Why It Hurts to Be Left Out:

The Neurocognitive Overlap Between Physical and Social Pain

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"Without friends no one would choose to live, though he had all other goods."
- Artistotle

Replace the word "friends," as quoted above, with the word "air," "water," or "food" and Aristotle's claim seems simple and indisputable. At most, some might argue for a more stringent statement suggesting that without air, water, or food one could no longer *choose* to live, one could simply *not* survive. Without amending his statement, however, Aristotle's claim seems more hyperbolic than truthful. If granted all the 'real' necessities of life, such as air, water, and food, would we not be able to live or, at least, not want to live, without the companionship of others?   Are social relationships something we actually need or are they better described as desirable but not necessary? In this chapter we will suggest that social connection is a need as basic as air, water, or food and that like these more traditional needs, the absence of social connections causes pain. Indeed, we propose that the pain of social separation or social rejection may not be very different from some kinds of physical pain.

We are not alone in this claim. For centuries, writers, musicians, playwrights, and poets have noted that the loss of social bonds can unleash the most profound forms of human pain and suffering. The legal systems of many countries have recognized this relationship as well, evidenced by their use of social isolation as one of the most extreme forms of punishment, at times issued interchangeably with the death penalty for the most severe crimes (Baumeister, 2000). Likewise, the pain of broken social bonds permeates the English language, illustrated by the use of physical pain words to describe episodes of socially painful experiences, such as when speaking of "broken hearts" or "hurt feelings" (Leary, 2001).   Indeed, the connection between broken social bonds and some of life's

most painful experiences seems to have left its imprint on most, if not all, human societies. Could Aristotle have been right?

Despite the wisdom of writers, until a half century ago, most psychologists would have responded with a resounding "no," maintaining that social connections were simply the remnants of a developmental need to satisfy certain biological drives that could not be satisfied on one's own. These psychologists held that an infant's attachment to his or her caregiver was exclusively the result of the association of the caregiver's face or form with the alleviation of certain drive states such as hunger or thirst (Dollard & Miller, 1950; Mussen & Conger, 1956). However, in a series of seminal studies, Harlow (1958, 1959) demonstrated that infant rhesus monkeys separated from their natural mothers preferred a cloth surrogate mother that provided them with contact comfort to a wire-mesh mother that provided them with food, indicating the existence of a need, over and above the need for food. This study, along with the others that have followed, emphasizes the importance of a mammalian drive that is primarily social, unrelated to hunger or thermoregulation, aimed at maintaining social closeness or social contact. Though it is possible that this need for social closeness may have originally evolved to support a drive for food or warmth, Harlow's studies indicate that it is now clearly a separate, autonomous need. In fact, these studies suggest that social closeness is a need paramount to the need for food or warmth, causing pain and discomfort when the need goes unmet.

We propose that along with the evolution of mammals, a species unique in their need for early nurturance and care, came a corresponding lifelong need for social connection. Indeed, this need has proved so essential to survival that social separation, like other unmet needs, is experienced as painful. Based on the lengthy period of

immaturity in mammalian infants and the critical need for maternal care and nurturance, we hypothesize that the pain mechanisms involved in preventing physical danger were co-opted to prevent social separation. In this chapter, we suggest that social pain and physical pain share the same underlying system and that this overlap has several consequences for the way that these types of pain are detected, experienced, and overcome. We call this theory "Social Pain / Physical Pain Overlap Theory" (SPOT) and will present evidence for four hypotheses derived from this proposed overlap.

Social Pain / Physical Pain Overlap Theory (SPOT)

Social Pain / Physical Pain Overlap Theory (SPOT) (Eisenberger & Lieberman, in press) proposes that social pain, the pain that we experience when social relationships are damaged or lost, and physical pain, the pain that we experience upon physical injury, share parts of the same underlying processing system. This system is responsible for detecting the presence or possibility of physical or social damage and recruiting attention once something has gone wrong in order to fix it. Evolutionarily, this overlap makes good sense. Based on mammalian infants' lengthy period of immaturity and their critical need for substantial maternal contact and care, it is possible that the social attachment system, the system that keeps us near close others, may have piggybacked onto the pre-existing pain system, borrowing the pain signal to signify and prevent the danger of social separation (Nelson & Panksepp, 1998; Panksepp, 1998).

This evolutionary hypothesis was first proposed to explain the similar effects of opiates on both social and physical pain. Panksepp noted that opiate-based drugs, known for their effectiveness in alleviating physical pain, were also effective in alleviating

distress vocalizations emitted by the young of different animal species when separated

from others (Herman & Panksepp, 1978; Panksepp, Herman, Conner, Bishop, & Scott,

1978; Panksepp, Vilberg, Bean, Coy, & Kastin, 1978). Panksepp suggested that the social

attachment system may have co-opted the opiate substrates of the physical pain system to

maintain proximity with others, eliciting distress upon separation and comfort upon

reunion (Nelson & Panksepp, 1998; for review, see Panksepp, 1998).[1]

For most mammalian species, an initial connection between mother and child is

essential for survival as mammalian infants are born relatively immature, without the

capacity to feed or fend for themselves. The Latin root of the word *mammal* is *mamma*

which means *breast* and bears a striking resemblance to the first word uttered by many

infants across many countries, namely the colloquial word for *mother* (English: *mom,*

mommy; Spanish: *mami, mama*; French: *maman*; German: *mami, mama*; Hindi: *ma*;

Korean: *ama*; Hebrew: *ima*). Thus, the need to maintain closeness with the mother is so

critical that the first word uttered by many human infants typically reflects this important

underlying motivation, the need for the mother.

Because maintaining closeness with caregivers for food and protection is

necessary for mammalian survival, at least in the early stages of development, a system

that monitors for distance from the caregiver and alerts the individual once a certain

distance has been exceeded is critical. Indeed, the pain system may have been co-opted

for just this purpose. Due to its aversiveness, pain grabs attention, interrupts ongoing

behavior, and urges actions aimed at mitigating painful experience (Williams, 2002). To

the extent that social distance is harmful to survival, experiencing pain upon social

separation would be an adaptive way to prevent social distance.

Thus, the essence of SPOT is that both physical and social pain share parts of a common underlying system, which monitors for harm and initiates affective distress once harm has been detected to motivate recuperation. The value of SPOT, however, comes from its corollary hypotheses. In this chapter, we will present four of these hypotheses along with the evidence relevant to each. SPOT provides an overarching structure and organization to these findings that on their own tend to be interesting but atheoretical. The first and most fundamental hypothesis of SPOT is that physical and social pain should share a common phenomenological basis and should rely on some of the same neural structures. Second, if both types of pain rely on some of the same neural structures, they should also share some of the same underlying cognitive or computational mechanisms. Third, potentiating or regulating one type of pain should similarly influence the other type of pain. Lastly, traits related to a heightened sensitivity to one kind of pain should also relate to a heightened sensitivity to the other type of pain. Before presenting evidence to support each of these hypotheses, we will first attempt to provide a more specific definition of the terms "physical pain" and "social pain" in the manner that they will be used throughout this chapter.

Physical pain has previously been defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (International Association for the Study of Pain; IASP, 1979). Social pain, however, is a bit trickier to define, as there is no pre-existing definition of this term that captures our intended meaning. We conceptualize social pain as analogous to Bowlby's description of the separation distress that occurs when an infant feels distress due to separation from a caregiver. Bowlby (1969) maintained that the purpose of the

attachment system is to keep infants near their caregivers in order to keep them safe from

predators and promote their survival. The primary function of the attachment system is

to monitor for distance from the caregiver and to elicit distress and attachment behaviors,

such as crying or approaching, aimed at regaining proximity with the caregiver. In a

similar manner, we define 'social pain' as *the distressing experience arising from the*

perception of psychological distance from close others or from the social group.

