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The Compassionate Brain: Humans Detect Intensity of Pain from Another's Face

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Understanding another person's experience draws on "mirroring systems," brain circuitries shared by the subject's own actions/feelings and by similar states observed in others. Lately, also the experience of pain has been shown to activate partly the same brain areas in the subjects' own and in the observer's brain. Recent studies show remarkable overlap between brain areas activated when a subject undergoes painful sensory stimulation and when he/she observes others suffering from pain. Using functional magnetic resonance imaging, we show that not only the presence of pain but also the intensity of the observed pain is encoded in the observer's brain—as occurs during the observer's own pain experience. When subjects observed pain from the faces of chronic pain patients, activations in bilateral anterior insula (AI), left anterior cingulate cortex, and left inferior parietal lobe in the observer's brain correlated with their estimates of the intensity of observed pain. Furthermore, the strengths of activation in the left AI and left inferior frontal gyrus during observation of intensified pain correlated with subjects' self-rated empathy. These findings imply that the intersubjective representation of pain in the human brain is more detailed than has been previously thought.

Keywords: anterior cingulate cortex, anterior insula, empathy, face, intensity, pain

Introduction

Human nonverbal behavior, consisting of postures, gestures, and facial expressions, carries a vast amount of information about people's emotions, aims, and internal states. The 7 basic emotions—sadness, happiness, anger, contempt, disgust, fear, and surprise—are all rather well recognized from facial expressions, but suffering pain seems to be harder for other people to interpret (Kappesser and Williams 2002). Although pain is often considered a private experience, recognition of pain in a conspecific has clear survival and communicative value. Distinct facial expression of pain can warn others of imminent danger and elicit helping behavior (Williams 2002).

The discovery of the human motor mirror-neuron system (see Rizzolatti and others 1996; Hari and Nishitani 2004; Rizzolatti and Craighero 2004), which is assumed to support the understanding of other people's actions and motor intentions, has led to the search of corresponding sensory mirroring systems that would form the neuronal basis for understanding other person's percepts and feelings. In a mirroring system, motor or sensory, corresponding brain areas are activated when the subjects themselves act, feel, or perceive and when they observe another individual in similar situations and infer their feelings or intentions from their nonverbal behavior. Such sensory mirroring systems have already been identified, by brain imaging methods, for touch (Avikainen and others 2002; Keysers and others 2004) and disgust (Krolak-Salmon and others 2003; Wicker and others 2003).

Similar mirroring mechanisms are starting to be revealed also for processing of pain. In direct intracranial recordings, 1 neuron in the human anterior cingulate cortex (ACC) was found to fire both when the subject perceived thermal pain and when he/she saw another subject receiving the same stimuli (Hutchison and others 1999). Similarly, functional magnetic resonance imaging (fMRI) studies indicate bilateral activation in the ACC and anterior insula (AI) during both self-experienced pain and during observed or implied pain in others, strongly suggesting a shared brain circuitry for first- and third-person experiences of pain (Singer and others 2004; Botvinick and others 2005; Jackson, Brunet, and others 2005).

Recently, brain activation for pain observed from another's face has been explored (Botvinick and others 2005; Saarela and others 2005). Botvinick and others (2005), using fMRI region-of-interest analysis that was based on meta-analysis of previous studies, found that facial expressions of pain activate the AI and ACC bilaterally, as in self-experienced pain. However, as their brief report did not present examples of the pain face stimuli, it remains unclear whether the stimuli contained some other cues of pain generation besides the facial expressions—such as arm manipulation. Furthermore, neither the empathy correlates of brain activation during observation of pain from the other's face nor the subjective estimates of pain intensity were taken into account.

Our aim was to further expand studies of mirroring systems from the motor to the sensory side. We imaged brain activity in 12 subjects while they viewed photographs of faces of patients, whose pain was transiently intensified for a few seconds. The subjects estimated the pain intensity in each face stimulus, and those estimates were incorporated into the fMRI data analysis. Thus, our study expands the earlier reports by searching for brain circuitry involved in the processing of the intensity of pain observed from the face of a conspecific.

As stimuli, we used real pain faces as did Botvinick and others (2005) because acted facial expressions of pain can differ from genuine pain expression (Hill and Craig 2004), and real pain has a meaning for the chronic patient which cannot be approximated by experimental pain in volunteers.

We expected that when healthy observers view facial expressions of chronic pain, their own affective pain network will activate, as has been shown for observers who view acute pain or receive cues of someone else in pain (e.g., Singer and others 2004; Botvinick and others 2005; Jackson, Meltzoff, and Decety 2005). Moreover, we predicted that if the human brain encoded the experience of pain similarly for both self-experienced pain and for pain observed in another, the intensity of the observed pain would also be encoded in the observer's brain—as happens during the individual's own pain experience (Coghill and others 1999). Thus, we envisioned that the intensity of pain experienced by the pain patient would be reflected in the intensity of the observers' brain responses and that the brain responses for faces showing more intense pain would be stronger than responses for faces with less intense pain. We also predicted that the personal empathic abilities of the observer would show a relationship to the detected brain responses.

