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Empathy examined through the neural mechanisms involved in imagining how I feel versus how you feel pain

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Abstract

Perspective-taking is a stepping stone to human empathy. When empathizing with another individual, one can imagine how the other perceives the situation and feels as a result. To what extent does imagining the other differs from imagining oneself in similar painful situations? In this functional magnetic resonance imaging experiment, participants were shown pictures of people with their hands or feet in painful or non-painful situations and instructed to imagine and rate the level of pain perceived from different perspectives. Both the Self's and the Other's perspectives were associated with activation in the neural network involved in pain processing, including the parietal operculum, anterior cingulate cortex (ACC; BA32) and anterior insula. However, the Self-perspective yielded higher pain ratings and involved the pain matrix more extensively in the secondary somatosensory cortex, the ACC (BA 24a'/24b'), and the insula proper. Adopting the perspective of the Other was associated with specific increase in the posterior cingulate/precuneus and the right temporo-parietal junction. These results show the similarities between Self- and Other-pain representation, but most interestingly they also highlight some distinctiveness between these two representations, which is a crucial aspect of human empathy. It may be what allows us to distinguish empathic responses to others versus our own personal distress. These findings are consistent with the view that empathy does not involve a complete Self–Other merging. © 2005 Elsevier Ltd. All rights reserved.

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1. Introduction

The issue of how we perceive the pain of other people provides an avenue for tackling the neural mechanisms involved in empathy. By virtue of its aversive properties, pain promotes the organism's health and integrity, and also provides a signal that motivates others to behave prosocially (e.g., to comfort or help). However, one does not need to feel the sensory aspect of pain to understand the plight of the person in need; imagining the distress of that individual is often sufficient to evoke feelings of concern. Recently, a number of neuroimaging studies on pain processing have demonstrated partial neural overlap between the experience of pain in Self and the observation

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of pain in Others (Botvinick et al., 2005; Morrison, Lloyd, di Pellegrino, & Roberts, 2004; Simon, Rainville, Craig, & Miltner, 2005; Singer et al., 2004) and the evaluation of pain for others (Jackson, Meltzoff, & Decety, 2005).

Although the actual experience of pain and the perception of pain in other individuals tap similar brain regions, such as the ACC and anterior insula, different activation sites were also detected for Self and Other (Singer et al., 2004). Interestingly, none of these above mentioned studies reported involvement of the somatosensory cortex in perceiving the pain of Others, contrary to what might be predicted from the perception—action hypothesis (see Jackson & Decety, 2004; Preston & de Waal, 2002). The perception—action model posits that perception of emotion activates the neural mechanisms that are responsible for the generation of emotions. Such a system prompts the observer to resonate with the emotional state of another individual, with the observer activating the motor representations and associated autonomic and

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somatic responses that stem from the observed target, i.e., a sort of inverse mapping (Adolphs, 2002; Hatfield, Cacioppo & Rapson, 1994; Preston & de Waal, 2002). Furthermore, psychological research has demonstrated that perception of an action activates action representations to the degree that the perceived and the represented action are similar (Knoblich & Flach, 2003). This perception—action coupling constitutes one important component in the neural architecture underlying empathy (Decety & Jackson, 2004; Goldman & Sripada, 2005; Meltzoff & Decety, 2003; Preston & de Waal, 2002).

In this study, we draw upon the findings of similarities between imagination and actual production of behavior that accumulated in the last two decades (Hesslow, 2002), but we also leave room for complementary interpretation and limits of this sharing mechanism. A number of neuroimaging studies demonstrated that mental simulation of actions taps similar neural networks to those involved in action execution (e.g., Decety et al., 1994; Jackson, Lafleur, Malouin, Richards, & Doyon, 2001; Parsons, 1994; Parsons & Fox, 1998). Notably, one study showed that mental imagery of action engages the somatotopically organized sections of the primary motor cortex in a systematic manner as well as activates some body-part-specific representations in the nonprimary motor areas (Ehrsson, Geyer, & Naito, 2003). Evidence for similar congruence was found for visual perception (Kosslyn, 1996; Kosslyn & Thompson, 2003), auditory perception (Halpern, Zatorre, Bouffard, & Johnson, 2004), and olfactory processing (Bensafi et al., 2003). We therefore expect that imagining oneself in a painful situation taps into the neural mechanisms of pain processing.

However, imagining how another person feels and how one would feel oneself in a particular situation require distinct forms of perspective-taking that likely carry different emotional consequences (Batson, Early, & Salvarini, 1997a). Research in social psychology (Batson et al., 1997b; Underwood & Moore, 1982) has documented this distinction by showing that the former may evoke empathy (defined as an Other-oriented response congruent with the perceived distress of the person in need; see also Davis, 1996; Hodges & Wegner, 1997), while the latter induces both empathy and distress (i.e., a Self-oriented aversive emotional response). We believe that these different outcomes of perspectivetaking arise from a combination of similar as well as distinct cognitive and neural processing, thereby extending the current account of the perception-action model in the context of human empathy (Decety & Jackson, 2004).

