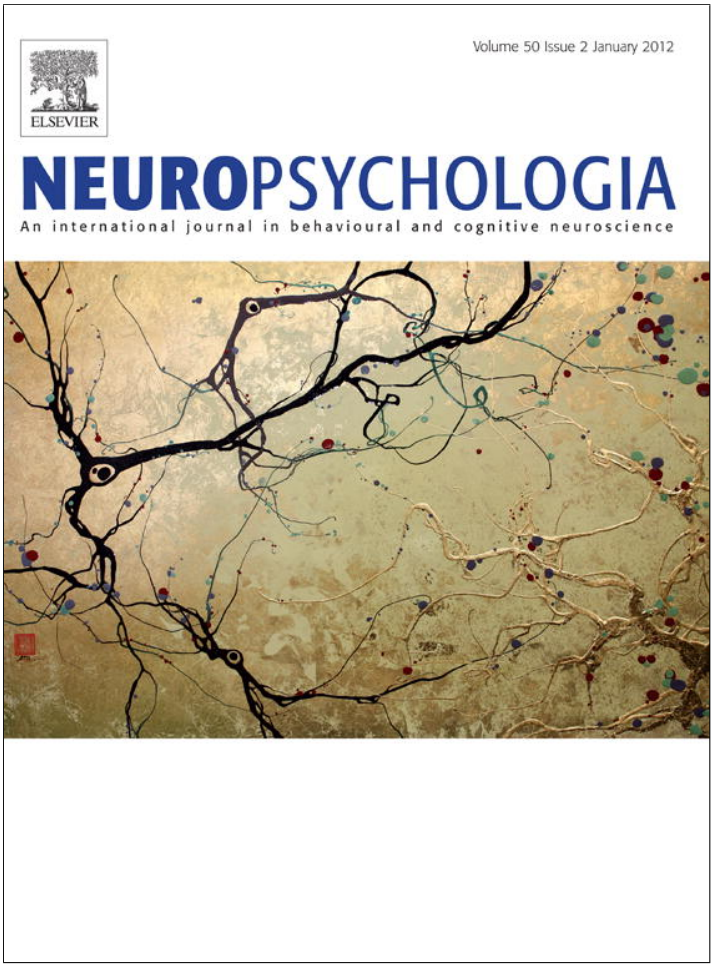

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Distinct roles of the 'Shared Pain' and 'Theory of Mind' networks in processing others' emotional suffering

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ABSTRACT

The brain mechanisms involved in processing another's physical pain have been extensively studied in recent years. The link between understanding others' physical pain and emotional suffering is less well understood. Using whole brain analysis and two separate functional localizers, we characterized the neural response profiles of narrative scenarios involving physical pain (PP), and scenarios involving emotional pain (EP) with functional magnetic resonance imaging (fMRI). Whole brain analyses revealed that PP narratives activated the Shared Pain network, and that the brain regions responsible for processing EP overlapped substantially with brain regions involved in Theory of Mind. Region of interest (ROI) analysis provided a finer-grained view. Some regions responded to stories involving physical states, regardless of painful content (secondary sensory regions), some selectively responded to both emotionally and physically painful events (bilateral anterior thalamus and anterior middle cingulate cortex), one brain region responded selectively to physical pain (left insula), and one brain region responded selectively to emotional pain (dorsomedial prefrontal cortex). These results replicated in two groups of participants given different explicit tasks. Together, these results clarify the distinct roles of multiple brain regions in responding to others who are in physical or emotional pain.

1. Introduction

Imagine watching a close friend slam a door on her fingers, breaking them. Now imagine watching that friend describe her recent divorce. In both cases, you would likely recognize your friend's pain, experience personal distress in response to her suffering, and feel motivated to help her. Accurately knowing what another is feeling, 'sharing' that experience, and feeling motivated to help, are all elements of empathy (Batson, 2009). But is the mechanism of empathy the same, when the target is broken bones versus a broken heart?

Previous studies on pain experience (and perception) have focused on physical pain. These studies have identified a number of brain regions that respond to the sensory aspects of pain (e.g. a strong, crushing pressure on the fingers). For example, primary and secondary sensory areas have been shown to help discriminate the location and quality of a painful stimulus (e.g. Craig, 2002; Rainville, Duncan, Price, Carrier, & Bushnell, 1997). Other brain regions are associated also with an affective or motivational reaction to the pain, including elements of anxiety and fear (e.g. feeling that the pain is unpleasant, anxiety that it will continue); this sense of threat associated with pain is necessary for the evolutionary function of pain in self-preservation. These aspects of pain are associated with activity in the anterior insula and anterior middle cingulate cortex (aMCC). For example, activity in insula and aMCC is modulated by participants' anticipation of pain, and feelings of threat from an injury (e.g. Atlas, Bolger, Lindquist, & Wager, 2010; Wiech et al., 2010). Anterior insula activity has also been associated with other negative affective experiences, including feeling and observing disgust (Jabbi, Bastiaansen, & Keysers, 2008). These three regions all show activity both while experiencing physical pain, and while watching someone else experience physical pain, across a large range of contexts and stimuli (Botvinick et al., 2005; Gu & Han, 2007a; Immordino-Yang, McColl, Damasio, & Damasio, 2009; Jackson, Meltzoff, & Decety, 2005; Lamm, Batson, & Decety, 2007; Singer et al., 2004; Xu, Zuo, Wang, & Han, 2009), and the amount of activity in these regions is correlated with trial-by-trial measurements of the intensity of physical pain experienced (e.g. Peyron, Laurent, & Garcia-Larrea, 2000), or observed (e.g. Saarela et al., 2007). Since the insula and aMCC respond to the first and second person experiences of pain (although see Morrison & Downing, 2007), they are referred to as the 'Shared Pain network', and have been hypothesized to serve as a "bridge" between an observer and a victim. Activity in common brain regions could

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enable 'shared' affective responses, which then support empathy (De Vignemont & Singer, 2006; Sommerville & Decety, 2006) and pro-social behavior (Preston & De Waal, 2002).

Along with the primary sensory and affective/motivational aspects of pain, however, there can also sometimes be a secondary emotional response: for example, feelings of sadness or anger, which can grow into full blown emotional states involving "uniquely human" emotions, such as sadness that broken fingers will prevent you from playing the piano in a concert, the resulting remorse or embarrassment as you anticipate telling colleagues, melancholy knowing that you may never play the same again, and so on. These same emotions often arise in the absence of physical pain. Do the brain regions involved in the 'Shared Pain network' form the basis of empathic reactions to another's emotional suffering that involves no physical pain at all, like a close friend's divorce? Some recent evidence suggests that they could.

Eisenberg and colleagues (Eisenberger, Lieberman, & Williams, 2003; Eisenberger & Lieberman, 2004; Masten, Morelli, & Eisenberger, 2010) have developed a paradigm to create 'social pain' in the laboratory. In this paradigm, called "Cyber Ball", three players pass a ball back and forth; after a short period, two of the players exclude the third player from the exchange. The first-hand social exclusion experienced by the third player is associated with activity in 'Shared Pain network' including anterior insula and middle cingulate regions.

One hypothesis is therefore that responding to others' misfortunes, across the whole gamut from broken fingers to a broken heart, depends on one common neural system, especially including the anterior insula and middle cingulate. However, there is another possibility. Recognizing another's emotional suffering may depend on a different group of brain regions involved in thinking about another person's mind. This so-called "Theory of Mind (ToM) network" includes bilateral temporo-parietal junction (TPJ), precuneus (PC), and medial prefrontal cortex (mPFC) regions (Saxe & Kanwisher, 2003). There is considerable evidence that these regions are recruited when thinking about others' emotional experiences. For example, there is activity in the ToM network when participants evaluate the mental states of characters in cartoons who are reacting to emotionally salient information (Atique, Erb, Gharabaghi, Grodd, & Anders, 2010; Hooker, Verosky, Germine, Knight, & D'Esposito, 2010; Hooker, Verosky, Germine, Knight, & DíEsposito, 2008; Schnell, Bluschke, Konradt, & Walter, 2010; Vollm et al., 2006). Interestingly, watching another person be excluded from a Cyberball game also leads to activation in ToM regions, especially mPFC and PC (Masten et al., 2010; though note that insula activity is also observed).

The prior literature thus raises a key question: what are the relative roles of the 'Shared Pain' and 'ToM' networks in processing (i.e. recognizing, representing and responding to) others' physical and emotional misfortunes?

To test this question, we sought to portray individuals' experiences of physical injuries versus emotional suffering in a single experimental paradigm. Short verbal narratives provide a useful modality for conveying rich information about another person's internal states. Previous studies of empathy for physical pain have used three kinds of stimuli: (i) images of the injury (e.g. pictures or movies of sharp objects threatening body parts) (Gu & Han, 2007a; Jackson et al., 2005; Morrison & Downing, 2007), (ii) images of facial expressions reacting to injury (Botvinick et al., 2005; Lamm et al., 2007; Saarela et al., 2007), or (iii) symbolic cues that predicted actual painful stimulation of a person who is present, next to the participant (Singer et al., 2004, 2006). All three kinds of stimuli robustly activate the 'Shared Pain' network. However, to our knowledge, only one previous study has found activation in the 'Shared Pain' network using verbal descriptions of painful events (Gu & Han, 2007b). We therefore first ask whether (and which) regions involved in representing another's physical pain can also be recruited by abstract verbal stories (cf. Jabbi et al., 2008).