Materials and Methods

Subjects

A total of 42 healthy adult volunteers participated in the experiment: 30 (16 females, 14 males; aged 21–38 years) in the stimulus selection study and 12 (7 females, 5 males; aged 18–37 years; mean ± standard deviation (SD) 27 ± 5; all right-handed by self-report) in the fMRI study that also included postscan questionnaires. None of the participants in the stimulus selection study took part in the fMRI study. The subjects for the stimulus selection study (with no fMRI recordings) provided verbal consent, and all subjects of the neuroimaging study gave written informed consent prior to the experiment. A written informed consent was also obtained from the chronic pain patients who were videotaped for the stimuli. All parts of the study were approved by the ethics committee of the Helsinki and Uusimaa Hospital district.

Stimulus Recording

The stimuli were photographs of faces of chronic pain patients (Fig. 1) and healthy volunteers, all unknown to the subjects. Seven patients were videotaped during provocation of pain (provoked pain) and at rest (chronic pain). The pain provocation procedure was carefully explained to the patients prior to their consent. Pain was transiently provoked by reproducing the patients' own pain, for example cautiously stretching or pressing the painful arm or leg, until patients themselves signaled the end of the provocation period by giving a sign with their hand. After each pain provocation, patients rated the peak intensity of their pain on a scale from 0 to 10, where 0 = no pain and 10 = worst possible pain; patients also rated their pain during the rest period between the provocations. Videos were carefully recorded to exclude all visual information except for the patient's face. Thus, the recordings from 2 patients were rejected because of too many qualitative differences between the conditions (e.g., eyes open during chronic pain and closed during provoked pain).

Stimulus Selection Study

From each of the 5 patients with high-quality videos, 25 still photos were selected for classification by 30 participants in the stimulus selection study. The photos were presented in a random order for 2.5 s with an interstimulus interval of 5 s, and the subjects estimated the intensity of pain in each photo on a scale from 1 to 10, where 1 = the person in the photo is suffering from pain of minimum intensity and 10 = the person in the photo is suffering from pain of maximum intensity. The photos of 1 patient did not obtain sufficient range of estimates and were discarded.

Thus, the set of photos for the fMRI stimuli was formed from photos of 4 pain patients (2 females and 2 males; aged 41–66 years). The patients suffered from complex regional pain syndrome, osteonecrosis due to chronic myeloid leukemia, spinal stenosis, and neuropathic pain. From each patient, 3 photos with the highest pain estimates were selected to represent "provoked pain," and 3 photos with the lowest ratings were selected to represent "chronic pain." Thus, altogether 12 photos of provoked pain and 12 photos of chronic pain served as stimuli in the neuroimaging study.

Stimulus Sequences in the fMRI Study

Brain scanning consisted of 2 sessions, one with the provoked and chronic pain faces and the other with the neutral faces of healthy individuals in their twenties. The neutral faces—gender matched with the pain patients—were originally recorded for another experiment and reused here with the healthy individuals' written consent (Schürmann and others 2005).

During the pain face sequence, the photos of provoked and chronic pain of the same patient were presented in pairs (Fig. 1). This procedure enabled the subject to better detect the quantitative variations in pain expressions within the same patient, instead of comparing faces of different patients. The order of provoked pain and chronic pain stimuli in the pairs was counterbalanced within the sequence, and the photos for different patients were randomized within the sequence.

The experiment always started with a sequence of control stimuli of the neutral facial photos, presented in a similar sequence of paired stimuli as described for the patient faces (photos of each volunteer presented pairwise); the photos of different volunteers were randomized within the sequence. The presentation order of conditions was fixed; the sequence of control faces always preceding the sequences of patient faces. Each photo was displayed for 2.5 s. The intrapair interval