2. Experiment 1—stimuli and tasks validation

We first conducted a behavioral experiment to test whether taking different perspectives while watching pictures of potentially painful scenarios leads to different ratings of pain. We expected that the perspective adopted by participants when they watched and assessed a painful scenario would influence their ratings of the perceived pain. It was anticipated that participants would give higher ratings during conditions in which they were asked to imagine themselves in painful situations than when the same situations were assessed while imagining the pain of someone else. Imagination of Self-pain should be more similar to the actual experience of pain than imagination of Other's pain. Consequently, the assessment of the level of pain should be easier and quicker for Self than for Other. Moreover, taking the perspective of a human being (ourselves or someone else) in painful situations should yield higher ratings than imagining an artificial limb in the same situations.

2.1. Methods

2.1.1. Participants

Thirty-four healthy individual aged 29 ± 6.5 years were recruited (20 females, 14 males). Participants gave informed consent according to the declaration of Helsinki.

2.1.2. Materials

A series of 96 digital color pictures showing right hands and right feet of people in painful and non-painful situations was used. All situations depicted familiar events that can happen in everyday life to people (e.g., pinching one's finger in a door, or catching one's toe under a heavy object). Various types (mechanical, thermal and pressure) and levels (neutral [no pain], low pain, medium pain, high pain) of pain inflicted to the limbs were depicted. Neutral pictures showed limbs in visually similar situations without pain component (e.g., a hand on the handle of a drawer as opposed to being caught in the same drawer). Using a picture editing software, the limbs were carefully centered and all pictures were then edited to the same size. Finally, a Gaussian filter was applied on the limb in order to reduce age and gender biases, and facilitate identification with the target. In addition, randomization and counterbalancing between conditions should even out this potential confounding factor across conditions of interest.

2.1.3. Procedure

Three different perspectives were manipulated through explicit instructions: the subject's own perspective (Self), that of a specific but unfamiliar person (Other), and that of a plastic limb (Artificial). In order to make the distinction between the three conditions more explicit, the Other was described to the participant as being a specific but unfamiliar individual, while Artificial limb referred to a plastic limb such as that of a manikin. Stimuli were presented with a computer running the Presentation software (Neurobehavioural SystemsTM) to manage the timing and presentation of the stimuli, as well as the recording of responses. Under each scenario a visual analogue rating scale ranging from "No Pain" to "Worst Possible Pain" was presented. Participants were instructed to evaluate the level of pain according to the perspectives previously

shown on an instruction panel. Note that in the Artificial limb trials participants were asked to rate the level of damage the scenario would inflict to the limb. Stimuli were grouped in blocks of four trials of the same condition. Each trial lasted 3 s and consisted of one of the pain scenarios. Prior to each block of trials, an instruction panel (2 s) informed the participants of the perspective they had to adopt (i.e., Self, Other, Artificial). The task was performed during four sessions of 15 blocks each. The limb and the level of pain of each trial were randomized across the experiment. Each different stimulus was presented three times (once per condition). Participants used two keys on the computer keyboard and used their left hand to move the cursor left or right on the scale. Note that the cursor initially appeared in the middle of the scale and the use of the left hand was favored in consideration for the next experiment (see Experiment 2). Participants were instructed to answer as quickly and as accurately as possible. Ratings and response times (ms) were recorded for each trial. The cursor position was later converted to a percent value and ratings were then normalized intra-individually within conditions. Each participant had a maximum of 3 s (trial duration) to enter each response after which the next trial would be presented. If no response was entered, an omission error was recorded and the trial was excluded from the analysis. Normalized ratings as well as response times were submitted to two-way repeated measure ANOVAs (Condition × Session) and a priori contrasts were computed the Bonferroni procedure. The alpha level was set at P < 0.05.

