The role of anterior insula and anterior cingulate in empathy for pain


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The understanding of others’ feeling and emotional states is commonly defined by the term ‘empathy’. Here, I discuss recent findings regarding the differential contribute of anterior insula and anterior cingulate cortices to this function. For the first time, Gu and colleagues showed no direct involvement of the anterior cingulate during observation of other’s pain and propose the anterior insula as the main neural substrate for the mental representation of empathy.

Empathy allows us to predict the emotional experience and behaviours of other people thereby prompting us to act accordingly. This is the reason why an increasing number of studies is attempting to uncover the neural underpinnings of such an important function.

The most useful model for studying empathy is the observation and/or the imagination of pain in others. Indeed, the structures reported to be involved in empathy for pain closely overlap those activated during perception of somatic pain. While on one hand some studies pinpoint to a central role of neural activity arising from the ‘sensory node’ of the so-called ‘pain matrix’ (i.e. primary and secondary somatosensory cortices [SI and SII], e.g. Bufalari et al. 2007), on the other hand several authors confirmed the involvement of neural activities arising from the ‘affective node’ (i.e. the frontoinsular cortex [FIC] and the
anterior cingulate cortex [ACC]), which were reported to be increased in virtually all
neuroimaging studies of empathy (e.g., Singer et al. 2004).

Interestingly, some scholars pointed out that different findings among studies (emphasis
on somatosensory rather than on anterior cingulate/insula activity and vice versa) during
empathy for pain, may be due to methodological-related factors such as passive versus
active observation, perspective-taking, emotional context, selective attention and cognitive
load (see Fitzgibbon et al. 2010 for a review).

In a recent study published in *The Journal of Neuroscience*, Gu and colleagues (2010)
importantly addressed for the first time one of these possible sources of variability, namely
the role of cognitive load during the experimental performance. Gu and co-workers
adopted a simple elegant task that required participants to either evaluate whether the
person depicted in the photograph was suffering from pain (task pain – TP), or to assess
the laterality of the represented hand/foot (task laterality – TL). These two tasks were
chosen according to their similar level of cognitive load, as assessed using reaction times
and accuracy measures in a pilot behavioral study. Their main study results show that,
though an effect of stimulus type was evident on accuracy (painful stimuli had lower
accuracy than non-painful stimuli, see their Fig.2), no significant effect of task on both
reaction times and accuracy was detected, thus suggesting a consistent matching of
cognitive load between TP and TL. Interestingly, though the interaction of task and
stimulus was not significant (p=0.07), the authors found a trend towards slower reaction
times when judging laterality of painful stimuli rather than when judging laterality of non-
painful stimuli (TL–painful vs TL–non-painful). This finding was interpreted as the
occurrence of a Stroop-type phenomenon, that is painful stimuli might attract attention and
interfere with laterality judgment even when the painful feature of the stimuli is unrelated to task requirements.

Such a behavioral pattern was paralleled by higher FIC activity during the observation of other's pain, irrespective of the task required to judge pain or laterality (Gu et al. 2010; their Fig. 3), while in contrast the ACC showed to be equally activated across tasks and stimuli. In fact, by conducting a region of interest analysis (ROI) of brain activity the authors revealed that only the FIC and not the ACC was involved during the observation of other's pain. Indeed, Pairwise comparisons between painful and non-painful stimuli under TP (painful>non-painful) yielded significant activation in bilateral FI, somatosensory, superior parietal, and occipitotemporal visual areas, but not in ACC (their Fig. 4, C).

Therefore, these findings suggest that ACC does not seem to represent a crucial node in the brain network subserving empathy, as classically reported in the literature. Conversely, FIC shows to be active when painful stimuli are observed regardless of task requirements, and even when subjects are not asked to directly evaluate pain (see Fig. 1).

However, It is worth noting that the method used for localizing the ROIs (by using an [all]-[baseline] contrast estimated on the same dataset) has the potential to miss regions that show task-related deactivations. An atlas-driven ROI selection (independent ROIs) or a metanalysis-based selection (see Jackson et al. 2006b) would have provided a confirmatory approach to the data analysis, able to strengthen the observation of experimentally induced deactivations.

The crucial finding of an automatic FIC activation for other's pain observation (i.e., even when judging only laterality) made the authors conclude that FIC "provides a neural mechanism for the perception–action model of empathy, which states that the sight of another person’s emotional state directly and immediately elicits a mental representation of that state in the observer" (Preston and de Waal 2002).
However, this interpretation should not easily be drawn due to the lack of trait/state empathy measures and due to a lack of correlation between personality trait and neural activity in this study. In addition, there is no strong evidence of a causal relationship between the well known insular activation functions (e.g., interoceptive representation) and their hypothesized higher level functions (empathy and shared representation), neither in this study, nor in the literature (see Decety 2010 for a critical review). Therefore, the call for caution when using the mirror neuron theory to make inferences regarding human behaviours is mandatory. Indeed, this theory has not been validated yet (Hickok 2009), and its application to typically human functions, such as empathy, is importantly less straightforward than its application to action understanding in monkeys.