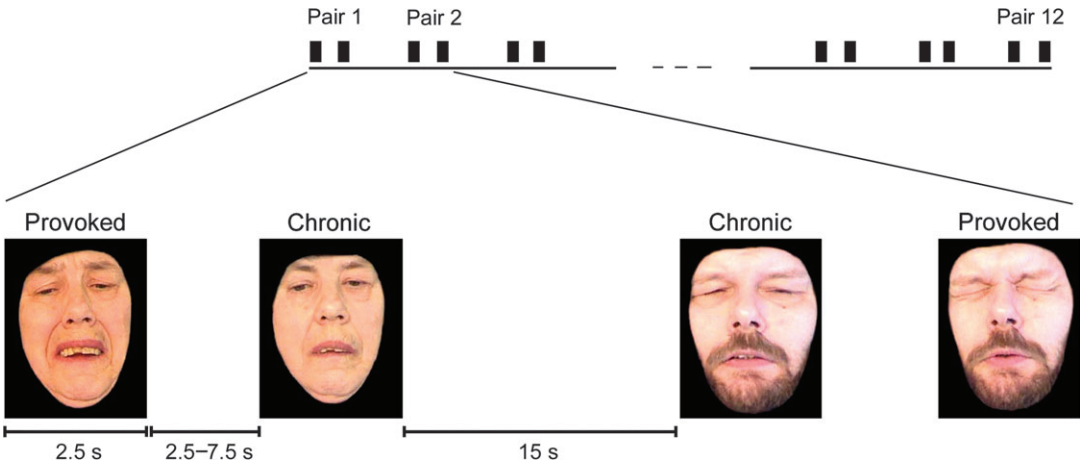

Figure 1. An example of the sequence of the pain face stimuli. Altogether 12 provoked pain photos (3 from each of the 4 patients) and 12 chronic pain photos (similarly 3 from each of the 4 patients) of the same patient were shown in pairs, each consisting of 2 photos of the same patient. Each photo was displayed for 2.5 s. The intrapair-interval varied between 2.5 and 7.5 s, and the interpair-interval was 15 s.

was 2.5–7.5 s, and the between-pair interval was 15 s. During all intervals, the subjects viewed a white fixation cross on a black background. In both conditions, each photo was shown only once, resulting in the total trial duration of 5 min 15 s.

Instructions to Subjects

Subjects were carefully explained the course of the study prior to the fMRI recording. They were instructed to view all stimuli attentively during the scan, so that they could answer questions concerning the stimuli afterward; all subjects confirmed that they had understood the task. Before the scan, the subjects were also informed that some of the photos were of persons experiencing pain. The aim was to ensure that the subjects were attentive to pain, instead of the other emotions sometimes mistaken for pain, such as fear or anger (Kappesser and Williams 2002).

Postscan Tests

Pain Intensity Estimation

Instantly after the scan, the subjects reviewed the patient faces, presented in the same order and for the same duration as during the scan, but this time the subjects themselves controlled the onset of stimuli by pressing a button. For each stimulus, the subjects were asked to provide 3 estimates on a scale from 0 to 10: the pain intensity of the patient (0 = the person in the photo does not suffer from pain, 10 = the person in the photo suffers from pain of maximum intensity), pain distress of the patient (0 = the person in the photo does not suffer from distress, 10 = the person in the photo suffers from the maximum possible distress), and the subjects' own self-distress (0 = I do not feel distressed when viewing the photo, 10 = I feel maximum distress when viewing the photo). Neutral control faces were not rated. Statistical differences in postscan estimates for provoked versus chronic pain were assessed with a nonparametric Wilcoxon test, as were differences in pain intensity and pain distress estimates for all pain faces.

Assessment of Empathy

The subjects also completed 2 self-report questionnaires addressing empathy: the 30-item Balanced Emotional Empathy Scale (BEES) (Mehrabian 2000) and the 28-item Interpersonal Reactivity Index (IRI) (Davis 1980). The BEES assesses the capacity to vicariously experience another's emotions, both positive and negative (including pain). The IRI has 4 subscales: "empathic concern" relating to others' hardships, "fantasy" mainly taking the place of characters in books or movies, "perspective taking" in relation to interpersonal conflicts, and "personal distress" concerning the subjects' tendency to become anxious when witnessing others' suffering or need for help.

Experimental Setup and Data Acquisition

During the fMRI scan, the subject was lying in the whole-body General Electric Signa® 3.0 T magnetic resonance imaging (MRI) scanner at the Advanced Magnetic Imaging Centre, Helsinki University of Technology. The visual stimuli were delivered to a semitransparent screen behind the head coil with a digital-light-processing micromirror data projector (Christie Vista X3, Christie Digital Systems Inc., Kitchener, Ontario). The subject viewed the screen from a distance of 35 cm via a mirror attached to the head coil. Stimulus presentation was controlled by the Presentation™ software (Neurobehavioral Systems, Inc., Albany, CA). Functional magnetic resonance (MR) images were acquired in an event-related design using a standard head coil and gradient-echo planar imaging sequence with the following imaging parameters: field of view = 200 × 200 mm^2, time of repetition = 2500 ms, time to echo = 32 ms, 31 slices with slice thickness of 4.0 mm in interleaved acquisition order, number of excitations = 1, and acquired matrix size 64 × 64. Structural MR images were acquired using a standard spoiled-gradient echo sequence.

Evaluation of fMRI Data

General Data Analysis

The fMRI data were evaluated with BrainVoyager QX (Brain Innovation B.V., Maastricht, The Netherlands). Preprocessing comprised 3-dimensional motion correction, temporal high-pass filtering at 0.01 Hz, slice scan-time correction, and spatial smoothing with an 8-mm Gaussian kernel. Both functional and anatomical data were subsequently normalized to the Talairach space (Talairach and Tournoux 1988).