2.2. Results and discussion

Analysis on the normalized ratings showed a significant main effect of Condition (F(1, 33) = 233.4, P < 0.0001), as well as Session (F(1, 33) = 6.45, P < 0.05). The interaction did not reach significance level. Pair-wise comparison based on a priori hypotheses showed that participants gave higher ratings in the Self-condition than in both the Other- and Artificial-conditions, as well as higher ratings in the Otherthan in the Artificial-condition ([mean ± standard deviation]; Self $Z = 0.3170 \pm 0.1628$; Other $Z = 0.1488 \pm 0.1765$; Artificial $Z = -0.4187 \pm 0.1757$; P < 0.05). Analysis of the response times also showed significant main effects of Condition (F(1, 33) = 6.1, P < 0.05) and Session (F(1, 33) = 49.0, P < 0.05)P < 0.0001), but no Condition × Session interaction. Pairwise comparisons showed that participants were faster in the Self- $(1381 \pm 249 \,\text{ms})$ than in the Other- $(1466 \pm 261 \,\text{ms})$ and Artificial-conditions (1434 \pm 276 ms; P < 0.05), but that the response times in the Other- and the Artificial-conditions did not differ significantly. It was thus demonstrated that on average both human perspectives led to significantly higher ratings than the non-human artificial perspective. Moreover, participants rated the scenarios as being significantly more painful when they imagined themselves (Self) as opposed to someone else (Other), and they were faster at providing their ratings when imagining themselves, as opposed to someone else.

3. Experiment 2—functional imaging

We then conducted an fMRI experiment with naïve participants to investigate differences in blood oxygenation dependent level (BOLD) signal in the cerebral networks involved in the distinct perspectives from which pain can be assessed. Predictions can be organized in three levels: (1) We predicted that taking the Self-perspective, which is closer to the situation of Self-pain, should provide the strongest activation in the pain-related cerebral network. In light of previous work on pain representation (Jackson et al., 2005; Morrison et al., 2004; Singer et al., 2004), modulation of the BOLD signal is likely to be higher in regions involved in the affective aspects of pain processing such as the anterior cingulate cortex and the anterior insula. (2) We further predicted that the pattern of cerebral activity between assessing pain for Self and for Other should vary within regions known to play a role in perspective-taking. Notably, the posterior cingulated cortex, the right temporo-parietal region, as well as the frontal poles have previously been identified as key regions to this process (e.g., Decety, 2005). (3) Finally, we expected that taking the perspective of a human being as opposed to an artificial limb should result in stronger activation of pain-related regions, as well as within the systems important for perspective-taking and most importantly those involved in the attribution of affective states. The medial prefrontal cortex is acknowledged to plays a critical role in such processes (Frith & Frith, 2003).

3.1. Methods

3.1.1. Participants

Eighteen healthy right-handed volunteers (10 females, 8 males) aged between 18 and 31 years (M = 25.2, S.D. = 4.4) participated in the study. None had participated in previous experiments on related topics, including the validation of the stimuli and tasks described in Experiment 1 of the current paper. Participants gave informed written consent and were paid for their participation. No participant had any history of neurological, major medical, or psychiatric disorder. The study was approved by the local Ethics Committees, and conducted in accordance with the Declaration of Helsinki.

3.1.2. Materials

The same stimuli described in Experiment 1 were used in the functional MRI study. The design was also very similar except that a few minor changes were made to comply with fMRI methods and constraints as described below.

3.1.3. Scanning method and procedure

Participants took part in three consecutive mixed-design (i.e., event-related block design) fMRI sessions on the same day. The number of sessions (three as opposed to four in the previous experiment) was used to comply with a stricter counterbalancing and randomization of stimuli across sessions. The different stimuli (hands/feet; three levels of pain/no pain)

were randomized and counterbalanced across the sessions and were presented following an event-related design. The instructions for perspective-taking (Self, Other, Artificial) were blocked in order for participants to engage and maintain specific mental sets. Each block consisted of three trials preceded by an instruction screen (2 s) indicating the perspective from which participants had to imagine the scenario. The duration of each trial varied randomly between 3.6, 4.2, 4.8 and 5.4 s within each block in order to introduce jittering. The use of jitter in the design allows extraction of the signal from each event even though the stimuli are presented rapidly one after the other (Donaldson & Buckner, 2001). The order of the perspective condition was randomized within sessions and each was presented eight times for a total of 24 blocks per session. Note that each individual scenario was presented three times during the whole experiment, so that they were each assigned to all three perspective conditions (randomized between runs). For every trial, participants used a two-button response box under their left hand to move a cursor horizontally on the scale, which appears below the pictures. Use of left hand response was favored to reduce interaction with a possible somatotopic representation of the right hands in painful situations. Participants were instructed to answer as quickly and as accurately as possible. They were provided with several training trials prior to the scanning sessions in order to learn to use the rating scale and perform the task accurately and within the allotted time. Ratings and response times (ms) were recorded for each trial. The cursor position was later converted to a percent value and ratings were then normalized intra-individually within conditions. Participants had a maximum of 3 s (trial duration) to enter their response after which the next trial would be presented. If no response was entered, an omission error was recorded and the trial was excluded from the analysis. Normalized rating as well as response times were submitted to two-way repeated measure ANOVAs (Condition × Session) and a priori contrasts were computed with the Bonferroni procedure. The alpha level was set at P < 0.05.

