frontal-central regions. P3 component was defined as the most positive component within 300–600 ms over the central-parietal region. LPP component was defined as the long-lasting positive component within 600–900 ms over the central-parietal region. Based on findings in previous studies (Cui, Zhu, Gu, et al., 2016; Peng et al., 2019), the mean amplitudes of N1 (measured from Fz, F1, F2, FCz, FC1, and FC2, within 110–140 ms), N2 (measured from Fz, F1, F2, FCz, FC1, and FC2, within 220–270 ms), P3 (measured from Pz, P1, P2, CPz, CP1, and CP2, within 400–600 ms), and LPP (measured from Pz, P1, P2, CPz, CP1, and CP2, within 600–800 ms) components were extracted from each participant. In addition, group-level scalp topographies at the latencies of the

N1, N2, P3, and LPP components were computed by spline interpolation.

2.2.7 | Statistical analyses

Descriptive statistics were provided for pain sensitivity (i.e., pain threshold and pain tolerance), subjective ratings (i.e., pain intensity and unpleasantness), and ERP responses (amplitudes and latencies of N1, N2, P3, and LPP components) in the empathy for pain task, and pain-related emotion/cognition (i.e., PASS, BDI, PCS, and FPQ scores). To assess the difference between painful and nonpainful conditions, paired-sample *t* tests were performed on subjective ratings (i.e., pain intensity and unpleasantness) and ERP responses (i.e., amplitudes and latencies of N1, N2, P3, and LPP components). Cohen's *d* was calculated to reflect the effect size for the *t* tests. To account for multiple comparisons in the analyses, an FDR procedure (Benjamini & Hochberg, 1995) was used to correct the significance level (*p* value).

The relationships between pain sensitivity, psychophysiological empathic responses to others' pain, and pain-related emotion/cognition were investigated using a series of Pearson correlation analyses. Please note that the differences in subjective ratings and ERP amplitudes between painful and nonpainful conditions were regarded as the psychophysiological empathic responses to others' pain. Other statistical procedures were identical to Experiment 1.

In light of the mediating effects of pain-related emotion/cognition on the relationship between pain sensitivity and self-report empathy revealed in Experiment 1, we also performed a similar mediation analysis, in which the self-report empathy scores were replaced by the psychophysiological empathic responses to other's pain. The possible influence of

gender on the relationship between pain sensitivity and psychophysiological empathic responses was not considered due to the limited sample size. The mediating effect was considered statistically significant when the 95% CI (based on 2,000 bootstrap samples) excluded zero.

3 | RESULTS

3.1 | Experiment 1: The relationship between pain sensitivity and self-report empathy

3.1.1 | Correlations between pain sensitivity, self-report empathy, and pain-related emotion/cognition

Descriptive statistics of pain sensitivity, self-report empathy, and pain-related emotion/cognition and their correlation results are summarized in Table 1. Pearson correlation analyses revealed that pain threshold was negatively correlated with PD score ($r(194) = -.22, p = .005$), and pain tolerance was negatively correlated with EC score ($r(194) = -.16, p = .047$) and PD score ($r(194) = -.23, p = .003$). In addition, pain threshold was negatively correlated with PASS score ($r(194) = -.24, p = .003$), PCS score ($r(194) = -.18, p = .023$), and FPQ score ($r(194) = -.20, p = .009$). Pain tolerance was negatively correlated with PASS score ($r(194) = -.16, p = .042$) and FPQ score ($r(194) = -.17, p = .027$). EC score was positively correlated with PASS score ($r(194) = .26, p < .001$), PCS score ($r(194) = .17, p = .034$), and FPQ score ($r(194) = .24, p = .003$). PD score was also positively correlated with PASS score ($r(194) = .53, p < .001$), BDI score ($r(194) = .31, p < .001$), PCS score ($r(194) = .34, p < .001$), and FPQ score ($r(194) = .45, p < .001$).

TABLE 1 Descriptive statistics ($M \pm SE$) of pain sensitivity, self-report empathy, and pain-related emotion/cognition, and their correlations

Categories	Variables	$M \pm SE$	Pain threshold	Pain tolerance	PT score	EC score	PD score
Pain sensitivity	Pain threshold (s)	1.05 ± 0.75	–	–	–	–	–
	Pain tolerance (s)	43.00 ± 4.26	–	–	–	–	–
Self-report empathy	PT score	13.69 ± 0.23	0.02	–0.14	–	–	–
	EC score	16.32 ± 0.25	–0.09	–0.16*	–	–	–
	PD score	10.90 ± 0.25	–0.22**	–0.23**	–	–	–
Pain-related emotion/cognition	PASS score	44.55 ± 1.02	–0.24**	–0.16*	0.13	0.26***	0.53***
	BDI score	1.80 ± 0.53	–0.11	–0.01	–0.16	–0.01	0.31***
	PCS score	21.10 ± 0.66	–0.18*	–0.08	0.05	0.17*	0.34***
	FPQ score	9.16 ± 1.22	–0.20**	–0.17*	0.10	0.24**	0.45***

