CHAPTER 39

Why Rejection Hurts: What Social Neuroscience Has Revealed About the Brain's Response to Social Rejection

Naomi I. Eisenberger

Abstract

This chapter reviews evidence from behavioral, pharmacological, and social neuroscience research that supports the notion that physical and social pain rely on shared neural substrates. It then reviews some of the unexpected and potentially surprising consequences that arise from such a physical-social-pain overlap. Specifically, it considers evidence showing that, even though experiences of physical and social pain seem very different from one another on the surface, individuals who are more sensitive to one kind of pain are also more sensitive to the other. It also reviews evidence demonstrating that factors that alter one kind of pain experience alter the other in a congruent manner. Finally, the chapter concludes by discussing what this shared neural circuitry means for our experience and understanding of social pain.

Keywords: social rejection, social pain, neural circuitry, physical pain, neural substrates

In 1989, Vivian Paley, a MacArthur Award-winning teacher, introduced a new rule into her kindergarten classroom: "You can't say you can't play." In other words, social exclusion or not being allowed to play with others—an experience that is almost synonymous with childhood—was banned. As simple as it sounds, Paley describes the mixed feelings that her kindergarten students had about instituting the rule and the difficulty that they had, at first, in following it (discussed in her book; Paley, 1993). However, Paley also describes the palpable sense of relief she observed in her class once this new rule was put into effect: "It was as if the children had been rescued from meanness. They were grateful for a structure that let them feel good about themselves and each other."

As we all know, being rejected or excluded is distressing and painful, even at this young age. Indeed, most of us have vivid childhood memories of the pain of social rejection and can easily imagine the relief experienced by the children in Paley's classroom who were granted at least a temporary safe haven from this dreaded experience. Yet, one question that comes to mind when reflecting on these experiences is: Why is it that social rejection exerts such a powerful effect on our emotional well-being? Or more simply put, why is it that social rejection "hurts"?

Over the past several years, social neuroscience research has transformed our understanding of this question by demonstrating that the experience of social rejection or exclusion ("social pain") is processed by some of the same neural regions that process physical pain (Eisenberger, Lieberman, & Williams, 2003; Eisenberger & Lieberman, 2004, 2005; MacDonald & Leary, 2005). In essence, individuals may describe experiences of rejection as being "painful" because they rely, in part, on pain-related neural circuitry.

In fact, it has been suggested that, because of the importance of social connection for human survival, the social attachment system—which ensures social connection—may have piggybacked directly onto the physical pain system, borrowing the pain signal itself to indicate when social relationships are threatened (Panksepp, 1998). Specifically, as a mammalian species, humans are born relatively immature without the capacity to feed or fend for themselves and must rely solely on the care and nurturance of a caregiver in order to survive. Later in life, being connected to close others as well as a social group increases chances of survival by providing access to shared resources as well as protection from predators (Axelrod & Hamilton, 1981; Buss, 1990). Thus, over the course of our evolutionary history, being separated from others significantly decreased chances of survival. Consequently, if broken social ties are experienced as "painful," an individual will be more likely to avoid situations that might threaten social ties or lead to rejection, hence increasing one's likelihood of inclusion in the social group and one's chances of survival. In short, to the extent that social rejection or exclusion is a threat to survival, feeling "hurt" by these experiences may be an adaptive way to prevent them.

In this chapter, I will review evidence from behavioral, pharmacological, and social neuroscience research that supports the notion that physical and social pain rely on shared neural substrates. I will then review some of the unexpected and potentially surprising consequences that arise from such a physical-social-pain overlap. Specifically, I will review evidence showing that, even though experiences of physical and social pain seem very different from one another on the surface, those individuals who are more sensitive to one kind of pain are also more sensitive to the other. I will also review evidence demonstrating that factors that alter one kind of pain experience alter the other in a congruent manner. Finally, I will end by discussing what this shared neural circuitry means for our experience and understanding of social pain.

Evidence for a Physical-Social Pain Overlap

Linguistic Evidence

One reason to believe that physical and social pain share overlapping mechanisms is that they share a common vocabulary. When individuals describe times when they have felt rejected or excluded, they will often describe these experiences with words typically reserved for physical pain experiences—complaining of "hurt" feelings and "broken" hearts. Indeed, there is no other way to describe socially painful experiences other than through the use of these physical pain words. Interestingly, the use of physical pain words to describe experiences of social pain is not unique to the English language and is observed across many other languages as well (MacDonald & Leary, 2005). However, while suggestive, linguistic evidence alone does not substantiate the claim that physical and social pain processes overlap. After all, it is possible that describing rejection as being "painful" may be no more than a convenient metaphor and social rejection may not actually be experienced as painful. One way to more convincingly demonstrate an overlap in the mechanisms that support physical and social pain processes is to show that they rely on shared neurochemistry or shared neural circuitry. Here, I will review pharmacological, neuropsychological, and neuroimaging research to support this overlap.

Pharmacological Evidence

Pharmacological studies provide evidence that physical and social pain rely on shared neurochemistry by showing that certain drugs have similar effects on both types of pain. For example, opiate drugs, such as morphine and heroin, known primarily for their pain-relieving qualities, have also been shown to reduce behaviors indicative of social pain in animals. Specifically, low, nonsedative doses of morphine have been shown to reduce distress vocalizations made by infants when separated from their mothers across multiple species, including monkeys, dogs, guinea pigs, rats, and chickens (Carden, Barr, & Hofer, 1991; Herman & Panksepp, 1978; Kalin, Shelton, & Barksdale, 1988; Panksepp et al., 1978; Warnick, McCurday, & Sufka, 2005). Moreover, some have suggested that in humans opiate abuse is due, in part, to its capacity to alleviate negative social experience, as opiate addiction is most common in environments where social isolation is pervasive (Panksepp, 1998). Consistent with this, animal research has demonstrated greater opiate consumption among animals who are separated from companions (Alexander, Coambs, & Hadaway, 1978). Similar to the effects of opiates, antidepressants (such as selective serotonin reuptake inhibitors or SSRIs), which are commonly prescribed to treat anxiety and depression often resulting from social stressors, also alleviate physical pain (Nemoto, Toda, Nakajima, Hosokawa, Okada, et al., 2003;

Shimodozono, Kamishita, Ogata, Tohgo, & Tanaka, 2002; Singh, Jain, & Kulkarni, 2001) and are now commonly prescribed to treat chronic pain conditions. Thus, both opiates and antidepressants seem to reduce social as well as physical pain.

Neural Evidence

Neuropsychological and neuroimaging research amassed over the past several decades has also provided support for a physical-social pain overlap by showing that some of the same neural regions that are involved in physical pain are also involved in separation distress behaviors in nonhuman mammals and social pain experience in humans.

The neural correlates of physical pain

Physical pain experience can be subdivided into two components: 1) a *sensory* component, which codes for the discriminative aspects of pain (e.g., location, intensity, duration) and 2) an *affective* component, which codes for the unpleasant aspects of pain (e.g., distressing, suffering). Because the experience of social rejection does not necessitate any direct sensory contact, the affective component of pain may be more relevant for understanding feelings of social pain and will be focused on here.