Second, we ask whether the same brain regions are recruited by stories about physically painful injuries, versus about emotional suffering without physical pain. As described above, physical injuries are often accompanied by affective experiences, even including complex emotions such as fear, loss, remorse, and humiliation; nevertheless, it is often possible to dissociate physical pain from emotional suffering, especially in misfortunes that involve intense emotional suffering in the absence of physical pain. We therefore presented participants with short stories from 6 conditions that described a protagonist experiencing: (1) physical pain [PP] (e.g. cutting a finger to the bone), (2) physical sensations without pain [PPC] (e.g. cutting vegetables), (3) emotional suffering [EP] (e.g. proposing marriage and being rejected), (4) emotions without suffering [EPC] (e.g. proposing marriage and being accepted), (5) a false belief causing emotional suffering [FBP] (e.g. falsely believing that a girlfriend is having an affair), or (6) a false belief that does not cause suffering [FBC] (e.g. falsely believing that your girlfriend just boarded a bus). Scenarios involving false beliefs were included because they have been shown previously to be particularly effective at activating the ToM network (Hooker et al., 2008).

Our design had two further elements. First, we manipulated the explicit task instructions of the participants in the scanner. Because verbal stimuli are rarely used in studies of empathy, especially empathy for pain, we tested whether the response in 'Shared Pain' regions to stories about misfortunes depends on task instructions. One group of participants was instructed to quantify the pain or suffering experienced by the protagonist of each story. Objectively quantifying the pain in the story may reduce participants' ability to react emotionally to the protagonist's misfortune. A second group of participants was therefore instructed to just 'try to imagine how the main character feels' (Batson et al., 1997).

Second, in order to relate our results directly to the previous literature, and to maximize the power and sensitivity of our analyses, we identified brain regions of interest in two separate "localizer" studies. In a "Pain Localizer Experiment," participants directly watched another person receive a painful electric shock, or received a shock themselves. In a "ToM Localizer Experiment," participants read about someone's false belief, or an outdated physical representation like a photograph or a map.

In sum, this design allowed us to test three key questions:

(1) How are verbal scenarios involving physical pain and emotional pain represented neurally?
(2) How are these representations related to brain regions recruited during traditional Pain and Theory of Mind tasks?
(3) Are these brain activations robust across different task demands?

2. Methods

2.1. Participants

Forty-one naive right-handed participants (18–37 years old (mean 23.0 ± 4.8 s.d.), 25 females) engaged in the Narrative Experiment, for payment. A separate group of fourteen participants (19–33 years old (mean 23.5 ± 4.1 s.d.), 8 female) engaged in the localizer experiments. All participants were proficient English speakers, had normal or corrected to normal vision, and gave written informed consent in accordance with the requirements of MIT's Committee on the Use of Humans as Experimental Subjects.

2.2. Design and materials

For the Narrative Experiment, 144 verbal scenarios were constructed to fit a 2 (Pain: Pain versus No Pain) × 3 (Condition: Physical Sensations, Emotions and False Beliefs) design. When creating the stimuli, 24 stories were created for each Condition, describing Painful experiences, and then a modified version of each scenario was created, in which outcomes were either neutral or positive, and were free of pain

Table 1
Sample stories from each Condition (Physical, Emotional, False Belief) and each Pain state (Pain, No Pain). Participants were presented with a random set of 12 of the total 24 stories from each Pain condition, and the remaining 12 stories in each No Pain condition. Stories in the No Pain condition involved either neutral or positive outcomes (see Supplemental Materials for full set of stimuli).

Physical pain	Joe was playing soccer with his friends. He slid in to steal the ball away, but his cleat stuck in the grass and he rolled over his ankle, breaking his ankle and tearing the ligaments. His face was flushed as he rolled over.
Physical no pain	Joe was playing soccer with his friends. He slid in to steal the ball; he kicked the ball away from the opposing player, got to his feet and began dribbling down the field. His face was flushed as he ran.
Emotional pain	John was on a hike with his girlfriend. He had an engagement ring in his pocket and at a beautiful overlook he proposed marriage. His girlfriend said that she could not marry him and began crying. John sat on a rock and looked at the ring.
Emotional no pain	John was on a hike with his girlfriend. He had an engagement ring in his pocket and at a beautiful overlook he proposed marriage. His girlfriend said that she would marry him and began crying. John held his new fiancée and looked at the ring.
False belief pain	Ellen took an important exam yesterday. She needed to pass in order to graduate. She passed but the professor switched her results with another student who failed. Ellen checks the results online and cannot hold back her tears.
False belief no pain	Ellen took an important exam yesterday. She needed to pass in order to graduate. She passed but the professor switched her results with another student who scored even higher. Ellen checks the results online and smiles.

or suffering. Thus, within each Condition, Pain and No Pain scenarios were matched for general semantic content. Across all conditions, scenarios were also matched for number of words (mean 46.9 ± 3.7 s.d.). (For sample scenarios, see Table 1; for full list of stimuli, see Supplemental Material.)

Participants in the Narrative Study read either the Painful or Non-Painful Control version of each story (counter-balanced across participants); in total each participant therefore read 72 total stories. Each story was presented for 16 s, followed by a 2 s inter-stimulus interval. However, because the first sentence of the story described the protagonist's background, we estimated that the painful versus control outcome was experienced mostly in the last 10 s of story presentation. Stories were presented in groups of 3 stories from different conditions. After each group of 3 stories, there was a 12 s rest period. Each run contained 12 stories, 2 per condition, and lasted 4.6 min. The whole experiment consisted of 6 runs. The order of conditions and scenarios were counterbalanced across runs and across participants.

Stimuli were presented in white 24-point font on a black background via Matlab 5.0 with an Apple G4 powerbook.

In order to examine the effects of task demands on processing the narratives, participants were all presented with the same stimuli, but were given different assignments in response to the stimuli. At the beginning of each run, prior to stimulus presentation, half of the participants ($n = 20$) were given the following instructions both verbally and in written text on the screen:

Task 1 (Pain Rating): "Read the following stories and when the prompt appears indicate how much pain or suffering the protagonist of the story feels at that moment."

During each story, a single response prompt appeared below the story for the final 4 s of the presentation. The prompt asked participants to judge the "Protagonist's pain or suffering" on the following scale: 1 (None) – 2 (A little) – 3 (Moderate) – 4 (A lot). Subjects made their response on an MR-safe button box. Average responses and reaction times (RTs) for each condition were determined for each individual, and were averaged across item for use in Item Analysis (see below). Behavioral data from 2 of the participants included in the study were lost due to a computer error.

The other half of the participants ($n = 21$) were instead given the following instructions:

Task 2 (Active Empathizing): "While reading each of the following stories try to imagine how the main character in the story feels about what has happened and how that affects his or her life. Do not worry about attending to all the details of the story, just concentrate on trying to imagine how the main character feels." (adapted from Batson et al., 1997).

Participants pressed a button when they were done reading each story.

Two localizer experiments were conducted in a separate group of participants (see Supplemental Materials for a description of the methods).

2.3. Image acquisition and analysis

Participants were scanned using a Siemens Magnetom Tim Trio 3T System (Siemens Solutions, Erlangen, Germany) in the Athinoula A. Martinos Imaging Center at the McGovern Institute for Brain Research at MIT using 30 4-mm-thick near axial slices with whole brain coverage (TR= 2 s, TE = 30 ms, flip angle = 90). Every experiment used a block design, and was modeled using a boxcar regressor.

MRI data were analyzed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm8/), SnPM5 (http://www2.warwick.ac.uk/fac/sci/statistics/staff/research/nichols/software/snpm/) and custom software. Each participant's data were motion corrected, and then normalized onto a common brain space (Montreal Neurological Institute, EPI Template). Data were smoothed using a Gaussian filter (full width half maximum = 5 mm) and high-pass filtered during analysis.

Functional images were analyzed using both whole brain random effects analyses, and using group-level regions of interest. For whole brain analyses, we first built a modified linear model of the experimental design, and used this model to analyze the BOLD response in each voxel. The model included both covariates of interest (the experimental conditions) and nuisance covariates (run effects, an intercept term, and global signal). We modeled the conditions as a box-car (matching the onset and duration of each block) convolved with a standard hemodynamic response function (HRF). Time-series data were subjected to a high-pass filter (128 Hz). To identify voxels in which effects of condition were reliable across participants, BOLD signal differences between conditions (linear combinations of the beta parameters for condition covariates) were submitted to second level, random-effects analysis. All whole brain analyses were conducted using SnPM and used corrected p thresholds, at $p < 0.05$, based on Monte Carlo simulations of the false positive rate in these data (Nichols & Holmes, 2004).

To define regions of interest, random effects analyses were performed on the localizer experiments, using a threshold of $p < 0.001$ (voxel-wise, uncorrected), and a cluster threshold of $k > 10$ on the data from 12 participants on the Theory of Mind task, and from 13 participants in the Pain task (Supplemental Figs. 1 and 2). For the Theory of Mind task the contrast (Belief > Photo) was used. For the Pain task, most regions were identified using the contrast OtherPain > OtherNoPain. One region was identified using the contrast SelfPain > SelfNoPain. See Supplementary Methods for more details.

Coordinates of the peak voxel in each ROI were identified, and all suprathreshold voxels within a 9 mm radius from the peak voxel defined the region of interest (ROI). The response at each time point for each story condition in the Narrative Study was calculated as the average BOLD response across all voxels in each ROI, across all participants; this response was then converted to percent signal change as follows: PSC = 100 × average_BOLD_response(condition, time)/average_BOLD_response(rest). The BOLD response at rest was calculated as the average response in each ROI during the rest period, excluding the 6 s immediately following a story. For the purposes of statistical analyses, we averaged 12–20 s after story onset. This time accounted for hemodynamic lag and story design: information about the negative or neutral outcome of each story was only available in the second part of each story (where painful and non-painful versions of each story deviated from each other). The data extracted from the ROIs were not filtered, other than averaging. All peak voxels are reported in MNI coordinates.