At the group level, hemodynamic responses were subjected to random-effects statistical analysis using a general linear model (GLM). The predictors for GLM were obtained by convolving the time course of the stimuli with a hemodynamic response function (Boynton and others 1996).

Contrasts

The blood oxygen level–dependent (BOLD) effect of viewing all faces was studied by using the contrast "patient face + neutral face – baseline" to show activations to face stimuli as such. The contrast between patient and neutral faces was meaningless due to the fixed scanning order (neutral faces always presented first).

The difference in brain activation with provoked and chronic pain faces was studied using both patient and neutral faces. First, a contrast of "provoked pain – chronic pain" was calculated. This procedure was repeated for paired neutral faces, using the same predictors in the same order, resulting in a contrast "neutral face 1 – neutral face 2." Thereafter, the result of contrast in neutral faces was subtracted from the result of contrast in patient faces, to achieve a contrast of provoked pain – chronic pain free from random differences in viewing nonemotional faces [provoked pain – chronic pain – (neutral face 1 – neutral face 2)], henceforth referred to as "provoked pain - chronic pain".

In all statistical maps, the threshold for cluster size was 5 activated voxels at the original acquisition resolution of functional images, corresponding to a volume of 200 mm^3. The default statistical threshold was $P < 0.005$ (uncorrected for multiple comparisons) for all other statistical maps except for "viewing all faces" (patient face + neutral face – baseline). For the latter, we used $P < 0.0005$ to clearly differentiate the activated anatomical areas.

The association of subjects' postscan estimates of pain intensity with brain activations was studied using separate models for each subject and 2 separate predictors in a GLM. The first predictor encoded onsets of the stimuli as in the previous contrasts, and it was the same for all subjects. The second predictor incorporated the subject's pain intensity estimates into the model, so that the predictor's amplitude depended linearly on the value of the subject's estimate for each stimulus—thus this value was different for each subject (for details of the method, see Büchel and others 1998). The amplitude of the modeled BOLD response during each separate patient face thus depended on the subject's pain intensity estimates.

Results

Brain Activation during Viewing All Faces (Patient Face + Neutral Face – Baseline)

Face stimuli, in contrast to baseline, elicited widespread activation (positive BOLD signal) in the occipital cortex, cingulate cortex, supplementary motor area (SMA), cerebellum, brainstem, pons, thalamus, amygdala, and hippocampal formation ($P < 0.0005$ uncorrected); all these activations were bilateral. Deactivation (negative BOLD response) occurred simultaneously bilaterally in the ventromedial prefrontal cortex, in the right posterior lateral sulcus, in the left superior frontal area, and in the left inferior parietal area.

Provoked Pain – Chronic Pain

Figure 2 shows that provoked pain faces, contrasted with chronic pain faces, elicited prominent activation bilaterally in the inferior frontal gyrus (IFG) conjoined with the AI, the bilateral SMA, the left ACC, left premotor cortex in the wall of the precentral sulcus, and in the left inferior parietal lobe (IPL) (for all areas $P < 0.005$ uncorrected; see Table 1). In the postscan behavioral tests, subjects rated their self-distress higher for viewing faces with provoked than chronic pain (mean ± SD 2.8 ± 1.3 vs. 1.1 ± 1.0; $P < 0.01$, Wilcoxon).