The "affective" or unpleasant component of physical pain is processed by various regions of the anterior cingulate cortex (specifically the dorsal portion: dACC) and insula (anterior insula) (Apkarian, Bushnell, Treede, & Zubieta, 2005; Peyron, Laurent, & Garcia, 2000; Price, 2000; Rainville, 2002). Thus, chronic pain patients who have undergone cingulotomy—a surgery in which a portion of the dACC is lesioned (Richter et al., 2004)—report that they can still feel and localize pain sensation (sensory component intact) but that the pain no longer "bothers" them (Foltz & White, 1968; Hebben, 1985). Similar reductions in emotional responses to painful stimuli have been observed following insular lesions as well (Berthier, Starkstein, Leiguardia, & Carrea, 1988).

Neuroimaging studies support these neuropsychological findings by showing that both the dACC and anterior insula track the affective component of pain. In one study, subjects who were hypnotized to selectively increase the "unpleasantness" of noxious stimuli (affective component) without altering the intensity (sensory component) showed increased activity in the dACC without changing activity in the primary somatosensory cortex (Rainville, Duncan, Price, Carrier, & Bushnell, 1997). Moreover, other work has shown that self-reports of pain unpleasantness correlate specifically with dACC activity (Peyron et al., 2000; Tolle et al., 1999). Similarly, the anterior insula has been shown to track the affective component of pain and self-reported pain unpleasantness correlates with bilateral anterior insular activity as well (Schreckenberger et al., 2005).

The ACC and separation distress in non-human mammals

Interestingly, the ACC—clearly implicated in perceptions of pain unpleasantness—is also a major contributor to attachment-related distress vocalizations. In many mammalian species, infants will emit distress vocalizations upon caregiver separation in order to signal the caregiver to return to the infant. These vocalizations are presumed to reflect some degree of distress due to separation and serve the adaptive purpose of reducing prolonged separation from a caregiver. Highlighting a role for the ACC in distress vocalizations, it has been shown that lesions to the ACC (that include both dorsal and ventral regions) eliminate the production of these distress vocalizations (Hadland, Rushworth, Gaffan, & Passingham, 2003; MacLean & Newman, 1988), whereas electrical stimulation of the ACC can lead to the spontaneous production of these vocalizations (Robinson, 1967; Smith, 1945). Similar findings have not been observed for the anterior insula. However, other regions that play a role in pain processing, such as the periaqueductal gray (PAG), are also known to be involved in attachment-related behaviors such as distress vocalizations (Bandler & Shipley, 1994).

The neural correlates of social pain in humans

Recent research has also started to reveal that the neural regions that are most often associated with pain unpleasantness (dACC, anterior insula) are also involved in the distressing experience of social exclusion. In the first neuroimaging study of social exclusion (Eisenberger, Lieberman, & Williams, 2003), participants were led to believe that they would be scanned while playing an interactive ball-tossing game over the Internet ("cyberball"), with two other individuals who were also in fMRI scanners. Unbeknownst to participants, they were actually playing with a preset computer program. Participants completed one round of the ball-tossing game in which they were included and a second round in which they were excluded partway through the game.

Upon being excluded from the game, compared to when being included, participants showed increased activity in both the dACC and anterior insula—a pattern very similar to what is often observed in studies of physical pain. Furthermore, individuals who showed greater activity in the dACC reported greater levels of social distress (e.g., "I felt rejected," "I felt meaningless") in response to the exclusion episode. In addition to activity in these pain-related neural regions, participants also showed significant activity (in response to exclusion vs. inclusion) in a neural region that is often associated with regulating painful or negative affective experience—the right ventral prefrontal cortex (RVPFC; Hariri, Bookheimer, Mazziotta, 2000; Lieberman, Jarcho, Berman, Naliboff, Suyenobu, Mandelkern, & Mayer, 2004; Lieberman, Eisenberger, Crockett, Tom, Pfeifer, & Way, 2007; Ochsner & Gross, 2005; Petrovic & Ingvar, 2002; Wager et al., 2004). Indeed, consistent with this region's role in emotion/pain regulatory processes, greater RVPFC activity was associated with lower levels of self-reported social distress in response to social exclusion and reduced activity in the dACC. Finally, we found that the dACC was a significant mediator of the RVPFC—distress relationship, such that the RVPFC may relate to lower levels of social distress by downregulating the activity of the dACC.

Although, we have not yet examined neural responses to physical and social pain within the same set of participants, Figure 39.1 shows the similarity in the neural responses to social pain, taken from the study of social exclusion described above (on the left; Eisenberger et al., 2003) and the neural responses to physical pain, taken from a neuroimaging study of irritable bowel syndrome patients undergoing painful visceral stimulation (on the right; Lieberman et al., 2004). Thus, not only are the general locations of the activations similar but the pattern of correlations between neural activity and self-reported pain or social distress is similar as well.

Subsequent research, using various experimental designs, has provided analogous findings. Thus, both our own group and others have found that greater self-reported social pain following the cyberball game was associated with greater activity in the dACC (Eisenberger, Taylor, Gable, Hilmert, & Lieberman, 2007; Onoda et al., 2009). Moreover, it has been shown that individual difference factors that typically moderate responses to social pain show the expected relationships with neural activity. Thus, individuals with higher levels of social support show reduced dACC activity in response to social exclusion (Eisenberger, Taylor et al., 2007).

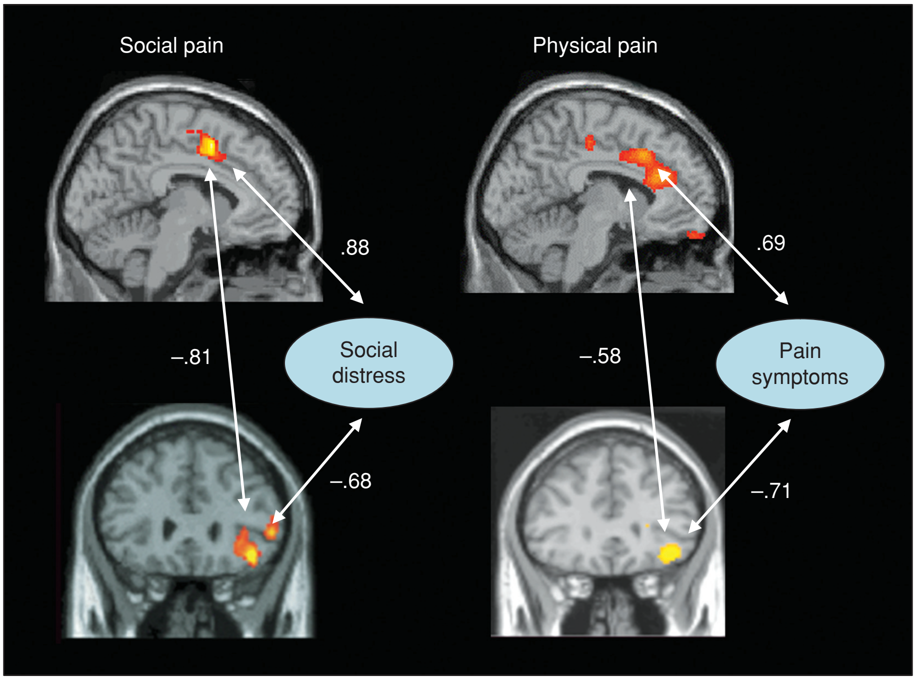

Fig. 39.1 The left side of the panel displays neural activity during social exclusion, compared to social inclusion, that correlates with self-reported social distress (from Eisenberger, Lieberman, & Williams, 2003). The right side of the panel displays the neural activity during painful visceral stimulation, compared to baseline, that correlates with self-reported pain experience.
From Lieberman, Jarcho, Berman, Naliboff, Suyenobu, Mandelkern, & Mayer, 2004. Reprinted with permission of Elsevier.

