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Why rejection hurts: a common neural alarm system for physical and social pain

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Numerous languages characterize 'social pain', the feelings resulting from social estrangement, with words typically reserved for describing physical pain ('broken heart', 'broken bones') and perhaps for good reason. It has been suggested that, in mammalian species, the social-attachment system borrowed the computations of the pain system to prevent the potentially harmful consequences of social separation. Mounting evidence from the animal lesion and human neuroimaging literatures suggests that physical and social pain overlap in their underlying neural circuitry and computational processes. We review evidence suggesting that the anterior cingulate cortex plays a key role in the physicalsocial pain overlap. We also suggest that the physicalsocial pain circuitry might share components of a broader neural alarm system.

When people speak of 'hurt feelings' or 'broken hearts', it is clear that these descriptions are meant to reflect painful experiences. Writers have long noted that some of the most painful experiences known to humankind are those that involve the loss of important social bonds. Indeed, the use of physical pain words to describe episodes of social estrangement is common across many different languages [1]. However, is feeling socially estranged truly comparable to feeling physical pain or is this merely poetic license? This review presents evidence suggesting that the similarity between physical and social pain does not end with this linguistic overlap but extends into how the human brain processes both kinds of pain. We propose that, based on similarities in purpose, process, and function, physical and social pain share parts of the same underlying system for their operation.

An overlap between physical and social pain

We have recently proposed that physical pain – the pain experienced upon bodily injury - and social pain - the pain experienced upon social injury when social relationships are threatened, damaged or lost – share neural and computational mechanisms [1]. This shared system is responsible for detecting cues that might be harmful to survival, such as physical danger or social separation, and then for recruiting attention and coping resources to minimize threat.

Such an overlap would be evolutionarily adaptive. Because of the prolonged period of immaturity and the critical need for maternal care in mammalian infants, it has been suggested that the pain mechanisms involved in detecting and preventing physical danger were co-opted by the more recently evolved social attachment system to detect and prevent social separation [2]. This hypothesis was first proposed to explain why opioids are effective in alleviating both physical pain and separation distress in several different animal species [2]. Because of its aversiveness, pain captures attention, disrupts ongoing behavior, and motivates action aimed at regaining safety and mitigating painful experience [3]. If the need to maintain close contact with the mother for nurturance and protection is crucial to mammalian survival, experiencing pain upon social separation would be an adaptive way to prevent the harmful consequences of maternal separation.

Before continuing, we briefly define physical and social pain. Physical pain is defined as the 'unpleasant sensory and emotional experience associated with actual or potential tissue damage' [4]. Social pain is defined as the distressing experience arising from the perception of actual or potential psychological distance from close others or a social group (see Box 1). This parallels Bowlby's conception of the infant attachment system that monitors for physical distance from the caregiver and elicits distress once a certain distance has been exceeded [5], but allows for the abstract and implied sense of psychological distance to which adults are sensitive.

A common neural basis

Several lines of evidence suggest that the anterior cingulate cortex (ACC), specifically the dorsal subdivision (dACC; areas 24' and 32'), is involved in the affectively distressing components of both physical and social pain. For decades, neurosurgeons have performed cingulotomies, a circumscribed lesioning of the ACC, to treat intractable chronic pain [6]. Patients who have undergone cingulotomies for chronic pain report that they are still able to feel the pain but that it no longer bothers them [6], highlighting the ACC's role in the distressing, rather than the sensory, component of physical pain.

More recently, pain researchers have subdivided pain experience into two psychological components: sensory processing and felt unpleasantness [7]. Numerous TRENDS in Cognitive Sciences Vol.not known No.not known Month 0000

Box 1. The link between social rejection and self-esteem

Many psychologists have assumed that high self-esteem is essential to positive psychological health [47]. Consistent with this view, high self-esteem has been associated with psychological well-being, whereas low self-esteem has been associated with greater depression, anxiety, and other psychological problems [48]. However, research suggests that it might not be 'self-esteem' per se that contributes to psychological well-being, but rather the state of social connectedness that underlies this construct.

