



## Topical review

# To what extent do we share the pain of others? Insight from the neural bases of pain empathy

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## 1. Introduction

In the representationalist framework generally adopted in cognitive neuroscience, pain is conceived as a subjective experience triggered by the activation of a mental representation of actual or potential tissue damage (nociception). This representation may involve somatic sensory features, as well as affective-motivational reactions associated with the promotion of protective or recuperative visceromotor and behavioral responses. Mental representation of nociception may provide the primary referent from which a rich associative network can be established to evoke the notion of pain in the absence of a nociceptive stimulus.

Here, we adopt the notion of a mental representation of pain<sup>1</sup> as a means to relate the experience of pain in oneself to the perception of pain in others. We review the functional neuroimaging studies supporting the hypothesis that the perception of pain in others relies at least partly on the activation of a mental representation of pain in the Self, and thus on common neural systems. However, we also demonstrate that there are

systematic differences in activation sites within pain-related areas that must be considered for a better understanding of the mechanisms underlying pain empathy.

## 2. Cerebral networks underlying the representation of pain

Neuroimaging studies performed in normal volunteers using pain stimuli demonstrate that nociceptive information is processed in several brain areas including the thalamus, contralateral primary somatosensory cortex (S1), secondary somatosensory cortices (S2), insula (IC), anterior cingulate cortex (ACC), as well as some prefrontal areas (Apkarian et al., 2005). Several studies further indicate that nociceptive responses in this network are strongly correlated with the subjective reports of pain and that different parts of the network code more specifically, but not exclusively, sensory (e.g., S1) and affective (e.g., ACC) aspects of this experience (Rainville, 2002). Activity in this network is highly sensitive to top-down processes, consistent with the notion that the mental representation of nociception and the pain experience result from the interaction between noxious sensory inputs and cognitive factors. However, studies have also shown that pain-related cortical responses may be evoked in the absence of a painful stimulus when a painful experience is anticipated (see Apkarian et al., 2005), and that this anticipatory activity seems correlated with the magnitude of the pain expected (Koyama et al., 2005). Activation of this mental representation of Self-experienced pain and its related

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<sup>1</sup> Note that pain is not a representation but a conscious experience. Here we use « representation of pain » to refer to a mental representation of nociception, the activation of which is normally associated with the experience of pain.

neural systems provides the fundamental means allowing us to relate to the pain of others.

### 3. Shared neural circuits

In recent years, many studies have documented that perception of a given behavior in another individual automatically activates one's own representation of that behavior (Jackson and Decety, 2004). Further support for this model was provided for different emotions (e.g., Carr et al., 2003; Ruby and Decety, 2004). These shared neural circuits between self and other prompt the observer to resonate<sup>2</sup> with the emotional state of others, and constitute one important component of the cognitive architecture underlying empathy (Preston and de Waal, 2002; Decety and Jackson, 2004; Goubert et al., 2005).

Current evidence shows that the perception of pain in others relies partly on the neural systems activated by noxious stimuli and involved in pain experiences (Lamm et al., in press; Morrison et al., 2004; Singer et al., 2004; Botvinick et al., 2005; Jackson et al., 2005). These findings are consistent with the idea that the perception of pain in others taps into the affective component of pain processing, notably through activation of the ACC and anterior IC. Furthermore, ACC activity was found to correlate with the intensity of the pain observed, as rated by the observer (Jackson et al., 2005).

### 4. ACC and insula contributions to pain representation

Peaks of activations in the ACC and IC reported in different neuroimaging studies were plotted together to examine possible distinctions between activity changes reported for pain in Self and perception of pain in others (Fig. 1). Activation sites in the ACC follow a clear caudo-rostral organization based on the target of the pain: Self or Other (Fig. 1A). Perception of pain in Self is associated with more caudal and somewhat more ventral activation, consistent with spino-thalamo-cortical nociceptive projections to Brodmann Area (BA24), while perception of pain in others is represented in two distinct clusters within more rostral regions of ACC (peri-genu BA24/BA33; subcallosal BA32/BA25). Interestingly, the mental imagination of Self-pain mapped onto the more caudal cluster of ACC (Jackson et al., 2006), consistent with the proposed self-other distinction.

<sup>2</sup> The term "resonance" is often used in the scientific literature related to the mirror neurons. We find it useful here as it conveys both the idea of a physical/physiological property (the reproduction in the observer of a pattern similar to the target), as well as a psychological relationship (i.e., relation of mutual understanding or trust and agreement between people).

Fig. 1B also demonstrates a rostro-caudal organization in the left IC, based on the target of the pain, with more caudal regions (posterior to mid-insula) activated for Self pain and more anterior regions for pain in others. The map of the right IC (Fig. 1C) shows a slightly different organization. While the anterior organization seems to hold in part for the pain in other conditions, the peaks of activation for pain in Self are found along the full caudo-rostral extent and regrouped on the most dorsal part of the IC, displaying a ventro-dorsal organization. Interestingly, painful sensations are evoked by direct electrical stimulation in the dorsal and posterior part (but not anterior) of the insula in epileptic patients (Ostrowsky et al., 2002).