3.1.4. fMRI data acquisition and analyses

MRI data were acquired on a 3 T head-only Siemens Magnetom Allegra System equipped with a standard quadrature head coil. Changes in blood oxygenation level-dependent (BOLD) T2* weighted MR signal were measured using a gradient echo-planar imaging (EPI) sequence (repetition time $TR = 2000 \,\text{ms}$, echo time $TE = 30 \,\text{ms}$, $FoV = 192 \,\text{mm}$, flip angle = 80° , 64×64 matrix, 32 slices/slab covering the whole brain including the cerebellum, slice thickness 4.5 mm, no gap, voxel size = $3.0 \, \text{mm} \times 3.0 \, \text{mm} \times 4.5 \, \text{mm}$). For each run, a total of 260 EPI volume images were acquired along the AC-PC plane. Structural MR images were acquired with a MPRAGE sequence (TR = 2500, TE = 4.38, FoV = 256 mm, flip angle = 8° , 256 × 256 matrix, 160 slices/slab, slice thickness = 1mm, no gap). Image processing was carried out using SPM2 (Wellcome Department of Imaging Neuroscience, London, UK), implemented in MATLAB 6.5 (Mathworks

Inc., Sherborn, MA). Images were realigned and normalized using the SPM templates. The normalized images of $2 \text{ mm} \times 2 \text{ mm} \times 2 \text{ mm}$ were smoothed by a FWHM $6 \times 6 \times 6$ Gaussian kernel. A first fixed-level of analysis was computed subject-wise using the general linear model with hemodynamic response function using event-related regressors for each of the conditions. Contrast images for each condition and the contrasts of interest for each participant were computed and transformed, after spatial normalization, into standard (MNI152) space. First-level contrasts were introduced in second-level random-effect analysis to allow for population inferences. One-sample t-tests including all subjects for each of the contrasts of interest, which yielded a statistical parametric map of the t-statistic (SPM t) were computed. A voxel-level threshold of P < 0.001 uncorrected for multiple comparisons (t = 3.65) and an extent threshold of k > 5 were used to identify significant activity changes in pain-related regions based on the results of previous studies (Jackson et al., 2005; Morrison et al., 2004; Singer et al., 2004). A threshold of P < 0.05 corrected was used for other brain areas.

Parametric analyses were also performed to determine the brain regions whose activity varies with the pain-ratings given by the participants during either the Self- or the Othercondition. Normalized ratings were introduced in first-level parametric analyses, at the subject level, taking into account only trials from Self- and Other-conditions. First-level statistics were introduced into second-level random effects analysis, which consisted of one-sample t-tests including all participants, for each condition separately. A voxel-level threshold of P < 0.001 uncorrected for multiple comparisons (t = 3.65) and an extent threshold of k > 5 voxels were used to identify clusters of activation within regions of interest based on a priori hypotheses. A threshold of P < 0.05 corrected was used for other brain areas.

Time courses in specific regions of interest were computed with MarsBaR region of interest toolbox v0.36.1 (http://www.sourceforge.net/projects/marsbar) for SPM2. The regions of interest were extracted from the corresponding clusters found in SPM contrasts (threshold P < 0.001). Thus, only data from significantly activated voxels were used to compute time courses. To compute individual time courses the percent signal change related to a specific category of event (i.e., Self and Other trials) was computed for a given participant at each time point. Then, individual time courses were averaged across the 18 participants to produce the mean hemodynamic response associated with an event.

3.2. Results

3.2.1. Behavioral results

This experiment replicated most of the behavioral results of Experiment 1. Analysis on the normalized subjective ratings showed significant main effects of Condition (F(1, 17) = 460.66, P < 0.0001), and Session (F(1, 17) = 8.78,

P < 0.01). The interaction did not reach significance level. Bonferroni contrasts on the normalized ratings showed that participants rated the scenarios as significantly more painful in the Self- than in the Other-condition, and also rated both of these conditions significantly higher than the Artificial one (Self $Z=0.4911\pm0.1696$; Other $Z=0.1719\pm0.2261$; Artificial $Z = -0.6631 \pm 0.2072$: P < 0.05). Analysis of the response times showed a significant main effect of Session (F(1, 17) = 36.16, P < 0.05), but not of Condition, nor of the Condition × Session interaction. Bonferroni a priori contrasts confirmed that participants were significantly faster at providing a rating when adopting the Self-perspective versus the Other-perspective (P < 0.05), and marginally faster in the Self- than in the Artificial-condition (P = 0.16). Response times did not differ significantly between Other and Artificial (Self = 1377 ± 233 ms; Other = 1469 ± 212 ms; Artifi $cial = 1439 \pm 183 \text{ ms}$).