Conversely, individuals with lower levels of self-esteem (vs. higher levels of self-esteem) report feeling more hurt in response to social exclusion (using the cyberball game) and also show greater activity in the dACC (Onoda et al., in press). Finally, individuals who reported feeling more socially rejected or disconnected in their real-world social interactions (assessed daily across a 10-day period) showed greater activity in the dACC and PAG in response to a cyberball-exclusion episode (Eisenberger, Gable, & Lieberman, 2007), suggesting a link between real-world experiences of social rejection and pain-related neural activation.

In addition to studies examining the neural correlates underlying the experience of social pain, studies using rejection-themed images or facial expressions have shown similar effects as well. Thus, Kross and colleagues (2007) have shown both dACC and anterior insula activity in response to rejection-themed images (paintings by Edward Hopper) compared to acceptance-themed images. Moreover, we have shown that for rejection-sensitive individuals, viewing videos of individuals making disapproving facial expressions—a potential cue of social rejection—was associated with greater activity in the dACC, but not other limbic regions (e.g., amygdala), suggesting that the dACC may be specifically responsive to these cues of rejection (Burklund, Eisenberger, & Lieberman, 2007).

Finally, other types of socially painful experiences, such as bereavement, have also been shown to activate pain-related neural regions. In one study (Gundel, O'Connor, Littrell, Fort, & Lane, 2003), bereaved participants were scanned while viewing pictures of their deceased first-degree relative or pictures of a stranger. In response to viewing pictures of the deceased, compared to pictures of a stranger, participants showed greater activity in regions of the dACC and anterior insula. A subsequent study, using a similar design, replicated these findings; bereaved individuals experiencing normal or complicated grief showed greater activity in both the dACC and anterior insula in response to viewing images of the deceased vs. images of a stranger (O'Connor et al., 2008). Thus, various types of socially painful experience—not just experiences of social rejection or exclusion—may activate pain-related neural regions as well.

Summary

Across diverse languages, individuals use the same words to describe the negative feelings associated with physical injury and social rejection. Pharmacological agents that affect one type of pain appear to have parallel effects on the other. Moreover, neural data from both animal and human subjects converge to show that some of the same neural regions support both physical and social pain experience. One of these regions, the dACC, has been shown to be involved in the experienced unpleasantness of physical pain, the elicitation of separation distress behaviors in non-human mammals, and the experience of distress following social rejection in humans. Other regions that have also been shown to play a role in these pain processes include the anterior insula and PAG, which encode physical pain experience (Aziz, Schnitzler, & Enck, 2000; Bandler & Shipley, 1994; Cechetto & Saper, 1987), as well as the RVPFC, which has been involved in regulating painful as well as generally negative affective experience (Hariri et al., 2000; Lieberman et al., 2004, 2007; Petrovic & Ingvar, 2002; Wager et al., 2004).

Taken together, these data provide convergent evidence for a physical-social pain overlap. In the next section, I will highlight some of the expected functional consequences of such an overlap and will review several studies that have examined the nature of these consequences. It should be noted, however, that even though there is evidence to support a functional overlap in physical and social pain processes, these processes certainly do not overlap completely. Intuitively, we know this to be true because we can differentiate between pain due to a relationship snub and pain due to physical injury. Moreover, research has identified specific differences between these two types of pain experience. For example, Chen and colleagues have shown that individuals can easily relive the pain of previous relationship breakups or other socially painful events; however, it is much harder, and sometimes impossible to relive the pain of physical injury (Chen, Williams, Fitness, & Newton, 2008). Nonetheless, even though there are certainly ways in which physical and social pain experiences are different, this next section will focus on ways in which these pain processes are similar and the consequences of this similarity.

Consequences of a Physical-Social Pain Overlap

One of the benefits of identifying a physical-social pain overlap is that it leads to several novel hypotheses regarding the functional consequences of such an overlap. The first hypothesis—*the individual differences hypothesis*—is that individuals who are more sensitive to one kind of pain should also be more sensitive to the other because both of these pain processes are governed, in part, by the same underlying system. The second hypothesis—*the manipulation hypothesis*—is that factors that either increase or decrease one kind of pain should affect the other in a similar manner, because altering one pain process should alter the underlying system that supports both pain types of painful experience. Here I will review evidence for each of these hypotheses. I will then discuss several other possible consequences of a social-pain overlap that have remained largely unexplored.

Individual Differences Hypothesis: Sensitivity to One Kind of Pain Should Relate to Sensitivity to the Other

One of the intriguing consequences of a physical-social pain overlap is that individuals who are more sensitive to one kind of pain (e.g., physical pain) should also be more sensitive to a seemingly different kind of pain (e.g., social pain). To test this notion, we have investigated whether baseline sensitivity to physical pain relates to self-reported sensitivity to social rejection (Eisenberger, Jarcho, Lieberman, & Naliboff, 2006). In this study, participant's baseline sensitivity to physical pain was assessed by asking participants to rate the temperature at which they perceived a painful heat stimulus delivered to their forearm to be very unpleasant ("pain threshold"). After this, participants completed one round of the cyberball game in which they were socially excluded and were subsequently asked to rate how much social distress they felt in response to being excluded. As predicted, individuals who were more sensitive to physical pain at baseline (e.g., lower baseline pain thresholds) were also more socially distressed by the social exclusion episode. Moreover, this relationship remained significant after controlling for neuroticism, suggesting that this relationship cannot be explained solely by a general tendency to report higher levels of negative experience.

Building on this, we have also examined whether a genetic correlate of physical pain sensitivity relates to social pain sensitivity as well (Way, Taylor, & Eisenberger, 2009). Previous research has shown that a polymorphism in the mu-opioid receptor gene (*OPRM1*; *A118G*) is associated with physical pain sensitivity, such that individuals with the variant G allele tend to experience more physical pain and need more morphine to deal with the pain (Chou et al., 2006a-b; Coulbault et al., 2006; Sia et al., 2008). To examine whether this polymorphism also related to social pain sensitivity, we examined whether allelic differences in the *OPRM1* gene related to both dispositional and neural sensitivity to social rejection. Participants (n = 125) were genotyped for the *OPRM1* gene and were asked to complete a self-report measure of trait sensitivity to rejection (Mehrabian Sensitivity to Rejection Scale; Mehrabian, 1976; e.g., "I am very sensitive to any signs that a person might not want to talk to me"). Following this, a subset of these individuals (n = 30) completed the cyberball game in the scanner in which they were socially excluded. Results demonstrated that G allele carriers—who have previously been shown to be more sensitive to physical pain—also reported significantly higher levels of rejection sensitivity. Moreover, neuroimaging analyses revealed that G allele carriers also showed greater pain-related neural activity (dACC, anterior insula) in response to social exclusion (Figure 39.2). Thus, a genetic correlate of physical pain sensitivity related to both dispositional and neural sensitivity to social pain as well.