Psychological distance could include perceptions of rejection, exclusion, non-

inclusion, or any socially-relevant cue that makes an individual feel unimportant to,

distant from, or not valued by important relationship partners. Whereas infants may only

be capable of detecting actual physical distance from a caregiver, emergent cognitive

capacities soon enable young children with the ability to monitor not only objective

distance from the caregiver, but also perceived psychological distance from the caregiver,

an assessment that relies on a more complex understanding of socio-relational

information.   In short, social pain can be thought of as the distressing experience

associated with *"perceived social distance."*

There are two factors that make social pain a broader and more expansive social

experience than Bowlby's conception of separation distress. First, unlike separation

distress, social pain is posited to be an experience that persists throughout the life span.

Typically, separation distress is thought to diminish as a child matures and becomes

capable of taking care of him/herself (Bowlby, 1969). However, if the social attachment

system borrowed the mechanisms underlying the physical pain system, perceived social

distance should continue to cause social pain for as long as the physical pain system is in

tact. Indeed this seems to be the case, as evidenced by the occurrence of grieving

responses, social anxiety disorders, and depression from social isolation in individuals of all ages. Whether this continued sensitivity to social distance remains adaptive in adulthood or is merely a vestige of the merging of these two systems is not yet known.

Second, based on expanding cognitive capacities that allow certain species to represent, manipulate, imagine, and predict complex social information, many more cues may be capable of eliciting social pain in non-infants than are capable of eliciting separation distress in infants. For example, human adults can experience social pain not only based on the perception of psychological distance from an individual but also based on the perception of psychological distance from a *social group*, a more complex mental representation. In addition, human adults can experience social pain or anxiety at the mere *possibility* of social distance. The capacity to represent complex ideas such as 'the social group' or 'the possibility of social distance' may only be possible for those species with enhanced cognitive resources that allow symbolic and propositional representations (Brothers, 1990; Deacon, 1992; Lieberman et al., 2002). For instance, human infants can only begin to show fear of anticipated situations once they have undergone a critical period of prefrontal cortex maturation, at the end of their first year (Bowlby, 1973; Schore, 2001). Species that show the most expansion of neocortical areas, such as primates, humans, and possibly cetaceans (whales and dolphins) (Panksepp, 1998) may be the only mammals capable of showing distress at these more subtle cues of social distance.

In the remainder of this chapter, we will present evidence for the four corollary hypotheses derived from SPOT. After presenting these, we will conclude with a brief

discussion of some areas of research that might benefit from a better understanding of the physical-social pain overlap.

Hypothesis #1: Physical and social pain should share a common phenomenological and neural basis.

The first and most fundamental hypothesis derived from SPOT elaborates on the underlying structures involved in the physical-social pain overlap. This hypothesis proposes that both physical and social pain should share a common phenomenological and neural basis.   We have already mentioned one reason to believe that physical and social pain share a common phenomenological experience; they share a common vocabulary. In the English language, the same words are used to describe instances of both physical and social injury (Leary, 2001). Thus, we can have a *broken* bone or a *broken* heart; we can feel the pain of a stomach*ache* or of heart*ache*; and we can be *hurt* by a dog's *bite* or by another's *biting* remark. Indeed, the use of pain words to describe episodes of physical and social pain is a phenomenon common to many different languages (Leary, 2003). However, linguistic evidence alone does not substantiate the claim that physical and social pain share the same underlying phenomenology. Perhaps a 'broken heart' is merely a figure of speech and is not actually experienced as painful. Showing that the same neural regions are activated to experiences of both physical and social pain provides more substantial evidence that these two types of pain share a common phenomenological experience.

In this section, we will review neuropsychological and neuroimaging research suggesting that the anterior cingulate cortex (ACC), a large structure on the medial wall

of the frontal lobe, is one of the key neural structures involved in the affective distress associated with the physical-social pain overlap. Though there may be several other neural structures involved in other aspects of this overlap (e.g. sensory intensity), such as the insula, periaqueductal grey, and the dorsomedial thalamus (Panksepp, 2003), we will focus primarily on the role that the ACC plays in the affective component of physical and social pain. We hope to show that the ACC is involved in the affective experience of physical and social pain, providing evidence for a shared phenomenological and neural basis underlying both types of painful experience.

Physical Pain and the ACC

For nearly a century, it has been known that the ACC plays a role in the experience of physical pain. Since the mid-1930s, neurosurgeons have used cingulotomy, a circumscribed lesioning of the ACC, for the treatment of intractable chronic pain disorders (Davis, Hutchison, Lozano, & Dostrovsky, 1994). Following cingulotomy for chronic pain, patients report still being able to feel the intensity of pain but report that the pain no longer bothers them (Foltz & White, 1968).[2] For example, following cingulotomy for chronic pain, one patient, upon being asked how he felt, replied: "Oh, the pains are the same, but I feel fine now, thank you" (Damasio, 1994. p. 266). Thus, the ACC seems to be involved in registering the *distress* as opposed to the *intensity* of physical pain.

Pain researchers have subsequently subdivided painful experience into two components: the intensity and the unpleasantness of painful experience (Price, 2000; Price, Harkins, & Baker, 1987; Rainville et al., 1997; Sawamoto et al., 2000). Rating the intensity of pain can be likened to rating the loudness of the volume on a radio. Rating

the unpleasantness of pain can be likened to rating the extent to which the volume on the radio is perceived as bothersome. While the ACC has been shown to be involved in the perceived unpleasantness of physical pain, other neural regions such as the somatosensory cortex and the insula have been shown to be involved in processing the intensity of somatic or visceral pain, respectively (Aziz, Schnitzler, & Enck, 2000). Pain disorders involving damage to somatosensory areas leave patients unable to identify where the pain is coming from or how intense it is but still able to experience the distress associated with having the pain in the first place (Nagasako, Oaklander, & Dworkin, 2003).

The first neuroimaging study linking pain distress to ACC activity used hypnotic suggestion to alter the perceived unpleasantness of painful stimulation without changing the perceived intensity (Rainville et al., 1997). Using positron emission tomography (PET), it was observed that ACC activity corresponded to changes in the perceived unpleasantness of painful stimuli whereas the activity of primary somatosensory cortex, typically associated with the perceived intensity of painful stimulation, remained unaltered. Since then, several neuroimaging studies have linked the unpleasantness of of painful stimulation to the activation of the ACC, with more ACC activity corresponding to more self-reported pain unpleasantness (Peyron et al., 2000; Ploghaus, et al., 1999; Sawamoto et al., 2000). In a similar manner, pain-sensitive individuals, who report more pain unpleasantness to less intense pain, show significantly more ACC activity to painful stimulation than do less pain-sensitive individuals (Coghill, McHaffie, & Yen, 2003).

Neuroimaging studies have also linked ACC activation to the anticipation or possibility of pain (Chua et al., 1999; Porro et al., 2002; Sawamoto et al., 2000). One

neuroimaging study has shown that the mere possibility of pain increases ACC activity to

nonpainful stimulation, making the experience of nonpainful stimulation more painful

(Sawamoto et al., 2000). In this study, participants either: a) expected and received a

nonpainful stimulus, or b) did not know what to expect and received either a painful or a

nonpainful stimulus. Results indicated that the expected nonpainful stimulation was the

least unpleasant and was associated with the least ACC activity; whereas the painful

stimulation was the most unpleasant and was associated with the most ACC activity.

