The painful side of empathy

Tania Singer & Chris Frith

Empathy refers to our ability to share emotions and sensations such as pain with others. Imaging studies on pain showed that the affective but not sensory component of our pain experience is involved in empathy for pain. In contrast, a new study using transcranial magnetic stimulation highlights for the first time the role of sensorimotor components in empathy for pain in other people.

We all have a remarkable and largely involuntary capacity to share the experiences of others. We yawn when those around us are yawning. We wince when we see a stranger shut her hand in a car door. We suffer when our loved ones are in pain. Brain imaging studies suggest that this capacity for empathy relies on neural systems that are specific to the content of the experience (such as touch, emotion, pain), but shared across having the experience ourselves and observing the experience in others. But can we share all aspects of the experience of others? Studies using fMRI (functional magnetic resonance imaging) have suggested that empathy is associated with activity in regions concerned with the unpleasantness of the pain rather than with its precise sensorimotor qualities. However, using transcranial magnetic stimulation (TMS), Avenanti and colleagues[1] show in this issue that watching a needle prick a specific hand muscle reduces motor excitability in the same muscle in the observer.

How can we know how it feels for another to be in pain, to be sad or to be hungry when we do not actually experience these feelings ourselves? Many authors have proposed that watching another person have a particular experience automatically activates the neuronal network that is usually involved in processing that same experience ourselves[2,3]. For example, activity in the insular cortex elicited by a disgusting smell is also elicited by the sight of the facial expression of disgust[4]. Activity in secondary somatosensory cortex elicited by being touched is also elicited by the sight of someone else being touched[5]. Activity elicited in anterior cingulate and anterior insular cortex by a painful stimulus is also elicited by the knowledge that a loved one is receiving a painful stimulus[6].

Avenanti and colleagues[1] now show that this neural response to the pain of others is specifically localized within the sensorimotor system. The authors used TMS to measure the sensitivity of corticospinal pathways. When a strong magnetic pulse is applied over the motor cortex, motor potentials (MEPs) are evoked in the associated muscles. The strength of the TMS signal required to elicit MEPs is a measure of corticospinal excitability. When a participant is experiencing pain, MEPs elicited by TMS indicate a marked reduction of corticospinal excitability[7]. Using this technique, Avenanti *et al.* found a similar reduction of corticospinal excitability when participants saw someone else receiving a painful stimulus. In this experiment, the participants watched a video showing a sharp needle being pushed into someone's hand (**Fig. 1**). No change in corticospinal excitability occurred when participants saw a Q-tip pressing the hand or a needle being pushed into a tomato. These control conditions show that the reduction in excitability was specifically associated with seeing someone else in pain.

However, the neural effects were much more precise than a general response to the observation of pain. In all experiments, MEPs were recorded simultaneously from the first dorsal interosseus muscle (FDI) and the abductor digiti minimi muscle (ADM) of the observers' right hands. Corticospinal excitability measured from these hand muscles was not affected by seeing a needle being thrust into someone's foot. Furthermore, MEPs recorded from the FDI muscle of the observers were affected by the sight of a needle entering the FDI muscle of someone's hand and not by the sight of the needle entering the ADI muscle. The reverse pattern was observed for MEPs recorded from the observers' ADI muscle. The authors interpret their findings as evidence for a pain resonance system that extracts basic sensory qualities of another person's painful experience (location and intensity of a noxious stimulus) and maps these onto the observers' own sensorimotor system in a manner that is somatotopically organized.

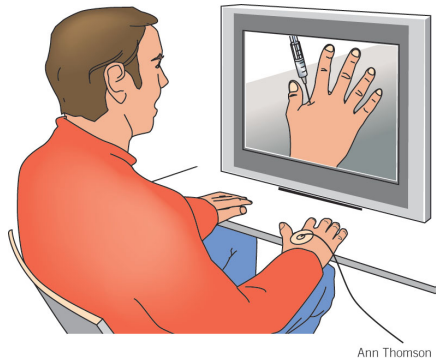

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Figure 1 Experimental protocol for the study of Avenanti *et al*[1]. The subject watched a video of someone's hand being pierced by a needle while the electrical excitability of the same muscle in the subject's hand was recorded.

These results are in striking contrast to the findings of our fMRI study of empathy for pain[6]. This study showed shared activity in the affective pain network (including anterior cingulate cortex (ACC) and anterior insula), but not in primary somatosensory cortex (SI). We concluded that empathy for pain involved the affective, but not the sensory components of the pain matrix. These differences could be due to the different material used to induce empathy in the two studies. In the study of Avenanti *et al.*[1], the participants saw needles inserted into the hand of an unknown person. This stimulus seems likely to emphasize the sensory qualities of the pain. In contrast, the participants in our study saw a symbolic cue (an arrow) indicating when their partner, who was sitting next to them

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in the scanning room, was receiving a painful stimulus. This protocol seems likely to emphasize the affective quality of the pain. However, this explanation is not the whole story.