Abbreviations: BDI, Beck Depression Inventory; EC, empathic concern; FPQ, Fear of Pain Questionnaire; PASS, Pain Anxiety Symptoms Scale; PCS, Pain Catastrophizing Scale; PD, personal distress; PT, perspective taking.

* $p < .01$; ** $p < .001$.

3.1.2 | Pain-related emotion/cognition mediates the relationship between pain sensitivity and self-report empathy

Since (a) PT score was not significantly correlated with any variable assessing pain sensitivity or pain-related emotion/cognition, and (b) BDI score was not significantly correlated with any variable assessing pain sensitivity (see Table 1), both measures were excluded in the mediation analysis. All other measures were fitted in the model, in which pain sensitivity was the predictor and loaded by pain threshold and pain tolerance, pain-related emotion/cognition was the mediator and loaded by PASS, PCS, and FPQ scores, and emotional empathy was the outcome and loaded by EC and PD scores (see Figure 2). In the fitted model, all observed variables had moderate to high loadings (b s range = [.35, .98]) in their respective unobserved variables. The model produced adequate fit indices: $\chi^2(11) = 19.07$, $p = .060$, $\chi^2/df = 1.73$, RMSEA = 0.06, GFI = 0.97, AGFI = 0.93, CFI = 0.98, NFI = 0.96. Pain sensitivity showed an indirect effect ($b = -.18$, $SE = 0.08$, $CI = [-0.34, -0.04]$, $p = .009$) on emotional empathy through pain-related emotion/cognition, but not a direct effect ($b = -.21$, $SE = 0.14$, $CI = [-0.48, 0.03]$, $p = .113$). These results revealed that pain-related emotion/cognition was an indirect-only mediator on the relationship between pain sensitivity and emotional empathy.

Independent-sample t tests showed that although no gender differences in pain threshold and pain tolerance were observed (both $p > .05$), there were significant gender differences in PD ($t(194) = -3.12$, $p = .002$, Cohen's $d = 0.46$), PASS ($t(194) = -2.30$, $p = .023$, Cohen's $d = 0.34$), PCS ($t(194) = -2.16$, $p = .032$, Cohen's $d = 0.32$), and FPQ ($t(194) = -3.33$, $p = .001$, Cohen's $d = 0.49$) scores (see Table S1). When gender was included as a confounder in the SEM, no significant effect of gender on pain sensitivity, emotional empathy, or pain-related emotion/cognition was observed (all $p > .05$; see Figure S1).

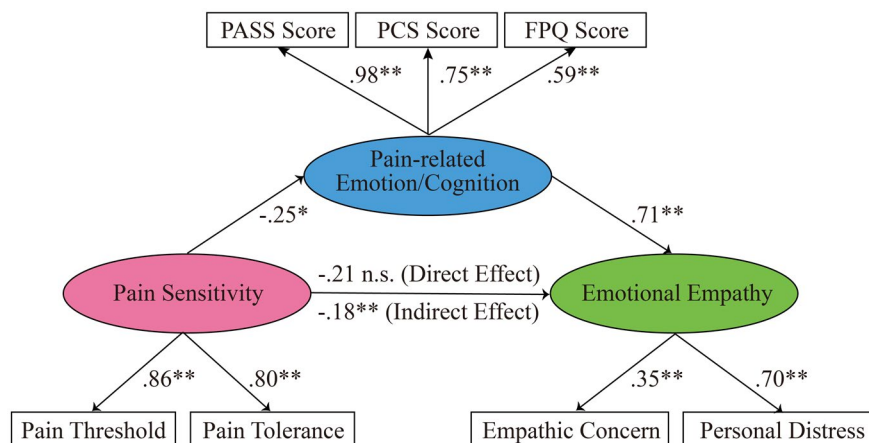
3.2 | Experiment 2: The relationship between pain sensitivity and psychophysiological empathic responses to others' pain

3.2.1 | Subjective ratings and ERP responses in the empathy for pain task

The descriptive statistics of the subjective ratings and ERP amplitudes, as well as their statistical comparisons between painful and nonpainful conditions, are summarized in Table 2. Paired-sample t tests showed there were significant differences in ratings of pain intensity ($t(49) = 22.23$, $p < .001$, Cohen's $d = 3.14$) and unpleasantness ($t(49) = 2.94$, $p < .001$, Cohen's $d = 2.95$) between painful and nonpainful conditions. As expected, both subjective ratings in the painful condition (pain intensity: 5.33 ± 0.22 ; unpleasantness: 5.51 ± 0.26) were significantly larger than those in the nonpainful condition (pain intensity: 0.54 ± 0.08 ; unpleasantness: 0.56 ± 0.08).