However, perhaps most surprising, was the finding that the unexpected nonpainful

stimulus was rated as more unpleasant than the expected nonpainful stimulus and was

correspondingly associated with significantly more ACC activity. Thus, the possibility of

pain appears to heighten the sensitivity of the ACC, making otherwise neutral sensory

experiences more unpleasant.

Social Pain and the ACC

Not only has the ACC been shown to be involved in physical pain but it has also

been shown to be involved in social pain, resulting from social distance or separation. As

noted by MacLean, "A condition that makes being a mammal so painful is separation

from a sustaining member or members of a group" (MacLean, 1985b, p. 220). According

to MacLean (1985a), the cingulate plays a critical role in producing this mammalian

condition. Here we will present evidence from animal and human populations pointing to

a role for the ACC in social pain.

Social Pain in Animals. The cingulate gyrus has no distinctive counterpart in the

reptilian brain, appearing for the first time, phylogenetically, in mammalian species

(MacLean, 1985a, 1993).[3] Several behavioral characteristics accompany the

development of mammals as well. These newly emerged characteristics, differentiating

mammals from their reptilian ancestors, include audiovocal communication for

maintaining maternal-offspring contact and the nursing of young along with maternal

care.[4] As the cingulate appeared on the evolutionary scene at the same time as these

characteristics, the cingulate may be a contributor to these uniquely mammalian

behaviors. Here we present evidence suggesting that the cingulate seems to play a

primary role in the production of distress vocalizations for maintaining mother-infant

contact and in the response to these distress vocalizations in the form of nursing and

maternal care.

Distress vocalizations are considered to be the most primitive and basic

mammalian vocalization with the original purpose of maintaining mother-infant contact

(Lorberbaum et al., 1999; MacLean, 1985a). Typically, infants emit distress

vocalizations when separated from their caregivers and the sound of distress

vocalizations elicits distress in the mother, motivating her to retrieve her young.

Consistent with the idea that distress vocalizations evolved in the context of parent-child

relations, reptilian newborns, which receive no parenting as they are born almost

completely mature, do not produce distress vocalizations (MacLean, 1977). In fact, the

most likely consequence of reptilian distress vocalizations would be the death of the

infant due to the parent discovering the infant and eating it.

To establish that the cingulate gyrus plays a causal role in the distress of social

distance and the production of distress vocalizations, lesions to the cingulate gyrus should

lead to: a) fewer distress vocalizations when socially separated and b) fewer attempts at

maintaining social closeness if social distance is no longer distressing. Consistent with

this causal role, ablation of the ACC in squirrel monkeys leads to decreased distress

vocalizations (Kirzinger & Jurgens, 1982; MacLean & Newman, 1988). Additionally,

cingulate lesions in macaques lead to decreases in affiliative behavior, as indicated by a

reduction in the amount of time spent in social interactions or in proximity with other

macaques (Hadland, Rushworth, Gaffan, & Passingham, 2003). This drop-off in social

affiliation may be the result of a reduced need for social closeness because social distance

is no longer experienced as aversive.

Additionally, if the ACC is one of the primary neural regions involved in the

production of distress vocalizations, localized stimulation of the ACC should elicit

distress vocalizations while stimulation of other language areas should not. To this end,

electrical stimulation of the ACC leads to the spontaneous production of distress

vocalizations in rhesus monkeys (Jurgens & Ploog, 1970; Ploog, 1981; Smith, 1945);

whereas, stimulation of the area corresponding to Broca's area in monkeys and in apes,

an area known to be involved in speech production, elicits movement of the vocal chords

but no distress vocalizations (Leyton & Sherrington, 1917; Ploog, 1981).

The cingulate gyrus also plays a role in caregiver responses to infant distress

vocalizations. Ablation of the cingulate gyrus in adult female rats results in deficits in

maternal behavior, including the nursing and retrieval of pups (Stamm, 1955).

Interestingly, ablation of the cingulate gyrus also interferes with the parental behavior of

male rats (Slotnick, 1967).   Following cingulate ablation in females, rat mothers become

less responsive to the distress vocalizations of their pups. The survival rate of rat pups,

with mothers having cingulate lesions, is only 12%. This rather dismal survival rate

highlights the importance of this structure in maintaining mother-infant contact and

promoting the survival of mammalian infants.

Social Pain in Humans. Much less is known about the neural correlates of social

pain in humans. However, if the ACC is involved in social pain in animals, it is

reasonable to assume that it is involved in human social pain as well. If this is true,

lesioning the ACC in humans should have social consequences, making individuals less

sensitive to social pain and potentially less interested in social affiliation as social

closeness is no longer relieving. An early study noted that lesioning the ACC for chronic

pain or anxiety disorders had social consequences. Following cingulotomy, patients

became less socially inhibited, less shy, and less socially sensitive (Tow & Whitty, 1953).

In other words, they became less socially reticent or concerned. These results imply that

human cingulotomy patients not only became less sensitive to the possibility of social

pain but they became more social as well. These results seem contradictory to the effects

of cingulotomy observed in animals. Whereas animals became less interested in social

connection following cingulotomy, human cingulotomy patients seemed to become less

socially apprehensive, thus appearing more social. Why might this be the case?

One possible explanation for the contradictory results of human and animal

cingulotomy studies is that humans can have a more complex representation of what

might be socially painful. For humans, the ACC may be monitoring not only perceived

social distance but the *possibility* of social distance as well, a more complex abstraction

that relies on the computations of the more recently evolved regions of the prefrontal

cortex (Deacon, 1992). For other animals, however, the ACC may only be capable of

monitoring for the online occurrence of social distance. Thus, for most animals, the

social environment is black-and-white: the presence of others is good and the absence of others is bad. With an intact cingulate, these animals experience distress upon social separation and comfort upon social reunion. With a lesioned cingulate, these animals are no longer distressed by social separation and thus may not find social closeness as rewarding or at least as relieving. However, for humans, the presence of others can be either good or bad depending on whether or not there is a possibility of social rejection. If the perceived possibility of social rejection is high, being in the presence of others can be distressing, even if no rejection occurs. Thus, for humans, ACC activity may be associated not only with the pain of social rejection but with an anxious social vigilance aimed at monitoring for or preventing social rejection. In humans, lesioning the ACC might be associated with a reduction in thoughts regarding the possibility of social rejection and thus to a less apprehensive approach to social relationships, potentially resulting in more social interaction. Nonetheless, common to both animal and human cingulotomy patients is a reduced 'concern' for social connection characterized by either less affiliative behaviors in animals or less caution within social interactions in humans.

Another frequent consequence of cingulotomy that might be relevant to the experience of social pain is akinetic mutism, in which patients temporarily do not initiate vocalization based on a lack of desire rather than a lack of ability (Laplane, Talairach, Meininger, Bancaud, & Orgogozo, 1977; Nemeth, Hegedus, & Molnar, 1988). While highly speculative, the disinclination to initiate vocalization may reflect a reduction in a concern for social connection. As discussed earlier, the initiation of vocalization associated with cingulate activity may represent a primitive attempt at establishing or reestablishing social connection (Lorberbaum et al., 1999; MacLean, 1985a).

Consequently, ablation of the cingulate, a structure associated with detecting social

separation and vocalizing to reestablish connection, may result in the temporary absence

of self-initiated vocalizations.

Perhaps the most direct evidence for the role of the ACC in human social pain

comes from a neuroimaging study investigating the neural correlates of one type of social

pain: social exclusion (Eisenberger et al., 2003). In this study, participants were led to

believe that they would be playing a virtual ball-tossing game with two other players over

the internet while in the fMRI scanner. In reality, there were no other players; rather, the

computer images of the other players were preprogrammed to include the participant

during one round of the ball-tossing game and to exclude the participant in another round

of the game by not throwing the ball to the participant. Upon being excluded from the

game, compared to when being included, participants showed increased activity in dorsal

ACC, the region most often associated with the affective distress of physical pain. In

addition, the amount of activity in this area correlated strongly (r = .88) with the amount

of self-reported social distress participants felt during the exclusion episode (how

rejected, excluded, meaningless they felt). Thus, mirroring the animal research, the ACC

seems to play a role in the distress associated with perceived social distance in humans as

well.

