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Pain sensation evoked by observing injury in others

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ABSTRACT

Observing someone else in pain produces a shared emotional experience that predominantly activates brain areas processing the emotional component of pain. Occasionally, however, sensory areas are also activated and there are anecdotal reports of people sharing both the somatic and emotional components of someone else's pain. Here we presented a series of images or short clips depicting noxious events to a large group of normal controls. Approximately one-third of this sample reported an actual noxious somatic experience in response to one or more of the images or clips. Ten of these pain responders were subsequently recruited and matched with 10 non-responders to take part in an fMRI study. The subjects were scanned while observing static images of noxious events. In contrast with emotional images not containing noxious events the responders activated emotional and sensory brain regions associated with pain while the non-responders activated very little. These findings provide convincing evidence that some people can readily experience both the emotional and sensory components of pain during observation of other's pain resulting in a shared physical pain experience.

1. Introduction

Observing another person in pain, or knowing that a loved one is in pain, activates brain areas known to process the emotional qualities of pain [22,29,34]. Brain areas associated with coding the location and intensity of pain are also occasionally reported when observing another person in pain [21,25]. Viewing a needle entering the hand activates primary (S1) and secondary (S2) somatosensory cortex and generates a somatomotor preparation [2,3,25]. Focusing on the intensity of the observed stimulus increases S1 activation and the somatomotor preparation [1,25]. Thus, modulating attention towards others' experienced pain intensity activates somatosensory areas similar to when subjects orient towards the intensity of a felt pain [24]. A series of EEG studies also suggest modulation of somatosensory evoked potentials when observing pain in others [9,15,37]. Thus there is a growing body of research linking vicarious pain to somatosensory processing, implying shared emotional *and* sensory pain components, and raising the possibility of pain being fully experienced because of vicarious observation.

Supporting this speculation, highly empathic touch synaesthetes find it difficult to distinguish between touch sensation evoked by observation and that evoked by physical touch [4]. In a case report, one subject reported feeling touch when observing another person being touched [5]. This vicarious experience of touch correlated with activity in S1, which presumably mediated the touch sensation.

Several anecdotal cases have described pain sensation without apparent noxious stimulation. Amputees sometimes have increased phantom limb pain when viewing or imagining another person in pain [17]. A patient with parietal lobe damage reported pain in his finger when observing his wife cut her finger [8]. A builder reported severe pain in his right foot after jumping down onto a 15 cm nail even though the nail passed directly between his toes leaving his foot uninjured [16]. Finally, a male, who suffered injuries following a bomb attack, reported over 40 flashbacks of pain sensation, especially when reliving the experience [40]. Clearly pain can occur because of sensory input that is not inherently noxious and, at least occasionally, pain might be directly shared with another person.

The long term presence of pain without injury characterizes a large group of patients that are largely refractory to treatment [39]. The persistence, intractability and apparent lack of peripheral cause for their pain have led to an increasing interest in neuropsychological mechanisms [6]. A major barrier to understanding pain without injury, however, is the absence of techniques to generate pain without injury under controlled conditions. To that end, we have generated pain without injury using hypnosis [11,12] and a signal detection task [23]. These methods, however, involve activities that patients are not likely to encounter including a hypnotic induction and uncertain pulses of heat.

Based on anecdotal reports of pain without injury, and the apparent ability of at least some people to share the sensory component of an observed injury or touch, we hypothesized that some

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normal subjects would report pain sensation when observing another person in pain.

2. Methods

2.1. Subjects

Fifteen subjects were recruited to take part in a pilot study (2 male; mean age 19.9). Further data were collected from 108 (27 male; mean age 23.5) psychology undergraduates with no current or past psychiatric illness. The procedures were approved by local ethics committee and all subjects gave informed consent. Subjects were rewarded with course credits.