Leary and colleagues have proposed 'sociometer theory' to explain why self-esteem appears to be crucial for psychological health [48,49], maintaining that self-esteem is a measure of the degree to which an individual is included or excluded by others. Because of the importance of social ties for human survival, it is important to be able to monitor one's acceptance or rejection within a social group. In the same manner that a fuel gauge provides a readout of the amount of gas in a car to prevent empty tanks, self-esteem might provide a read-out of a person's inclusionary status to prevent exclusion [48]

Several studies have provided direct evidence for this theory showing that increasing degrees of rejection are associated with more negative self-feelings and reductions in self-esteem [48,49]. Additionally, being socially ostracized or excluded during a computerized, interactive ball-tossing game (Cyberball) played over the internet, ostensibly with others, causes reductions in self-esteem [50]. Perhaps most surprising, though, is that even when participants are told they are playing with a computer program and that the computerized players are going to stop throwing the ball to them, participants still report lower self-esteem following the game [51].

Similarly, in an fMRI study of social exclusion [24], participants were prevented from playing a ball-tossing game, ostensibly because of technical difficulties, in an 'implicit exclusion' condition. Participants watched the others play the game without them, in what looked like exclusion, although participants consciously knew the other players were not excluding them. Nevertheless, implicit exclusion produced dACC activity indistinguishable from explicit exclusion. These studies suggest that the capacity for social exclusion to cause social pain and decrease self-esteem might be so powerful that simply viewing a scene that bears a resemblance to rejection produces these effects. Just as conscious knowledge of a visual illusion does not prevent it from occurring, conscious knowledge that one is not actually being actively excluded does not prevent dACC activity or diminished self-esteem.

neuroimaging studies have pointed to the role of the dACC in the felt unpleasantness of physical pain [8–11]; whereas the somatosensory cortex and posterior insula have been associated with the sensory-discriminative aspects of pain [11]. Specifically, increasing levels of dACC activity correspond with increasing levels of selfreported pain unpleasantness [8-11]. Thus, individuals who are dispositionally pain-sensitive show more dACC activity and report greater levels of perceived unpleasantness to painful stimulation [12].

The dACC has also been shown to relate to social pain distress in humans and other mammals. The experience of social pain might be exclusive to mammals because of their extended need for maternal care, and thus might specifically relate to behaviors and neural structures unique to mammalian species. Two behavioral characteristics that separate mammals from their reptilian ancestors are vocal communication for maintaining mother-infant contact and the nursing of young along with maternal care [13]. Paralleling these newly acquired behaviors, the cingulate gyrus also appears for the first time, phylogenetically, in mammals and thus might contribute to these behaviors [13].

Distress vocalizations, emitted by young animals when separated from caregivers, rely on an intact cingulate gyrus for their production [13–15]. Consistent with a causal role for the ACC in the production of social pain and distress vocalizations, ablating the dACC in squirrel monkeys eliminates the spontaneous production of distress vocalizations [16,17], whereas electrically stimulating the dACC in macaques leads to the spontaneous production of distress vocalizations [18,19]. In addition, ablating the ACC in macaques leads to decreases in affiliative behavior [20,21], potentially reflecting a reduced need for social closeness as social separation is no longer distressing.

The cingulate gyrus also plays a role in maternal responses to distress vocalizations. Ablating the cingulate gyrus in rodent mothers disrupts maternal responses to distress vocalizations, including retrieving pups and keeping them near [22,23]. In one study, the survival rate of rat pups whose mothers had cingulate lesions was only 12% [23], highlighting the importance of the cingulate in promoting mother-infant contact and facilitating offspring survival. Two human neuroimaging studies are generally consistent with these findings [14,15].

To date, only one study has examined the neural correlates of social pain in humans. This neuroimaging study investigated the neural correlates of social exclusion [24]. Participants were scanned while playing a computerized ball-tossing game, supposedly with two others, and were ultimately excluded from the game (see Figure 1a). When examining neural activity during exclusion, compared with inclusion, participants showed increased activity in dACC (see Figure 1b). The magnitude of dACC activity correlated strongly with self-reports of social distress felt during the exclusion episode (see Figure 1c and Box 2).

A common computational basis

Processes that share the same neural circuitry often share some of the same computational mechanisms [25]. Across several neuroimaging and computational modeling studies, it has been shown that the dACC acts as a conflict or discrepancy detector, activated by behavioral response conflicts, such as those produced in the Stroop task [26]. In addition, the dACC might be sensitive to goal conflicts, expectation violations, and errors more generally [27,28] (see Box 3). Discrepancy detection in dACC leads to prefrontal activations that promote contextually-appropriate, top-down responses to resolve the discrepancy [29].