Although less work has examined whether individual differences in social pain sensitivity relate to physical pain sensitivity, correlational research has shown that adolescents with higher levels of attachment anxiety (increased sensitivity to rejection from an attachment figure) also reported greater pain severity over a one-month assessment period (Tremblay & Sullivan, 2009). Moreover, depressed individuals who reported increases in levels of state rejection sensitivity also reported increases in symptoms of pain (e.g., chest pain, headaches, body aches and pains) (Ehnvall, Mitchel, Hadzi-Pavlovic, Malhi, & Parker, 2009). Thus, individuals who tend to be more sensitive to rejection may also be more sensitive to physical pain.

Manipulation Hypothesis: Factors that Increase or Decrease One Kind of Pain Should Affect the Other in a Similar Manner

To the extent that physical and social pain processes overlap, factors that alter one type of painful experience should affect the other type of pain in a similar manner. Thus, factors that increase or decrease social pain should have similar effects on physical pain, and, likewise, factors that increases or decrease physical pain should have parallel effects on social pain. Although few studies have directly examined this hypothesis, as it is not necessarily intuitive to measure feelings of social and physical pain in the

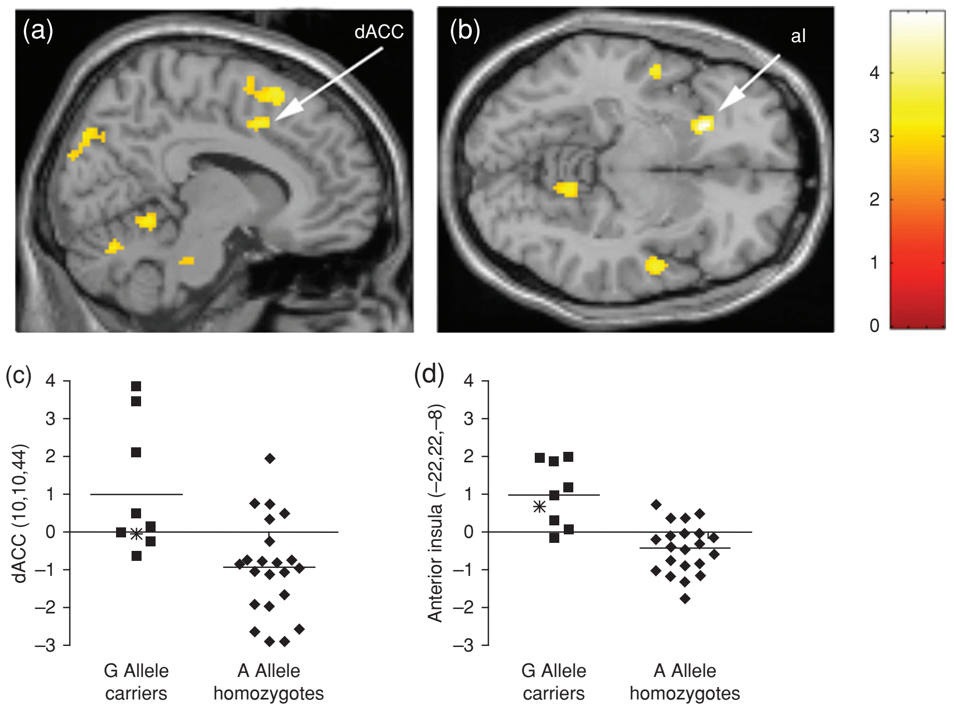

Fig. 39.2 Sagittal (a; dACC) and axial (b; anterior insula, denoted by arrow) sections of neural activations during social exclusion vs. inclusion that showed significantly greater activity ($p < 0.001$, 20 voxel extent) for G allele carriers than A allele homozygotes. c) Parameter estimates from the dACC (8,12,44; $t_{(24)} = 4.06$, $p < 0.001$); d) Parameter estimates from the left anterior insula (–22,24,–8; $t_{(24)} = 5.07$, $p < 0.001$). * denotes G allele homozygote.

same study, the number of studies that have started to explicitly test this notion is increasing. I will begin by reviewing the studies that have examined whether factors that increase or decrease social pain (social pain potentiation/regulation effects) affect physical pain and will then review the studies that have examined whether factors that increase or decrease physical pain (physical pain potentiation/regulation) affect social pain as well.

Social pain potentiation effects

To explore whether factors that increase social pain increase physical pain as well, we tested whether an episode of social exclusion increased subsequent physical pain sensitivity (Eisenberger et al., 2006). In this study, participants were randomly assigned to play a round of the cyberball game in which they were either included or excluded. Then, as participants were either being included or excluded from the game, they were exposed to three painful heat stimuli (the level of heat was customized so that each participant received heat stimuli that he/she had previously rated as "very unpleasant") and were asked to rate the unpleasantness of each. Following this, participants rated how much social distress they felt during the cyberball game (e.g., "I felt rejected," "I felt meaningless"). Although we did not find that excluded individuals reported feeling more pain in response to the heat stimuli than included individuals, we did find that, among subjects who were excluded, those who felt the most social distress also reported the highest pain ratings in response to the heat stimuli. Moreover, this effect remained after controlling for neuroticism, suggesting that the positive correlational relationship between social distress and pain distress was not due solely to a greater tendency to report negative affect and could reflect a more specific relationship between physical and social pain processes. Thus, even though this finding is correlational, it suggests that augmented sensitivity to one type of pain is related to augmented sensitivity to the other.

It should be noted, however, that these findings are somewhat different from those of another study that examined the effect of social exclusion (using a different manipulation) on physical pain sensitivity (DeWall & Baumeister, 2006). This study was based on the observation that extreme physical pain can sometimes turn off the pain system itself, leading to temporary analgesia or numbness (Gear, Aley, &

Levine, 1999). Based on this observation, it was hypothesized that, to the extent that physical and social pain overlap, extreme forms of social exclusion should lead to numbness, not only to negative social experiences, but to physical pain as well. In this study (DeWall & Baumeister, 2006), social exclusion was manipulated by telling participants that they would be alone in the future. Participants in this "future alone" condition, compared to those who were given no feedback or who were told that they would have satisfying relationships in the future, showed a reduced (rather than an increased) sensitivity to physical pain.

Differences between these two sets of findings could be due to the underlying nature of the pain system, such that mild pain (e.g., being excluded by strangers during the cyberball game) augments pain sensitivity whereas more intense pain (e.g., being told that one will be alone in the future) leads to analgesia (Gear et al., 1999; Price, 2000). It is also possible that the "future alone" manipulation may have induced more depression-like affect, which in some cases has been associated with reduced experimental pain sensitivity (Adler & Gattaz, 1993; Dickens, McGowan, & Dale, 2003; Orbach, Mikulincer, King, Cohen, & Stein, 1997), whereas the cyberball manipulation may have induced more anxiety-like affect, which has been linked with increased experimental pain sensitivity (Cornwall & Donderi, 1988; Lautenbacher & Krieg, 1994; Melzack & Wall, 1999). Nonetheless, it is important to note that in both studies, physical and social pain sensitivity still appear to be working in parallel. In the first study, greater sensitivity to social rejection was correlated with greater sensitivity to physical pain; in the second, an extreme form of social exclusion resulted in general emotional insensitivity, both to social and physical pain.