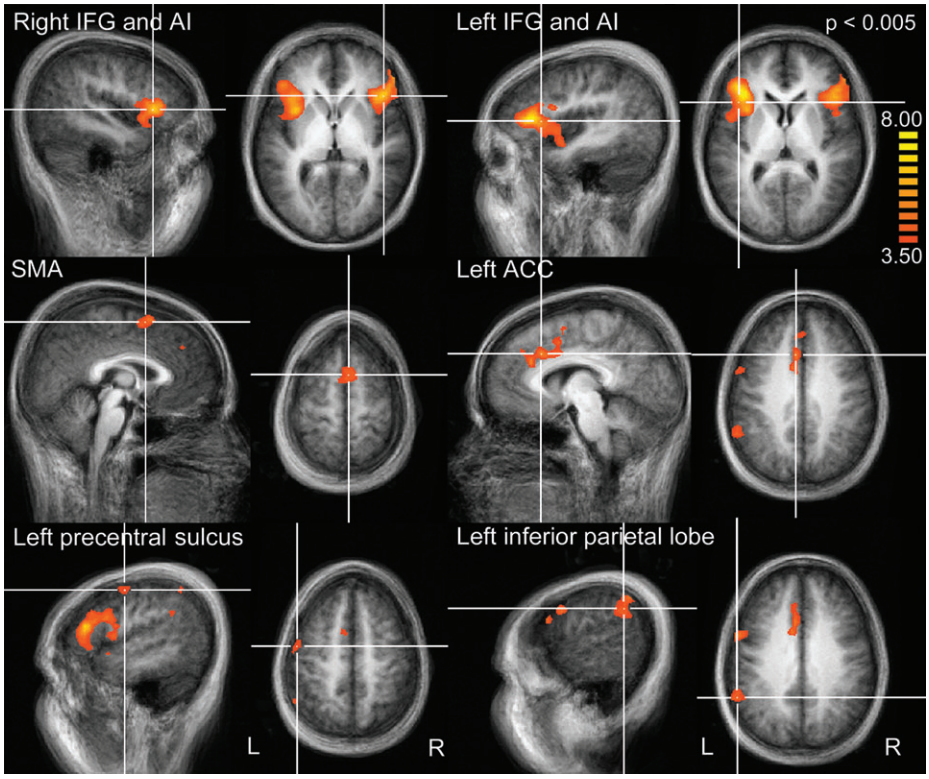

Figure 2. Statistical maps in the provoked pain – chronic pain contrast superimposed on the averaged structural MR image of all 12 subjects. The colored areas indicate statistically significant activations at $P < 0.005$, and the color bar indicates the *t*-value scale.

Due to the conjoined cluster of AI and IFG in the group analysis, we inspected the activation on IFG of all 12 subjects at individual level. Based on the work by Amunts and others (2004), and by comparing the activations with individual brain gyration, the IFG activation was identified to pars triangularis in 10 out of 12 subjects (mean ± SD coordinates for centers of gravity: $x = -47 \pm 2$, $y = 23 \pm 8$, $z = 6 \pm 9$ and $x = 50 \pm 3$, $y = 26 \pm 4$, $z = 4 \pm 8$ in the left and right hemisphere, respectively).

Pain Intensity–Dependent Activation

After the fMRI recording, subjects estimated the intensity of pain and pain distress in each face stimulus, as well as their self-distress in viewing the stimulus. All 3 estimates were higher for faces with provoked than with chronic pain (mean ± SD intensity 5.4 ± 1.9 vs. 2.3 ± 1.7, $P < 0.01$, Wilcoxon; distress 5.5 ± 2.1 vs. 2.3 ± 1.8, $P < 0.01$, Wilcoxon; self-distress 2.8 ± 1.3 vs. 1.1 ± 1.0, $P < 0.05$, Wilcoxon). No statistically significant difference was found between subjects' pain intensity and pain distress estimates ($P = 0.72$, Wilcoxon). The subjects' intensity estimates were consistently lower (in 45 out of 48 cases) for provoked pain faces than the patients' own pain ratings (see Fig. 3). The subjects' intensity estimates for chronic pain faces were also lower than the patients' own pain ratings (in 41 out of 48 cases). The differences between patient's own pain ratings and the subjects' pain intensity estimates for provoked pain and chronic pain were 2.7 ± 1.7 and 1.7 ± 2.0 (mean ± SD), respectively.

Next, the subjects' postscan estimates of pain intensity in each stimulus face were individually incorporated into the fMRI model. Figure 4 shows the resulting statistical parametric maps, obtained using linear regressors (Büchel and others 1998).

Table 1

Mean ± SD Talairach coordinates (*x*, *y*, and *z*) for the centers of gravity of activation clusters > 200 mm^3 both in the contrast of provoked pain − chronic pain and in the pain intensity–dependent model at $P < 0.005$ uncorrected

Condition	Region	L/R	*x*	*y*	*z*	*t*(11)	*P*	Area (mm^3)
Provoked − chronic	AI-IFG	L	−40	18	7	3.5	0.001	18616
	AI-IFG	R	43	22	3	4.4	0.001	8355
	ACC	L	−6	20	33	3.9	0.002	1997
	SMA	R	2	6	56	3.9	0.002	1576
	IPL	L	−56	−48	31	3.9	0.002	2479
	PS	L	−48	−6	47	3.7	0.003	274
Pain intensity model	IPL	L	−58	−58	28	3.8	0.003	1768
	AI	R	37	17	−4	3.8	0.003	525
	ACC	L	−9	23	43	3.8	0.003	436
	AI	L	−37	12	−7	3.7	0.004	225

Note: Statistical *t*(11) and *P* values are averaged across all voxels of a cluster and across all subjects. PS, precentral sulcus.

These results indicate that estimates of pain intensity correlated with activation strengths of the left ACC, left IPL, and AI bilaterally (Table 1).

Empathy for Pain in Others

Figure 5 shows that the strength of activation in the left AI-IFG region during provoked pain faces correlated positively with the subjects' individual scores on the personal distress subscale of the IRI (explained variance 49%, $P = 0.012$, Spearman) and BEES (explained variance 37%, $P = 0.035$). Other IRI subscales failed to reach statistical significance; Table 2 lists results for all scales.