As showed in Figure 3, ERP responses displayed two evident negative components at early latencies (N1 and N2 components) and a dominant positive component at late latencies (P3 component), which was followed by a long-latency positive deflection (LPP component). Scalp topographies showed that N1 and N2 components were maximal at the frontal region, and P3 and LPP components were maximal at the parietal region. For the amplitude, paired-sample t tests revealed no significant differences in N1 and N2 amplitudes between the two conditions (both $p > .05$). However, significant amplitude differences between the two conditions were observed for P3 ($t(49) = 3.08$, $p = .003$, Cohen's $d = 0.43$) and LPP components ($t(49) = 5.43$, $p < .001$, Cohen's $d = 0.77$). As expected, P3 and LPP amplitudes were significantly larger in the painful condition (P3: $7.52 \pm 0.49 \mu V$; LPP: $6.08 \pm 0.54 \mu V$) than those in the nonpainful condition (P3: $6.31 \pm 0.43 \mu V$; LPP: $3.58 \pm 0.48 \mu V$). For the latency, paired-sample t tests revealed no significant differences in N1 latency between the two conditions ($p > .05$). N2 latency in the painful condition

FIGURE 2 Pain-related emotion/cognition mediates the relationship between pain sensitivity and emotional empathy (Experiment 1). Displayed values are standardized regression coefficients. FPQ, Fear of Pain Questionnaire; PASS, Pain Anxiety Symptoms Scale; PCS, Pain Catastrophizing Scale. n.s. $p > .05$, * $p < .05$, ** $p < .01$



Variables	Painful	Nonpainful	<i>t</i> (49)	<i>p</i>	Cohen's <i>d</i>
Pain intensity	5.33 ± 0.22	0.54 ± 0.08	22.23	<.001***	3.14
Unpleasantness	5.51 ± 0.26	0.56 ± 0.08	2.94	<.001***	2.95
N1 amplitude (μV)	-1.75 ± 0.30	-2.24 ± 0.23	1.65	.105	–
N2 amplitude (μV)	-3.79 ± 0.46	-3.78 ± 0.46	-0.06	.954	–
P3 amplitude (μV)	7.52 ± 0.49	6.31 ± 0.43	3.08	.003**	0.43
LPP amplitude (μV)	6.08 ± 0.54	3.58 ± 0.48	5.43	<.001***	0.77

p* < .01; *p* < .001.

TABLE 2 Descriptive statistics (*M* ± *SE*) of subjective ratings and ERP amplitudes, and their comparisons between painful and nonpainful conditions