Although the phenomenological experience of pain distress and the computational process of discrepancy detection have been shown to activate neighboring and sometimes overlapping regions of dACC [30], the phenomenological and computational correlates of dACC activity have seldom been investigated together. Typically, studies of physical or social pain have examined the role of dACC in distress rather than in discrepancy detection, whereas studies of the computational mechanisms underlying dACC function have examined its role in discrepancy detection rather than in distress. In one study that investigated dACC activity to both a discrepancy-detection task and a pain task, it was found that these tasks activated mostly adjacent, but sometimes overlapping sections of TRENDS in Cognitive Sciences Vol.not known No.not known Month 0000

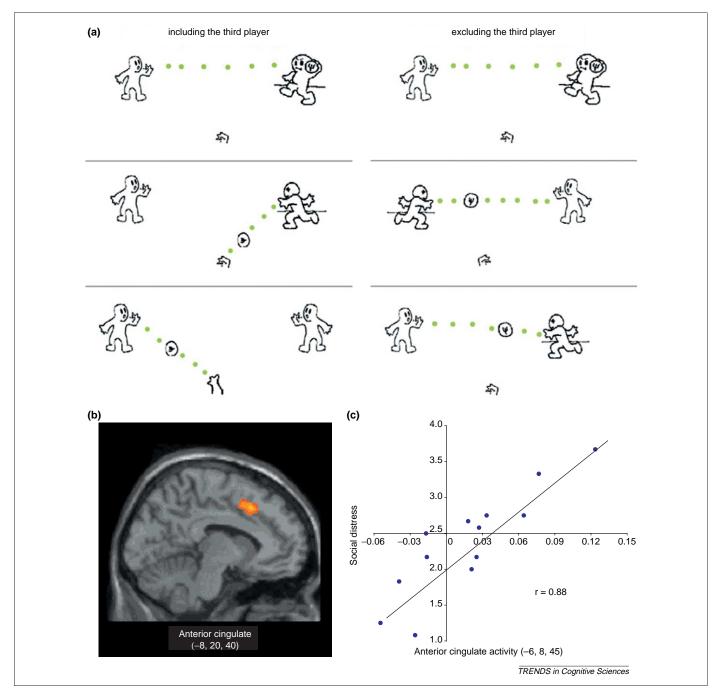


Figure 1. Methodology and results from an fMRI study of social exclusion [24]. (a) Example of what participants viewed while in the scanner. Participants were included in the ball-tossing game during one round and excluded during another. (b) Participants showed increased dorsal anterior cingulate cortex (dACC) activity during the exclusion compared with the inclusion episode. (c) Participants' levels of self-reported distress correlated highly with dACC activity during the exclusion episode compared with the inclusion episode.

dACC in six subjects [30]. In another study that examined dACC activity to both a cognitive task (although not a discrepancy-detection task) and a pain task, it was found that the cognitive task activated a more anterior and superior part of dACC; whereas the pain task activated a more posterior part of dACC [31]. However, no studies have investigated whether true discrepancy-detection tasks and pain tasks activate the same region of dACC within a large sample.

One way to triangulate the relationships between distress, discrepancy detection, and general dACC activity is by conceptualizing the dACC as a neural 'alarm system'. For an alarm system to function properly, two components are needed: a discrepancy monitoring system, which detects deviations from desired standards (e.g. detecting an excessive amount of smoke), and a sounding mechanism which signals that there is a problem that needs to be addressed (e.g. an alarm bell ringing). The discrepancy-detection function of the dACC can be likened to the detection of excessive smoke whereas pain distress can be likened to the sound of an alarm bell ringing. Thus, rather than discrepancy detection and distress being two competing

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Box 2. The neural regulation of pain

In addition to dorsal anterior cingulate cortex (dACC), right ventral prefrontal cortex (RVPFC) was also found to be active in response to social exclusion (see Figure Ia) [24]. This same prefrontal region was also activated in a neuroimaging study of placebo effects when participants received painful stimulation to the gut [8] (Figure Ib) and has been reported in more than a dozen neuroimaging studies of pain [52]. Although RVPFC was activated along with dACC in the social pain and placebo studies, there was a strong negative relationship between these activations such that greater RVPFC activation was associated with less dACC activation and less self-reported distress across participants (c.f. [53]). These results suggest that RVPFC might serve a self-regulatory function by disrupting the pain distress associated with dACC activity.

RVPFC activity might be set in motion by thinking about, rather than merely experiencing, pain. Several studies have reported increased RVPFC activity when thinking about, labeling, or evaluating affective stimuli, particularly when thinking about negative stimuli [8,54]. Additionally, RVPFC has been implicated in the inhibition of motor, cognitive and affective processes and possesses efferent connections projecting to dACC [55,56].