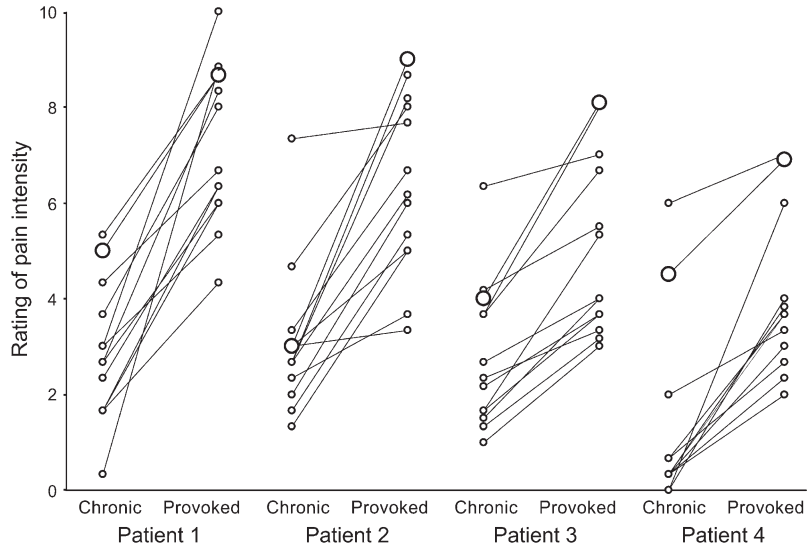

Figure 3. Individual estimates of pain intensity by the 12 subjects participating in the neuroimaging experiment. The subjects evaluated the chronic and provoked pain photos of patients 1–4: smaller circles represent average evaluations of 3 photos of the same situation. The patients' own ratings of average pain intensity during pain provocation and rest periods are indicated by larger circles.

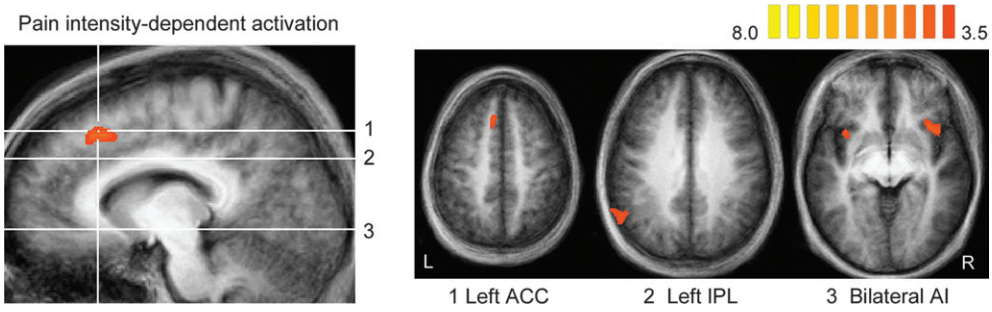

Figure 4. Brain areas where the BOLD response correlated with the subjects' estimates of observed pain intensity. The statistically significantly activated areas are the left ACC (Talairach *x*, *y*, *z* coordinates for center of gravity –9, 23, 43), the left IPL (–58, –58, 28), and the bilateral AI (–37, 12, –7 and 37, 17, –4). The locations of the axial slices are shown on the left, and the color bar indicates the *t*-value. All statistical maps are superimposed on group averages (n = 12) of structural images.

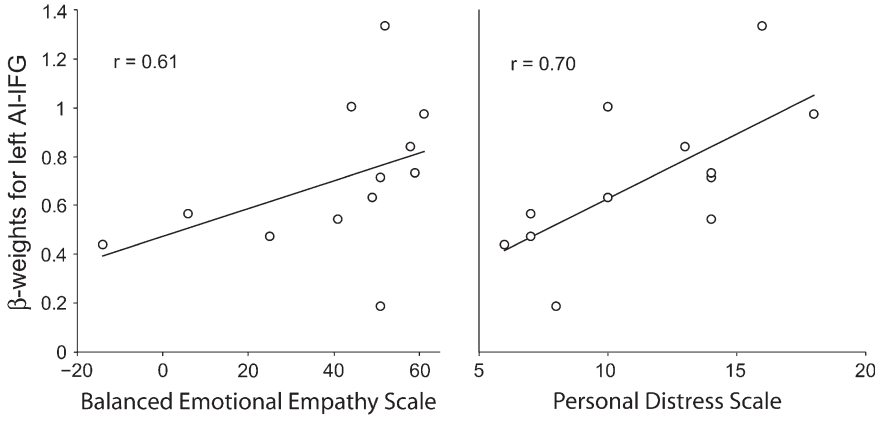

Figure 5. Activation strengths as β-weights in the left AI-IFG region (see Fig. 2) during provoked pain faces presented as a function of the individual scores in personal distress scale (right) and BEES (left). The lines represent the linear best fits. The correlation coefficients for both scales differed from zero at $P < 0.05$ (see Table 2).