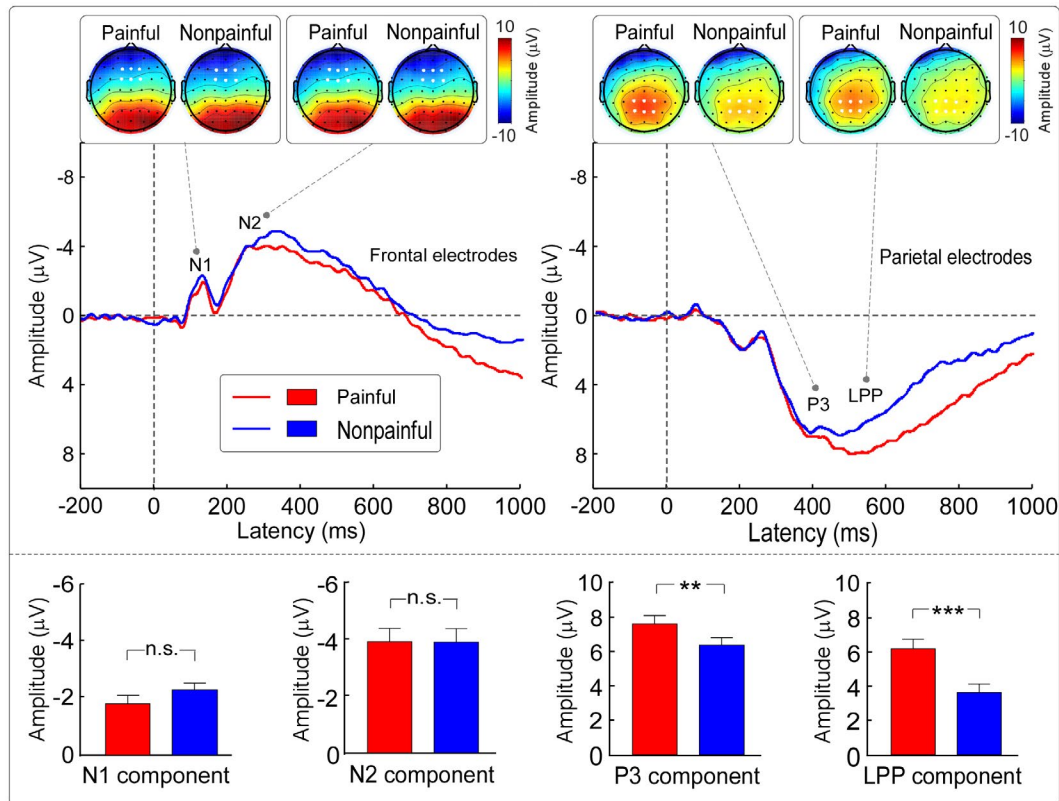


FIGURE 3 ERP responses in painful and nonpainful conditions (Experiment 2). ERP waveforms elicited by painful and nonpainful pictures are marked in red and blue, respectively. Scalp topographies of N1, N2, P3, and LPP components in painful and nonpainful conditions are showed at their respective latencies. Electrodes displaying the maximal responses are marked using enlarged white dots (frontal electrodes for N1 and N2 components, parietal electrodes for P3 and LPP components). Whereas N1 and N2 amplitudes were not significantly different between painful and nonpainful conditions, P3 and LPP amplitudes were significantly larger in the painful condition than those in the nonpainful condition. Data are expressed as *M* ± *SE*. n.s. *p* > .05, ** *p* < .01, *** *p* < .001

(240.68 ± 4.43 ms) was significantly shorter than that in the nonpainful condition (253.80 ± 4.94 ms; *t*(49) = -2.12, *p* = .039, Cohen's *d* = 0.30). No condition differences were observed in P3 and LPP latencies (both *p* > .05; see Table S2).

3.2.2 | Correlations between pain sensitivity, psychophysiological empathic responses, and pain-related emotion/cognition

Descriptive statistics of pain sensitivity, psychophysiological empathic responses, and pain-related emotion/cognition

and their correlation results are summarized in Table 3. Pain threshold was negatively correlated with several psychophysiological empathic responses (pain intensity: *r*(48) = -.37, *p* = .029; P3 amplitude: *r*(48) = -.45, *p* = .006; LPP amplitude: *r*(48) = -.40, *p* = .020) and FPQ score (*r*(48) = -.36, *p* = .038). Similarly, pain tolerance was negatively correlated with two psychophysiological empathic responses (P3 amplitude: *r*(48) = -.34, *p* = .044; LPP amplitude: *r*(48) = -.42, *p* = .011). In addition, both empathic P3 and LPP amplitudes were positively correlated with FPQ score (P3 amplitude: *r*(48) = .35, *p* = .039; LPP amplitude: *r*(48) = .34, *p* = .044).

TABLE 3 Descriptive statistics ($M \pm SE$) of pain sensitivity, empathic responses, and pain-related emotion/cognition, and their correlations

Categories	Variables	$M \pm SE$	Pain threshold	Pain tolerance	Pain intensity	Unpleasantness	N1 amplitude	N2 amplitude	P3 amplitude	LPP amplitude
Pain sensitivity	Pain threshold (s)	1.45 $\pm$ 1.49	-	-	-	-	-	-	-	-
	Pain tolerance (s)	46.91 $\pm$ 8.03	-	-	-	-	-	-	-	-
Empathic responses	Pain intensity	4.78 $\pm$ 0.22	-0.37*	-0.32	-	-	-	-	-	-
	Unpleasantness	4.95 $\pm$ 0.24	-0.31	-0.24	-	-	-	-	-	-
	N1 amplitude (μV)	0.49 $\pm$ 0.29	-0.01	-0.17	-	-	-	-	-	-
	N2 amplitude (μV)	-0.01 $\pm$ 0.26	-0.16	-0.23	-	-	-	-	-	-
	P3 amplitude (μV)	0.68 $\pm$ 0.33	-0.45**	-0.34*	-	-	-	-	-	-
Pain-related emotion/cognition	LPP amplitude (μV)	2.18 $\pm$ 0.43	-0.40*	-0.42*	-	-	-	-	-	-
	PASS score	45.72 $\pm$ 2.23	-0.27	-0.26	0.22	0.26	0.12	0.04	0.09	0.24
	BDI score	9.22 $\pm$ 0.88	-0.23	-0.08	-0.01	0.07	0.06	-0.01	0.03	0.10
	PCS score	22.36 $\pm$ 1.47	-0.30	-0.25	0.14	0.09	0.21	0.15	0.10	0.22
	FPQ score	89.40 $\pm$ 2.63	-0.36*	-0.25	0.24	0.25	0.12	0.10	0.35*	0.34*