As a final example of the effect of social pain potentiation on physical pain, Gray and Wegner (2009) examined whether an intentional interpersonal transgression (i.e., stepping on someone's toe on purpose), which is typically more emotionally "hurtful" than an accidental transgression, was also more physically painful. Participants believed that another subject, who was actually a confederate, was going to choose which of two tasks the participant was going to complete. In the intentional transgression condition, the confederate chose a task that involved the participant receiving electric shock; in the unintentional transgression condition, the confederate chose a pitch judgment task for the participant to complete, but the participant still received shock due to study constraints. Participants were told which task the confederate chose for them and then rated pain unpleasantness as they received a series of electric shocks. Results demonstrated that physical pain ratings following the intentional transgression were higher than those following the unintentional transgression. In addition, while participants in the unintentional transgression condition showed habituation to repeated painful stimulation, those in the intentional transgression condition did not. Thus, social factors that are primarily thought to increase emotional pain seem to affect physical pain in a congruent manner.

Social pain regulation effects

A great deal of correlational research has shown that factors that reduce social pain—such as social support—are associated with less physical pain as well. Thus, individuals with more social support report feeling less pain during childbirth (Chalmers, Wolman, Nikodem, Gulmezoglu, & Hofmeyer, 1995; Kennell, Klaus, McGrath, Robertson, & Hinkley, 1991), following coronary artery bypass surgery (King, Reis, Porter, & Norsen, 1993; Kulik & Mahler, 1989), and during cancer (Zaza & Baine, 2002). However, because of the correlational nature of these studies, it is not clear if social support directly reduces physical pain or whether some third variable (e.g., extraversion) explains these effects.

A few experimental studies have provided evidence to suggest that social support may directly reduce physical pain by demonstrating that participants receiving interactive support during a painful task reported less pain than participants completing the task alone or during nonsupportive interactions (Brown, Sheffield, Leary, & Robinson, 2003; Jackson, Iezzi, Chen, Ebnet, & Eglitis, 2005). However, given the nature of these studies, some of the pain-attenuating effects of social support could have been due to other factors unrelated to social support, such as distraction due to the presence of the support figure or reappraisal due to the support figure actively helping the participant to cope with the pain.

Thus, in a recent study, we examined whether a very minimal social support manipulation could directly reduce physical pain experience (Master, Eisenberger, Taylor, Naliboff, Shirinyan, & Lieberman, 2009). In this study, female participants received a series of painful heat stimuli and were asked to rate the unpleasantness of each while they went through a number of different tasks, including holding their partner's hand, a stranger's hand, or a squeeze-ball and viewing a picture of their partner, a stranger, or a neutral object (a chair). We found that participants reported significantly less pain while holding their partner's hand compared to when they were holding a stranger's hand or an object. Interestingly, participants also reported feeling significantly less pain while simply viewing pictures of their partner compared to when they were viewing pictures of a stranger or an object. Thus, simple reminders of one's social support figure may be capable of directly reducing physical pain, in addition to social pain.

Physical pain potentiation effects

Although there is not a lot of research that has directly examined whether potentiating physical pain experience potentiates social pain experience as well, there is some correlational research that supports the notion that these two experiences are related. For example, Bowlby noted that when children experience physical pain, they become much more sensitive to the whereabouts of their caregiver, experiencing distress more frequently and easily upon noting distance from a caregiver (Bowlby, 1969). Similarly, compared to healthy controls, adults with chronic pain are more likely to have an anxious attachment style, characterized by a heightened sense of concern with their partner's relationship commitment (Ciechanowski, Sullivan, Jensen, Romano, & Summers, 2003).

In the only experimental study (to our knowledge) to examine whether factors that increase physical pain also increase experiences of social pain, we examined the effect of inflammatory activity on feelings of social disconnection (Eisenberger, Inagaki, Mashal, & Irwin, 2010). Previous research has shown that pro-inflammatory cytokines, which are involved in fighting off foreign agents such as bacteria, facilitates physical pain experience as well, presumably to promote recovery and recuperation from infection or disease (Watkins & Maier, 2000). Here, we wanted to see if inflammatory processes might also increase social pain experience.

In this study, participants were randomly assigned to either receive placebo or endotoxin—a bacterial agent that has been shown to trigger an inflammatory response in a safe manner. Participants were then asked to complete hourly self-report measures of their feelings of social disconnection (e.g., "I feel disconnected from others," "I feel overly sensitive around others (e.g., my feelings are easily hurt)") for six hours. Results demonstrated that individuals in the endotoxin condition reported significantly greater increases in feelings of social disconnection (from baseline to two hours post-drug treatment) than those in the placebo condition. Thus, activating inflammatory processes, known to increase experiences of physical pain, increased self-reports of social disconnection as well.

Physical pain regulation effects

Finally, we have also examined whether factors that regulate physical pain also regulate social pain. Specifically, we have explored whether Tylenol (generic name: acetaminophen), a well-known physical pain reliever, could also reduce social pain (DeWall et al., 2010). In a first study, participants were randomly assigned to take either a daily dose of Tylenol (1000 mg/day) or placebo for 3 weeks and were asked each night to report on their daily "hurt feelings" (e.g., "Today, I rarely felt hurt by what other people said or did to me" (reverse-scored)). Results demonstrated that individuals in the Tylenol condition showed a significant reduction in hurt feelings across the 3-week period, whereas individuals in the placebo condition showed no significant change in hurt feelings over time. In fact, the average participant in the Tylenol group reported significantly lower daily hurt feelings than the average participant in the placebo group starting on Day 9 and continuing through Day 21.

To further examine the neural mechanisms that might underlie these effects, in a second study, participants were randomly assigned to take a daily dose of Tylenol (2000 mg/day) or placebo for 3 weeks and then completed the cyberball task in the scanner at the end of the 3-week period. Consistent with the results from the first study, participants in the Tylenol condition, compared to those in the placebo condition, showed significantly less pain-related neural activity (dACC, anterior insula) in response to social exclusion (Figure 39.3). Thus, Tylenol, a well-known physical pain reliever, appears to have similar effects on experiences of social pain.

Other Consequences of a Physical-Social Pain Overlap?

There are several other possible consequences of a physical-social pain overlap that have not yet been directly explored. One of these may be the aggressive behaviors that are observed following both physical and social pain. Aggressive action makes sense if one is in danger of being physically harmed, and not surprisingly, one consequence of painful stimulation in animals is aggressive attacks on a con-specific (Berkowitz, 1983). However, aggressive acts make less sense if one is being socially harmed,