In order to validate the stimuli, a separate group of participants were asked to rate the amount of physical pain ("How much physical pain is the main character in?") and the amount of emotional suffering ("How much emotional suffering did the main character experience?") in each of the stories on a scale from (1) none at all to (9) extreme. Stories were rated on Amazon Mechanical Turk. Each story was rated on each dimension by 60 participants. If participant responses were unreasonably fast (representing a reading time of >10 words per second), were >3 standard deviations from the mean, or if they did not answer a 'check' question ("I have read the story completely and answered all questions honestly") with anything other than "(9) completely agree", their responses were eliminated. This resulted in the exclusion of ~15% of the responses.

Statistical analysis (behavioral and fMRI experiments) utilized post hoc paired-samples t-tests and repeated-measures ANOVAs, both conducted with an alpha level of 0.05. When the significance level of the Mauchly's test was $p < 0.05$, we corrected for sphericity using the Greenhouse–Geisser correction, and we report corrected degrees of freedom.

3. Results

3.1. Behavioral results

Emotional Pain and False Belief Pain stories were defined in the current study as scenarios that involved others experiencing emotional suffering that did not have a physical cause. Physical Pain stories were defined as others experiencing physical pain that did not have an emotional cause. Although physical pain and emotional suffering are often confounded in real-life situations, in the current stimuli the PP scenarios described more physical pain than

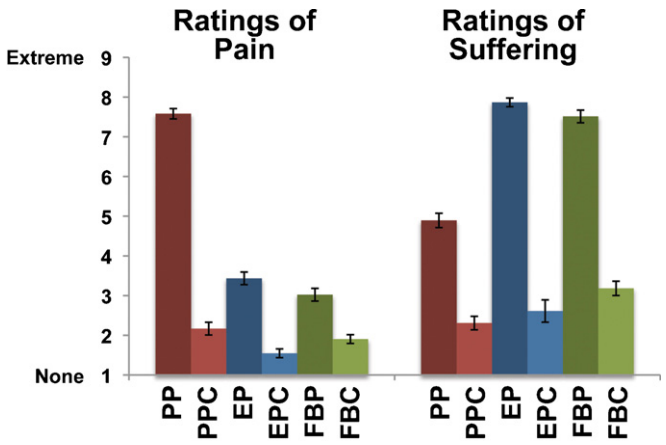

Fig. 1. Average ratings of pain and suffering for stories in each of the conditions. Stories involved physical pain (PP), physical sensations without pain (PPC), emotional pain (EP), emotional states without pain (EPC), false beliefs resulting in emotional pain (FBP), and false beliefs resulting in no pain (FBC). Each story was rated by a group of participants not involved in the fMRI study across two dimensions: "How much physical pain is the main character in?" and "How much emotional suffering did the main character experience?" on a scale from (1) none at all to (9) extreme. Ratings were then averaged across all of the stories within each condition. Bars represent average ratings for all stories within each condition (±s.e.m.).

emotional suffering, and the EP and FBP scenarios described more emotional suffering than physical pain. To confirm this, an independent group of participants ($n = 40$ per story) rated the "amount of physical pain" and "amount of emotional suffering" experienced by the main character in each of the stories on a scale of 1 (none at all) to 9 (extreme). PP scenarios were rated to involve more physical pain (mean = 7.7 ± 0.6 s.d.) than emotional suffering (mean = 5.1 ± 0.8; paired samples *t*-test, $t(23) = 20.6$, $p < 0.001$), and EP and FBP scenarios to involve more emotional suffering (EP: mean = 8.0 ± 0.6; FBP: mean = 7.6 ± 0.7) than physical pain (EP: mean = 3.6 ± 0.6; FBP: mean = 3.3 ± 0.7; both $t(23)$s > 35.0, both ps < 0.001). Relative to the EP and FBP scenarios, the PP scenarios were rated to involve significantly more physical pain (independent samples *t*-tests, both $t(46)$s > 23.0, both ps < 0.001) and significantly less emotional suffering (both $t(46)$s > 10.0, both ps < 0.001). Overall, there was a significant interaction between the condition and the rating, such that PP stories were rated to involve more "physical pain" than EP and FBP stories (ANOVA, $F(1,2) = 207.6$, $p < 0.001$), and PP stories were rated to involve less "emotional suffering" than the EP and FBP stories ($F(1,2) = 30.2$, $p < 0.001$) (Fig. 1).

In the Narrative Experiment, participants' judgments of the characters' "pain or suffering" from Task 1 (in the scanner) were analyzed using a 2 × 3 within-subjects ANOVA of Pain (pain versus no-pain control) by Mental State Condition (physical states, emotions, false beliefs). Over all, participants judged that the character experienced more pain/suffering in the Pain stories (main effect of Pain, $F(1,18) = 627.0$; $p < 0.001$; $\text{eta}^2 = 0.97$). There was also an interaction of Pain and Condition ($F(2,36) = 18.6$, $p < 0.001$, $\text{eta}^2 = 0.51$), because participants judged the Emotional Pain stories to involve more pain/suffering than either the Physical Pain (paired-samples *t*-test, $t(18) = 3.1$, $p < 0.01$) or False Belief Pain ($t(18) = 3.6$, $p < 0.01$) stories. There was no main effect of Condition on pain judgements ($F(2,36) = 2.0$, $\text{eta}^2 = 0.10$) (Table 2).

Reaction time data were analyzed in the same way as the pain judgments (Table 2). The analysis revealed a significant main effect of Condition ($F(1.41,25.3) = 14.6$; $p < 0.001$, $\text{eta}^2 = 0.45$). Participants were slower when judging stories involving false beliefs than physical states (paired-samples *t*-test, $t(18) = 3.8$, $p = 0.001$) or emotional states ($t(18) = 4.7$, $p < 0.001$) (averaged by participant across painful and non-painful stories within each condition). Participants were also slower judging the subset of False Belief stories involving pain compared to the stories involving Physical Pain ($t(18) = 3.4$, $p = 0.003$) or Emotional Pain ($t(18) = 3.4$, $p = 0.003$). There were no other main effects or interactions.

3.2. Neuroimaging results

3.2.1. Narrative Experiment: whole brain analysis

An initial whole brain analysis identified brain regions that responded to painful stories versus non-painful control stories, regardless of condition, across both tasks. The contrast for the main effect of Pain revealed activity in regions of the Shared Pain network: the left insula, the cingulate cortex (posterior, middle and anterior), left secondary sensory cortex, and bilateral thalamus, as well as brain regions associated with Theory of Mind: precuneus, and medial and dorsomedial prefrontal cortex (Fig. 2). We next separately examined the brain response to the subset of stories involving physical pain (versus physical pain control stories), and the brain responses to stories involving emotional pain (versus emotional pain control stories). Relative to control stories, physical pain stories resulted in activity in bilateral insula cortex and middle and posterior cingulate cortex (Fig. 3). These brain regions are consistent with Shared Pain network brain regions found previously in studies involving witnessing others in physical pain (Botvinick et al., 2005; Lamm, Decety, & Singer, 2010; Singer & Frith, 2005). Emotional pain stories, on the other hand, resulted in activity in regions in the medial and dorsomedial prefrontal cortex, and a region of the posterior cingulate (largely distinct from the region reported for physical pain) (Fig. 4). These regions are often associated with Theory of Mind (Gallagher & Frith, 2003; Saxe & Kanwisher, 2003). Conjunction analysis revealed two regions in the cingulate, one anterior and one posterior to the aMCC, that were super-threshold for both physical pain and emotional pain (over their respective control conditions) (Fig. 5). These results suggest that representations of others' physical pain and others' emotional pain are largely distinct, but share activity in small regions within the cingulate cortex. For peak coordinates for all contrasts, see Table 3.

To find regions that respond specifically to Emotional Pain, we also examined the contrast (EP-EPC) – (PP-PPC). This contrast revealed activity in dmPFC, along with regions along the middle temporal gyrus, when using a voxel-wise threshold of $p < 0.001$, uncorrected; however this result did not survive the conservative correction for multiple comparisons used in our whole brain analyses. Relatedly, the contrast (PP-PPC) – (EP-EPC) did not reveal any voxels in the whole brain analysis.

We then turned to regions of interest (ROI) analysis. Statistical tests in ROI analyses are more sensitive (because there are fewer ROIs than voxels in the whole brain, reducing the multiple comparisons problem), and also allowed us specifically to test how these results are related to prior studies in the literature.

Table 2
Average pain/suffering ratings (standard deviation) and reaction time means (standard deviation) for each of the four experimental conditions. Pain was rated in the scanner by subjects engaged in Task 1 on a four-point scale from (1) no pain to (4) a lot of pain. Reaction time was measured in seconds.