### 5. Differences between Pain in Self and Pain in others: what is Pain Empathy?

The available evidence for shared pain representations shows that pain-related activations within the ACC and IC are systematically more posterior when noxious stimuli are applied, imagined, or suggested to Self than to others. Evidence for such a rostro-caudal organization adds nuance to the conception that the perception of pain in others involves comparable cerebral systems than the first-hand perception of nociceptive stimulation.

Several functional models of the ACC and IC have been proposed (e.g., Bush et al., 2000; Craig, 2002; Vogt, 2005), but our review suggests a new organization based, not on the constructs of emotion, motor, attention and monitoring, but on the subject of the experience (self vs other) and consequently the experiential proximity, tangibility, or self-embodiment of the pain. We argue that the self vs other distinction forms a continuum along which other forms of pain representation can also be mapped. There is a proximo-distal continuum of triggers for the representation of pain with somatic inputs (e.g., nociceptive pain) producing the more robust activation of pain representation and a corresponding vivid pain experience, and pain-related cues (e.g., the word "pain") producing a weaker activation of pain representation. Moreover, it is clear that pain in Self is not restricted to pain felt during a nociceptive stimulation but also extends to the mental evocation of pain from a self-perspective (Jackson et al., 2006). Other forms of pain or suffering, such as that associated with social exclusion (e.g., Eisenberger et al., 2003), might also be characterized by a similar functional organization.

How does the self-other distinction relate to the sensori-discriminative and motivational-affective components of pain? Does pain in Self imply more robust activation of areas subserving sensory component of pain? Most of the fMRI data reviewed here were interpreted in favor of the view that pain representations triggered from the observation of pain in others are mostly

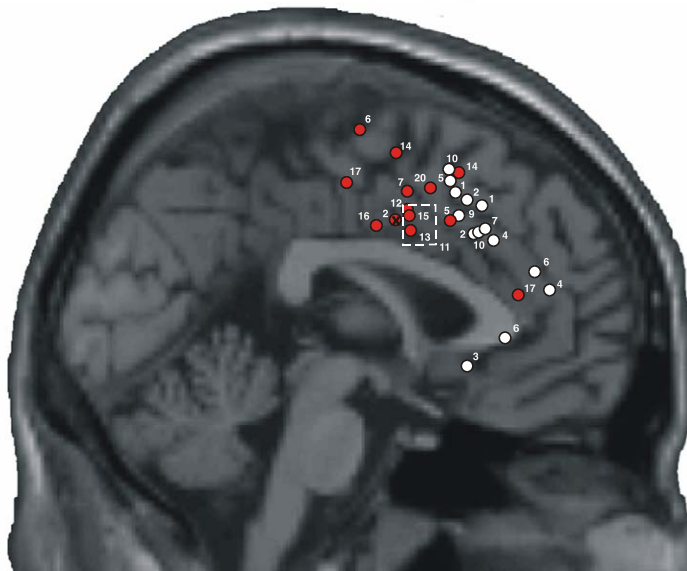
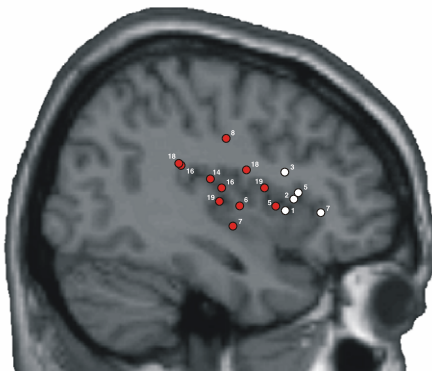
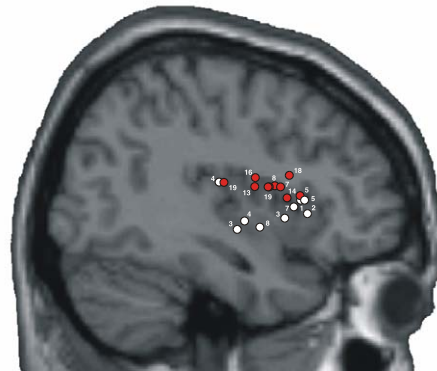
**A Anterior cingulate cortex****B Left insula****C Right insula**