39-Decety-39.indd 594 1/19/2011 6:05:02 PM

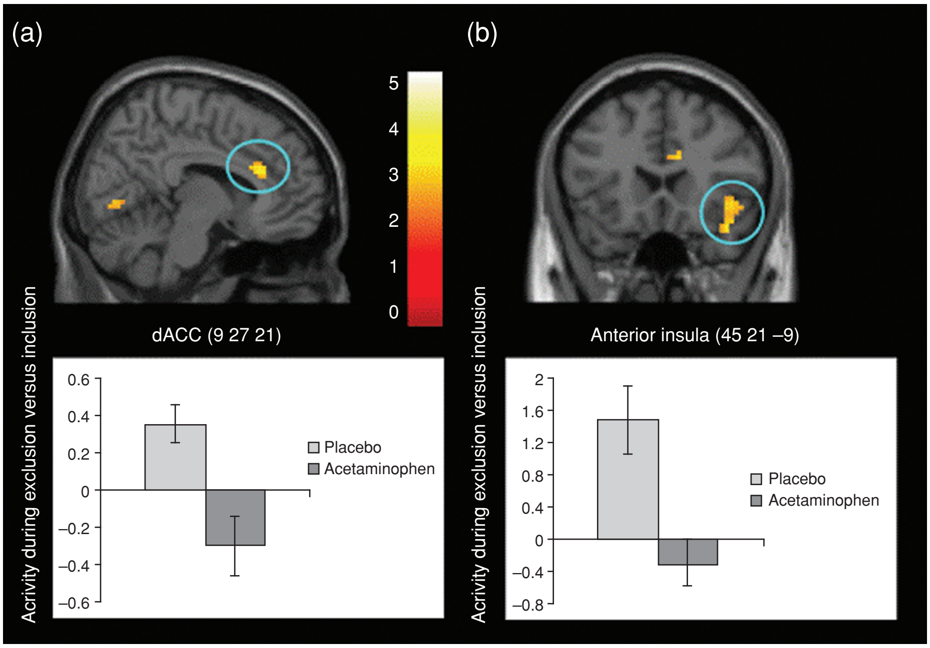

Fig. 39.3 Whole-brain, between-group analysis displaying neural activity (parameter estimates during exclusion vs. inclusion) that was greater for participants who took placebo (vs. those who took acetaminophen) in the (a) dACC and (b) right anterior insula ($p < .005$, 20 voxels). Bar graphs (with standard error bars) for each region show the activity during exclusion compared to inclusion, averaged across the entire cluster, for the acetaminophen and placebo groups.

as aggression is presumably not conducive to strengthening or mending social ties. Nonetheless, it has been well documented that the experience of social rejection can lead to aggressive acts as well (Twenge, Baumeister, Tice, & Stucke, 2001). Thus, it is possible that aggressive responses to rejection may be a by-product of an adaptive response to physical pain, which was subsequently co-opted by the social pain system. In other words, although aggressive responses to rejection may be maladaptive in recreating social bonds, this response may reflect a conservation of behavioral responses that are adaptive following physical pain.

Another possible consequence of this overlap may be the similar physiological stress responses that are observed to both physical threat and social threat. It is well known that physical threat induces physiological stress responses to mobilize energy and resources to deal with the threat (Taylor, 2003), and this makes good sense. Escaping a predator or navigating some other life-threatening situation may require a significant amount of physical energy. However, these same physiological responses are responsive to social threats as well, such as being socially evaluated (Dickerson & Kemeny, 2004). Although this may not seem surprising to stress researchers who have witnessed these effects repeatedly, from a functional perspective, it makes little sense that the body would require significant energy resources to manage the stress of social evaluation. After all, how much physical energy is needed to give a public speech or to worry about one's performance? However, if the threat of social rejection is interpreted by the brain in the same manner as the threat of physical harm, biological stress responses might be triggered to both for the simple reason that these two systems overlap.

Summary

Identifying an overlap in the neural substrates that underlie physical and social pain leads to several novel hypotheses regarding the ways in which these two types of painful experiences interact. For examples, studies reviewed here demonstrated that those more sensitive to physical pain were also more sensitive to social pain and that factors that regulate or potentiate one kind of pain have similar effects on the other. There are likely many other consequences of this functional overlap and future research will be needed to further explore and uncover these effects.

Conclusions

Taken together, the research presented here puts forth a strong case for the notion that being rejected "hurts."

Indeed, social neuroscience research has fundamentally changed the way that we understand experiences of social rejection by demonstrating that some of the same neurochemistry and neural circuitry that underlies physical pain, underlies social pain too. One of the implications of these findings is that episodes of rejection or relationship dissolution can be just as damaging and debilitating to the person experiencing those events as episodes of physical pain. Thus, even though we may treat physical pain conditions more seriously and regard them as more valid ailments, the pain of social loss can be equally as distressing, as demonstrated by the activation of pain-related neural circuitry to social disconnection as well.

It is important to remember, though, that while painful in the short-term, feelings of distress and heartache following social exclusion or broken social relationships also serve a valuable function, namely to ensure the maintenance of close social ties. Thus, returning to our opening example, although the pain of social rejection on the kindergarten playground is palpable, it also serves as a reminder of our inherent need for social connection. To the extent that being rejected hurts, individuals are motivated to avoid situations in which rejection is likely. Over the course of evolutionary history, avoiding social rejection and staying socially connected to others likely increased chances of survival, as being part of a group provided additional resources, protection, and safety. Thus, the experience of social pain, while distressing and hurtful in the short-term, is an evolutionary adaptation that promotes social bonding and ultimately survival.

References

Adler, G. & Gattaz, W. F. (1993). Pain perception threshold in major depression. *Biological Psychiatry*, *15*, 687–689.

Alexander, B. K., Coambs, R. B., & Hadaway, P. F. (1978). The effect of housing and gender on morphine self-administration in rats. *Psychopharmacology*, *58*, 175–179.

Apkarian, A. V., Bushnell, M. C., Treede, R. -D., & Zubieta, J. -K. (2005). Human brain mechanisms of pain perception and regulation in health and disease. *Journal of Pain*, *9*, 463–484.

Axelrod, R. & Hamilton, W. D. (1981). The evolution of cooperation. *Science*, *211*, 1390–1396.

Aziz, Q., Schnitzler, A., & Enck, P. (2000). Functional neuroimaging of visceral sensation. *Journal of Clinical Neurophysiology*, *17*, 604–612.

Bandler, R. & Shipley, M. T. (1994). Columnar organization in the midbrain periaqueductal gray: Modules for emotional expression? *Trends in Neurosciences*, *17*, 379–389.

Berkowitz, L. (1983). Aversively stimulated aggression: Some parallels and differences in research with animals and humans. *American Psychologist*, *38*, 1135–1144.

Berkowitz, L. (1993). *Aggression: Its causes, consequences and control*. Philadelphia, PA: Temple University Press.

Berthier, M., Starkstein, S., Leiguardia, R., & Carrea, R. (1988). Asymbolia for pain: A sensory-limbic disconnection system. *Annals of Neurology*, *24*, 41–49.

Bowlby, J. (1969). *Attachment & loss, Vol. I: Attachment*. New York: Basic Books.

Brown, J. L., Sheffield, D., Leary, M. R., & Robinson, M. E. (2003). Social support and experimental pain. *Psychosomatic Medicine*, *65*, 276–283.

Burklund, L. J., Eisenberger, N. I., & Lieberman, M. D. (2007). Rejection sensitivity moderates dorsal anterior cingulate activity to disapproving facial expressions. *Social Neuroscience*, *2*, 238–253.

Carden, S. E., Barr, G. A., & Hofer, M. A. (1991) Differential effects of specific opioid receptor agonists on rat pup isolation calls. *Brain Research, Development, Brain Research, 62*, 17–22.

Cechetto, D. F. & Saper, C. B. (1987). Evidence for a viscerotopic sensory representation in the cortex and thalamus in the rat. *Journal of Comparative Neurology*, *262*, 27–45.

Chalmers, B., Wolman, W. L., Nikodem, V. C., Gulmezoglu, A. M., & Hofmeyer, G. J. (1995). Companionship in labour: Do the personality characteristics of labour supporters influence their effectiveness? *Curationis*, *18*, 77–80.