Abbreviations: BDI, Beck Depression Inventory; FPQ, Fear of Pain Questionnaire; PASS, Pain Anxiety Symptoms Scale; PCS, Pain Catastrophizing Scale.

* $p < .05$; ** $p < .01$.

3.2.3 | Pain-related emotion/cognition mediates the relationship between pain sensitivity and psychophysiological empathic responses

According to the correlation results, the mediation model (see Figure 4) was established based on pain threshold (assessing pain sensitivity), FPQ score (assessing pain-related emotion/cognition), and empathic ERP responses (assessing psychophysiological empathic responses to others' pain). Pain threshold demonstrated both a direct ($b = -.37$, $SE = 0.13$, 95% CI = $[-0.61, -0.08]$, $p = .013$) and an indirect effect ($b = -.08$, $SE = 0.05$, 95% CI = $[-0.22, -0.01]$, $p = .023$) on empathic P3 amplitude through FPQ score. Similarly, pain threshold demonstrated both a direct ($b = -.32$, $SE = 0.12$, 95% CI = $[-0.54, -0.08]$, $p = .014$) and an indirect effect ($b = -.08$, $SE = 0.05$, 95% CI = $[-0.23, -0.01]$, $p = .017$) on empathic LPP amplitude through FPQ score. These results suggested that FPQ score was a complementary mediator on the relationship between pain threshold and empathic ERP responses.

4 | DISCUSSION

By investigating the detailed relationship between pain sensitivity and empathy for pain at both behavioral and electrophysiological levels, we obtained two main findings. First, across participants, pain sensitivity was positively correlated with both emotional empathy (i.e., EC and PD scores) and pain intensity ratings as well as empathic P3 and LPP amplitudes in the empathy for pain task. However, no significant correlation was observed between pain sensitivity and cognitive empathy (i.e., PT score). Second, the effect of pain sensitivity on emotional empathy was mediated by pain-related anxiety, pain catastrophizing, and pain-related fear, and the effect of pain sensitivity on ERP responses to others' pain was mediated by pain-related fear. Therefore, even a significant correlation between pain sensitivity and emotional empathy (not cognitive empathy) was confirmed in the present study, their relationship was mediated by some nonnegligible psychological factors. Our findings suggest that the strategy of using pain sensitivity to quantify empathy level should be treated with caution, as their relationship could be disturbed by experimental manipulations or pathological modulations that could influence individual emotional states or cognitive processes.

4.1 | The relationship between pain sensitivity and emotional empathy

One of the main findings is that both emotional empathy (i.e., EC and PD scores) and empathic ERP responses in the