Discussion

Encoding of Intensity of Another Person's Pain

The most striking and novel result of the present study is the correlation—during pain observation—of activation strength in the observer's brain with the intensity estimates for pain in the patients' facial expressions. This result is a notable expansion of recent findings on shared brain representations for first- and third-person perspectives of pain. The more widespread neural correlates of estimated pain intensity in our study than when subjects viewed pictures of human limbs in painful situations (Jackson, Meltzoff, and Decety 2005) could reflect the

Table 2

Correlation coefficients (*r*, Spearman) and statistical significances (*P*) of all the empathy scales, and the brain activation during viewing provoked pain faces in the brain area defined by provoked − chronic pain contrast

Brain region	Empathy scale									
	IRI								BEES	
	PT		FS		EC		PD			
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Right AI-IFG	0.30	0.34	0.48	0.11	0.30	0.34	0.48	0.11	0.39	0.20
Left AI-IFG	0.03	0.93	0.54	0.07	0.37	0.24	0.70	0.01*	0.61	0.04*
Left ACC	−0.24	0.45	0.42	0.17	0.36	0.25	0.42	0.18	0.37	0.24
Right SMA	−0.11	0.72	0.32	0.31	−0.06	0.85	0.39	0.21	0.35	0.26
Left IPL	−0.24	0.46	0.27	0.39	0.07	0.81	0.39	0.22	0.32	0.32
Left precentral sulcus	0.06	0.85	0.28	0.38	0.00	1.00	0.35	0.27	0.42	0.17

Note: PT, perspective taking; FS, fantasy scale; EC, emotional concern; PD, personal distress.
*$P < 0.05$

importance and survival value of detecting pain directly from the face of another person.

AI and ACC are widely accepted to contribute to the affective components of pain processing (Morrison and others 2004; Singer and others 2004; Jackson, Meltzoff, and Decety 2005), although activation in both ACC (Davis and others 1997; Peyron and others 1999; Longe and others 2001; Bantick and others 2002) and AI (Longe and others 2001; Bantick and others 2002; Brooks and others 2002) also seem to covary with attention to pain. During first-person pain experience, AI activation increases proportionally to intensity of the applied pain (for review, see Peyron and others 2000), as do subjects' own percepts of pain intensity (Coghill and others 1999).

In addition to pain, the AI is involved in the experience of disgust, both in first- and third-person perspectives (Krolak-Salmon and others 2003; Wicker and others 2003), as well as in integrating autonomic and visceral information (Mesulam and Mufson 1982). As a result, AI involvement with appreciation of others' pain is not surprising. Importantly, however, our findings suggest "alteroceptive" rather than interoceptive activation that has been typically assigned to insula (for a review, see Craig 2004).

Many functions of the ACC include activation during tasks related to affect, response selection, interoception, attention, conflict, and autonomic arousal (for a review, see Critchley 2004). Cytoarchitectonically, ACC comprises at least 6 regions (Vogt and others 1995, 2003; Gittins and Harrison 2004). In monkeys, the midcingulate cortex receives abundant input from the inferior parietal cortex (Vogt and Pandya 1987), and it can be further divided into 2 parts due to different neural discharging properties (Vogt and others 2003). In humans, the midcingulate skeletomotor region is usually activated during noxious stimulation (Hutchison and others 1999; Derbyshire 2000; Peyron and others 2000; Raij and others 2005) that suggests selection of motor response after pain (Vogt and others 2003). In our contrast provoked – chronic pain, the observed activation centered mainly on area 24 of the midcingulate cortex (see Fig. 2). In contrast, the activation that covaried with the pain intensity estimates was slightly more dorsal, corresponding to area 32 that has been claimed to signal the occurrence of conflicting input (for a review, see Botvinick and others 2004).

Besides responding to direct noxious stimulation, the ACC is also consistently implicated in processing of pain unpleasantness and affect (Rainville and others 1997; Fulbright and others 2001). The role of the ACC in coding subjective pain intensity is, however, controversial. Coghill and others (1999) showed ACC and AI involvement in coding of both subjective pain intensity and applied physical strength of the stimulus, whereas other studies have emphasized involvement of ACC in attentional (Peyron and others 1999) or modulative (Petrovic and Ingvar 2002; Rainville 2002) function of pain perception. Altogether, the information on pain intensity may require precursors from affect, feature extraction, attention, and motor control (Coghill and others 1999).

In our study, the subjects' estimates of pain intensity and pain distress in the observed pain faces did not differ, suggesting that these features are hard to differentiate from each other when they are mediated only by observing another person. When the direct sensory experience is missing, the intensity of another's pain can only be derived from the other person's overt expression of distress. Therefore, our results suggest involvement of the ACC, besides its multiple functions in the direct pain experience, also in estimating pain intensity in others.