Subjects who reported pain to at least one of the images used were invited to take part in a further fMRI study. Ten subjects (4 male; mean age 27.5) provided consent for this further study. A further 10 (4 male; mean age 24.6) subjects who had not reported pain to any of the images or clips also provided consent for the fMRI study. The 10 responders and 10 non-responders were matched for trait empathy using the Interpersonal Reactivity Index (IRI) [10]. The index consists of four independent subscales with items designed to measure aspects of empathy. The subscales are labeled perspective taking, empathic concern, fantasy and personal distress. The ratings were as follows: empathic concern, pain responders 21.4 (5.1), non-responders 19.7 (3.5); perspective taking, responders 20.4 (3.2) non-responders 17.3 (4.9); personal distress, responders 12.4 (5.5) non-responders 12.9 (4.0); and fantasy, responders 16.1 (4.5) non-responders 19.9 (4.7). None of these differences reached criteria ($p < 0.05$) for significance although perspective taking trended very close to a higher score in the responders ($p = 0.06$) and fantasy trended towards a higher score in the non-responders ($p = 0.09$).

Subjects were paid £15 for completing the fMRI procedure.

2.2. Visual stimuli

Seven images and three movie clips were selected from the internet using an image search facility. Fig. 1 shows the selected images. The three movie clips included a person's hand receiving an injection, a tennis player turning over their left ankle and a soccer player breaking their right leg.

2.3. Behavioural procedure

Subjects viewed a computer screen at a comfortable distance of approximately one metre. A standardized set of instructions were used to explain the procedure. Subjects were informed that they were to view a series of images and short movie clips. Immediately after viewing each image they reported if they felt any sensation of pain while viewing the image. It was emphasized that the pain should be felt in the body and that general feelings of disgust or unease should not be recorded as painful. The subjects were then shown the visual analogue scale (VAS) used to rate the pain (anchored at 0 for no pain and at 10 for most pain imaginable) and the short-form McGill Pain Questionnaire (MPQ) [28]. The MPQ includes 15 pain descriptors (e.g. throbbing, shooting, gnawing, and sickening), linked to the sensory, affective and evaluative aspects of pain experience, and a pictorial presentation of the front and back of a body. Subjects were told to indicate the intensity of any pain felt in response to any of the images or clips using the VAS and the quality and location of the pain using the MPQ.

After addressing any questions or concerns, the seven images and three movie clips were presented in a counterbalanced sequence using PowerPoint. Each image and clip was presented for 6 s except for the soccer movie clip, which played for 18 s. If the subject reported pain after viewing any one of the images or clips then he or she completed the VAS and MPQ.

After the pilot study, additional questions were introduced to explore the nature of the pain experience and to ensure that feelings of unpleasantness or visceral reaction were clearly discriminated from somatic signs of noxious experience. All further subjects were therefore asked: "How long did the pain sensation last?", "How would you describe the pain sensation you felt?", "How did it feel?", "Have you previously experienced a similar kind of pain following an injury or other problem?" and "Do you get this type of pain in everyday life or when you watch a movie?". The investigator asked additional questions to clarify the nature of the experience as somatic, rather than just visceral or emotional, when necessary.

All subjects rated disgust, unpleasantness, sadness and fear following each image using a 0–10 VAS. The subjects also rated their