	Physical pain	Physical no pain	Emotional pain	Emotional no pain	False belief pain	False belief no pain
Pain/suffering (mean, s.d.)	3.26 (0.45)	1.26 (0.25)	3.53 (0.34)	1.2 (0.22)	3.28 (0.46)	1.47 (0.37)
Reaction time (mean, s.d.)	1.52 (0.83)	1.61 (0.9)	1.56 (0.87)	1.57 (0.95)	1.96 (1.1)	1.98 (1.06)

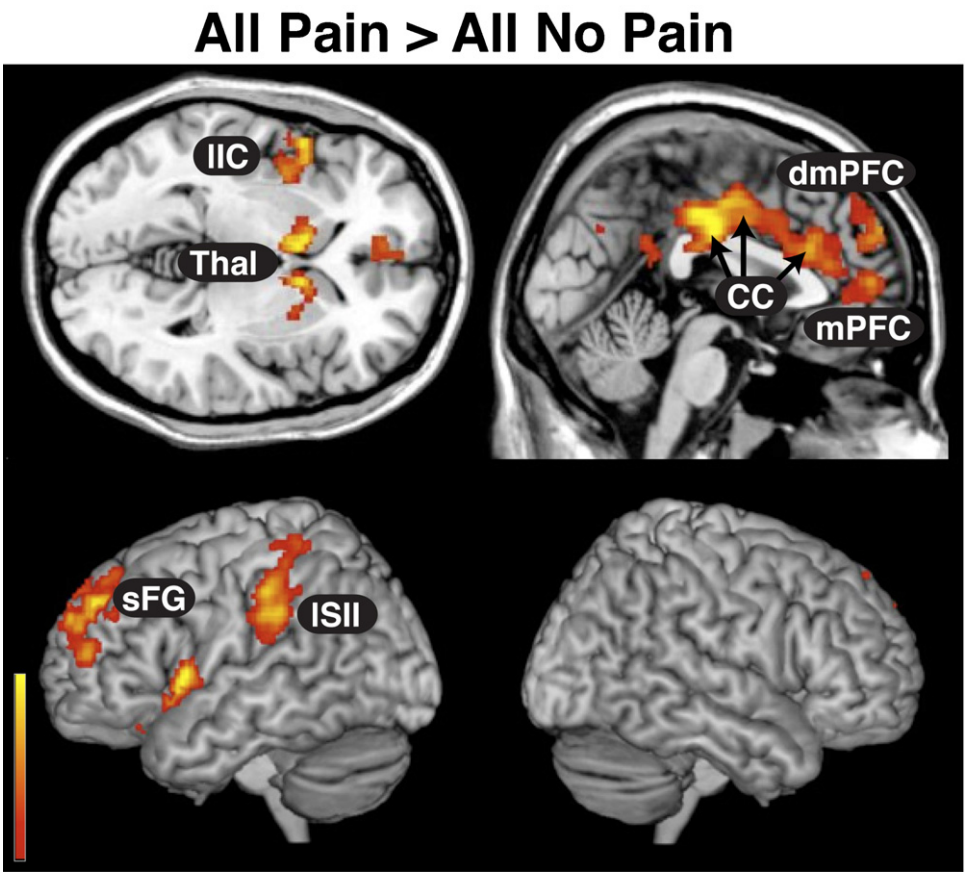

Fig. 2. Brain regions responding to stories involving Pain (PP, EP, FBP) versus matched control stories involving No Pain (PPC, EPC, FBC). This contrast revealed activation in regions of the "Shared Pain network": left insula cortex (IC), posterior, middle and anterior regions of the cingulate cortex (CC), and left secondary sensory regions (lSII), as well as left superior frontal gyrus (sFG), and regions of the medial prefrontal cortex (mPFC). Random effects analysis performed at $p < 0.05$ (corrected) and $k > 10$. Color scale indicates t-values from 3 (red) to 6 (yellow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Table 3
Coordinates of peak brain activity for each of the contrasts. MNI coordinates and the t-value of the peak voxel in each region are listed for each of the contrasts used in the study. All analyses performed using statistical non-parametric mapping (SnPM), and performed at $p < 0.05$ (corrected).

Contrast	Cluster		Cluster-voxel combo				Voxel-level peak t	Brain area
	k	w	P_{combo}	x	y	z		
AllPain > AllNoPain	3508	9.52	0.0002	−4	−24	42	6.72	Posterior cingulate cortex
	522	6.18	0.0084	−56	10	2	6.17	Left frontal operculum
				−38	2	4	4.96	Left insula cortex
	784	6.38	0.007	−8	10	0	6.07	Left anterior thalamus
				−20	−2	−20	5.11	Left amygdala
	221	5.14	0.0236	10	8	2	5.77	Right anterior thalamus
	492	4.84	0.0302	−4	−48	28	5.32	Dorsomedial prefrontal cortex
	649	5.33	0.02	−60	−32	32	5.32	Motor cortex
PP > PPC	1585	8.42	0.0012	2	−18	32	6.28	Posterior/mid cingulate cortex
				2	16	28	5.55	Anterior middle cingulate cortex
				−4	12	40	5.17	Dorsal cingulate cortex
	446	5.53	0.0158	46	6	−2	5.84	Right insula cortex
	627	6.12	0.0088	−56	8	6	5.63	Left frontal operculum
				−48	0	−2	5.26	Left insula cortex
EP > EPC	366	6.88	0.0040	−2	−26	42	6.46	Posterior cingulate cortex
	1923	7.57	0.0024	−6	50	20	6.46	Medial prefrontal cortex
				0	54	36	5.35	Dorsomedial prefrontal cortex
				−6	40	24	5.28	Anterior cingulate cortex
Task 2 – Task 1	205	5.15	0.0094	42	−80	12	5.87	Right occipital cortex
(AllPain > AllNoPain)	296	4.55	0.03	36	2	−14	5.39	Right insula cortex
Task 2 – Task 1	50	4.51	0.0430	52	−12	−8	5.68	Right occipital cortex
(PP > PPC)	386	5.04	0.0260	32	−42	−18	5.65	Right inferior temporal cortex
	475	4.50	0.0430	36	6	−2	4.75	Right insula cortex
Task 2 – Task 1 (EP > EPC)	No superthreshold voxels at $p < 0.05$, corrected							

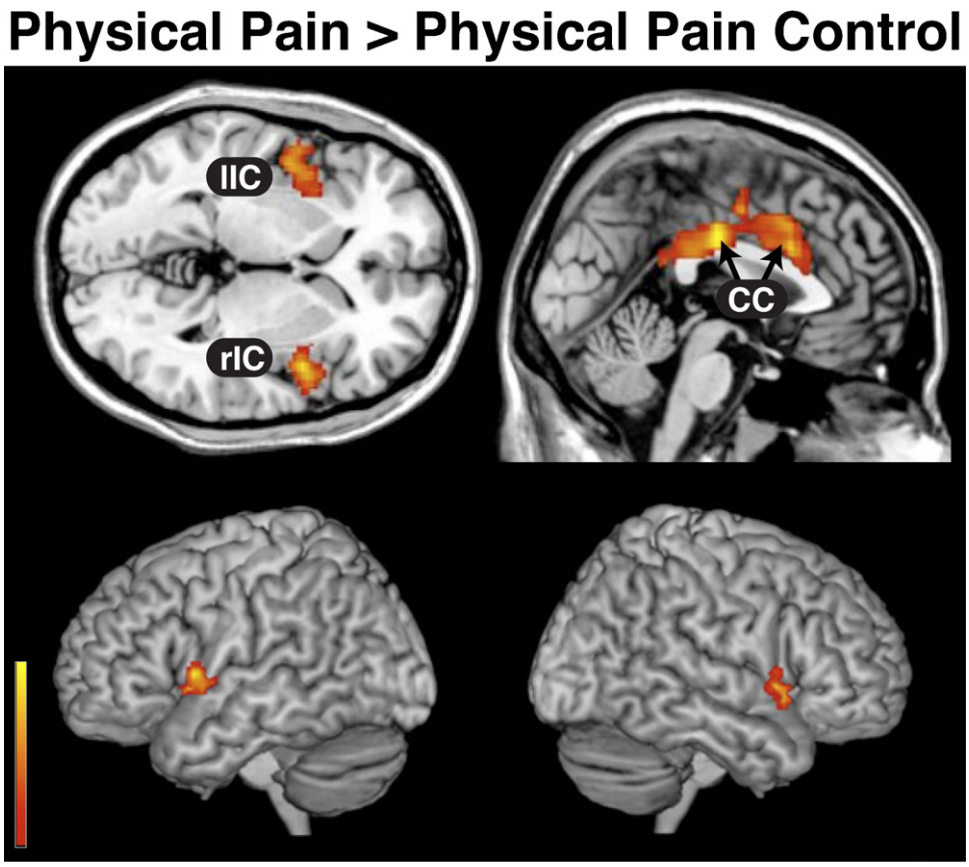

Fig. 3. Brain regions responding to stories involving physical pain (PP) versus matched control stories involving physical sensations that were non-painful (PPC). Stories involving PP activated regions previously shown to be active during observing others in physical pain ('Shared Pain network' regions): bilateral insula cortex (IC), and regions in the cingulate cortex (CC), including anterior middle and posterior regions. Random effects analysis performed at $p < 0.05$ (corrected) and $k > 10$. Color scale indicates t-values from 3 (red) to 6 (yellow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

3.2.2. Regions of interest analyses

We identified unbiased regions of interest in a separate group of participants using two tasks. Using a standard localizer for Theory of Mind brain regions (reading stories about Beliefs > Photographs) we identified the components of the "Theory of Mind network": the bilateral TPJ, PC, dmPFC and vmPFC (Fig. S2). We used a version of a standard task (directly observing someone else receive Painful or Non-Painful electrical stimulation) to identify regions in the pain network – bilateral secondary sensory areas (SII), bilateral insula, bilateral anterior thalamus – as well as the dmPFC (Fig. S3A). One other brain region commonly identified as part of the Shared Pain network, the aMCC, was not significantly recruited by the pain observation task, but did show significant activity when participants themselves experienced a Painful (versus Non-Painful) electric shock. This region was also included in the ROI analyses (Fig. S3B).

We analyzed the data in each ROI using a $2 \times 3 \times 2$ mixed ANOVA, including within-subjects factors of Pain (Pain, No Pain) and Mental State Condition (Physical States, Emotions, False Beliefs), and the between-subject factor of Task (explicitly rating, actively empathizing).