Similar reciprocal effects have been observed for RVPFC and the amygdala. Hariri et al. found that labeling emotionally expressive faces produced more RVPFC, and less amygdala, activity than matching emotionally expressive faces to other faces [57]. Paralleling the pain findings, in this study, the participants who generated more RVPFC activity during the labeling task tended to generate weaker amygdala activations.

Evolutionarily, such a feedback mechanism from RVPFC to alarm systems such as the ACC and amygdala makes good sense. These alarms often trigger a change in our attention to deal with the source of the threat or to cope in the aftermath. If the alarms continue to sound at full volume, however, they could detract from the limited processing capacity of executive processes in prefrontal cortex. A feedback mechanism in RVPFC might assure that the partial dampening down of an alarm only occurs after attention has been turned to the source of the alarm, the point at which continued alarm sounds become maladaptive.

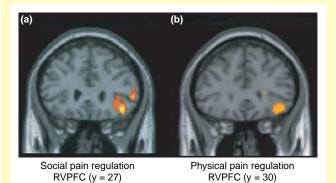


Figure I. Right ventral prefrontal cortex (RVPFC) activation associated with (a) social pain regulation, and (b) physical pain regulation. (Part a reproduced with permission from [24]).

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explanations of dACC activity, they might actually be complementary processes underlying the functioning of this neural alarm system.

One way to test whether discrepancy detection and distress are complementary processes in the broader functioning of an alarm system, is to examine whether individuals who chronically experience more distress also show greater dACC reactivity during discrepancy detection. This would suggest that individual differences operate at the level of the alarm system rather than at the level of the component processes. In a recent neuroimaging study [32], individuals with obsessive-compulsive disorder (OCD), an anxiety disorder characterized by heightened levels of distress, doubt and worry, were scanned while performing a conflict monitoring task. Individuals with OCD, compared with healthy controls, showed significantly more dACC activity to high-conflict trials. In addition, there was a trend such that within the OCD group, patients with more severe symptoms showed more ACC activity to conflict than those with less severe symptoms. In a study we conducted (reported in [1]), neuroticism, the dispositional tendency to experience distress and negative affect, correlated strongly (r = 0.76) with ACC activation to a non-distressing discrepancy-detection task. Together, these studies suggest that discrepancy detection and distress might be two complementary processes supporting the brain's alarm system in the ACC.

Consequences of the overlap

One of the hypotheses derived from the physical-social pain overlap is that endogenous and exogenous factors that enhance sensitivity to one type of pain should enhance the sensitivity of this alarm system and thus potentiate sensitivity to the other type of pain as well. Alternatively, factors that downregulate the sensitivity to one type of pain should downregulate the sensitivity of the alarm and thus diminish sensitivity to the other type of pain. Existing evidence supports both of these claims.

First, when young children experience physical pain, they experience social pain more easily and more frequently in response to separation from their caregiver [5]. Similarly, individuals with chronic pain disorders are more likely than healthy controls to have an anxious attachment style, characterized by a preoccupation with the commitment status of relationship partners [33] and to have heightened fears of social evaluation and rejection [34]. Lastly, rejection-sensitive, compared with non-rejection-sensitive, individuals report more distress when watching video clips of people experiencing physical pain [35]. These findings provide evidence that an enhanced sensitivity to one type of pain accompanies an enhanced sensitivity to the other.

Second, increased social support, which reduces social pain [36], is also associated with a reduction in pain from chronic ailments, during cancer, following heart surgery, and during childbirth [37-40]. Experimental evidence demonstrates similar effects in animals and humans. In animals, shock punishment is less effective in training groups of rats than in training rats individually [41], leads to less immobility in rats in the presence of a companion [42], and elicits fewer emotional reactions in infant goats in the presence of their mother [43]. Similarly, in humans, the presence of social support increases tolerance of electric shock stimulation [44] and decreases levels of selfreported pain during a cold-pressor task [45].