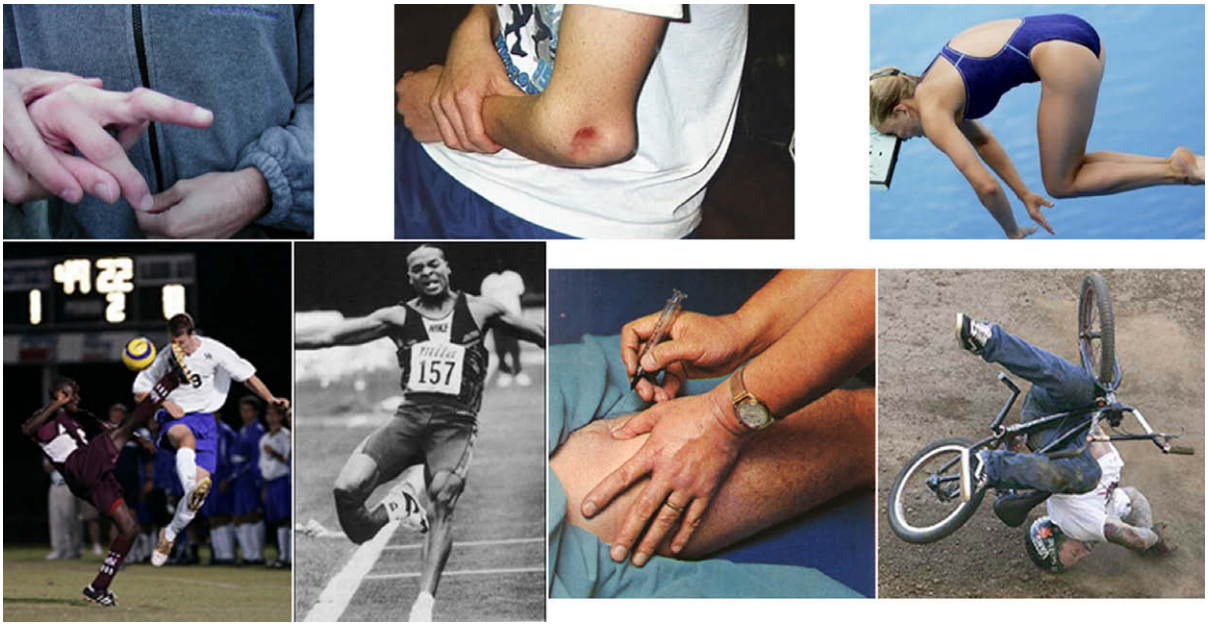

Fig. 1. The images used to elicit pain for the behavioural study and fMRI study.

empathic feelings towards the person in the image or clip using an adapted state empathy scale [31].

Once the questionnaires were complete, and the investigator was satisfied that she had sufficient information about the nature of any pain experience, the experiment continued with the next image or movie clip. In total, the experiment lasted 15–30 min depending on the range of responses.

2.4. fMRI visual stimuli

Before the fMRI study, the seven pain images were matched for emotional content to seven non-pain emotional images selected from the international affective picture system [26]. Fourteen new subjects (mean age 23; 2 male) were asked to observe the pain images and a series of emotional images and rate each image for emotional qualities (unpleasantness, fear, disgust, sadness). Emotional images rated as equivalent to the pain images were selected for use with fMRI.

2.5. fMRI procedure

Brain activation was inferred based on measurement of the blood oxygen level dependent (BOLD) contrast [30]. These measurements were acquired at 3 T using a Philips system. $T2^*$ weighted MR signal were measured using gradient echo-planar imaging (EPI) sequence (repetition time TR = 3000 ms, echo time TE = 2000 ms, FoV = 220 mm, 40 slices, 2.75 isotropic voxels). For the functional run, 215 dynamics were acquired from the AC-PC line. Hi-resolution (1 mm isotropic voxels) structural images were acquired using T1TFE technique.

Following acquisition of the structural image, each subject completed a functional run lasting 643 s and then a further series of shorter runs for a separate experiment that will be reported elsewhere. During functional acquisition subjects viewed a series of images: (1) images of people experiencing pain, (2) scrambled versions of the pain images, (3) images depicting emotional situations matched for emotional content with the painful images, and (4) images depicting neutral situations matched for content with the painful images. Fig. 2 illustrates part of a typical run.

The functional run consisted of 28 trials (seven pictures in each condition). Each trial consisted of a fixation crosshair (6 s), followed by one of the four condition images (6 s) and then a variable period to rate experience (ranging from 8 to 14 s). Order of stimuli presentation was rotated and each set of stimuli was presented once per subject. Immediately after each image subjects were instructed to rate how much pain they experienced and then how unpleasant they found the image. Ratings were delivered using a slider connected directly to CHEPS (Medoc, Israel) using the Computerised Visual Analogue Scale (COVAS), which was placed in a comfortable position on the subject. Subjects familiarized themselves with the slider in a short practice session before scanning. During the practice session the experimenter explained that start point (left hand side) referred to "no pain" and the end point (right hand side) referred to "worst pain imaginable". COVAS ratings were recorded online via CHEPS.

2.6. Data analysis

Data analysis was performed using the FMRIB Software Library (FSL release 4.1 – Oxford Centre for Functional Magnetic Resonance Imaging of the Brain), described in detail elsewhere [35]. In summary, head movement between scans was corrected by aligning all subsequent scans with the first. Each re-aligned set of scans from every subject was coregistered with his or her own hi-res structural MRI image, with the non-brain components edited out, and reoriented into the standardized anatomical space of the average brain provided by the Montreal Neurological Institute (MNI). To increase the signal to noise ratio and accommodate variability in functional anatomy, each image was smoothed in *X*, *Y*, and *Z* dimensions with a Gaussian filter of 6 mm (FWHM).