3.2.2. Regions involved in pain representation

The BOLD signal elicited by the painful nature of the stimuli was first assessed by contrasting the hemodynamic response to the painful stimuli with those that did not depict any pain (Neutral), for both Self- and Other-perspectives combined. Significant changes in signal intensity were detected in a number of brain regions related to pain processing (Table 1), including the ACC (Brodmann's area 32; BA32), anterior insula, ventral striatum, thalamus, parietal operculum, posterior parietal cortices and cerebellum. In addition, changes in activity were observed in the inferior frontal gyrus bilaterally. Note that hand versus foot contrasts did not yield robust findings related to a possible somatotopic organization of the pain representation and those conditions were collapsed thus forth. Note that the same analyses performed separately with the Self- and the Other-conditions also yielded bilateral activation of the posterior parietal cortex, the anterior insula, and the anterior cingulate (not shown).

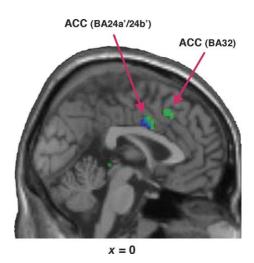


Fig. 1. ACC activity in pain representation is related to pain intensity. Cluster of activation in the contrast Self-pain vs. Other-pain (blue; x = 0, y = 0, z = 36 [t = 4.33]) and different clusters from the parametric analysis for the Self-condition (green). Coordinates in MNI system refer to local cluster maxima.

3.2.3. Parametric analyses of the pain representation

In order to further support the interpretation that the changes in activity reported in the pain-related regions are related to the intensity of the pain depicted, parametric analyses were performed for the Self- and the Other-conditions using each participant's normalized ratings (Fig. 1). These analyses confirmed that changes in activity in both the insula and the ACC were related to the level of pain imagined but some interesting differences were noted between the patterns of results from the Self- and Other-conditions. Activation in the anterior insula was restricted to the right hemisphere for the Other-condition, while it was found bilaterally for Self. Moreover, activation in the medial wall was restricted to the paracingulate/SMA region (BA 32) in the Other-condition, while for the Self an additional and spatially distinct cluster was found in the ACC (BA 24a'/24b'). Note that

Table 1 Pain-related sites of activation

Pain-related regions	L/R	MNI coordina	t-Score		
		\overline{x}	у	z	
Anterior cingulate cortex (BA 32)	L	-6	24	39	6.62
Anterior cingulate cortex (BA 32)	R	6	21	42	6.41
Anterior insula	R	33	21	0	8.31**
Anterior insula	L	-30	18	3	7.22**
Inferior frontal gyrus	R	60	12	24	7.73**
Inferior frontal gyrus/anterior insula	L	-48	9	3	7.90**
Ventral striatum	L	-21	9	0	4.24
Ventral striatum	R	15	6	0	4.53
Thalamus	L	-12	-12	0	4.30
Parietal operculum	R	63	-18	36	6.17
Parietal operculum	L	-60	-21	33	7.69**
Posterior parietal cortex	R	42	-45	51	5.53
Posterior parietal cortex	L	-30	-51	54	6.99
Cerebellum	L	-36	-48	-39	4.99

Clusters of significant signal change in the right (R) and left (L) hemispheres, from anterior to posterior coordinates, when the participants watched painful stimuli vs. neutral stimuli, for the Self- and Other-conditions collapsed (voxel threshold P < 0.001 uncorrected [t = 3.65]; [k > 5]; **P < 0.05 corrected [t = 7.14]).

Table 2 Self vs. Other contrast

Region	L/R	MNI coordinates			t-Score
		x	у	z	
Insula	R	42	3	-6	4.42
Insula	L	-42	3	-6	4.51
Insula	L	-42	-3	12	4.48
Anterior cingulate cortex	L/R	0	0	36	4.33
(BA 24a'/24b')					
Globus pallidus/thalamus	L	-21	-15	3	3.89
Parietal operculum/SII	L	-63	-24	36	6.41
Parietal operculum/SII	R	66	-27	42	4.39
Parietal operculum/SII	R	63	-30	27	4.56
Postcentral gyrus	R	30	-36	63	3.93
Postcentral gyrus	L	-15	-54	66	4.35

Clusters of significant signal change in the right (R) and left (L) hemispheres, from anterior to posterior coordinates, when the participants watched painful stimuli and imagined it from the Self-perspective vs. the Other-perspective (voxel threshold P < 0.001 uncorrected [t = 3.65]; [k > 5].

neurons that respond specifically to painful stimulation have been identified with intracortical electrodes recordings in a very similar region of the ACC (Hutchison, Davis, Lozano, Tasker, & Dostrovsky, 1999; x=3-5, y=3-13, z=26-36).