Chen, Z., Williams, K. D., Fitness, J., & Newton, N. (2008). When hurt won't heal: Exploring the capacity to relive social and physical pain. *Psychological Science*.

Chou, W-Y., Yang, L.-C., Lu, H. F., Ko, J. Y., Wang, C.H., Lin, S. H. et al. (2006a). Association of mu-opiod receptor gene polymorphism (A118G) with variations in morphine consumption for analgesia after total knee arthroplasty. *Acta Anaesthesiol Scandanavica*, *50*, 787–792.

Chou, W. Y., Wang, C. -H., Liu, P. -H., Liu, C. -C., Tseng, C.- C., & Jawan, B. (2006b). Human opioid receptor A118G polymorphism, affects intravenous patient-controlled analgesia morphine consumption after total abdominal hysterectomy. *Anesthesiology*, 105334–105337.

Ciechanowski, P., Sullivan, M., Jensen, M., Romano, J., & Summers, H. (2003). The relationship of attachment style to depression, catastrophizing and health care utilization in patients with chronic pain. *Pain*, *104*, 627–637.

Cornwall, A. & Donderi, D. C. (1988). The effect of experimentally induced anxiety on the experience of pressure pain. *Pain*, *35*, 105–113.

Coulbalt, L., Beaussier, M., Verstuyft, C., Weikmans, H., Dubert, L., Trégouet, D., et al. (2006). Environmental and genetic factors associated with morphine response in the postoperative period. *Pharmacogenetics and Genomics*, *79*, 316–324.

DeWall, C. N. & Baumeister, R. F. (2006). Alone but feeling no pain: Effects of social exclusion on physical pain tolerance and pain threshold, affective forecasting, and interpersonal empathy. *Journal of Personality and Social Psychology*, *91*, 1–15.

DeWall, C. N., MacDonald, G., Webster, G. D., Masten, C., Baumeister, R. F., Powell, C., et al. (2010). Tylenol reduces social pain: Behavioral and neural evidence. *Psychological Science*, *21*, 931–937.

Dickens, C., McGowan, L., & Dale, S. (2003). Impact of depression on experimental pain perception: A systematic review of the literature with meta-analysis. *Psychosomatic Medicine*, *65*, 369–375.

Dickerson, S. & Kemeny, M. E. (2004). Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. *Psychological Bulletin*, *103*, 355–391.

Eisenberger, N. I., Gable, S. L., & Lieberman, M. D. (2007). fMRI responses relate to differences in real-world social experience. *Emotion*, *7*, 745–754.

Eisenberger, N. I., Inagaki, T. K., Mashal, N. M. & Irwin, M. R. (2010). Inflammation and social experience: An inflammatory challenge induces feelings of social disconnection in addition to depressed mood. *Brain, Behavior, & Immunity*, *24*, 558–563.

Eisenberger, N. I., Jarcho, J. M., Lieberman, M. D., & Naliboff, B. D. (2006). An experimental study of shared sensitivity to physical pain and social rejection. *Pain*, *126*, 132–138.

Eisenberger, N. I. & Lieberman, M. D. (2004). Why rejection hurts: The neurocognitive overlap between physical and social pain. *Trends in Cognitive Sciences*, *8*, 294–300.

Eisenberger, N. I. & Lieberman, M. D. (2005). Broken hearts and broken bones: The neurocognitive overlap between social pain and physical pain. In K. D. Williams, J. P. Forgas, & von Hippel (Eds.), *The social outcast: Ostracism, social exclusion, rejection, and bullying* (pp. 109–127). New York: Cambridge University Press.

Eisenberger, N. I., Lieberman, M. D., & Williams, K. D. (2003). Does rejection hurt: An fMRI study of social exclusion. *Science*, *302*, 290–292.

Eisenberger, N. I., Taylor, S. E., Gable, S. L., Hilmert, C. J., & Lieberman, M. D. (2007). Neural pathways link social support to attenuated neuroendocrine stress responses. *Neuroimage*, *35*, 1601–1612.

Ehnvall, A., Mitchell, P. B., Hadzi-Pavlovic, D., Malhi, G. S., & Parker, G. (2009). Pain during depression and relationship to rejection sensitivity. *Acta Psychiatrica Scandinavica*, *119*, 375–382.

Foltz, E. L. & White, L. E., (1968). The role of rostral cingulotomy in "pain" relief. *International Journal of Neurology*, *6*, 353–373.

Gear, R. W., Aley, K. O., & Levine, J. D. (1999). Pain-induced analgesia mediated by mesolimbic reward circuits. *The Journal of Neuroscience*, *15*, 7175–7181.

Gray, K. & Wegner, D. M. (2009). The sting of intentional pain. *Psychological Science*.

Gündel, H., O'Connor, M.-F., Littrell, L., Fort, C., & Richard, L. (2003). Functional neuroanatomy of grief: An fMRI study. *Journal of Psychiatry*, *160*, 1946–1953.

Hadland, K. A, Rushworth, M. F. S., Gaffan, D., & Passingham, R. E. (2003). The effect of cingulate lesions on social behaviour and emotion. *Neuropsychologia*, *41*, 919–931.

Hariri, A. R., Bookheimer, S. Y., & Mazziotta, J. C. (2000). Modulating emotional response: Effects of a neocortical network on the limbic system. *NeuroReport*, *11*, 43–48.

Hebben, N. (1985). Toward the assessment of clinical pain. In G. M. Aronoff (Ed.), *Evaluation and treatment of chronic pain* (pp. 451–462). Baltimore: Urban & Schwarzenburg.

Herman, B.H. & Panksepp, J. (1978). Effects of morphine and naloxone on separation distress and approach attachment: Evidence for opiate mediation of social affect. *Pharmacology and Biochemical Behavior*, *9*, 213–220.

Jackson, T., Iezzi, T., Chen, H., Ebnet, S., & Eglits, K. (2005). Gender, interpersonal transactions, and the perception of pain: An experimental analysis. *The Journal of Pain*, *6*, 228–236.

Kalin, N. H., Shelton, S. E., & Barksdale, C. M. (1988). Opiate modulation of separation-induced distress in non-human primates. *Brain Research*, *440*, 285–292.

Kennell, J., Klaus, M., McGrath, S., Robertson, S., & Hinkley, C. (1991). Continuous emotional support during labor in US hospital: A randomized control trial. *Journal of the American Medical Association*, *265*, 2197–2201.

King, K. B., Reis, H. T., Porter, L. A., & Norsen, L. H. (1993). Social support and long-term recovery from coronary artery surgery: Effects on patients and spouses. *Health Psychology*, *12*, 56–63.

Kirzinger, A. & Jurgens, U. (1982). Cortical lesion effects and vocalization in the squirrel monkey. *Brain Research*, *233*, 299–315.

Kulik, J. A. & Mahler, H. I. (1989). Social support and recovery from surgery. *Health Psychology*, *8*, 221–238.

Kross, E., Egner, T., Ochsner, K., Hirsch, J., & Downey, G. (2007). *Journal of Cognitive Neuroscience*, *19*, 945–956.

Lautenbacher, S. & Krieg, J. C. (1994). Pain perception in psychiatric disorders: A review of the literature. *Journal of Psychiatric Research*, *28*, 109–122.