Another fMRI study examined the role of human maternal behavior in response to

infant distress vocalizations. In the first functional neuroimaging study of human

maternal behavior, researchers examined the neural regions activated in response to

hearing infant cries (Lorberbaum et al., 1999). In this study, mothers were imaged while

listening to infant cries or white noise. Results indicated that mothers had more ACC

activity to infant cries compared to white noise (Lorberbaum et al., 1999; 2002),

consistent with the animal data demonstrating the cingulate's involvement in the

caregiver's response to distress vocalizations (MacLean, 1985a, 1985b; MacLean &

Newman, 1988; Slotnick, 1967; Stamm, 1955).

Hypothesis #2: Physical and social pain should rely on the same computational

mechanisms.

The second hypothesis derived from SPOT is that physical and social pain should

rely on the same underlying computations or cognitive processes. Because the ACC is

involved in the experience of both physical and social pain, it is plausible that the

underlying computational processes of the ACC are relevant in the processing of both

types of pain. In this section, we will review the underlying computations of the ACC

and will demonstrate how these mechanisms are related to physical and social pain

processes. Understanding the computations underlying this shared neural circuitry is

important for building a more complete model of the physical-social pain overlap.

Through a series of elegant studies, Cohen and colleagues have shown that the

ACC acts as a conflict or discrepancy monitor, detecting when an automatic habitual

response is contextually inappropriate or conflicts with current goals (Botvinick et al.,

2001; Carter et al., 1998, 2000; MacDonald et al., 2000). One simple example of

conflict, often used to elicit ACC activation, is the Stroop task in which the automatic

word-reading response conflicts with the goal of color naming (e.g., name the ink color

of the word 'RED' printed in blue ink) (Barch, Braver, Akbudak, Conturo, Ollinger,

Snyder, 2001; Carter et al., 1998, 2000; Leung, Skudlarski, Gatenby, Peterson, & Gore,

2000; MacDonald et al., 2000).

A number of other studies suggest that the ACC may be sensitive to goal conflicts

and unexpected events more generally (Weissman, Giesbrecht, Song, Mangun, &

Woldorff, 2003), detecting discrepancies between automatic responses and current goals,

between actual and expected events, and between new stimuli and pre-existing

representations that do not map onto each other. When the ACC detects these

discrepancies, the prefrontal cortex is 'notified' of the problem so that it can exert

executive control (Miller & Cohen, 2001) by overriding automatic processes and

retrieving information from the medial temporal lobe to assist in dealing with exceptions

to the rules (McClelland, McNaughton, & O'Reilly, 1995). The ACC, itself, is thought to

be primarily involved in the detection of discrepancy, rather than in its resolution.

Though much research supports this account of the ACC as a discrepancy

detector, it is not clear how this function relates to physical or social pain processes. On

the one hand, the ACC has been characterized as a discrepancy detector, producing

activity to simple response conflicts such as those evidenced in the Stroop task

(Botvinick et al., 2001), while others have characterized the ACC as a 'distress center,'

producing activity to instances of both physical and social pain (Eisenberger et al., 2003;

Rainville et al., 1997). How can these two characterizations of ACC function be

integrated together?

If one conceptualizes the ACC as the brain's alarm system, the connection

between discrepancy detection and the experience of physical and social pain quickly

makes more sense. Most real world alarm systems (e.g. fire alarms) have two

components. The first component of an alarm system, the component that we are most familiar with, is the sound of the alarm bell, the part of the alarm that signals that there is a problem, interrupts ongoing activity, and directs attention at solving the problem. This part of the alarm may be analogous to the experience of physical or social pain, which, like the sound of the alarm bell, is distressing, attention-getting, and disruptive. The second component of the alarm, the part of the alarm that we rarely have a chance to see or sense, is the machinery that actually initiates the sounding of the alarm bell in the first place. This is the part of the alarm that detects when something has gone wrong or has strayed from a desired set point (e.g. too much smoke in the room in the case of a firm alarm). In essence, this part of the alarm system detects discrepancies from some standard, initiating the sounding of the bell, and may be analogous to the discrepancy detection function of the ACC. Rather than discrepancy detection and distress being two competing accounts of ACC functioning, the analogy to an alarm system suggests that they may actually be two sides of the same coin: the two complementary processes of a neural alarm system. Based on this account, the 'physical pain alarm' should be triggered once the underlying machinery has detected physical damage, a discrepancy from the healthy state of the body. Likewise, the 'social pain alarm' should be triggered once the underlying machinery has detected social distance, a discrepancy from the desired state of social inclusion or social closeness.

Though it seems reasonable that the ACC might act as a neural alarm system, detecting discrepancy and producing the subsequent feelings of distress, these two properties of ACC activity have yet to be linked. Typically, studies of the ACC as a discrepancy detector do not assess the phenomenological distress resulting from

discrepancy detection and studies of the ACC's involvement in distress do not measure its involvement in discrepancy detection. In order to examine whether these two properties of ACC function are two sides of the same coin, we examined two hypotheses: 1) whether individuals who tend to be distressed more often are more sensitive to discrepancy as evidenced by increased ACC activation during a discrepancy detection task and 2) whether activating discrepancy detection processes heightens an individual's sensitivity to distress.

In a study testing the first hypothesis, we examined whether individuals high in neuroticism, who tend to experience distress more often, are more sensitive to discrepancy detection, as evidenced by more ACC activity to a simple discrepancy detection task (Eisenberger, Satpute, & Lieberman, 2003). Because neuroticism is defined as the tendency to experience negative affect (Costa & McCrae, 1985; Eysenck, 1967; McCrae & Costa, 1996), neurotics should show a greater sensitivity to discrepancy, if discrepancy detection and distress go hand-in-hand. Though much research has focused on the phenomenological correlates of neuroticism (e.g., the tendency to experience stress, nervousness, or moodiness), much less research has attempted to pinpoint the causal factors that might contribute to the experience of negative affect in the first place. If part of the reason that neurotic individuals are distressed more often is because they have a more sensitive alarm system, detecting smaller discrepancies and experiencing distress more frequently, then neurotic individuals should show greater ACC reactivity to simple discrepancies.

In this study, participants were scanned while performing an "oddball" task, a simple discrepancy detection task in which a sequence of letters is presented, one at a

time, on a computer screen. In this task, eighty percent of the letters are the letter 'X',

but participants are instructed to press a button only when they see a letter other than 'X.'

Because the base-rate expectation of seeing an 'X' is 80%, seeing other letters violates

this expectation and leads to activation of the ACC (Braver, Barch, Gray, Molfese, &

Snyder, 2001; Weissman, Giesbrecht, Song, Mangun, & Woldorff, 2003). Self-reported

neuroticism (EPQ: Eysenck & Eysenck, 1975) was assessed 5 to 14 days after

participants were scanned.

It was found that heightened ACC reactivity to the oddball trials, relative to non-

oddball trials, was significantly correlated with higher levels of self-reported neuroticism

($r = .76$). In other words, individuals higher in neuroticism showed more ACC reactivity

to this simple discrepancy detection task, implying that the more distressed an individual

tends to be, the more strongly that individual's alarm system responds to simple

discrepancy.