3.2.4. Self versus Other

Direct contrast between imagining Self and imagining Other in painful situations also revealed clusters of activation in a number of pain-related regions of interest (Table 2). Activations associated with the Self-condition were detected in the ACC (BA 24a'/24b'; in the same region identified through the parametric analysis; Fig. 1), the insula bilaterally (Fig. 2A), the left striatum, as well as in the parietal operculum/SII bilaterally (Fig. 2B). The reverse comparison (i.e., Other versus the Self in painful situations) resulted in bilateral clusters of activity in the posterior cingulate/precuneus and in the right temporo-parietal region, as well as a cluster in the middle frontal gyrus (Table 3).

Table 3
Other vs. self contrast

Region	L/R	MNI coordinates			t-Score
		x	у	z	
Middle frontal gyrus (BA 8)	R	51	18	48	4.75
Supramarginal gyrus (temporo-parietal junc)	R	48	-57	27	5.18
Sup temporal gyrus (temporo-parietal junc)	L	-45	-60	27	3.89
Inferior parietal lobule	L	-51	-69	39	4.60
Posterior cingulate/precuneus	L	-12	-60	36	7.23**
Posterior cingulate/precuneus	R	3	-66	39	6.16

Clusters of significant signal change in the right (R) and left (L) hemispheres, from anterior to posterior coordinates, when the participants watched painful stimuli an imagined it from the Other-perspective vs. the Self-perspective (voxel threshold P < 0.001 uncorrected [t = 3.65]; [k > 5]; **P < 0.05 corrected [t = 7.14]).

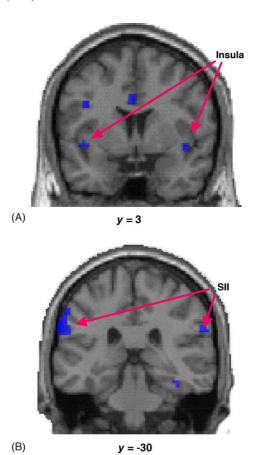


Fig. 2. Greater pain representation in the Self-condition. (A) Bilateral clusters of significant activation in the insula proper for the contrast Self-pain vs. Other-pain. (B) Bilateral clusters of significant activation in secondary somatosensory cortex (SII) for the contrast Self-pain vs. Other-pain.

3.2.5. Human perspectives versus artificial limb

The contrast between imagining Self and Other in painful situations versus imagining damage to an artificial limb points out the neural activity associated with adopting the perspective of a human being (Fig. 3). Part of our hypothesis is thus confirmed, showing significant clusters in the medial prefrontal cortex (MPFC) bilaterally (centered at x = -12, y = 54, z = 36 and x = 9, y = 57, z = 39), extending laterally in the left hemisphere, as well as in the posterior cingulate cortex bilaterally (x = -6, y = -51, z = 24, and x = 12, y = -48, z = 27, as well as x = 0, y = -15, z = 39). Finally, additional clusters were located in the inferior parietal lobule bilaterally (x = -57, y = -66, z = 21, and x = 48, y = -54, z = 24).

4. General discussion and conclusion

Our study showed that taking the Self-perspective while assessing the pain of hands and feet in potentially harmful situations reliably yields higher subjective ratings and shorter response time than when the perspective of another person is adopted. One interpretation for the higher ratings is that imagining painful scenarios from a Self-perspective is more

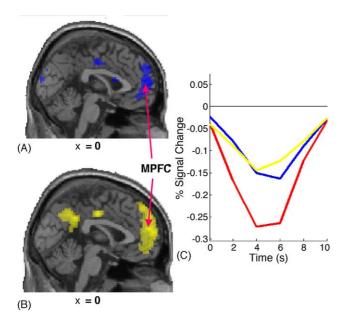


Fig. 3. Medial prefrontal activity related to taking a human perspective. (A) Cluster of significant activation in the medial prefrontal cortex (MPFC) for the contrast Self-pain vs. Artificial damage and (B) for the contrast Other-pain vs. Artificial damage. (C) Hemodynamic response in the medial prefrontal cortex at x = 9, y = 57, z = 39 for the Self- (blue), Other- (yellow) and Artificial- (red) conditions.

closely related to the one's own actual experience of pain than taking the perspective of a stranger. Similarly, the faster response times in the Self-condition suggest that less computation has to be performed in order to determine a pain rating from this perspective. Assessing the pain of Others is likely to require an additional frame of reference (which can be the Self, or not), which is not necessary when assessing pain in Self.

Further, our study demonstrates that imagining the Self and imagining the Other in painful situations are both associated with activation of the pain-related neural network. These findings are compatible with previous neuroimaging studies on pain perception, whether it is actually experienced (Morrison et al., 2004; Rainville, Duncan, Price, Carrier, & Bushnell, 1997; Singer et al., 2004), visually perceived (Botvinick et al., 2005; Jackson et al., 2005; Morrison et al., 2004), inferred (Singer et al., 2004), or even conveyed by words (Osaka, Osaka, Morishita, Kondo, & Fukuyama, 2004). Furthermore, the fact that we obtained similar findings with imagined pain is compatible with the general assumption of the simulation theory. This theory states that behavior can be simulated by activation of the same neural resources for acting and perceiving, and in both cases yield its expected consequences (Hesslow, 2002).