Lieberman, M. D., Eisenberger, N. I., Crockett, M. J., Tom, S. M, Pfeifer, J. H., & Way, B. M. (2007). Putting feelings into words: Affect labeling disrupts amygdala activity to affective stimuli. *Psychological Science*, *18*, 421–428.

Lieberman, M. D., Jarcho, J. M., Berman, S., Naliboff, B. D., Suyenobu, B. Y., Mandelkern, M., et al. (2004). The neural correlates of placebo effects: A disruption account. *Neuroimage*, *22*, 447–455.

MacDonald, G. & Leary, M. R. (2005). Why does social exclusion hurt? The relationship between social and physical pain. *Psychological Review*, *131*, 202–223.

MacLean P. D. & Newman, J. D. (1988). Role of midline frontolimbic cortex in production of the isolation call of squirrel monkeys. *Brain Research*, *45*, 111–123.

Master, S. L., Eisenberger, N. I., Taylor, S. E., Naliboff, B. D., Shirinyan, D., & Lieberman, M. D. (2009). A picture's worth: Partner photographs reduce experimentally induced pain. *Psychological Science*, *20*, 1316–1318.

Mehrabian, A. (1976). Questionnaire measures of affiliative tendency and sensitivity to rejection. *Psychological Reports*, *38*, 199–209.

Melzack, R. & Wall, D. (1999). *Textbook of pain*. Edinburgh: Churchill Livingstone.

Nemoto, H., Toda, H., Nakajima, T., Hosokawa, S., Okada, Y., Yamamoto, K., et al. (2003). Fluvoxamine modulates pain sensation and affective processing of pain in human brain. *Neuroreport*, *14*, 791–797.

Ochsner, K. N. & Gross, J. J. (2005). The cognitive control of emotion. *Trends in Cognitive Sciences*, *9*, 242–249.

O'Connor, M. F., Wellisch, D. K., Stanton, A., Eisenberger, N. I., Irwin, M. R., & Lieberman, M. D. (2008). Craving love? Enduing grief activates brain's reward center. *NeruoImage*, *42*, 969–972.

Onoda, K., Okamoto, Y, Nakashima, K, Nittono, H., Ura, M., & Yamawaki, S. (2009). Decreased ventral anterior cingulate cortex activity is associated with reduced social pain during emotional support. *Social Neuroscience*, *4*, 443–454.

Onoda, K., Okamoto, Y., Nakashima, K, Nittoni, H., Yoshimura, S., Yamawaki, S., et al. (in press). Does low self-esteem enhance social pain? The relationships between trait self-esteem and anterior cingulate cortex activation induced by ostracism. *Social Cognitive and Affective Neuroscience*.

Orbach, I., Mikulincer, M., King, R., Cohen, D., & Stein, D. (1997). Thresholds and tolerance of physical pain in suicidal and nonsuicidal adolescents. *Journal of Consulting and Clinical Psychology*, *65*, 646–652.

Paley, V. (1993). *You can't say you can't play*. Cambridge, MA: Harvard University Press.

Panksepp, J. (1998). *Affective neuroscience*. New York: Oxford University Press.

Panksepp, J., Herman, B., Conner, R., Bishop, P., & Scott, J. P. (1978). The biology of social attachments: Opiates alleviate separation distress. *Biological Psychiatry*, *13*, 607–618.

Petrovic, P. & Ingvar, M. (2002). Imaging cognitive modulation of pain processing. *Pain*, *95*, 1–5.

Peyron, R., Laurent, B., & Garcia-Larrea, L. (2000). Functional imaging of brain responses to pain. A review and meta-analysis. *Neurophysiological Clinics*, *30*, 263–288.

Price D. D. (2000). Psychological and neural mechanisms of the affective dimension of pain. *Science*, *288*, 1769–1772.

Rainville, P. (2002). Brain mechanisms of pain affect and pain modulation. *Current Opinion in Neurobiology*, *12*, 195–204.

Rainville, P., Duncan, G. H., Price, D. D., Carrier, B., & Bushnell, M. D. (1997). Pain affect encoded in human anterior cingulate but not somatosensory cortex. *Science*, *277*, 968–971.

Richter, E. O., Davis, K. D., Hamani, C., Hutchison, W. D., Dostrovsky, J. O., & Lozano, A. M. (2004). Cingulotomy for psychiatric disease: Microelectrode guidance, a callosal reference system for documenting lesion location, and clinical results. *Neurosurgery*, *54*, 622–628.

Robinson, B. W. (1967). Neurological aspects of evoked vocalizations. In S. A. Altmann (Ed.), *Social communication among primates* (pp. 135–147). Chicago, IL: The University Press.

Shimodozono, M., Kawahira, K., Kamishita, T. Ogata, A., Tohgo, S., & Tanaka, N. (2002). Reduction of central poststroke pain with the selective reuptake inhibitor fluvoxamine. *International Journal of Neuroscience*, *112*, 1173–1181.

Schreckenberger, M., Siessmeier, T., Viertmann, A., Landvogt, C., Buchholz, H.-G., Rolke, R., et al. (2005). The unpleasantness of tonic pain is encoded by the insular cortex. *Neurology*, *64*, 1175–1183.

Singh, V.P., Jain, N.K., & Kulkarni, S.K. (2001). On the anitnociceptive effect of fluoxetine, a selective serotonin reuptake inhibitor. *Brain Research*, *915*, 218–226.

Smith, W. (1945). The functional significance of the rostral cingular cortex as revealed by its responses to electrical excitation. *Journal of Neurophysiology*, *8*, 241–255.

Taylor, S. E. (2003). *Health psychology* (5th Edition). New York: McGraw Hill Publishers.

Tölle, T. R., Kaufmann, T., Siessmeier, T., Lautenbacher, S., Berthele, A., Munz, F., et al. (1999). Region-specific encoding of sensory and affective components of pain in the human brain: A positron emission tomography correlation analysis. *Annals of Neurology*, *45*, 40–47.

Tremblay, I. & Sullivan, M. J. L. (2009). Attachment and pain outcomes in adolescents: The mediating role of pain catastrophizing and anxiety. *Journal of Pain, in press.*

Twenge, J. M., Baumeister, R. F., Tice, D. M., & Stucke, T. S, (2001). If you can't join them, beat them: Effects of social exclusion on aggressive behavior. *Journal of Personality and Social Psychology*, *81*, 1058–1069.

Wager, T. D., Rilling, J. K., Smith, E. E., Sokolik, A., Casey, K. L., Davidson, R. J., et al. (2004). Placebo-induced changes in fMRI in the anticipation and experience of pain. *Science*, *303*, 1162–1167.

Warnick, J. E., McCurdy, C. R., & Sufka, K. J. (2005). Opioid receptor function in social attachment in young domestic fowl. *Behavioral Brain Research*, *160*, 277–285.

Watkins, L. R. & Maier, S. F. (2000). The pain of being sick: Implications of immune-to-brain communication for understanding pain. *Annual Review of Psychology*, *51*, 29–57.

Way, B. M., Taylor, S. E., & Eisenberger, N. I. (2009). Variation in the mu-opioid receptor gene (OPRM1) is associated with dispositional and neural sensitivity to social rejection. *Proceedings of the National Academy of Sciences*, *106*, 15079–15084.

Zaza, C. & Baine, N. (2002). Cancer pain and psychosocial factors: A critical review of the literature. *Journal of Pain and Symptom Management*, *24*, 526–542.