At the individual subject level a box-car model with a hemodynamic delay function was fitted to each voxel generating a statistical image corresponding to condition. A high pass filter removed baseline drifts. Brain regions with a large statistic correspond to structures whose BOLD response shares a substantial amount of variance with the induced changes in the subject's experience. Parameter estimate images for each individual subject were then combined at the second level to generate maps indicating within and between group effects. Critically, direct contrast of the brain response during the pain images with that during the emotional images provided an estimate of brain activation during pain experience excluding attendant emotional processing. The multiple comparisons problem of simultaneously assessing all the voxel statistics was addressed via cluster based thresholding. Clusters of voxels that exceeded a Z score >2.3 and $p < 0.05$ (corrected for multiple comparisons) were considered statistically significant. For display purposes, images are thresholded at $Z > 2.3$ and $k > 3$.

Region of interest (ROI) analysis was also performed for the anterior cingulate cortex, insula, S1 and S2. ROIs were drawn using MRIcro (http://www.sph.sc.edu/comd/rorden/mricro.html) and were then used as masks in FSL running FEATquery to extract the mean percentage change in BOLD signal for each ROI for each condition. The ROI data were entered into SPSS (Statistics for Research & Analysis, V16.0) and assessed using a repeated measures ANOVA.

3. Results

3.1. Behavioural experiment

Thirty one of the 108 subjects felt pain in response to at least one of the 10 images. All 31 felt their pain in the same location as the observed injury. For example, if the subject observed a finger injury, he or she marked a cross on the finger of the figure on the MPQ. The subjects selected a wide range of somatic descriptors from the MPQ. 'Tingling' was chosen as a descriptor most often (21 times) followed by 'aching' (18), 'sharp' (13), 'shooting' (11), 'throbbing' (8), 'sickening' (5), 'splitting' (5), 'heavy' (5), 'stabbing' (5), and 'tender' (1).

The duration of the pain was described as lasting for a "few seconds", "fleeting" or "for a split second as soon as the picture

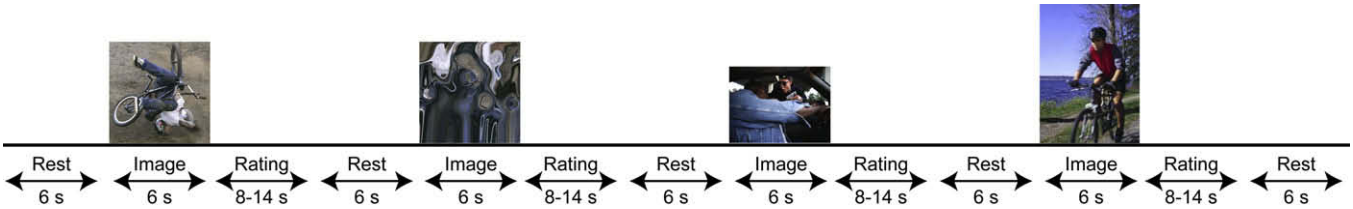

Fig. 2. Part of a functional run with the four image conditions illustrated from left to right: pain image, scrambled pain image, emotional image, and neutral image.

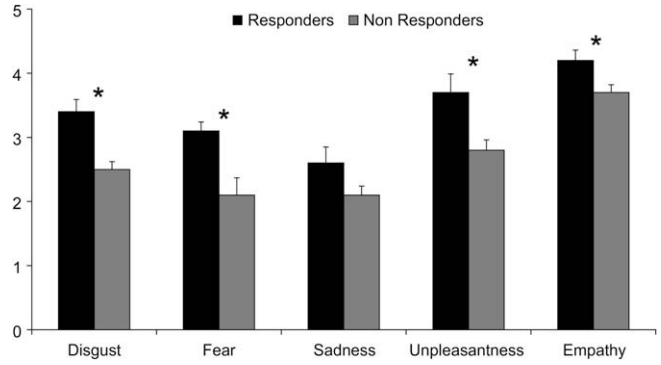

Fig. 3. Mean ratings for disgust, fear, sadness, unpleasantness, and state empathy for subjects who responded with pain (pain responders) to at least one of the images or clips in comparison to mean ratings for subjects who did not report any pain (non-responders). Asterisks indicate significant differences ($p < 0.05$) and error bars show standard errors.

appeared". The picture of the athlete with the broken leg generated the highest pain intensity (mean rating 3.7) and the most frequent pain reports (17 of the 31 responders reported pain in response to this picture). The picture of the man fallen from his bike generated the lowest pain intensity (mean rating 0.5) and the least frequent pain reports (4 of the 31 responders reported pain). The average pain intensity reported by the responders across all the images was 1.9 (SD = 2.4). The average pain unpleasantness reported by the responders across all of the images was 2.8 (3.0) and 1.1 (2.1) for the non-responders.