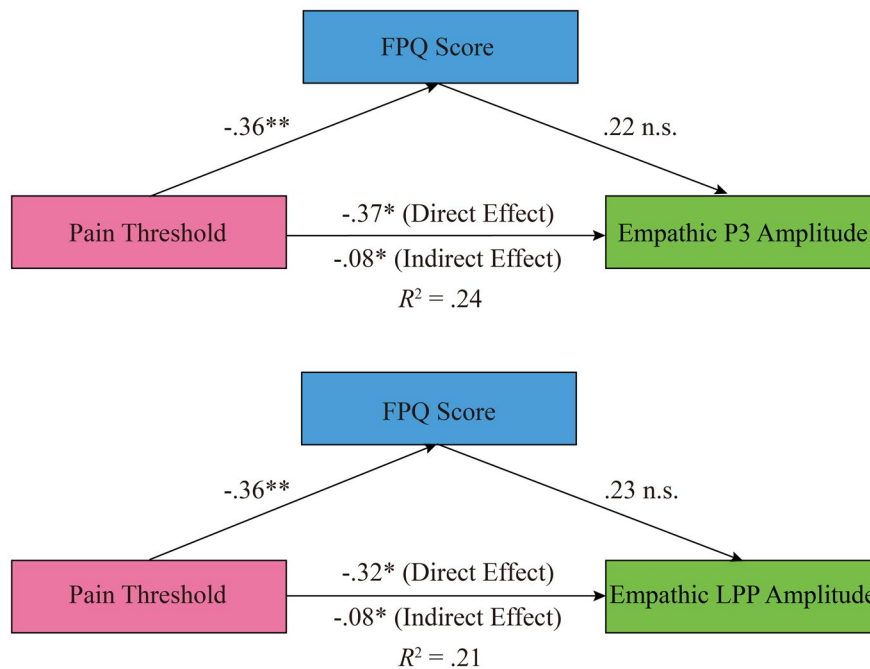


FIGURE 4 PFQ score mediates the relationship between pain threshold and empathic P3/LPP responses (Experiment 2). Displayed values are standardized regression coefficients. Empathic P3/LPP amplitudes are evaluated by the differences of P3/LPP amplitudes between painful and nonpainful conditions. FPQ, Fear of Pain Questionnaire. n.s. $p > .05$, * $p < .05$, ** $p < .01$

empathy for pain task (i.e., P3 and LPP amplitudes) were positively correlated with pain sensitivity (i.e., pain threshold and pain tolerance). It should be noted that IRI scores reflect participants' stable dispositions in understanding and sharing others' feelings (Davis, 1980; Giummarra et al., 2014), whereas empathy for pain reflected by increased amplitudes of ERP components (i.e., P3 and LPP) emphasizes the instant psychophysiological empathic responses to the situation involving pain-related events (Coll, 2018). Namely, whereas empathy measured by IRI in Experiment 1 represents general empathy, empathic ERP responses in Experiment 2 reflect empathy for pain. However, both variables are closely connected, given that many studies have shown that IRI scores were highly correlated with empathic ERP responses (e.g., P3 and LPP amplitudes) in the empathy for pain task (Choi & Watanuki, 2014; Gonzalez-Liencre, Brown, Tas, Breidenstein, & Brüne, 2016). In other words, both IRI scores and empathic ERP responses can reflect one's mental sensitivity to others' pain. Taken the fact that pain sensitivity reflects one's physical sensitivity to self-pain into consideration (Nielsen, Staud, & Price, 2009), the correlation results also indicated that the sensitivities to self-pain and others' pain were highly coupled in healthy participants.

This claim is supported by two lines of evidence. Existing studies performed on healthy volunteers suggested that the change of self-pain sensitivity strongly affected psychophysiological empathic responses to others' pain (Mischkowski et al., 2016; Rütgen, Seidel, Riečanský, et al., 2015; Rütgen, Seidel, Silani, et al., 2015). For example, after taking acetaminophen, a physical painkiller, reduced pain sensitivity to noxious stimuli was accompanied by reduced subjective ratings and empathic brain responses to others' pain in healthy

adults (Mischkowski et al., 2016). Similarly, naltrexone, an opioid antagonist, administrated after placebo manipulation recovered not only self-pain sensitivity, but also brain responses to others' pain (Rütgen, Seidel, Silani, et al., 2015). Another line of evidence from patient studies showed that people with abnormal inherent pain sensitivity had impaired empathy for others' pain (Danziger et al., 2006, 2009; Fan et al., 2013). For instance, individuals with autism spectrum disorder who were hypersensitive to self-pain exhibited exaggerated empathic brain responses in the primary and secondary somatosensory cortices to pictures depicting others' body injuries (Fan et al., 2013).

Importantly, we observed that pain sensitivity was correlated with emotional empathy (i.e., EC and PD scores), but not with cognitive empathy (i.e., PT score). Conceptually, emotional empathy refers to the automatic emotional reaction to the emotions of others, whereas cognitive empathy represents the ability to recognize others' mental states (Decety & Jackson, 2004). Therefore, our results suggest that individuals with higher pain sensitivity tended to have greater automatic emotional reactions to others' emotions, but not stronger ability to recognize others' mental states. This finding is consistent with previous studies showing that healthy participants with higher pain sensitivity to nociceptive heat stimuli had higher empathic concern toward others' pain (Loggia, Mogil, & Bushnell, 2008). Similarly, patients with congenital insensitivity to pain had impaired immediate affective resonance to others' pain, manifested as lesser occipitotemporal activation than healthy controls (Danziger et al., 2009).