The brain regions identified in the Theory of Mind Localizer are hypothesized to play a role in mental state attributions. Consistent with that hypothesis, all of these regions showed a significant main effect of Condition: in the Narrative Experiment, False Belief (FBP and FBC) and Emotional (EP and EPC) stories elicited a significantly higher response than Physical stories (PP and PPC) across all ROIs (F-statistic for mixed model ANOVAs in each brain region > 27.0, all p-values < 0.001) (Fig. 6A) (see Fig. 7A for sample timecourse). Most of these regions did not respond more to stories involving Pain over stories involving No Pain. Indeed, pairwise t-tests within each condition revealed that rTPJ and lTPJ responded more to *non*-painful compared to painful physical experiences (rTPJ: $t(40) = 2.8$, $p = 0.008$; lTPJ: $t(40) = 3.9$, $p < 0.001$). Of all the Theory of Mind brain regions, only the dmPFC showed a main effect of Pain. In pairwise comparisons, the dMPFC discriminated between False Belief stories involving Pain or No Pain (FBP > FBC: $t(40) = 3.2$, $p = 0.003$), while not discriminating between EP and EPC stories ($t(40) = 1.4$, $p = 0.16$), or painful and non-painful Physical stories (PP versus PPC, $t(40) = 0.7$, $p = 0.50$). The interaction between Pain and Condition in the dmPFC did not reach significance ($F(2,78) = 2.0$, $p = 0.14$).

The pattern of activity in these brain regions was remarkably similar across the two Tasks (see Fig. S4): there were no main effects of Task, or any interaction involving Task, in any of the Theory of Mind ROIs (mixed model ANOVAs; all p-values > 0.05).

In general, brain regions identified in the Pain Localizer experiment were hypothesized to be involved in responding to another's physical pain. The Pain Localizer experiment identified a region of interest very near, and partially overlapping, the dmPFC region identified by the ToM Experiment. Interestingly, this region responded selectively to stores about emotional pain (for timecourse see Fig. 7B): main effects of Condition ($F(1.7,65) = 47.8$, $p < 0.001$) and Pain ($F(1,39) = 19.3$, $p < 0.001$) were modulated by an interaction, such that Emotional but not Physical Pain led to an enhanced response ($F(1.7,67.8) = 5.4$, $p = 0.009$). Within-condition pairwise comparisons further showed a stronger response to EP > EPC ($t(40) = 4.3$, $p < 0.001$) and FBP > FBC ($t(40) = 4.5$, $p < 0.001$), but not for PP > PPC ($t(40) = 1.3$, $p = 0.19$) (Fig. 6B).

Otherwise, the patterns of activity in the regions in the Shared Pain network were consistently different from those of the

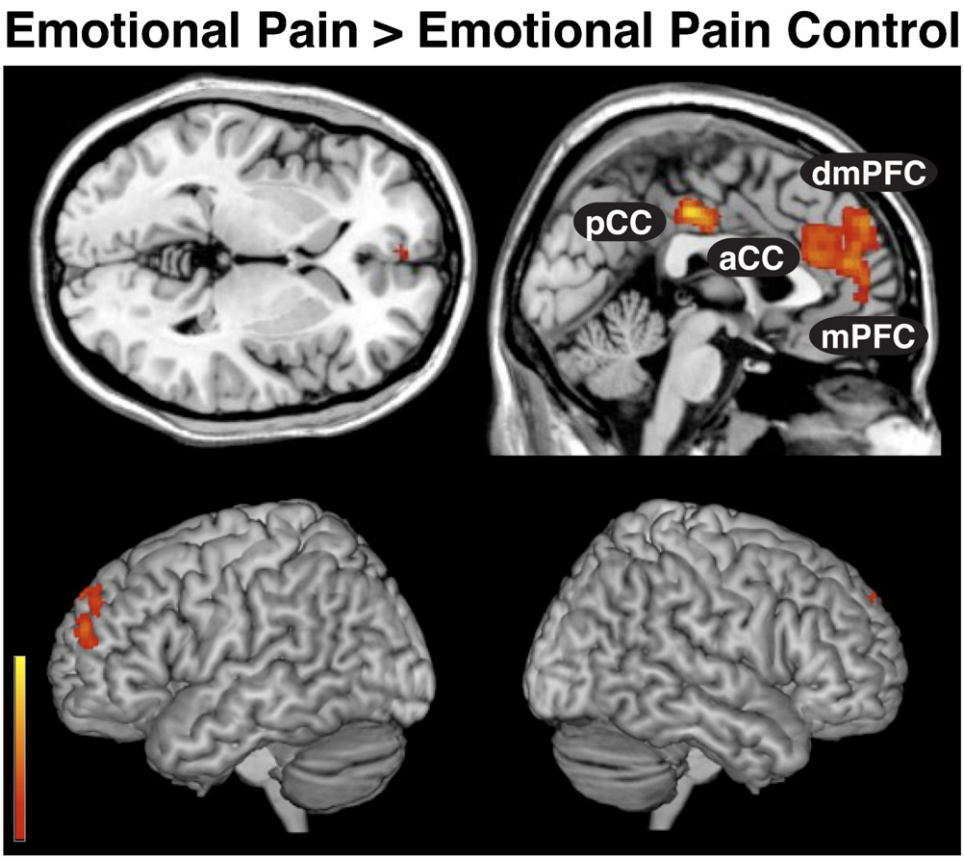

Fig. 4. Brain regions responding to stories involving emotional pain (EP) versus matched control stories involving emotional states without pain (EPC). This contrast revealed activation in medial frontal regions: dorsomedial prefrontal cortex (dmPFC) and medial prefrontal cortex (mPFC) extending into the anterior cingulate cortex, as well as a region in the posterior cingulate cortex (pCC). Random effects analysis performed at $p < 0.05$ (corrected) and $k > 10$. Color scale indicates t-values from 3 (red) to 6 (yellow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Theory of Mind regions. The insula, for example, showed a preference for stories describing physical experiences, especially painful ones (for timecourse see Fig. 7C). In the Left Insula, main effects of Condition (physical > emotion and false belief, $F(1.7,64.7) = 58.6$, $p < 0.001$) and Pain (pain > control, $F(1,39) = 14.2$, $p = 0.001$) were mediated by a Pain × Condition interaction ($F(2,78) = 4.6$, $p = 0.013$). Physical pain stories elicited higher responses than non-painful physical control stories ($t(40) = 5.7$, $p < 0.001$), whereas pain did not affect the response to stories about emotions or false beliefs (both $ps > 0.20$). The left insula also showed a main effect of Task, showing higher activation across all conditions when participants were instructed to actively empathize ($F(1,39) = 4.4$, $p = 0.043$).

Right insula showed a similar pattern: a significant main effect for Condition (physical > emotion and false beliefs, $F(1.5,59.4) = 10.3$, $p = 0.001$) and a Pain × Condition interaction ($F(2,78) = 4.9$, $p = 0.010$). Physical pain stories elicited the highest response of any condition, especially when participants were instructed to actively empathize (Pain × Mental State × Task interaction, $F(2,78) = 3.4$, $p = 0.038$). For data separated by task, see Fig. S5.

The right and left Thalamus showed a robust main effect of Pain > No Pain, across all conditions (lThal: $F(1,39) = 30.5$, $p < 0.001$; rThal: $F(1,39) = 22.6$, $p < 0.001$); all pairwise comparisons were significant for painful over non-painful versions within each condition (all p-values < 0.01). The Thalamus also showed a trend towards a main effect of Mental State Condition, with higher responses to Emotions and False Beliefs than Physical experiences: lThal: $F(1.7,65.6) = 3.2$, $p = 0.055$; rThal: $F(1.6,62.7) = 4.0$, $p = 0.031$.

The anterior middle cingulate cortex similarly showed a robust main effect of Pain > No Pain across all Conditions ($F(1,39) = 36.1$, $p < 0.001$), and all pairwise comparisons were significant for painful over non-painful versions within each condition (all $ts > 3.9$, all $ps < 0.001$). Interestingly, the aMCC was also sensitive to condition, but in the opposite direction from the thalamus: the aMCC showed a stronger response to stories involving Physical Sensations than Emotions or False Beliefs ($F(2,78) = 41.7$, $p < 0.001$) (for timecourse see Fig. 7D).

Finally, right and left SII both showed higher responses for stories involving Physical sensations than for stories involving Emotions or False Beliefs, independent of Pain (main effect of Condition: lSII $F(2,78) = 35.9$, $p < 0.001$; rSII $F(2,78) = 20.8$, $p < 0.001$) (for timecourse see Fig. 7E). The rSII also showed a higher response overall when participants were instructed to actively empathize (main effect of Task, $F(1,39) = 5.4$, $p = 0.025$), especially for physically and emotionally painful stimuli (Task by Condition by Pain interaction, $F(2,78) = 4.0$, $p = 0.023$).

A number of the brain regions identified in the SelfPain–SelfNoPain contrast overlapped with similar regions in the OtherPain–OtherNoPain contrast: bilateral SII, bilateral insula (slightly more anterior in SelfPain than OtherPain), right thalamus (slightly posterior in SelfPain than OtherPain). When these regions from the SelfPain contrast were used as ROIs to examine the narratives, they produced similar results as the ROIs generated from the OtherPain ROIs (see Supplemental Results).