The second study investigated whether increasing the activity of the alarm

system's discrepancy detector would simultaneously make distress-related cognitions

more accessible, particularly in neurotics who are posited to have a more sensitive alarm

system to begin with. In this study (Eisenberger & Gable, 2004), participants were

exposed to either a normal Stroop task involving discrepancy detection, in which

individuals were asked to name the ink color of various color words (the word "RED"

printed in blue ink), or a modified Stroop task containing no discrepancy (neutral task), in

which individuals were simply asked to name the color of different shapes (a triangle

printed in blue ink). Following the manipulation of discrepancy detection processes,

participants completed a lexical decision task in which reaction times to different

categories of words were assessed. Faster reaction times to a certain class of words were presumed to be indicative of cognitions that were more readily accessible. Participants were exposed to five categories of words including: 1) social rejection words ('abandonment,' 'rejection'), 2) negative trait words ('lazy,' 'dullness') to control for the negativity of the social rejection words without the social component, 3) social comfort words ('love,' 'support'), 4) positive trait words ('charming,' 'clever') to control for the positivity of the social comfort words without the social component, and 5) non-words ('tlinking,' 'worls').

In general, participants did not become more sensitive to social rejection words following discrepancy. However, individuals higher in neuroticism did. It was found that, controlling for reaction times to negative trait words, individuals higher in neuroticism were significantly faster to social rejection words following the discrepancy detection task compared to the neutral task. There were no between-group differences in reaction times to social comfort words, controlling for positive trait words, and there were no neuroticism by condition interactions. This makes good sense, as heightening the activity of the alarm system should sensitize it to indicators of social harm, such as 'rejection' or 'abandonment' but not to other social indicators such as 'love' or 'support.' This same pattern of results held for individuals high in trait anxiety and for individuals high in trait negative affect. Thus, inducing minimal discrepancy detection processes made neurotics more sensitive to social rejection, suggesting that for those with a sensitive system to begin with, activating the system can make these individuals more sensitive to distressing cues such as those indicating social pain. This study, along with the one described before it, provides evidence for the notion that discrepancy detection

and distress are two complementary processes that underlie the functioning of the ACC, the brain's alarm system.

Hypothesis #3: Inducing or regulating one type of pain should similarly influence the other type of pain.

The third hypothesis derived from SPOT is that inducing or regulating one type of pain should have a congruent influence on the other. In this section, we will first elaborate on the predictors of physical and social pain and will then provide evidence showing that enhancing one type of pain or its predictors should heighten an individual's sensitivity to the other type of pain (pain potentiation effects). Alternatively, reducing one type of pain or its predictors should diminish an individual's sensitivity to the other type of pain (pain regulation effects).

Predictors of Physical and Social Pain

Predictors of Physical Pain. The presence of bodily injury that could threaten survival typically predicts the experience of physical pain. Once physical harm occurs, the experience of pain is necessary for the recruitment of resources aimed at withdrawing from the harmful situation, inhibiting behaviors that might cause further bodily damage, and promoting recuperative efforts (Williams, 2002). However, because the experience of pain typically occurs once the physical damage has already occurred, it is also of great biological advantage to be able to learn to recognize potentially pain-inducing situations from distal cues that have predicted pain in the past (Bowlby, 1973). Feeling fear or anxiety in response to cues that have predicted pain in the past is an adaptive way to avoid the harmful situation in the future (Crombez, Vlaeyen, Heuts, & Lysens, 1999).

Thus, the immediate presence of physical harm (e.g., physical injury) predicts physical pain, leading to behavioral interruption and recuperative efforts, while cues associated with the possibility of physical harm predict anxiety, signaling that pain is imminent so that harm can be avoided. However, in addition to anxiety, cues predicting physical harm might also heighten an individual's sensitivity to physical pain in order to encourage more rapid retreat and recovery from danger. In line with this, it has been shown that cues that may have indicated the presence of physical harm or pain throughout our evolutionary history (snakes, blood) trigger a heightened sensitivity to physical pain. Participants exposed to these unpleasant cues through pictures (International Affective Pictures System; IAPS; Lang, Bradley, & Cuthbert, 1995) showed lower pain tolerance to a painful cold pressor task than did participants exposed to pleasant (puppy), or neutral (dish) pictures (de Wied & Verbaten, 2001).

Indeed, the presence of physical harm is so tightly connected to the experience of pain that individuals born without the experience of pain upon injury lead significantly shorter lives (Damasio, 1994; Wall, 1999), presumably because they lack this adaptive warning signal to determine what is harmful and needs to be avoided. Likewise, the experience of fear or anxiety is so closely connected to predictors of physical pain or harm that individuals low in trait anxiety are also more likely to die prematurely (Neeleman, Wessely, & Wadsworth, 1998), possibly because they lack a sense of vigilance to these cues.

Predictors of Social Pain. Analogous to the presence of physical harm producing physical pain, actual or perceived social distance (e.g., social rejection, social exclusion) produces social pain. Several lines of research support this claim. Leary and colleagues

have shown that perceiving that one is not valued in a relationship can lead to 'hurt feelings,' characterized by an experience of general distress and upset, similar to our conception of social pain (Leary, Springer, Negel, Ansell, & Evans, 1998). In fact, the extent to which an individual feels rejected or socially disassociated directly correlates with the intensity of his or her hurt feelings (Leary et al., 1998).

Williams and colleagues have shown that perceived social distance resulting from being socially ostracized or excluded results in social pain as well, evidenced by more negative moods, reduced feelings of social belongingness, reduced levels of social self-esteem, and heightened feelings of social rejection (Williams & Sommer, 1997; Williams et al., 1998, 2000, 2002). In fact, the capacity for ostracism to elicit social pain is so powerful that simply imagining or role-playing being ostracized results in negative self-evaluations (Williams, Bernieri, Faulkner, Gada-Jain, & Grahe, 2000; Zadro & Williams, 1998).

Perceptions of social distance can, at times, lead to such intense social pain that the consequence may be suicide. Over a century ago, Emile Durkheim, a French sociologist, highlighted the pain of perceived social distance through his work showing that suicide is most prevalent among those lacking social ties (Durkheim, 1897/1951). Consistent with the hypothesis that social distance directly contributes to the social pain that leads to suicide, the most frequent topics addressed in suicide notes or suicidal communications are social isolation, emotional pain, and relationship breakups (Darbonne, 1969; Leenaars, Lester, & Wenckstern, 1999).

Pain Potentiation Effects

Whereas it seems quite intuitive that physical harm produces physical pain and social harm produces social pain, the notion that experiencing or enhancing sensitivity to one type of pain might potentiate one's sensitivity to the other type of pain is far from obvious. However, there is at least some evidence supporting this hypothesis. Correlational accounts suggest that the experience of one kind of pain directly correlates with a heightened sensitivity to the other. For example, Bowlby noted that when a child experiences physical pain, he/she becomes much more sensitive to the whereabouts of his/her caregiver, experiencing distress more frequently and easily upon noting distance from the caregiver (Bowlby, 1969). Thus, a child experiencing more physical pain also becomes more reactive to and more distressed by predictors of social pain, specifically those that suggest separation from the caregiver. 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 a partner's relationship commitment (Ciechanowski, Sullivan, Jensen, Romano, & Summers, 2003). Here too, a heightened sensitivity to physical pain, in the form of a chronic pain condition, is associated with a heightened sense of vigilance and concern at the possibility of perceived distance from an attachment figure.

To date, no studies have experimentally manipulated physical pain to investigate the consequences for social pain or have manipulated social pain to investigate the consequences for physical pain. However, several studies have investigated the effects of failure on the experience of physical pain. The experience of failure may share some similarities with the experience of social pain if there is a possibility that the failure might lead to or indicate social rejection. In other words, if the perceived consequence of failing

is that one is not or would not be accepted or liked by others, failure could trigger feelings of social pain. This might occur for individuals who have been told that they have failed at something that they consider important for their social identity or for their acceptance or inclusion in a certain group.

