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Opinion

The Anatomy of Suffering: Understanding the Relationship between Nociceptive and Empathic Pain

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Pain features centrally in numerous illnesses and generates enormous public health costs. Despite its ubiquity, the psychological and neurophysiological nature of pain remains controversial. Here, we survey one controversy in particular: the relation between nociceptive pain, which is somatic in origin, and empathic pain, which arises from observing others in pain. First, we review evidence for neural overlap between nociceptive and empathic pain and what this overlap implies about underlying mental representations. Then, we propose a framework for understanding the nature of the psychological and neurophysiological correspondence across these types of 'pain'. This framework suggests new directions for research that can better identify shared and dissociable representations underlying different types of distress, and can inform theories about the nature of pain.

Nociceptive and Empathic Pain

Imagine accidentally hitting your hand with a hammer. This experience would induce a spectrum of physical and psychological events: tissue damage, visceral discomfort, shifts in attention, arousal, negative affect, and a desire to avoid repeating the experience. These events contribute to the broad phenomenon of 'pain', and, more specifically to **nociceptive pain** (see Glossary), which originates in peripheral nociceptive fibers (see Box 1 for detailed definitions). Although pain helps individuals to avoid future harm, it also impairs wellbeing and generates an enormous public health burden [1].

Now imagine observing a friend hit themselves with a hammer. This experience typically generates **empathic pain**, a phenomenon that, despite differences in origin, shares features with nociceptive pain. Here, we explore the relation between nociceptive and empathic pain. What does it mean to label both of these experiences as 'pain?' And, how grounded are these labels in shared neurophysiological representation?

The Debate

Decades of evidence in humans and animals suggest at least some overlap between nociceptive and empathic pain [2,3]. Witnessing others in pain can create or intensify behavioral signs of nociceptive pain [4–6], and individuals with congenital insensitivity to nociceptive pain exhibit blunted responses to empathic pain [7]. Neuroscientists have further demonstrated that brain structures, such as anterior insula (AI) and parts of the cingulate cortex (CC), commonly respond when humans experience nociceptive and empathic pain [8–15] (Figure 1A). In some cases,

Trends

Neuroimaging evidence has suggested both overlapping and nonoverlapping representations across nociceptive and empathic pain, leading to debates as to whether empathic experience should be considered a type of pain or a distinct experience.

Here, we advocate dispensing with binary definitions of pain versus nonpain, and instead considering the constellation of phenomena that comprise pain.

This approach, in conjunction with cumulative efforts testing the specificity and generalizability of brain measures across labs, can help us move beyond debates about which experiences are or are not pain, and towards a more comprehensive understanding of aversive experiences and their constituent representations.

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Box 1. Definitions of Pain

The International Association for the Study of Pain (IASP) defines pain as 'An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage' [89]. This includes not only effects of noxious physical stimulation, but also other experiences that 'hurt'. After witnessing a friend hit herself with a hammer, for instance, you might feel a 'crushing' sensation in your own hand, or discomfort in your stomach. Such empathic pain includes bodily sensations described in terms of tissue damage, meeting the IASP criteria for pain.

The IASP definition of pain contrasts with its narrower definition of nociceptive pain: 'pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors.' This definition privileges etiology and excludes empathic pain, which is not triggered by nociceptors in the person experiencing empathy.

Definitions by nature are operational: they serve the study of a phenomenon in a particular context. If scientists investigate a phenomenon such as pain at multiple levels (e.g., nociceptors, cortical neurons, patterns of BOLD activity, psychological experience, behavior, and pathology), operational definitions useful at one level may lose their relevance at another, potentially impeding vital efforts to link these levels. At some levels, such as the response of certain neurons in the cingulate cortex, nociceptive and empathic pain might trigger identical responses [78]. At the psychological level, both might feel aversive, trigger strong motivations and be described in terms of tissue damage. Yet, at the level of peripheral nociceptors, they will seem fundamentally different. Scientists specializing in each of these three levels may then disagree about whether empathic pain is a form of 'true' pain. These scientists would disagree not about data, but rather about definitions.

Instead of a universal definition of pain to settle resulting arguments, here we argue for an agnostic approach: investigating particular pain-related dimensions at various levels of analysis, and mapping similarities and dissimilarities between empathic and nociceptive experiences with respect to each dimension. This could allow scientists to more precisely shed light on how nociceptive and empathic experiences relate, as well as how practitioners can effectively intervene to reduce the burden of pain. This approach further allows for a common ground from which each investigator can decide whether they believe empathic experiences constitute 'pain', based on relevant data.

Glossary

Component: a subset of a brain pattern inferred to track a specific dimension of psychological experience (e.g., attention shifts or location coding).
Constructionism: an approach to psychology and neuroscience positing that complex states (e.g., emotions) can be best understood not as irreducible entities, but rather as combinations of psychological 'ingredients'.
Empathic pain: pain that arises from observing actual or threatened tissue damage in another person.
Marker: a pattern or component that displays sensitivity and specificity to one psychological state, allowing for reverse inference about that state based on the activation of that pattern.
Nociceptive pain: pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors.
Pattern: the set of voxels activated (and their accompanying intensity) by a stimulus or task.
Sensitivity: the probability of engaging a neural marker given that a particular mental state is present.
Separate modifiability: a state under which activity in two patterns or components is modulated by differing tasks; for example, activity in pattern A tracks psychological variable X but not variable Y, and activity in pattern B tracks psychological variable Y but not variable X.
Specificity: the probability of not engaging a neural marker when a particular mental state is not present.

empathic experiences also activate somatosensory cortex [9] and facilitate motor programs associated with nociceptive pain [16]. Brain responses to others' pain in AI and CC correlate with subjective experiences of pain empathy [2,17,18] and willingness to shoulder costs to reduce others' pain [3,19]. Finally, brain responses to empathic pain diminish after placebo analgesia pain [20,21].

These findings signal important relations between nociceptive and empathic pain, but do not necessarily imply that they rely on the same psychological representations. For instance, AI and CC respond to nonpain states, including arousal and attention [22–28]. Manipulations that affect nociception, such as placebo analgesia, likewise influence not only pain, but also stress and anxiety [29]. Critics suggest that conclusions about the overlap between empathic and nociceptive pain rely heavily on spurious reverse inference (*cf*. [30]; Box 2), and that social and nociceptive experiences might not in fact share pain-specific processes [31].

Often, questions about pain states are posed as a binary: empathic pain either 'counts' as pain or does not. We believe that understanding the nature of empathy and pain requires moving away from this simple distinction and instead: (i) decomposing pain into its **component** 'ingredients'; (ii) identifying brain **markers** of these ingredients; and (iii) using those markers to identify exactly which ingredients empathic and nociceptive pain share. This approach transforms the binary question of whether both empathic and nociceptive experiences constitute pain into a graded question: how far from one another do these experiences fall in the multidimensional space of pain ingredients?

Multidimensional Pain

Pain includes a complex suite of processes. Consider the moment in which you hit yourself with a hammer. This event triggers a multidimensional experience, including, but not restricted to, processing: (i) the location of pain (in your hand, not foot); (ii) its intensity (strong); (iii) qualities (crushing, aching); (iv) generalized discomfort; the negative (v) valence and (vi) high arousal characterizing your emotional response; (vii) redirection of attention to your hand; (viii) motivation