As a control, we also examined brain activity for the 6 narrative conditions in an ROI identified in the OtherPain > OtherNoPain contrast that was thought to be unrelated to representations of pain. Activity in the right primary motor cortex (MI) was thought to be related to movement of the left hand observed in the Pain condition (involuntary twitching in response to electrical shock) that did

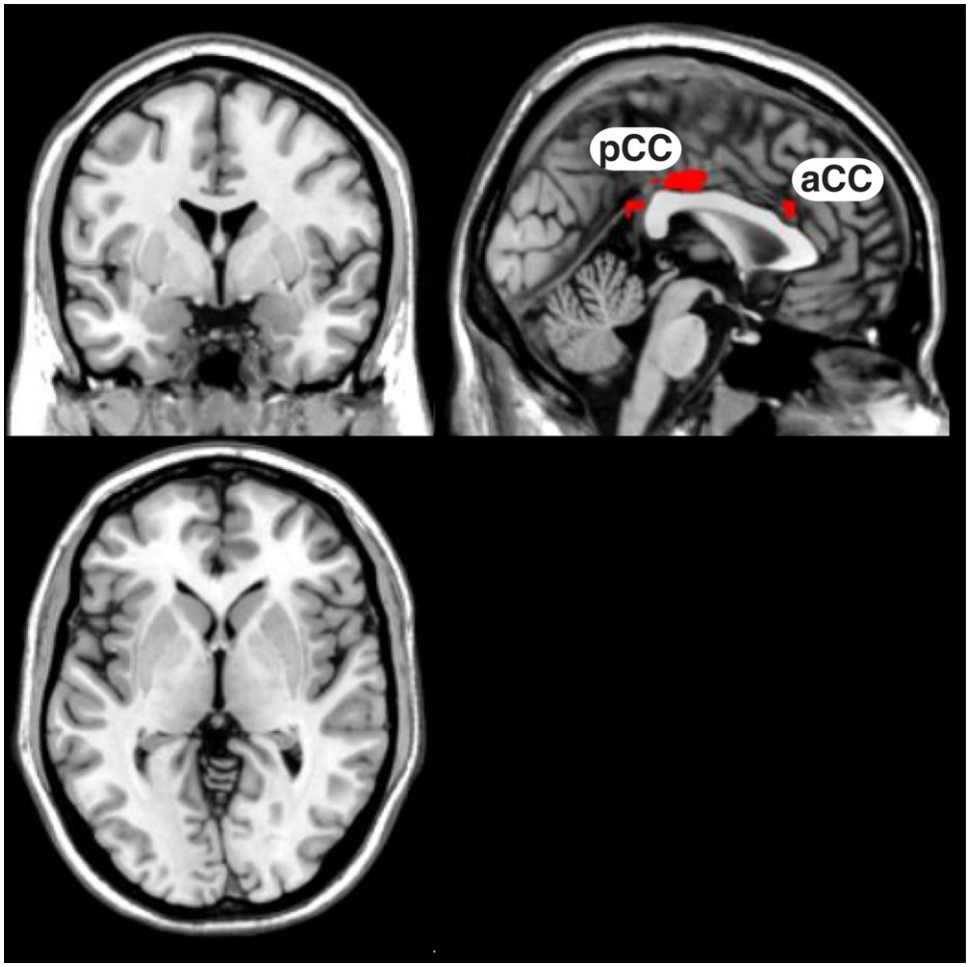

Fig. 5. Conjunction analysis of PP-PPC and EP-EPC. Whole brain analysis shows areas of overlap for the two contrasts, each performed at $p < 0.05$ (corrected) and thresholded at $t > 3.0$. Overlap was localized to a posterior region of the cingulate cortex (pCC) and an anterior region of the cingulate cortex (aCC). No overlap was present in any other brain regions.

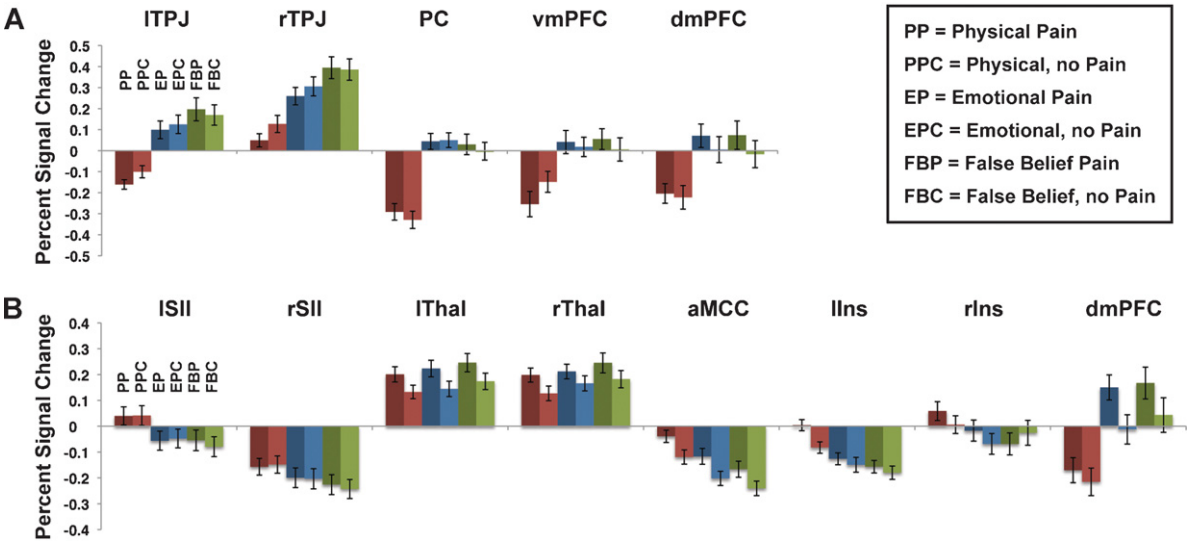

Fig. 6. Region of Interest (ROI) analysis. (A) Theory of Mind regions of interest were identified in a separate group of participants who read stories that involved making mental state attributions of others. Regions of interest were localized in the right temporoparietal junction (rTPJ), left temporoparietal junction (lTPJ), precuneus (PC), ventromedial prefrontal cortex (vmPFC) and dorsomedial prefrontal cortex (dmPFC). (B) Shared Pain network regions of interest were identified in a separate group of participants who experienced and watched someone else receive a painful electric shock. Regions were defined in the following regions: left secondary sensory (lSII), right secondary sensory (rSII), left thalamus (lThal), right thalamus (rThal), anterior middle cingulate cortex (aMCC), left insula (lInsula), right insula (rInsula) and dorsomedial prefrontal cortex (dmPFC). Bars represent average percent signal change by brain region for stories involving each of the 6 conditions: physical pain (PP), physical pain control (PPC), emotional pain (EP), emotional pain control (EPC), false belief pain (FBP) and false belief control (FBC). Bars represent percent signal change in each condition relative to rest ± s.e.m.

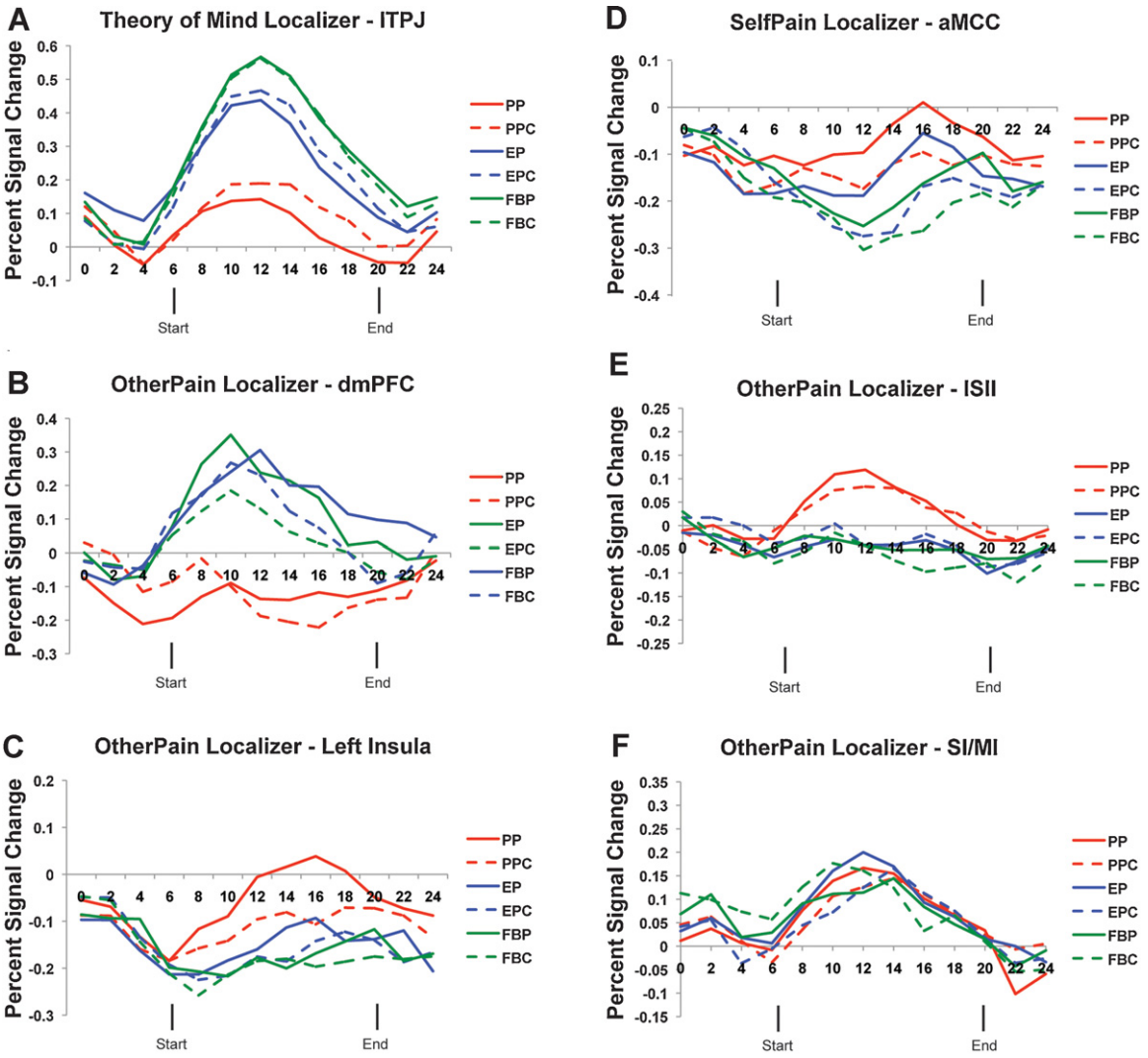

Fig. 7. Time-courses for sample brain regions of interest (ROI). In each ROI, percent signal change is shown for each story type. Labeled are the times of story onset (start) and end of story presentation (end), accounting for hemodynamic lag. Data are averaged across all participants at each time point. These time courses sometimes appear to start above or below zero, because the average hemodynamic response to the previous stimulus did not return completely to baseline before the story onset (since stories were presented with an ISI of 2 s). However, the *y*-axis correctly reflects percent signal change from the true baseline – i.e. response during rest periods – in each region.

not occur in the Other No Pain condition. This ROI showed positive activity for each of the narratives, but there were no significant effects of Pain, Condition or Task, or any interaction between them (for all mixed-model ANOVAS, F-statistics < 2.7, p-values > 0.05) (for timecourse see Fig. 7F).