Two recent fMRI studies used visual material similar to that used by Avenanti *et al.* but found no SI involvement in empathy for pain. In one study, participants saw still pictures of unknown people experiencing pain to their hands and feet (for example, a hand trapped in a car door)[8]. The sight of such pictures elicited activity in ACC and anterior insula, but not SI. In another fMRI study[9], the authors presented videos very similar to those used by Avenanti *et al.*, showing needles pricking the fingertips of unknown people. Again, these videos elicited activity in ACC, but not in SI. ACC and anterior insula might well have been activated in the Avenanti *et al.* study, but such activity would not be detectable using their method. The question is rather why SI activity has not been detected in fMRI studies of empathy for pain.

One possibility is that TMS, the method used by Avenanti *et al.*, may be able to pick up subtle changes in the sensorimotor system that are below the significance threshold in fMRI techniques. Activation in SI is not always detected by fMRI, even when the participants themselves receive painful stimuli. A meta-analysis of brain imaging studies of pain report that SI activity was observed in only 50% of the studies[10]. Similar discrepancies are present in the action observation literature. Using TMS, action observation can be shown to alter corticospinal excitation with direct mapping to the muscles used in the action[11]. In contrast, studies of action observation using fMRI typically implicate the inferior parietal lobule and the inferior frontal gyrus, rather than primary sensorimotor cortex[12].

Nevertheless, SI activity has been detected in fMRI studies on empathy. The experimental protocols in our study[6] and another one[9] were sensitive enough to activate SI, as such activity was observed when painful stimuli were applied to the participant. Thus the lack of SI activity in the empathy condition is unlikely to be a problem of methodology. Likewise, a recent study of 'empathy' for touch[13] revealed activation in the sensorimotor cortex that was somatotopically mapped. The precise location of activity in SI elicited by the presentation of a video of someone being touched was determined by the side (left versus right) and the location of the touch (face versus neck).

The key variable is likely to be the mental attitude of the participants when thinking about the pain of others. Somatotopically organized sensorimotor activity can be elicited by attending to the part of the body that is about to be touched[14]. In both the studies that have observed somatosensory mapping, the participants were explicitly asked to rate the intensity of the touch[13] or the pain that was applied to the model in the videos[1]. Such an instruction is likely to direct attention to target body part. In contrast, ACC and anterior insula activity is elicited when participants anticipate the unpleasantness of the painful stimulus that they are about to receive[15]. This aspect of pain was emphasized in studies that did not show SI activity for pain empathy[8,9]. It is precisely this ability to anticipate our experience of pain before it occurs and to attend to a specific part of our body before it is stimulated, that enables us to share the experiences of others. Therefore we will need to be careful to take the mental attitudes of our participants into account when studying empathy for pain.

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Adult neurogenesis: a tale of two precursors

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The rodent brain constantly generates new granule and periglomerular interneurons to replenish the olfactory bulb. New work shows that the two subtypes are derived from distinct progenitor populations, revealing unexpected diversity among adult neural stem cells.

The discovery over the last decade that the adult brain produces large numbers of new neurons throughout life has raised hopes that we will eventually be able to mimic this natural phenomenon and replace neurons lost in brain disease and injuries[1,2]. Studies so far have drawn a fairly simple picture of adult neurogenesis, further increasing its appeal as an experimental system. At the major site of neurogenesis in the adult brain, the olfactory bulb, only two major types of neurons are produced. Moreover, just a few types of progenitors, including stem cells and transit-amplifying cells, have been implicated in the generation of these neurons[3]. This simplicity contrasts favorably with the multiple neuronal types generated in any region of the embryonic brain, and the bewildering complexity of embryonic progenitor populations[4,5].

Is this simple view of the adult neurogenic process an accurate reflection of reality, or a mere illusion resulting from our superficial understanding of the system? A paper in this issue[6] demonstrates that the two types of neurons produced in the adult olfactory bulb are generated by distinct progenitors present at different locations and expressing different markers, thus throwing into disarray the prevalent idea of a simple lineage that would lead from adult stem cells to adult olfactory neurons in a few simple steps.

Key to this new finding was the use of a powerful method, based on stereotaxic injection of retroviral vectors, to stably label defined populations of progenitors and their progeny in the adult rodent brain[7]. Stem cells that give rise to olfactory bulb interneurons are known to reside in the subependymal zone (SEZ) lining the walls of the lateral ventricles. SEZ stem cells generate transit-amplifying progenitors, which divide rapidly before producing neuroblasts. Neuroblasts in turn

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