In line with this, college-age participants who were informed by the experimenter that they performed far below average on a college entrance exam and that this should be considered a personal failure, reported heightened pain ratings to a cold-pressor task (van den Hout, Vlaeyen, Peters, Engelhard, & van den Hout 2000). For the college undergraduates who participated in this study, intelligence is likely to be a characteristic that is valued by the participants and their families. Failing on an academic test could signify that their family or other important social relationship members would disapprove or reject them, thus eliciting social pain and a corresponding sensitivity to physical pain. In a similar study, college-age participants who were given computerized feedback indicating that they had performed poorly compared to others on a reading comprehension task, also reported higher pain ratings to a cold-pressor task (Levine, Krass, & Padawer, 1993). Another study reported the opposite pattern of results such that failure feedback led to decreased pain behaviors (van den Hout, Vlaeyen, Houben, Soeters, & Peters, 2001); however, this study was conducted among individuals with chronic low back pain who as a group may evidence different pain responses than healthy individuals.

Pain Regulation Effects

Diminishing one type of pain or diminishing an individual's sensitivity to one type of pain has been shown to reduce an individual's sensitivity to the other type of pain

as well. A great deal of correlational research has shown that individuals with more social support experience less cancer pain (Zaza & Baine, 2002), are less at risk for back pain (Hoogendoorn, van Poppel, Bongers, Koes, & Bouter, 2000), take less pain medication, are less likely to suffer from chest pain following coronary artery bypass surgery (King, Reis, Porter, & Norsen, 1993; Kulik & Mahler, 1989), report less labor pain, and are less likely to use epidural anasthesia during childbirth (Chalmers, Wolman, Nikodem, Gulmezoglu, & Hofmeyer, 1995; Kennell, Klaus, McGrath, Robertson, & Hinkley, 1991). Thus the perception or presence of social support, presumably indicative of a lesser likelihood of social harm, appears to regulate physical pain in a number of different health domains.

Experimental evidence has demonstrated similar effects. Animal research has shown that the presence of another animal lessens the distressing experience of painful stimulation (Epley, 1974). For example, electric shock punishment was less effective in training rats that were tested in groups than rats that were tested alone (Rasmussen, 1939), suggesting that the shocks were less aversive and thus a less effective training device when the rats were in a social group. In addition, a rat's immobility due to electric shocks was reduced by the presence of a companion rat (Davitz & Mason, 1955). Finally, baby goats displayed fewer emotional reactions to electric shock when their mother was present than when she was absent (Liddell, 1954).

Human research has shown similar effects as well (Epley, 1974). The presence of companions has been shown to reduce the amount of self-reported fear associated with electric shocks (Amoroso & Walters, 1969; Buck & Parke, 1972) and to increase participant's tolerance of intense electric shock, suggesting that painful stimulation is

experienced as less painful when in the presence of a companion (Seidman, Bensen, Miller, & Meeland, 1957). More recently it has been shown that participants in the presence of either a friend or a supportive stranger reported less pain to a cold-pressor task than when alone (Brown, Sheffield, Leary, & Robinson, 2003). In short, experimentally manipulating the presence of supportive others can reduce pain sensitivity.

More evidence for pain regulation effects comes from drug studies. Opiate-based drugs, known to reduce physical pain, have also been shown to reduce separation distress vocalizations, elicited by infant animals when separated from their caregivers or the social group (Nelson & Panksepp, 1998; Panksepp, 1998; Panksepp, Herman, Conner, Bishop, & Scott, 1978; Panksepp, Vilberg, Bean, Coy, & Kastin, 1978). In fact, one of the surest ways to increase a rat's consumption of opiates (especially for female rats) is to socially isolate it (Alexander, Coambs, & Hadaway, 1978), as the increased consumption of opiates seems to regulate the animal's experience of social isolation distress. Part of the reason that opiate-based drugs, such as morphine or heroin, are so addictive is because they alleviate not only physical pain but the pain associated with poor or damaged social relationships as well (Panksepp, 1998).

Antidepressant medications or selective serotonin reuptake inhibitors (SSRIs) also have similar effects on both physical and social pain. Antidepressants, typically prescribed for treating anxiety and depression, often related to or resulting from social pain, are effective in alleviating physical pain as well (Nemoto et al., 2003; Shimodozono, Kamishita, Ogata, Tohgo, & Tanaka, 2002; Singh, Jain, & Kulkarni, 2001). In fact, antidepressants are now regularly prescribed to treat chronic pain

conditions. However, antidepressants, like morphine and heroin, seem to have their

effect on physical and social pain through opiate-based processes rather than through an

independent mechanism. Some studies have suggested that the analgesic effects of SSRIs

may be due to the effect of the serotinergic system on the opioid system, as blocking

opioid receptors can prevent the analgesic effects of SSRIs (Singh, Jain, & Kulkarni,

2001). Thus, even though SSRIs seem capable of alleviating physical and social pain,

this process may rely on some of the same underlying mechanisms as opiate-based drugs.

Hypothesis #4: Trait differences relating to one type of pain should relate to the other

type of pain as well.

The last hypothesis that will be considered in this chapter is that trait differences

related to the sensitivity to one type of pain should also be related to the sensitivity to the

other type of pain. Because neuroticism has been shown to link to both aspects of the

alarm, a heightened sensitivity to discrepancy (Eisenberger et al., 2003) and heightened

distress (Costa & McCrae, 1985; Eisenberger & Gable, 2004), neuroticism may well

represent a trait amplification of this alarm system. As such, neuroticism should be

associated with a greater sensitivity to and a more distressing experience of both physical

and social pain.

Some observational evidence already exists that suggests this might be the case.

Beck noted that the two of the most frequent types of anxious thoughts that neurotic

individuals had, revolved around the possibility of physical harm, such as being attacked

or being in a car accident, and the possibility of social harm, such as being rejected,

ostracized, or humiliated by others (Beck, Laude, & Bohnert, 1974). In addition, Twenge

(2000) has shown that increases in the levels of neuroticism and anxiety in the United

States, over the past 40 years, directly correspond with increases in indicators of social

distance (divorce rates) and increases in the prevalence of physical dangers (crime rates).

In the following section, we will review evidence suggesting that neuroticism is

associated with a heightened sensitivity to physical pain and is also associated with a

heightened sensitivity to social pain.

Neuroticism and Physical Pain Sensitivity

Neuroticism is frequently associated with the tendency to be hypersensitive to

physical symptoms, such as pain or discomfort, and to be distressed by these symptoms

more often (Watson & Pennebaker, 1989). Epidemiological studies report that 50% of

patients seeking treatment for medically unexplained physical symptoms, often visceral

or somatic pain, are either anxious or depressed (Katon, Sullivan, & Walker, 2001).

Neuroticism, along with similar constructs such as trait negative affect and trait anxiety,

has also been shown to be associated with lower pain thresholds (Bisgaard, Klarskov,

Rosenberg, & Kehlet, 2001; Pauli, Wiedemann, Nickola, 1999; Phillips & Gatchel, 2000;

Shiomi, 1978; Wade & Price, 2000) and higher pain unpleasantness ratings (Wade,

Dougherty, Hart, Rafii, & Price, 1992). In addition, neuroticism predicts greater levels of

postoperative pain following cholecystectomy (Bisgaard, Klarskov, Rosenberg, & Kehlet,

2001), is associated with higher pain severity ratings to chest pain symptoms (Costa,

1987; Costa, Zonderman, Engel, Baile, Brimlow, & Brinker, 1985), and is associated

with higher levels of psychological distress due to pain in individuals with low back pain

(BenDebba, Torgerson, & Long, 1997).