4. Discussion

We find that activity in both the 'Shared Pain' and 'ToM' brain regions is modulated by the content of short verbal narratives. Overall, brain regions implicated in ToM responded more to stories about individuals' mental and emotional, versus physical, experiences, and brain regions previously implicated in observing others in pain responded more to stories about physical than emotional experiences. A subset of these regions also showed a specific response to painful, versus non-painful, experiences. Descriptions of physically painful events led to a specifically higher response in the left insula, and descriptions of emotional painful events led to a specifically higher response in the dorsal medial prefrontal cortex (dmPFC). A few regions, including the thalamus bilaterally and a region of middle cingulate cortex, showed a higher response to both kinds of pain. Finally, whereas the pattern in most of these brain regions was strikingly similar across two groups of participants and two task contexts, instructions to focus on feeling for the character led to stronger responses across all conditions in the left insula, and stronger responses specifically to painful experiences in the right insula and right secondary sensory region. These results provide a novel, detailed picture of the neural response to complex verbal descriptions of people in pain and suffering.

4.1. Responding to others' physical pain

This study is one of the first to investigate neural responses to verbal descriptions of physically painful events. Previous neuroimaging studies of empathy have typically used photographs of faces in pain, body parts suffering injuries, or live people receiving actual painful stimulation (Botvinick et al., 2005; Budell, Jackson, & Rainville, 2010; Decety, Yang, & Cheng, 2010; Lamm, Meltzoff, & Decety, 2010; Morrison, Lloyd, Di Pellegrino, & Roberts, 2004; Saarela et al., 2007; Singer et al., 2004, 2006).

Understanding empathic responses elicited by verbal scenarios is valuable for a number of reasons. First, the response to verbal scenarios may reveal the function performed by each region of the canonical 'Shared Pain network'. Some regions in this network may

respond only to stimuli that are associated with actual threat to the participant, and not to abstract conceptual representations of that threat. Second, many kinds of painful experience (especially emotionally painful experiences) are much easier to describe and transmit through language, than through nonverbal stimuli alone. For example, it is hard to convey in a photograph meanings like "the wood carving he broke was given to him by his mother just before she died," or "his step-daughter just told him that she hates him" (cf. Rameson et al., 2011). Third, in contemporary culture, people often need to make decisions based on empathic responses to individuals who are far away: for example, people must decide whether and how to help victims of cultural conflicts and natural disasters on the other side of the world. Verbal narratives (e.g. in books, magazines, newspapers and blogs) are one of the dominant modalities through which we are asked to exercise our empathy for others.

In the present study, we first asked whether verbal descriptions of physically painful experiences elicit activity in the same brain regions as directly witnessing another person in physical pain (cf. Jabbi et al., 2008). Key brain regions in the 'Shared Pain network', including bilateral anterior insula, the middle cingulate cortex, bilateral secondary sensory regions and the anterior thalamus all showed higher responses to descriptions of physical pain than descriptions of non-painful physical events. The correspondence between these regions, and the previously identified Shared Pain regions, was corroborated by functional region of interest analyses.

For the most part, our results show striking convergence with the only previous study to compare neural responses to verbal descriptions of physically painful and non-painful events (Gu & Han, 2007b). In that study, participants read one- or two-character long descriptions of events (in Chinese), and evaluated how painful the event would be. Compared to neutral events, descriptions of painful events elicited activity in insula, bilateral SII, and a left lateral occipital region, exactly as in the current study. Activity in the secondary sensory regions is especially interesting, since the response of SII was previously hypothesized to be restricted to the sensory-discriminative component of a pain response, and not recruited by observation of pain (Singer et al., 2004). Of interest, we found that both painful and non-painful physical experiences elicited SII activity, compared to stories about emotions. The response in SII may reflect imagery of the sensory experiences described in the stories (cf. Keysers et al., 2004).

Our study found one significant difference from the prior (Gu & Han, 2007b) study of pain words: the cingulate cortex did not significantly distinguish between painful and non-painful events in Gu and Han (2007b), but did in the current results. Based on the absence of cingulate activity, Gu and Han (2007b) concluded that "the processing of pain induced by rating pain intensity of actions depicted in words is essentially different from the processing of pain induced by noxious stimuli and the processing of imagined pain." By contrast, the current results show that the cingulate cortex is also modulated by verbal descriptions of pain. The verbal narratives presented here may have been more vivid than the one- and two-word phrases in the prior study.

The present study lends support for the idea that the role of the Shared Pain network, particularly the insula and middle cingulate, in processing painful experiences is very general (cf. Fan, Duncan, de Greck, & Northoff, 2010), not tied to any specific stimulus (e.g. Lamm, Decety, et al., 2010; Lamm, Meltzoff, et al., 2010), and is instead influenced by participants' task and construal. Activity in these regions, for first-person painful experiences, is modulated by anticipation and expectations (Atlas et al., 2010; Carlsson et al., 2006; Ploner, Lee, Wiech, Bingel, & Tracey, 2010). Identical physical stimuli result in higher insula activity (and higher pain intensity ratings) if participants believe it is more likely to cause physical injury (Wiech et al., 2010). Similarly, when observing another person in pain, the insula and cingulate responses depend not on the stimulus, but on the observers' construal. Pain experienced by a loved one leads to more activity in insula and cingulate regions (Cheng, Chen, Lin, Chou, & Decety, 2010; Singer et al., 2004), while pain experienced by a disliked individual or group leads to less activity in these regions (Hein, Silani, Preuschoff, Batson, & Singer, 2010; Singer et al., 2006). Participant's construal can even reverse the stimulus-based response. If the observer believes that the person in the photograph experiences penetration by a needle as non-painful, and a light touch by a Q-tip as painful, then the insula and middle cingulate regions show greater activity to the image of the Q-tip than of the needle (Lamm, Meltzoff, et al., 2010). Over all, representing another person's physical pain appears to depend on a highly similar network, whether the pain is depicted visually or verbally, whether anticipated, experienced, observed, or inferred, and whether real or hypothetical.

Nevertheless there was a hint that verbal descriptions elicit less activity overall, in the 'Shared Pain' regions, than direct observations. The cingulate, insula and secondary sensory regions all showed significantly negative BOLD responses, below the resting baseline, for all stories except physical pain, and the response of these regions to verbal stimuli overall was small in magnitude. One consideration may be the use of group functional ROIs. Because inter-subject alignment of anatomical and functional features is imperfect, group ROIs only partially capture each individual's true corresponding regions, leading to underestimates of the magnitude and selectivity of the regions' responses (Saxe, Brett, & Kanwisher, 2006). It is also possible that imagining (or reading about) physical events leads to less robust activation than direct experience. In prior studies, adding cognitive load or other distracting tasks substantially reduced activity in the insula, in response to both words and pictures depicting painful events (Gu & Han, 2007a, 2007b; Kim et al., 2009 but see Gu et al., 2010). On the other hand, at least one prior study has found stronger responses to imagined than actual experiences: the right insula response while vividly imaging a disgusting experience was larger in magnitude than when tasting or smelling a disgusting substance (Jabbi et al., 2008). The magnitude of response to verbal stories may therefore be sensitive to how vividly participants imagine the contents of the stories.

In our experiment, we found relatively small task effects in the response of 'Shared Pain' regions. Instructing participants to "imagine how the character feels" did lead to higher responses in the insula and secondary sensory regions than asking them to rate the pain/suffering experienced. In general, though, the response to verbal stimuli was largely replicable across groups and tasks. However, the current task manipulation was relatively subtle. Both tasks focused attention on the pain and suffering of the protagonist. Tasks that direct participants' attention away from the painful content of the stimuli would likely have larger effects on the neural response (Gu & Han, 2007a; Gu et al., 2010).

4.2. Responding to others' emotional suffering

Verbal descriptions of emotional experiences elicited a large response in brain regions implicated in thinking about others' thoughts, including bilateral temporo-parietal junction, medial precuneus and medial prefrontal cortices. Most of these regions showed equally high responses to stories about emotional suffering and those about non-painful emotional experiences. That is, while these brain regions clearly distinguished between stories describing emotional (mental) versus physical experiences (see also Bedny, Pascual-Leone, & Saxe, 2009; Saxe & Powell, 2006), they mostly did not show higher responses to stories describing painful emotions. These results are consistent with many prior studies showing that these regions of the 'ToM network' are involved in inferences

about a wide range of beliefs, intentions, and emotions (Atique et al., 2010; Hooker et al., 2008, 2010; Schnell et al., 2010).

Since the TPJ and PC regions do not respond more to emotionally painful events than emotional controls, should we conclude that these regions are not involved in representing emotional suffering? We suggest that the ToM brain regions are involved in processing a large range of mental and emotional experiences, but distinctions between specific categories of mental states are not detectable in the average magnitude of response. For example, the magnitude of response in TPJ also does not distinguish between justified and unjustified beliefs, good and bad beliefs, or deductive and inductive inferences about beliefs (Jenkins & Mitchell, 2010; Young, Nichols, & Saxe, 2010). Instead, subtle distinctions between categories of mental experiences – e.g. between positive and negative emotions – may only be distinguished by the pattern of responses across voxels (i.e. neural populations) within these regions (Atique et al., 2010), or by the interaction with other Theory of Mind brain regions.