Yet, one important aspect of our findings, which adds to this interpretation, is the differentiation between imaging the Self and Other in pain. The similarity between pain processing related areas is more extensive when participants imagined themselves in a painful situation than when they imagined the Other in the same situations.

Differences in the neural responses between the two perspectives are organized on two different levels. First, imagining Self engaged the pain matrix more extensively than imagining Other as evidenced by specific activity in the ACC (BA 24), insula proper, thalamus, as well as in the secondary somatosensory cortex. The latter two brain areas are considered part of the sensory component of pain processing (Bushnell et al., 1999). This suggests that the Self-perspective drives participants to tap beyond the affective aspects of pain processing and is able to trigger part of the sensory aspects as well. Further evidence for this interpretation comes from the results of the parametric analyses, which showed a relationship between the ACC (BA 24a'/24b') and the pain rating of subjects, but only in the Self-condition. Activation in the ventral striatum, which is part of the limbic system and involved in reward mechanisms, is another evidence that Selfperspective taps into affective processes to a greater extent than Other-perspective.

Another difference between the two perspectives emerges from the activation patterns within the insula. While the Self-perspective engages the insula bilaterally, it seems that the Other-perspective involves mainly the insula in the right hemisphere. One interpretation for this difference could be that, while the insula is generally involved in representing the homeostatic state of the body from its sensory pathways, only the right insula would serve to compute a higher order "metarepresentation of the primary interoceptive activity", which is related to the feeling of pain and its emotional awareness (Craig, 2003). Thus, activation of the left insula in the Self-condition only could be interpreted as further evidence of a partial sensory representation specific to this condition.

Failure to observe any activation of the primary somatosensory cortex in imagined pain conditions is not too surprising. In fact, even actual noxious stimuli yield inconsistent results in the neuroimaging literature. One of the interpretations for this inconsistency is that the different tasks used across experiments vary in terms of the type and the focus of the attention required from the subjects (Bushnell et al., 1999). The hypothesis is that SI would be involved when subjects are required, for instance, to make a fine discrimination judgment about the location or the type of pain (i.e., sensory aspects of pain). When attention is drawn mainly to the affective components of pain, as it is likely the case in our study (with the exception of the Self-condition), then less change in SI would be expected. However, some contemporary models of pain processing (e.g., Price, 2002) do not view the affective and sensory components as two processes based on distinct parallel pathways, but rather suggest that the extensive networks that subserve pain mechanisms involve both serial and parallel circuitry that are themselves modulated by other regions. Recently, a transcranial magnetic stimulation study reported changes in corticospinal motor representations of hand muscles in individuals observing needles penetrating hands or feet of a human model (Avenanti, Bueti, Galati, & Aglioti, 2005). This shows that the observation of pain can involve the somatosensory-motor representations.

Second, imagining the Other in painful situations as compared to neutral ones yielded activations restricted to the affective component of pain-processing. This affective component is mediated notably by the ACC and the insula (Rainville, 2002). Moreover, as compared to Self, this condition was associated with greater activations in the right temporo-parietal region, which is known to play a crucial role in perspective-taking and the sense of agency (Blanke & Arzy, 2005; Decety, 2005; Decety & Sommerville, 2003; Jeannerod, 2003; Meltzoff & Decety, 2003).

The fact that there is a partial overlap between imagining the Self and imagining the Other is coherent with the shared representations theory (see Decety & Sommerville, 2003; Jeannerod, 1999). The non-overlapping part of the neural circuit, including the right temporo-parietal area, is hypothesized to play a critical role for the sense of agency and self-identification (see Jeannerod & Pacherie, 2004). We believe that agency is an important aspect of our theory of empathy, which postulates that affective sharing must be modulated and monitored by a sense of whose feelings belong to whom (see Decety & Jackson, 2004).