Fig. 3 shows the average ratings for disgust, fear, sadness, unpleasantness, and state empathy evoked by the images and movie clips for the pain responders and non-responders. Responders had significantly elevated responses for all categories except sadness. Pain intensity, however, was not significantly correlated with state empathy ($r = 0.17$), empathic concern, ($r = -0.50$), perspective taking ($r = -0.35$), fantasy (-0.33), personal distress ($r = 0.25$), unpleasantness ($r = 0.03$), fear ($r = 0.15$), disgust ($r = 0.01$), sadness ($r = 0.27$), age ($r = 0.02$), or gender ($r = 0.17$).

Subjects were asked about previous pains due to injury or other sources but none reported the pain experienced from the images as equivalent to a previous pain and their previous injuries were in different parts of the body from those in the images. Subjects were asked if they get this type of pain in everyday life or at the movies. Most of the sample answered that they did get unexpected sensations of pain, or explained that they cannot watch films or documentaries that include images or scenes of pain because of these accompanying pain sensations. Subjects spoke about their pain experience during observation of another in pain as if it was normal; something they assumed was representative of the population as a whole.

3.2. fMRI experiment

None of the non-responders reported any pain while viewing the images in the scanner while the responders reported an average of three images as generating definite pain (mean rating 3/10). Contrasting the brain activation when viewing emotional images not depicting injury with those depicting injury should reveal pain related activation only for the subjects reporting vicarious pain. Critically, in subjects who do not report pain the two images should produce a similar emotional reaction and a similar pattern of activation resulting in little or no difference when contrasting activation across the conditions. This critical contrast is shown here. All other contrasts can be found in Supplementary materials. In summary, the responders consistently activated the anterior midcingulate cortex (aMCC), anterior insula, prefrontal cortex and S1 and S2 across all contrasts. The non-responders consistently activated aMCC and prefrontal cortex but did not activate insula, S1 or S2 and occasional deactivation of the insula was observed.

Fig. 4 illustrates that subjects reporting pain to the images depicting injury activate the ACC (especially the aMCC), insula, S1 and S2 in comparison with emotional (no injury) images whereas subjects not reporting pain show little activation for the same contrast.

The ROI data were entered into a repeated measures ANOVA to reveal a significant difference between groups for the overall profile of responses in these ROIs ($F_{1,18} = 5.0$, $p = 0.04$). The interaction of group with region was also significant ($F_{7,126} = 4.5$, $p < 0.01$). Post hoc *t*-tests revealed significantly greater responses in the responder group in right insular cortex (R IC), left insular cortex (L IC), right secondary sensory cortex (R S2) and left secondary sensory cortex (L S2).

4. Discussion

Our study provides convincing evidence that a significant minority of normal subjects can share not just the emotional component of an observed injury but also the sensory component. These subjects describe observing at least some injuries as painful and they activate regions of the brain known to be involved in pain (Fig. 4). Similar to our previous work with hypnosis, the current study provides good evidence that these regions are not just passively recording injury or threats to tissue but are actively generating painful experience [11].

Previous responses to observations of non-noxious touch have also produced somatic (S1 or S2) activation and our findings provide further support for the idea that mirror or empathic responses do not rely exclusively on motor imitation and can involve a shared sensory response [2,3,9,21,25]. Other investigators have also suggested that sources not typically considered noxious can generate pain and this experience is physical rather than metaphorical, or purely emotional, in nature [14,33]. Thus it is possible that at least some people might experience pain directly even in a non-painful scenario such as when observing another in pain.