Neuroticism and Social Pain Sensitivity

Perhpas less intuitive than the neuroticism-physical pain link is the hypothesis that neuroticism is associated with a heightened sensitivity to social pain as well. Though some have made the claim that the experience of anxiety is fundamentally a fear of social rejection or exclusion (Baumeister, 1991; Baumeister & Tice, 1990), most do not intrinsically equate neuroticism or trait anxiety with a specific sensitivity to social rejection. However, studies suggest that neuroticism is at least partly associated with a heightened sensitivity to the possibility or actuality of social pain.

Several studies have shown that neuroticism correlates well with measures assessing sensitivities to social pain, such as measures of rejection sensitivity or interpersonal sensitivity. Rejection sensitivity is defined as the tendency to expect rejection and is assessed by questions such as "How concerned or anxious would you be over whether or not this person would want to go out with you?" (Downey & Feldman, 1996). Interpersonal sensitivity is defined as the tendency to react with excessive sensitivity to the interpersonal behavior of others, social feedback, or the perceived or actual negative evaluation by others and is assessed by statements such as "I worry about what others think of me" (Boyce & Parker, 1989). Recent studies have demonstrated that self-reported neuroticism is related to both higher levels of rejection sensitivity (r = .36) (Downey & Feldman, 1996) and to higher levels of interpersonal sensitivity (r = .48 to r = .61) (Boyce & Parker, 1989; Gillespie, Johnstone, Boyce, Heath, Martin, 2001; Luty et al., 2002; Smith & Zautra, 2002). Self-reported neuroticism also correlates highly with self-reported generalized social anxiety (r = .58), the tendency to experience anxiety in social situations in which individuals feel that they are being scrutinized or evaluated (Norton et al., 1997). Similarly, substance abusers who are high in neuroticism are more

likely to relapse specifically from episodes of social rejection (r = .47) (McCormick, Dowd, Quirk, & Zegarra, 1998). Lastly, there is some evidence to suggest that not only are neurotics more sensitive to the possibility of social rejection but they also experience greater and longer-lasting levels of grief following the actual loss of close others (Bailley, 2001; Ogrodniczuk, Piper, Joyce, McCallum, & Rosie, 2003).

Conclusion

> "There is something in staying close to men and women, and looking on them, and in the contact and odor of them, that pleases the soul well…"
>   - Walt Whitman, "I Sing the Body Electric," 1855

We began this chapter with a quote from Aristotle, who suggested that no individual would want to live without social connections. We now end this chapter with a quote by Walt Whitman, written nearly 2000 years later, indicating a similar idea—that part of what makes life worth living is being close to others. Indeed, if asked to pinpoint the best and worst experiences of life, most of us would pick those experiences involving the making and breaking of social bonds. For most, no occasion could be happier than a marriage or the birth of a child, and none could be sadder than the loss of the ones we love. Increasingly, evidence is pointing to the importance of social connections not only for our happiness and well-being but for our survival as well. Through the studies reviewed here, we are beginning to appreciate that the need for social connection is so essential to survival, at least in mammalian species, that being left out or disconnected from the social group is processed by the brain in a manner similar to physical pain. Just as physical pain has evolved to alert us that 'something has gone wrong' with our bodies, social pain is a similarly potent signal that alerts us when 'something has gone wrong'

with our social connections to others, an equally important threat to the survival of our species.

In this chapter we have reviewed Social pain / Physical pain Overlap Theory (SPOT), which advances the notion that physical and social pain rely on parts of the same underlying system for their operation. We have also provided evidence for several hypotheses that can be derived from this theory. We have shown that the ACC acts as one of the neural substrates of the physical-social pain overlap and that it is involved in both the detection of physical and social danger and in the alarming experience that follows. We have shown that potentiating or regulating one of these forms of pain influences the other form of pain in a congruent manner. Lastly, we have provided some evidence to suggest that neuroticism is associated with a heightened sensitivity to indicators of both types of pain. These are not the only implications that can be derived from SPOT. Other hypotheses that remain to be explored include whether physical and social pain have similar behavioral consequences, result in similar health outcomes, or share other common neural structures or neurotransmitters not reviewed here.

Having a better understanding of the neural processes underlying the physical-social pain system may provide researchers with better leverage when trying to understand certain intriguing but elusive findings, such as how social processes influence morbidity and mortality. Studies linking social relationships to physical health outcomes have burgeoned in the past several decades, repeatedly showing that social support enhances physical health while a lack thereof has deleterious health consequences (Taylor et al., 2003). In a seminal study investigating the influence of social relationships on longevity, Berkman and Syme (1979) found that individuals with fewer social ties

were 2-3 times more likely to die during a 9-year follow-up period than individuals who had more social ties. The relationship between social ties and mortality held even after controlling for physical health status, socioeconomic status, and health practices. Another influential study demonstrated that individuals with more diverse social networks were less likely to develop a cold from a rhinovirus inoculation than those with less diverse social ties, even after controlling for age, sex, season, body mass index, education, and race (Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997).

While studies such as these give weight to the notion that social ties are vitally important to health and longevity, they remain silent on the mechanism whereby social relationship processes influence morbidity or mortality. Using what is now known about the neural responses to social exclusion may give us a clearer picture of how social support or social isolation relates to health and longevity. The ACC may be a starting point for investigating this relationship, as we know that this neural structure is involved in detecting disrupted social connections. Indeed, one potentially fruitful avenue for understanding how the ACC might contribute to social-health processes might come from investigating the opioid system. The ACC has been shown to have the highest density of opioid-receptors in the entire central nervous system (Vogt et al., 1995) and endogenous opioids, released upon social contact, have been shown to have both analgesic and stress-reducing effects. Opioids may prevent negative health consequences by alleviating feelings of pain and distress, thus preventing downstream stress responses that might typically be triggered by the ACC.

In addition, having a better understanding of the physical-social pain overlap may help to grant social pain the same status that physical pain has achieved in the medical

and clinical communities, as evidenced by the amount of time and attention dedicated to its treatment and prevention. For example, while we would never admonish someone for allowing themselves time for recuperation from a physical injury, we seem to have a double standard when it comes to social pain. We often hold people responsible for their painful experiences associated with social rejection, expecting them to 'move on' or 'get over it.' Few would try to rush the healing of a broken leg, yet we often try to hurry others (and sometimes ourselves) through the healing of social pain.

One very tangible consequence of assuming that social pain is not as valid or legitimate as physical pain is a societal acceptance of certain elicitors of social pain, such as prejudice and racism. It is a well-known fact that African Americans suffer from elevated rates of hypertension, and researchers have hypothesized that social stress, such as exposure to racism, may account for some of these between-group differences in the prevalence of hypertension (Brondolo, Rieppi, Kelly, & Gerin, 2003). It is possible that understanding the neural mechanisms underlying the detection and response to social rejection or social distance may shed light on the relationship between perceived racism and biological and health outcomes. Opioid processes may be important here too as inhibition of the cardiac sympathetic nervous system via opioid receptor binding may be a potential mechanism of cardioprotection, limiting infarct size and cellular injury in the heart (Schultz & Gross, 2001). Individuals who are less socially integrated because of lower societal status may show deficits in these socially-related opioid processes and thus may not benefit from their heart-protective effects.

In conclusion, accumulating evidence is revealing that physical and social pain are similar in experience, function, and underlying neural structure. Continuing to

explore the underlying commonalities between physical and social pain may provide us

with new ways of treating physical pain and new techniques for managing social pain.