Fig. 1. Coordinates for the peaks of activation in the ACC and IC were taken from 10 studies that explored the perception of pain in others as well as 10 key papers on the cerebral response to nociceptive stimuli (see Supplemental Material for a complete list of references). It is worth noting that these studies used various stimuli to induce pain in the self and evoke pain in others, and they relied on various experimental designs, tasks, and analysis parameters (see Table 1 in Supplemental Material). The reported coordinates for the peaks of activation were converted from Talairach to MNI coordinates when necessary using the formula developed by Matthew Brett (<http://www.mrc-cbu.cam.ac.uk>). Red dots, Pain in Self; Red dot marked with an “x” = Self vs Other condition in Jackson et al. (2006); White dots, Pain in Other; White dash square, coordinate range from Hutchison et al. (1999). (A) ACC: Peaks from both hemispheres were selected within 15 mm of the midline. No distinction was made between left and right hemisphere activations, and all peaks were mapped onto a representative middle sagittal section of the MNI template. ( $x = 0$ ). IC: left (B) and right (C) hemisphere activations were mapped separately on sagittal sections of the MNI template ( $x = 40$  and  $x = -40$ , respectively).

affective in nature. This implies that the perception of pain in others reaches beyond a direct matching of the Self pain representation, and could explain, for instance, the failure to find S1 activation or any somatotopic organization in the pain observation conditions. However, results from a study in which participants were asked to change the perspective they adopted while assessing painful scenarios did yield activation of S2 specific to the Self condition (Jackson et al., 2006). Moreover, results from two recent transcranial magnetic stimulation (TMS) studies have challenged this view (Avenanti et al., 2005, 2006). The authors proposed that pain

observation is highly bottom-up (stimulus-driven) because motor changes (reduction in amplitudes of motor-evoked potentials) were found to be specific to the muscle that was being targeted in the observed scenarios. Even though these changes correlated with rating of pain intensity, the relationship between the motor changes and somatosensory processing during pain observation has yet to be clarified. Failure to find sensory (and primary motor) activation in fMRI studies on pain empathy is perhaps related to a difference in threshold of activation and specificity of the stimuli used, which differ between fMRI and TMS. Primary

and secondary sensory areas are more strongly bounded by sensory inputs and stimuli that focus on a specific sensory target, while areas related to pain-affect may be more susceptible to internally generated global evocation of the pain representation.

Our interpretation for a rostro-caudal functional organization of the ACC and IC is also compatible with the bulk of evidence from studies on mentalizing (Amodio and Frith, 2006). Indeed, there is strong support for a predominant role of the medial prefrontal cortex (MPFC) in tasks requiring inference of the mental states of others. Observation and more specifically explicit assessment of the pain of others requires this type of cognitive processing and it is likely that connections between the MPFC and key pain regions such as ACC and IC are found mainly at the most anterior sites of these latter two regions (Vogt, 2005). A similar shift from posterior to anterior regions of the insula cortex as the activity is re-represented to guide the subjective evaluation of the interoceptive state was proposed (Craig, 2002). We suggest that the functional organization in the ACC and IC is based on the level of abstraction and the self-proximity with the pain experience.

One important consideration for the interpretation of the results on pain representation is related to the dual function of pain communication (e.g., Prkachin and Craig, 1995; Williams, 2002). Seeing another individual in pain in a naturalistic context can alert us of danger and promote a withdrawal response. This response is likely automatic (and non-conscious) and relies on more basic cerebral systems such as the amygdala and motor regions like M1 and supplementary motor area (SMA) [c.f., Simon et al., *in press* for an fMRI study on the implicit processing of pain and angry facial expressions]. Activation in the mid-ACC in conjunction with the pre-SMA is not necessarily specific to the first-hand experience of pain, but is related to other processes such as somatic monitoring, negative stimulus evaluation, and the selection of appropriate skeletomuscular movements of aversion (Isomura and Takada, 2004). In more controlled situations, as in most experiments where the observation of pain in others does not signal a threat to the observer, this automatic response is likely reduced. However, such situations do favor prosocial responses or attitudes towards the person experiencing pain, which perhaps qualifies better as pain empathy. Perspective-taking instructions as in the studies by Jackson and colleagues (2006) and Lamm and colleagues (*in press*) have demonstrated that one can consciously revert to a more “basic” route by focusing on the self-perspective as opposed to the others’.

A final argument which supports the notion that Self pain and others pain, while sharing some similarities, do not completely overlap is based on the fact that should pain resonance be complete and uncontrolled, emotional distress could result from the mere observation of others

in pain. Such an extreme response of being overwhelmed by the painful states of others would not be adaptive in most cases. Some level of sharing the other person’s pain without complete mapping onto oneself is likely necessary to allow for a controlled empathic response (Goubert et al., 2005; Decety and Jackson, 2006).

## 6. Conclusions

The comparison between the cerebral systems subserving the representation of pain in Self and pain in others is important for understanding not only the pain experience, but more broadly empathy. The appeal of the shared representation model renewed by the discovery of mirror neurons in monkeys may cast shadow over the sometimes subtle but crucial differences between the cerebral basis for a behavior and that of its mental evocation. Finally, our understanding of the relationship between pain in Self and pain in others should also evolve through the study of clinical populations (e.g., Danziger et al., 2006), as well as cross-species mechanisms (Langford et al., 2006).

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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.2006.09.013](https://doi.org/10.1016/j.pain.2006.09.013).

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