In addition, consistent with previous studies (Birkett, 2014; Edwards et al., 2004; Osman et al., 1994; Roelofs et al., 2005),

significant gender differences in PD scores, pain-related anxiety, pain catastrophizing, and pain-related fear were observed in the present study. However, females and males did not differ significantly in pain threshold or pain tolerance. Although some previous studies reported that females were more sensitive to pain compared with males (Edwards et al., 2004; Hirsh et al., 2008), recent qualitative and quantitative reviews have generally concluded that gender differences in pain sensitivity were highly variable across different studies (Hashmi & Davis, 2014; Mogil, 2012; Racine et al., 2012). For cold pain sensitivity, it was reported that 77% and 20% of the studies did not find significant gender differences in pain threshold and pain tolerance, respectively (Racine et al., 2012). Therefore, the lack of gender differences in pain sensitivity in the present study was not surprising. When gender was included as a potential confounding factor in the SEM, no significant effect of gender on pain sensitivity, emotional empathy, or pain-related emotion/cognition was observed, and pain-related emotion/cognition still mediated the relationship between pain sensitivity and emotional empathy after controlling gender. These results indicated that the influence of gender on the relationship between pain sensitivity and emotional empathy was not evident in the present study.

As for empathic ERP responses, a recent meta-analysis suggested that late ERP components (i.e., P3 and LPP) rather than early ERP components (i.e., N1 and N2) were reliably associated with the observation of others' pain (Coll, 2018). P3 and LPP responses were widely accepted to be involved in emotional regulation and social understanding in empathy for pain (Cheng, Hung, & Decety, 2012; Decety et al., 2010; Fan et al., 2013). Besides, it was found that empathic LPP response was greater in participants who had higher emotional empathy, that is, higher EC score (Ikezawa, Corbera, & Wexler, 2013). In line with these findings, our study showed that (a) P3 and LPP amplitudes were significantly greater in response to painful than non-painful pictures, and (b) pain sensitivity was positively correlated with empathic P3 and LPP amplitudes. Therefore, our results suggested that individuals with higher pain sensitivity would have stronger emotional reactions, represented as larger empathic ERP responses to others' pain.

Combined with the claim that pain threshold and pain tolerance reflect the sensory-discriminative and affective-motivational aspects of pain, respectively (Kim et al., 2017), the observation that both pain threshold and pain tolerance were significantly correlated with emotional empathy and empathic ERP responses would suggest that the relationship between pain sensitivity and empathy for pain would be associated with both sensory-discriminative and affective-motivational aspects of pain. This is consistent with existing neuroimaging evidence suggesting that empathy for others' pain was involved in not only the brain regions processing the sensory-discriminative aspect of pain, for example, the

somatosensory cortices, but also brain regions associated with the affective-motivational aspect of pain, for example, the anterior insula and the dorsal anterior cingulate cortex (Betti & Aglioti, 2016; Lamm et al., 2011; Zaki et al., 2016).

Besides, the CPT can elicit profound activation of the sympathetic nervous system and the baroreflex activity, for example, increasing skin conductance (Buchanan, Tranel, & Adolphs, 2006), elevating blood pressure (al'Absi, Petersen, & Wittmers, 2002), and increasing subjective stress ratings (Schwabe, Haddad, & Schachinger, 2008). Previous studies indicated that both self-pain and empathy for others' pain were involved in modulating the sympathetic nervous system activity and the baroreflex activity (Block, 1981; Ho, Konrath, Brown, & Swain, 2014; Konvalinka et al., 2011; Lamm, Porges, Cacioppo, & Decety, 2008; Leone et al., 2006). Therefore, it is possible that these shared physiological processes could be a part of the mechanisms underlying the relationship between self-pain sensitivity and empathy for others' pain.

4.2 | The relationship between pain sensitivity and empathy was mediated by pain-related emotion/cognition

Mediation analysis indicated that the effect of pain sensitivity on emotional empathy was mediated by pain-related anxiety, pain catastrophizing, and pain-related fear; meanwhile, the effect of pain sensitivity on empathic ERP responses was mediated by pain-related fear. These findings are consistent with the simulation theory of empathy, which proposed that empathy for others' pain relies on psychological and neural representations that are similar to those needed for the perception of self-pain (Decety & Jackson, 2004; Lamm & Majdandžić, 2015). It is widely recognized that pain perception in healthy volunteers not only depends on noxious inputs (Hu & Iannetti, 2019), but also is influenced by emotions and beliefs about the pain that they have (Zhang, Lu, Bi, & Hu, 2019; Zhou et al., 2019), such as pain-related anxiety (Wiech & Tracey, 2009), pain catastrophizing (Kjogx et al., 2016), and pain-related fear (Hirsh et al., 2008). Accordingly, it is reasonable to hypothesize that others' pain would be spontaneously matched to the prepared schema for the processing of self-pain, thereby instigating similar pain-related emotional and cognitive processing. This hypothesis could also be supported by the neural processing of empathy for pain *per se*. Specifically, empathy for pain is regarded as the product of both bottom-up and top-down processes (Craig et al., 2010). Bottom-up information is derived through the automatic processing of painful cues applied to others (Ochsner et al., 2008), and top-down information appraised and refined the bottom-up information by implicating personal beliefs, thoughts, or prior knowledge (Craig et al., 2010). Therefore,

both pain sensitivity and empathy are highly associated with pain-related emotion/cognition, which provided a solid basis for the mediation effect of pain-related emotion/cognition on the relationship between pain sensitivity and empathy.