One brain region, however, did show a selectively larger response to stories about emotional pain: the dmPFC. Prior studies have found dMPFC activation while reading stories, looking at cartoons, and making inferences about characters' emotions (Hooker et al., 2008, 2010) and while watching another person experience social exclusion (in Cyberball, though this contrast also led to recruitment of insula and cingulate regions, which we did not find in the current study, Masten et al., 2010). Other recent studies have identified the dmPFC as a key region mediating empathic *responses* to others' suffering. In two studies, individuals with more activity in dmPFC while observing others' suffering later offer more help to alleviate that suffering. Individuals with more dmPFC response to photographs of Hurricane Katrina victims later donated more money to help those victims (Mathur, Harada, Lipke, & Chiao, 2010); and individuals with more dmPFC response to watching someone be excluded from Cyberball later wrote more pro-social, consoling emails to the victims (Masten et al., 2010; though note that a similar correlation was observed in the right insula). Activity in dmPFC was also related to real-world empathy: individuals who reported more frequently helping friends in their daily lives (in a diary study) also show greater dmPFC response to depictions of emotional suffering (Rameson et al., 2011).

Both current and previous data therefore suggest that the dmPFC plays a particular role in recognizing, representing, and/or responding to others' emotional suffering and negative emotional states. One puzzle for this interpretation, however, arises in our own data. We find that the same region of dmPFC was recruited while observing another person receive a physically painful electric shock (the Other Pain localizer) although *not* while participants experienced the same pain (the Self Pain localizer, and see also Zaki, Ochsner, Hanelin, Wager, & Mackey, 2007). Similarly, in the previous literature on empathy for pain, some studies do report dmPFC activation, while others do not. dmPFC activity is typically not observed when participants look at photographs and videos of human body parts being exposed to noxious stimuli (e.g. needles or knives, Benuzzi, Lui, Duzzi, Nichelli, & Porro, 2008; Gu & Han, 2007a; Han et al., 2009; Jackson et al., 2005; Morrison & Downing, 2007; Morrison et al., 2004). By contrast, dmPFC activity is observed when participants view complex images of people in the midst of personal tragedy (e.g. surrounded by post-hurricane devastation, Mathur et al., 2010), or watch the facial expressions of people experiencing painful events (Botvinick et al., 2005; Decety et al., 2010; Lamm et al., 2007). A recent meta-analysis of these studies found that witnessing another's pain in photographs of injuries and in live painful events (like our Pain Localizer) both elicit common activity in insula and middle cingulate; however, only the live events, when witnessing someone else actually receiving a painful stimulus, elicit activity in the dmPFC and other ToM brain regions.

Thus, overall, the dmPFC appears to be recruited while witnessing another person's physical pain in live events, but not in photographs (Lamm, Decety, et al., 2010) and not in verbal descriptions (current data); on the other hand, the dmPFC is recruited when considering another's negative emotional experiences, both in live events (Cyberball, Masten et al., 2010) *and* in verbal narratives (current data). How should these results be integrated? One possibility is that both patterns reflect a common role of the dmPFC in responding to negative emotional states. It is possible that when witnessing live painful events, participants spontaneously attribute more negative emotional experience to the person being shocked – possibly including fear, anxiety and/or sadness. Directly witnessing a live person actually being harmed may encourage participants to infer rich emotional and affective experiences. Similarly, images of faces or entire tragic scenes may evoke more spontaneous consideration of others' mental/emotional states than photographs of injured body parts.

An alternative possibility is that responses to physical pain (in live events) and emotional pain (in verbal narratives) reflect distinct subregions within the mPFC, with different functional roles, or different aspects of a more general response to socially salient stimuli. In other studies the dmPFC has been implicated in a wide range of social cognitive processes, not specifically linked to empathy (Amodio & Frith, 2006), including making judgments about personality traits and preferences of the self, and salient others (Krienen, Tu, & Buckner, 2010; Macrae, Moran, Heatherton, Banfield, & Kelley, 2004; Mitchell, Macrae, & Banaji, 2006), regulating emotional behavior (Ochsner et al., 2004), and engaging in joint attention (Redcay et al., 2010; Schilbach et al., 2010). Thus future research will be necessary to test whether activity in the dmPFC during live observation of physical pain reflects spontaneous attribution of negative emotional states to the target.

4.3. The link between emotional suffering and physical pain

Reading stories about physical pain and emotional suffering lead to both common and distinct patterns of brain activity.

Both stories about physical pain (compared to physical control) and about emotional pain (compared to emotional control) led to activity in regions of posterior cingulate cortex (in the whole brain conjunction analysis) and in thalamus and middle cingulate (in regions of interest analysis). These results, especially in the middle cingulate, are consistent with the hypothesis that understanding others' physical pain and emotional suffering depends on a common neural representation, as do first-person experiences of physical pain and social rejection (Eisenberger et al., 2003). An interesting alternative possibility is that activity during all painful stories may reflect the observer's own personal distress, caused by reading about pain and suffering (Batson, 2009; Lawrence et al., 2006), especially since activity in these regions is not associated with helping the victim (e.g. Masten et al., 2010).

In addition to the overlapping responses, many brain regions distinguished between stories describing emotional and physical experiences. Most brain regions we tested showed some preference for either physical or emotional events: in general, brain regions in the Shared Pain network showed higher responses to stories about physical experiences, and regions in the Theory of Mind network showed higher responses to stories about emotional experiences. In addition, the dmPFC and left insula both showed significant interactions between pain and emotional versus physical experiences: the dmPFC response was highest to stories describing emotional pain, and the left insula response was highest to stories describing physical pain. A plausible interpretation of these results is that representations of others' physically and emotionally painful experiences depend on at least partially distinct neural mechanisms.

One puzzle is that these results appear to conflict with the only previous study that directly compared responses to others' physically versus emotionally painful experiences/events (Immordino-Yang et al., 2009). Participants in that study first watched detailed documentary-style videos, each narrating an individuals' (i) physically painful experience, (ii) emotionally painful experience, (iii) physical accomplishment or skill, (iv) prosocial (altruistic) accomplishment, or (v) a neutral event. Later, in the scanner, participants were briefly reminded of the whole narrative; neural activity was measured in response to the reminders. Compared to neutral events, all four conditions elicited activity in a substantially overlapping group of brain regions, including middle cingulate and bilateral insula. Contrary to much of the previous literature, Immordino-Yang et al. (2009) did not report any regions of greater activity for descriptions of negative/painful events, compared to positive events; contrary to the current results, Immordino-Yang et al. (2009) did not report significant differences between emotionally and physically painful events in the dmPFC and left insula (or indeed, anywhere).

There are a number of possible explanations of these discrepancies. First, the patterns of activation reported here may apply only to verbal stimuli. Neural responses to physical pain, versus social rejection, may be more similar when elicited by live events (Masten et al., 2010) or 5-min-long documentaries (Immordino-Yang et al., 2009); perhaps live and highly detailed stimuli elicit stronger emotional reactions than our short narratives, revealing subtle patterns of shared activation that we could not detect. For example, in a recent meta-analysis, Fan et al. (2010) found that direct observation of facial expressions of a range of (basic) negative emotions in photographs and videos evokes activity in the insula, whereas in our Narrative Experiment, the insula response was limited to stories describing physically painful events. Future research should test whether these patterns of neural responses to other people's negative emotions is predicted by the modality of the stimuli (e.g. live people and photographs versus verbal narratives) or the content (e.g. primary emotions including pain, fear and disgust versus secondary or complex emotions, including loss, shame and regret). Second, Immordino-Yang et al. (2009)'s method – in which participants see all of the documentaries, and are then cued to retrieve only one – may have led to a blurring the responses across conditions because of imperfect recall. Third, profiles of neural activation may be different while initially detecting and encoding another person's experience, versus while later deliberately recalling that experience. Future research will be necessary to test these possibilities.

In some respects, though, the results of Immordino-Yang et al. (2009) do appear to converge with the current results. They did observe most activity in the dmPFC when considering an emotionally painful experience, and least activity (significantly deactivated) when considering a physically painful experience. Also, consistent with our main results, Immordino-Yang et al. (2009) suggest that there is an important neural distinction between responses to psychological states versus physical states, although they observe the largest difference in medial parietal regions. Taken together, the results of the current study and Immordino-Yang et al. (2009) suggest that an important dimension to consider, in future neuroimaging studies of empathy, will be whether the stimuli focus on emotions versus physical pain.

5. Conclusion

Verbal narratives – in novels, newspapers, magazines and blogs – serve as one of the dominant modalities through which we are asked to empathize with other people. A single sentence can conjure a vivid representations of a stranger's mental and physical experience, in some cases much more effectively than a photograph. The current study helps to clarify how narratives of others' pain and suffering are represented neurally: some brain regions are tuned to physical sensations, regardless of pain (e.g. SII); some brain regions are tuned to emotions, regardless of suffering (TPJ, PC, vmPFC); some brain regions are tuned to pain, regardless of whether it is physical or emotional (thalamus, anterior middle cingulate); one brain region is tuned selectively to physical pain (left insula); and one brain region is tuned selectively to emotional suffering (dmPFC). While task demands modulate activity in some brain regions (especially right insula), these results were remarkably consistent across two separate studies. Future studies can therefore use these profiles as a foundation to investigate how and when empathy for pain and suffering fails (Cikara, Bruneau, & Saxe, 2011).

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neuropsychologia.2011.11.008.

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