Thus, one might re-interpret the observed differences as rather associated to a process of pain recognition rather than to the subjective feeling of empathy itself (see Morrison et al. 2007). The higher the saliency of the stimulus condition (noxious versus neutral) the higher the attentional resources to be allocated, especially in those areas related to the understanding of other’s experience (both emotional and cognitive evaluation). Noteworthy is that pain recognition may be necessary but not sufficient for empathy and may occur independently of it. Recently, other authors suggested an even more conservative scenario (Lamm et al. 2007): when the subject knows in advance that the hand’s owner is not going to feel pain (e.g., due to medical anesthesia), the vision of a hand inflicted by a syringe elicits activity in a set of structures (including FIC and ACC) similar to that recruited when the subject is certain that the effector will provoke a painful percept in the model. Therefore, Lamm et al. concluded that such an activation might not be specific to pain as such, but to the exposure to aversive and potentially threatening situations in general.
A compelling research strategy relies on a more scrupulous approach which address the complexity of empathy. Indeed, it is well known how empathy depends on other sub-functions as ‘mimicry’, ‘emotional contagion’, ‘perspective taking’, ‘sympathy’, ‘concern’ and ‘compassion’ for it to take place (for a review see Singer and Lamm 2009). Thus, whereby researchers isolate those sub-functions that are thought to shape the neural correlates of empathy in order to reduce the complexity of their observations and thus increasing the experimental power and the heuristic value of their interpretations (e.g. Lamm et al. 2008; Kim et al. 2009; Li and Han 2010).

On the basis of Gu et al.’s results at least four crucial issues remain to be addressed in future studies (see Fig. 1, panel B). First, can we exclude that FIC activity is a specific correlate of empathy for pain (or of its sub-functions) rather than being a more general non-specific correlate of potential threat and harm detection in the peri-personal space? Future studies should compare the observation of other’s pain to the observation of other categories of aversive and potentially threatening situations, possibly measuring the impact of autonomic activity on brain functioning (e.g., heart rate), especially in view of Critchley’s findings about insula activation being related to interoceptive awareness (2004). Well controlled studies are needed both to dismiss the specific involvement of anterior cingulate activity as empathy processor and to discard a possible interpretation of insula activity as a general sensory and affective magnitude estimator not specifically mediating the function of empathy. Second, Gu and co-workers did not report any information on the connectivity between FIC and ACC (if any), conversely several previous study on empathy reported the two structures as being coupled in providing the affective processing of pain related stimuli (both self- and other-oriented). Effective connectivity analysis (e.g. dynamic causal modelling) is needed to disentangle the causal direction of
information flow between FIC and ACC during empathy or its sub-functions. Third, the same set of stimuli used in the reviewed Gu et al.’s study significantly activated somatosensory cortices in the previous two studies where it was applied (Jackson et al. 2005, Jackson et al. 2006a). Thus, the lack of significant somatosensory activation in Gu et al’s was likely due to task requirements. An alternative version of cognitive load control task may ask the subjects to judge whether the body part showed is a foot or a hand rather than judging laterality. According to data reported by Gu and co-workers, during this version of the task we may expect a heightened activation of SI and SII following the observation of body parts being harmed. Such extension of the paradigm may help researchers to further investigate the role of somatosensory cortices during empathy-like brain activities, when the subject’s attention is directed to somatic features of other’s pain. Fourth, the functional interaction between sensory and affective structures may be crucial during the assessment of hemeostatic meaning of a stimulus (both during self-referred and other-referred experience). At present, we do not have a clear-cut picture of what are the interaction between anterior insula and somatosensory cortices (especially SII) when a subject is asked to focus on different sensory aspects of the observed noxious experience. For instance, anterior insula may interact with somatosensory cortices (especially SII) in assessing intensity of vicarious pain experience while it may be deactivated during evaluation of other sensory features, such as spatial localization and duration of pain experience.

Gu and co-workers introduced an elegant and sensitive experimental paradigm able to characterize the different contribution of anterior cingulate and anterior insula cortices during observation of other’s pain. This methodological improvement will possibly pave the
way to a series of neuroimaging and electrophysiological studies aimed to address the representation of empathy and of their sub-functions in the brain.
FIG. 1. Comparative diagram representing the classical simplified model of affective and sensory processing of vicarious pain processing in the brain and its update on the basis of Gu et al.’s findings. The distinction between the affective and pain processing (hexagons) of noxious information is represented respectively by two different set of structures (circles) within the so-called “pain matrix”. A. The classical model poses that the frontal insular cortex (FIC) and anterior cingulate cortex (ACC) process the affective and motivational features of pain, while the somatosensory cortices (SI and SII) process the sensory-discriminative features. B. Gu and co-workers identified a functional differentiation between FIC and ACC. Once controlling for the confounding effect of experimental cognitive load, FIC would be the structure actually involved in automatic affective-empathetic processing whereas ACC would be involved in motor preparation, response selection and task control, being non specific for the empathy function.
References


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Nociceptive Information
Sensory Processing
Affective Processing

Experimental factors (e.g., cognitive load)

FIC
ACC
SI
SII

Pre-Motor Processing

ACC

FIC
SI
SII

Nociceptive Information