Finally, certain drugs have similar regulatory effects on both physical and social pain. Opiate-based drugs, known for their effectiveness in alleviating physical pain, lessen social pain in animals and humans [2]. Additionally, antidepressants, often prescribed for anxiety or depression

Box 3. The function of rostral versus dorsal ACC

In recent years, the activity of the ACC has received a great deal of attention, showing engagement during cognitive tasks involving attention, error monitoring and target detection [26], during painful stimulation [11], and during emotional tasks involving the recollection of emotional experiences [58]. An influential review of this literature suggested that dorsal ACC (dACC) is involved in cognitive processes, whereas the rostral-ventral ACC (rACC) is involved in emotional processes [58]. However, this analysis did not include studies of physical pain. Intuitively, pain studies should cluster within the rostral, affective division of the ACC, but instead typically activate dACC [11]. Thus, dACC activations to pain remain either unexplained or surprisingly relegated to the 'cognitive' subdivision of the ACC. This poses a challenge to the cognitive/affective explanation of ACC activity.

One prominent computational explanation that might more adequately characterize ACC activity is an account of the ACC as a conflict monitor. Based on theories of cognitive control, it has been suggested that the ACC is specifically involved in detecting conflicts in information processing to signal situations requiring cognitive control [26]. This theory has been primarily applied to cognitive conflict and has thus typically been associated with dACC activity. However, some theories of emotion suggest that conflicts or interruptions to goals and plans result in strong emotional responses [59,60]. Thus, conflict detection might be an important computational process underlying emotional processes as well.

Both dACC and rACC might be involved in conflict detection but be sensitive to different forms of conflict. Thus, an alternative account to the cognitive/affective description of ACC activity is that rACC is involved in detecting conflict when there is an explicit symbolic representation of the stimulus or event that constitutes conflict, whereas dACC is involved in more bottom-up conflict that is either sensorimotor or lacks an explicit symbolic representation of the object of conflict (see Figure I).

For instance, conflict detection processes that activate dACC are well characterized by subsymbolic parallel constraint satisfaction models in which competing behavioral responses produce 'tension' in the network as the conflict increases. However, error detection, which activates rACC [61], involves a symbolic representation of the conflict that just occurred, namely the error. Similarly, discrete emotions are often defined as having a focal object or event, in contrast to moods, such as anxiety, which do not [62]. At least some studies of affect and emotion demonstrate a dorsal/rostral split such that emotion inductions

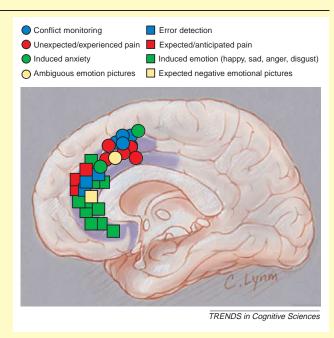


Figure I. A subsample of studies that activated rostral ACC (rACC) vs. dorsal ACC (dACC). Tasks involving conflict that contained a symbolic representation of conflict (denoted by squares) activated rostral-ventral ACC, whereas tasks involving conflict that did not contain a symbolic representation of conflict (circles) activated dACC.

activate rACC whereas anxiety inductions activate dACC [63,64]. Finally, Ploghaus et al. [65] recently reviewed data suggesting that expected pain activates rACC, whereas unexpected pain activates dACC. This distinction suggests that, as with physical pain, expected social rejection should activate rACC, whereas unexpected rejection should activate dACC. A thorough review of the literature is needed to determine how much of the existing findings fit with this alternative account. Nevertheless, pain studies present a challenge to the current cognitive/affective conception of ACC function and warrant further investigation.

resulting from social stressors, have recently been found to alleviate physical pain as well [46] and are now prescribed regularly to treat chronic pain.

Conclusion

The findings reviewed here suggest that social and physical pain might rely on overlapping neural processes

Box 4. Questions for future research

- How do individual differences in the reactivity of the ACC predict individual differences in the experience of physical or social pain? Would an individual who is highly sensitive to the possibility of one type of pain also be more sensitive to the possibility of the other?
- When does discrepancy detection elicit distress and when does it not? To what extent do these two processes activate overlapping or distinct parts of the ACC?
- Aside from the ACC and the opioid system, what are the other neural regions and relevant neurotransmitters involved in the physical-social pain overlap?
- If physical and social pain overlap in parts of their underlying neural circuitry, might these two types of pain show similar behavioral or health consequences?

in the form of a common neural alarm system. Such an overlap is adaptive for mammalian survival given the extended period of immaturity in mammalian young. Nevertheless, evolution's solution to ensured nurturance might have unintentionally produced a lifelong need for social connection and a corresponding sense of distress when social connections are broken. A more complete understanding of the elicitors and regulators of social pain will benefit from further investigations into its links with physical pain (see Box 4).

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