The stronger involvement of the medial prefrontal cortex extending to the frontal poles in imagining Self and Other compared to an artificial limb supports its role in the attribution of mental states (Frith & Frith, 2003), which are not imagined when the stimulus is processed as an artificial object. A number of brain imaging studies as well as clinical neuropsychological examinations have confirmed that a rather restricted group of brain regions (notably the medial prefrontal cortex) are reliably activated when individuals perform a variety of theory of mind tasks (e.g., Brunet, Sarfati, Hardy-Baylé, & Decety, 2000; Happé, Brownell, & Winner, 1999). A recent functional MR study has documented the specific involvement of the medial prefrontal cortex while adults watched video-clips of human interaction, but not when the clips depicted robots (Han, Jiang, Humphreys, Zhou, & Cai, 2005). In addition, the cluster found in the human conditions extends to the most anterior aspect of the medial prefrontal cortex, into the frontopolar cortex. There is evidence that this latter region is generally involved in the process of evaluation of self-generated responses, and is recruited when the task requires monitoring and manipulation of information that has been internally represented (Christoff & Gabrieli, 2000). It is worth mentioning that the apparent activation of the medial prefrontal cortex has been shown to reflect less deactivation of this region compared to the contrast condition in a number of studies (e.g., Pochon et al., 2002). Although specific details of the experimental design are required to be able to demonstrate this (such as a fixation cross baseline, which was not present in the current design), this alternate interpretation cannot be excluded, especially in light of the time course plotted for this region (Fig. 3C).

Altogether, our findings can also be interpreted based on the theory that two different emotional responses can be expected when taking the perspective of Self and that of Other (Batson et al., 1997a). These in turn can be linked to the distinction between empathy and personal distress. Previous studies in social psychology demonstrated that imagining how you would perceive a situation in the Other's position and how you would feel as a result leads to more physiological arousal and engenders different emotional constellation than imagining how the Other perceives the situation and feels as a result (Batson et al., 1997b). Focusing on our own thoughts and feelings reduces empathy, whereas focusing on those of distressed Others increases empathy (Thompson, Cowan, & Rosenhan, 1980). Recent cognitive neuroscience research has found that imagining actions (Ruby & Decety, 2001), beliefs (Ruby & Decety, 2003), feelings (Ruby & Decety, 2004), or food preferences (Seger, Stone, & Keenan, 2004) from the first (Self) and third person (Other) perspectives produce some overlap in terms of brain activation patterns. However, the posterior cingulate, right temporo-parietal junction, and prefrontal cortex are generally associated with third-person perspective. It can be argued that the more extensive involvement of pain-related regions that share connections with limbic structures (such as the insula, and the ventral striatum) when imagining the Self is associated with feelings of discomfort that arise from this egocentric perspective. Note that in the present experiment, the Self-condition was associated with stronger subjective ratings of pain, and that the clusters in both the insula and the ACC (BA 24a'/24b') correspond to subregions subserving visceral responses (Dupont, Bouilleret, Hasboun, Semah, & Baulac, 2003; Paus, 2001) and pain processing (Hutchison et al., 1999). Importantly, the part of the anterior cingulate gyrus specifically activated by Self-perspective contains pyramidal neurons that project directly and indirectly to subcortical brain regions associated with homeostasis and autonomic control, including the hypothalamus, and periaqueductal grey matter (Vogt, Hof, & Vogt, 2004). A number of studies with both healthy controls and patients have shown that this aspect of the ACC is implicated in mediating changes in arousal according to context as evidenced changes in heart rate (e.g., Critchley et al., 2003). It is thus interesting that this region is specifically recruited during Self-perspective, which is hypothesized to trigger emotional distress. Combined with the result of the parametric analysis, showing a correlation between pain ratings and activity in this region again specific to the Self-condition, the findings support the idea that the Self-condition put participants in a significantly different emotional state than the Other-condition.

It thus seems that changes in the perspective adopted by the subjects modulate the evaluation processes related to pain, and consequently the brain response associated to those processes. However, it remains difficult to convincingly tease apart modifications of the BOLD signal which are related to the changes in perspectives itself from those that are associated with different degrees of pain ratings (and likely stimuli-related arousal). Matching the subjects' responses in the different perspective conditions with regards to pain ratings, and then comparing the effect of changing the perspective would be worth exploring in future studies.

Our results nevertheless strongly suggest that empathy for pain does not rely on a full overlap between Self and Other. This is in agreement with a number of scholars who have argued that to experience empathy, Self and Other must be distinguished rather than merged (Batson et al., 1997a; Decety, 2005; Decety & Jackson, 2004; Ickes, 2003; Reik, 1949). By contrast, experiencing another's person's pain or distress in the same way as one's own experience would lead to "empathic over-arousal," in which the focus then becomes one's own feelings of stress rather than the Other's need (Eisenberg, 2000). This further argues that Selfperspective elicits a more egocentric affective response than when empathizing for others. Consistent with this idea, imagining Self in pain was associated with a cluster of activation in the left parahippocampal gyrus (albeit this cluster did not reach our strict threshold for whole brain analysis), a region known to play a key role in emotional episodic memory retrieval (Smith, Henson, Dolan, & Rugg, 2004). In light of our findings, it would be worthwhile to investigate further the role of memory and experience in the empathic response to pain, which stems from the conflict between the short-term goal of avoiding unpleasant situations for the Self and the motivation to feel for the Other.

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