The Relation of Motor Preparation to Pain

In the provoked – chronic pain contrast of our study, the SMA was activated bilaterally. In fact, the experience of pain has many connections with motor function; for example, experimental noxious stimuli activate the primary motor cortex (Raij and others 2004) as well as the midcingulate skeletomotor area (Hutchison and others 1999; Derbyshire 2000; Peyron and others 2000). Viewing faces expressing pain might thus trigger motor plans that facilitate escape or helping behavior, corresponding to the observed SMA activation in our study. Similarly, body positions expressing fear activate the SMA (de Gelder and others 2004), and so do the direct experiences of noxious stimuli (Becerra and others 1999; Coghill and others 1999; Kwan and others 2000; Ohara and others 2004). Thus, the interpretation of pain-induced motor preparation, suggested by previous work, is supported by our results.

Emotional Perspective Taking

The correlation of left IPL activity with pain intensity estimates could be related to emotional—rather than cognitive—perspective taking (see also Discussion on the correlations of empathy scales). During mental simulation of motor actions, the IPL is activated with left-hemisphere dominance for first-person perspective, and with right-hemisphere dominance for third-person perspective (Ruby and Decety 2003). In this sense, the left-hemisphere IPL correlation with pain intensity estimates in our study points toward the first-person perspective of pain and the related preparation for escaping or helping action.

Interpretation of the Facial Expression of Pain

In the provoked – chronic pain contrast, the IFG was activated bilaterally as a continuous cluster with the AI, but the strength of activation bore no relation to intensity estimates. IFG has an important role in the motor mirror-neuron system that likely supports understanding and imitation of action (Rizzolatti and Craighero 2004; Nishitani and others 2005); IFG, mainly area 44, is also effectively activated by still pictures of expressive faces that imply motion (Nishitani and Hari 2000). The right IFG has been specifically related to interpretation of facial expression (Nakamura and others 1999). The most consistent IFG activation in our study occurred in pars triangularis (Brodmann area 45) which, according to a recent meta-analysis of fMRI studies (Molnar-Szakacs and others 2005), is activated by observation of motor acts in contrast to the more posterior area 44 which, in addition to observation, is also related to imitation.

Empathy for Pain in Others

We found that the activation of the left AI-IFG region in subjects who viewed provoked pain faces correlated positively with the BEES (Mehrabian and Epstein 1972; Mehrabian 2000) as well as with the personal distress subscale of the IRI empathy questionnaire (Davis 1980), which measures individual's own discomfort at observing a negative experience of another. Singer and others (2004) also found a correlation between left AI activation and BEES and with the IRI empathic concern subscale, which samples compassion toward others. In our study, correlations of empathy subscales with brain activity varied across scales and brain areas, and only two of them reached statistical significance (personal distress subscale accounted for 48% and BEES scale for 37% of the variance of the signal strength in the left AI-IFG). Only 1 scale, cognitive perspective taking, clearly bore no relation to brain activation in any of the areas tested. Empathy is still a relatively loosely defined construct, with several models and measures in use whose content differs somewhat and whose psychometric properties are still to be fully described (Goubert and others 2005). Nevertheless, the consistency of our findings strongly suggests empathic processing of the pain face of a stranger.

Different IRI correlates of AI activation in our study and in the study by Singer and others (2004) agree with the separate features of empathy measured by the subscales. AI appears to be involved in more than one feature of empathy measured by the IRI, thus these findings seem supportive rather than controversial. Furthermore, the suggested hemispheric difference in the insular function (Jackson, Brunet, and others 2005) brings an interesting addition to these results. If the self-perspective engages the insula bilaterally and other-perspective activates only the right insular area as suggested by Jackson, Meltzoff, and Decety (2005), our results on bilateral insular response in both provoked – chronic pain contrast and the pain intensity–covariant model point to a lesser self/other boundary when viewing the faces of others than when mentalizing the perspective of another.

Situations where the subject has a close relationship with a person in pain (as in Singer and others 2004) might most likely evoke empathy, and those where the subject is viewing a painful cue applied to an isolated limb (Avenanti and others 2005; Jackson, Meltzoff, and Decety 2005) are perhaps less likely to show relationships between empathy and physiological responses. Our photos of chronic pain patients whose faces expressed long lasting suffering augmented by transient intensification of the pain, evoked strong distress in the observers (as suggested by AI-IFG and IRI subscale personal distress correlation, and the self-distress ratings of subjects) although the patients were unknown to them. Such findings confirm that the subjects truly internalized the other person's distress.

The Compassionate Brain

Even though pain is not as clearly recognized from the face as the other emotions and although others' suffering is often underestimated (Prkachin and others 1994; Kappesser and Williams 2002), we now demonstrate that the observers' brains react to the intensity differences in pain, when observed in the facial expressions of another human being. Our results agree with previous results of the existing shared sensory mirroring systems for pain. Moreover, they suggest that the encoding of another person's pain in the observer's brain is more detailed than has been previously thought: the observer's own brain circuitry for pain encodes, besides the occurrence of pain, also the intensity of pain suffered by another person.

Notes

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