Here we demonstrate that a significant minority of normal volunteers can experience pain when observing others in pain. This finding was maintained despite extensive questioning of subjects and significant effort to exclude responses restricted to visceral, or general unpleasant, feelings. Pain descriptors provided by the subjects included a high frequency of clearly somatic terms such as stabbing, shooting, sharp and tingling. Supporting these subjective pain reports, brain activation was higher in all areas associated with the pain matrix for those who experienced pain compared with the non-responders who felt no pain. Studies investigating the neural underpinnings of empathy have also generated activation in regions of the pain matrix [22,29,34]. In these studies, activation of the ACC and the insula was found when subjects viewed or anticipated somebody else in a painful situation but the subjects did not actually report experiencing pain in these studies and sensory areas (S1 and S2) were not activated.

Empathy has been implicated in a number of studies involved in perception of others in pain [22,29,34]. As similar areas of the pain matrix are activated for vicarious pain as for physical pain, the perception action model of empathy is often used to explain the neural correlates of empathy [32]. This model states that there is a representation of the action that is directly shared and drives the shared experience. A smile, for example, provides information about the happy state of the person observed and, through motor mimicry, leads to a shared happy state. Our results, however, provide little support for a motor representation of pain. Observation of the subjects did not indicate any overt grimacing or bracing

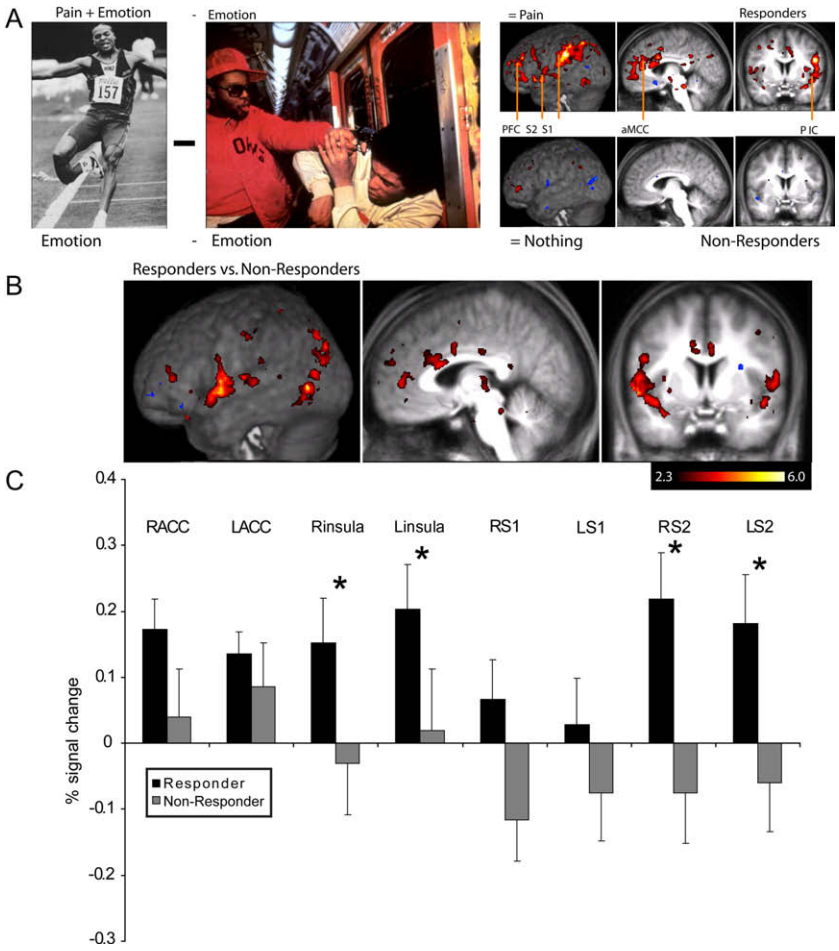

Fig. 4. Top left (A) illustrates a typical pain image shown to all subjects during fMRI. This image generated pain and emotion in the responders but only emotion in the non-responders. A typical non-pain emotion picture is shown to the right and generated emotion in both groups. Subtracting the brain activation during the non-pain emotion images from brain activation during the pain images reveals regions of the pain neuromatrix (labeled) in the responders but not in the non-responders. These differences between the groups are shown below (B) thresholded at $p < 0.01$ (uncorrected) to show the profile of difference. Whole brain analysis demonstrated significantly ($p < 0.05$, corrected) greater activation in the responders versus the non-responders in the left prefrontal cortex (MNI coordinates: −4, 52, 32; Z(height) = 5.2; k(extent) = 698). The results of the ROI analysis are graphed at the bottom (C). Asterisks indicate significant differences ($p < 0.05$) and error bars show standard errors.

action and the fMRI results provided little indication of motor preparation or response. Nevertheless, other studies have demonstrated motor preparation using more sophisticated behavioural and TMS techniques [2,3] that we will adopt in future work.