Notably, in Experiment 1, significant correlations were observed between pain sensitivity, as well as between emotional empathy, and PASS, PCS and FPQ scores. However, in Experiment 2, pain sensitivity and empathic ERP responses were merely correlated with the FPQ score. This discrepancy could be explained by two reasons: first, the sample size was much smaller in Experiment 2 than that in Experiment 1 (50 participants vs. 196 participants); second, the measures used to evaluate empathy were different in the two experiments (ERP vs. questionnaire). Besides, these pain-related psychological factors (i.e., pain-related anxiety, pain catastrophizing, and pain-related fear) have distinct psychological constructions, which may contribute to their difference in influencing the relationship between pain sensitivity and empathy for pain. Specifically, pain-related fear represents a present-oriented emotive state associated with nociceptive stimuli, whereas pain-related anxiety represents a more general and future-oriented emotive state that occurs in the anticipation of nociceptive stimuli (Carleton & Asmundson, 2009). Besides, compared with pain catastrophizing, pain-related fear played a more prominent role in the processing of pain (Hirsh et al., 2008). Therefore, it is reasonable that pain-related fear was more robust in mediating the relationship between pain sensitivity and empathy than pain-related anxiety and pain catastrophizing. The involvement of pain-related anxiety and pain catastrophizing in mediating the relationship between pain sensitivity and empathy for pain should not be neglected and needs to be further investigated. It is also worth mentioning that the BDI score was not correlated with pain sensitivity in the present study. This result could be attributed to the low level of depression in healthy participants, considering that previous evidence showing that depression was accompanied by altered pain sensitivity was mostly obtained from depressive individuals (Thompson, Correll, Gallop, Vancampfort, & Stubbs, 2016).

4.3 | Limitations

There are several limitations in the present study that merit consideration. First, instead of using a scale specifically developed for measuring empathy for others' pain (i.e., Empathy for Pain Scale; Giummarra et al., 2014), we adopted IRI since the Chinese version of Empathy for Pain Scale has not been validated. Second, even the influence of gender on the relationship between pain sensitivity and empathy for pain was ruled out in Experiment 1, the gender was not considered as an experimental factor in Experiment 2 due to the limited sample size (33 females and 17 males). Third, the possible influence of the menstrual cycle on pain sensitivity

and pain catastrophizing in female participants was not considered. To date, the influence of the menstrual cycle on pain sensitivity in healthy and pain-free women is still controversial. Although there are several studies demonstrated that pain sensitivity varied across the different stages of the menstrual cycle (Isselée, De Laat, Bogaerts, & Lysens, 2001; Wiesenfeld-Hallin, 2005), the more recent, well-controlled studies suggested a lack of variability in pain sensitivity across the different stages of the menstrual cycle (Bartley & Rhudy, 2013; Klatzkin, Mechlin, & Girdler, 2010; Rhudy & Bartley, 2010). Moreover, to our best knowledge, only one published study directly investigated the effect of the menstrual cycle on pain catastrophizing, which showed that pain catastrophizing scores on the 1st, 12th, and 20th days of the menstrual cycle were significantly different (Casic et al., 2013). However, the authors emphasized that such difference might be confounded by the assessment order, namely, the first measurement of pain catastrophizing was always collected on the first day of the cycle (Casic et al., 2013). Therefore, the influence of the menstrual cycle on pain catastrophizing remains to be corroborated.

4.4 | Conclusion

Our study elucidated the detailed relationship between pain sensitivity and empathy for pain in healthy participants. Individuals with higher pain sensitivity tended to have stronger empathy for pain, manifested as larger emotional reaction to others' pain. Importantly, the relationship between pain sensitivity and empathy for pain was mediated by pain-related emotion/cognition (e.g., pain-related fear). These findings provided new perspectives on the psychological and neurophysiological nature of empathy for pain. Besides, although the conventional strategy of measuring empathy by the change of pain sensitivity (mostly in animal studies) was partially supported by our findings, cautions should be taken to avoid misinterpretation in future studies since pain-related psychological processes take an indispensable part in the linkage between pain sensitivity and empathy for pain.

CONFLICT OF INTEREST

All authors declared no competing interests.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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