There was also no significant correlation between reported pain intensity and empathy or unpleasantness or disgust. A shared emotion with another person in pain is often referred to as an empathic experience but that experience might be quite different from shared pain experience. While some people may readily share the emotional perspective of others that shared empathic experience might have surprisingly little relation to the shared experience of pain intensity demonstrated here. Others have also failed to demonstrate a significant correlation between trait empathy and measures of sensory experience [3]. When S1 activation has previously been reported the activation was stronger when subjects were specifically asked to focus on the intensity of the observed painful stimuli. A vicarious sensory painful experience, therefore, may be linked to attention and vigilance towards pain rather than to empathy.

Overall, activation in regions associated with the emotional component of pain were activated more strongly and consistently than regions associated with the sensory component. Specifically, activation was observed in the rostral, rather than caudal, regions of ACC. The rostral ACC is linked with the emotional component of pain and with observing pain in others rather than with pain due to noxious heat or cold [20,38]. Subjects with high state empathy also report higher heat pain experience during noxious somatic stimulation [27]. In our experiment pain responders had significantly increased pain unpleasantness and state empathy. Thus, higher state empathy in our pain responders and a stronger response to the emotional component of the image may drive a secondary somatic reaction that is felt as pain. On the other hand, although ACC activation was greater in the responders, this difference did not reach criteria for significance in the ROI analysis. It is possible that pain in responders is more dependent on a larger somatosensory response driving a secondary emotional response. Other imaging technologies such as MEG or EEG can formally test this speculation [19].

Here we have focused on the critical analysis comparing pain images with non-pain emotional images. Other contrasts are included in Supplementary materials and generally support previous findings [20,21,25,26]. Insula activation, however, was only apparent in the responders and there was insula deactivation in the non-responders when comparing pain images to crosshair fixation. It is possible that the non-responders had an attenuated sensory and emotional reaction to the pain images relative to the responders resulting in reduced insula response. Previous studies using cartoon depictions have failed to activate the insula possibly because the subjects failed to see the images as real [18]. Our non-responders

might also fail to see the images as 'real' because of their extreme content but this speculation will require further investigation to substantiate.

The precise nature of the individual differences driving pain experience in the responders remains open to further investigation. Previous studies have reported variability in pain empathy dependent on trait-cognitive empathy and personal distress [1], self-centred versus other-centred stance [37], feelings of exclusion [13], and catastrophising [36]. Studies are ongoing in our laboratory to investigate whether responders can more readily adopt the perspective of the other, more readily incorporate a prosthetic limb into their body schema and are more readily suggestible than non-responders. We note that perspective taking did trend very close to significance in this study and this difference and others might be revealed as significant when using larger samples. A further possibility is that certain features of the images, such as the presence of a facial grimace [7] or a particular type or intensity of injury [1,25], contribute to the pain experience.

The responder group did not respond with pain to every image and different images elicited pain across our responders. If future studies can identify the features of an image most likely to yield a pain response then it could be instructive to compare pain evoking versus non-pain evoking injury images. The current study demonstrates a considerable activation difference between responders and non-responders and the clearest behavioural correlate with that activation difference is the report of pain for at least some of the images. It remains uncertain whether there is a qualitative or quantitative difference when responders view injury images and report pain versus viewing injury images and not reporting pain. Our speculation is that the difference is quantitative (there is a threshold of some sort that responders are able to tip over) but we need further studies to substantiate that claim.

Regardless of the precise mechanism of vicarious pain experience our findings add to a body of evidence that pain can be experienced without injury. Our results go substantially further than previously, however, by directly associating the tendency to report a somatic noxious experience, when observing another in pain, with activation in both emotional and somatic regions of the brain. Such findings have important implications for our understanding of sensory experience in general and for pain in particular. Observation of pain directly generating pain, for example, could form part of the etiology of functional pain. By increasing the understanding of pain without injury we might develop better insight into the mechanisms and causes of functional pain.

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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.pain.2009.11.007.

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