Perhaps most importantly, understanding this overlap may provide us with answers to

two of our most fundamental questions: why it 'hurts' to lose those we love and why

being close to others "pleases the soul well."

Footnotes

1. Though we will focus more specifically on the common neural structures underlying physical and social pain, we recognize that the shared opiate substrates are an important part of the physical-social pain overlap and will refer to them in a general manner throughout the chapter.

2. Though we can use the behavioral consequences of cingulotomy to inform our working knowledge of the phenomenology of ACC activation, it should be kept in mind that cingulotomies are only performed in the most extreme and severe cases of pain or anxiety. Thus, one should use caution when extrapolating from cingulotomy patients to the general population as the functioning of this neural region may be different for healthy individuals.

3. In non-primates, the *cingulate gyrus* is the primary unit of analysis; whereas in primates and humans, *anterior* and *posterior* sectors of the gyrus are treated separately.

4. The evolution of play is also a uniquely mammalian behavior; however, a complete discussion of the evolution of play behavior will not be discussed here (for a full review and discussion of play, see MacLean, 1985a or Panksepp, 1998, chapter 15).

References

Adler, C.M., Mcdonough-Ryan, P., Sax, K.W., Holland, S.K., Arndt, S., & Strakowski, S.M. (2000). fMRI of neuronal activation with symptom provocation in unmedicated patients with OCD, Journal of Psychiatric Research, 34, 317-324.

Alexander BK, Coambs RB, Hadaway PF. (1978). The effect of housing and gender on morphine self-administration in rats. Psychopharmacology, 58, 175-179.

Amoroso, D.M., & Walter, R.H. (1969). Effects of anxiety and socially mediated anxiety reduction on paired-associated learning. Journal of Personality and Social Psychology, 11, 388-396.

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

Azrin, N.H., Hutchinson, R.R., & Sallery, R.D. (1964). Pain-aggression toward inanimate objects. J Exp Anal Behav, 17, 223-228.

Baer, L., Rauch, S.L., Ballantine, T., Martuza, R., Cosgrove, R., Cassem, E., Giriunas, I., Manzo, P.A., Dimino, C., & Jenike, M.A. (1995). Cingulotomy for intractable obsessive-compulsive disorder: Prospective long-term follow-up of 18 patients. Archives of General Psychiatry, 52, 384-392.

Bailley, S.E. (2001). Personality and grieving in a university student population. Unpublished doctoral dissertation.

Barch DM, Braver TS, Akbudak E, Conturo T, Ollinger J, Snyder A. (2001). Anterior cingulate cortex and response conflict: effects of response modality and processing domain. Cerebral Cortex, 11, 837-848.

Baumeister, R.F. (1991). Anxiety and deconstruction: On escaping the self. (1990). In: Olson, J. M. (Ed); Zanna, M. P. (Ed). Self-inference processes: The Ontario symposium, Vol. 6. Ontario Symposium on Personality and Social Psychology (pp. 259-291). Hillsdale, NJ, England: Lawrence Erlbaum Associates, Inc.

Baumeister, R. F. & Leary, M. R. (1995). The need to belong: Desire for interpersonal attachments as a fundamental human motivation. Psychological Bulletin, 117, 497-529.

Baumeister, R. F. & Tice, D. M. (1990). Anxiety and social exclusion. Journal of Social & Clinical Psychology, 9, 165-195.

Beck, A.T., Laude, R., & Bohnert, M. (1974). Ideational components of anxiety neurosis. Archives of General Psychiatry, 31, 319-325.

BenDebba, M., Torgerson, W.S., & Long, D.M. (1997). Personality traits, pain duration and severity, functional impairment, and psychological distress in patients with persistent low back pain. Pain, 72, 115-125.

Benkelfat, C., Gradwejn, J., Meyer, E., Ellenbogen, M., Milot, S., Gjedde A., & Evans, A. (1995). Fucntional neuroanatomy of CCK4-induced anxiety in normal healthy volunteers, American Journal of Psychiatry, 152, 1180-4.

Berkman, L.F., & Syme, S.L. (1979). Social networks, host resistance, and mortality: A nine-year follow-up study of Alameda county residents. American Journal of Epidemiology, 109, 186-203.

Bisgaard, T., Klarskov, B., Rosenberg, J., & Kehlet, H. (2001). Characterisitics and prediction of early pain after laparoscopic cholecystectomy. Pain, 90, 261-269.

Boshuisen, M.L., Hortst, G.J.T., Paans, A.M.J., Reinders, A.A.T.S., & den Boer, J.A. (2002). rCBF differences between panic disorder patients and control subjects during anticipatory anxiety and rest, Biological Psychiatry, 52, 126-135.

Botvinick MM, Braver TS, Barch DM, Carter CS, Cohen JD. (2001). Conflict monitoring and cognitive control. Psychological Review, 108, 624-652.

Boyce, P, & Parker, G. (1989). Development of a scale to measure interpersonal sensitivity. Australian and New Zealand Journal of Psychiatry, 23, 341-351.

Braun, K., & Poeggel, G. (2001). Recognition of mother's voice evokes metabolic activation in the medial prefrontal cortex and lateral thalamus of octodon degus pups. Letter to Neuroscience, 103, 861-864.

Braver, T. S., Barch, D. M., Gray, J. R., Molfese, D. L. & Snyder, A. (2001). Anterior cingulate cortex and response conflict: effects of frequency, inhibition and errors. Cerebral Cortex 11, 825-836.

Breiter H.C., Rauch, S.L., Kwong, K.K., Baker, J.R., Weisskoff, R.M., Kennedy, D.,N., Kendrick, A.D., Davis, T.L., Jiang, A., Cohen, M.A., Stern, C.E., Belliveau, J.W., Baer, L., O'Sullivan, R.L., Savage, C.R., Jenike, M.A., & Rosen, B.R. (1996) Functional magnetic resonance imaging of symptom provocation in Obsessive-compulsive disorder, Archives of General Psychiatry, 53, 595-606.

Brondolo E, Rieppi R, Kelly KP, Gerin W. (2003). Perceived racism and blood pressure: a review of the literature and conceptual and methodological critique. Annals of Behavioral Medicine, 25, 55-65.

Brothers, L. (1990). The neural basis of primate social communication. Motivation and Emotion, 14, 81-91.

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

Buck, R.W., & Parke, R.D. (1972). Behavioral and physiological response to the presence of a friendly or neutral person in two types of stressful situations. Journal of Personality and Social Psychology, 24, 143-153.

Bush, G., Luu, P. & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends Cog. Sci.* **4**, 215-222.

Byrne, R., & Whiten, A. (Eds.). (1988). Machiavellian intelligence: Social expertise and the evolution of intellect in monkeys, apes, and humans. Oxford, England: Clarendon Press.

Bystritsky, A., Pontillo, D., Powers, M., Sabb, F.W., Craske, M.G., & Bookheimer, S.Y. (2001). Functional MRI changes during panic anticipation and imagery exposure, Brain Imagin, 12, 3953-57.

Carter, C. S., Braver, T. S., Barch, D. M., Botvinick, M. M., Cohen, J. D., & Noll, D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science, 280*, 747-749.

Carter, C. S., MacDonald, A. W., Botvinick, M. M., Ross, L. L., Stenger, V. A., Noll, D., & Cohen, J. D. (2000). Parsing executive processes: Strategic vs. evaluative functions of the anterior cingulate cortex. *Proceedings of National Academy of Sciences, 97*, 1944-1948.

Carver, C. S. & Scheier, M. F. (1981). *Attention and Self-Regulation: A Control Theory Approach to Human Behavior*. New York: Springer-Verlag.

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.

Cheney, D.L., & Seyfarth, R.M. (1980). Vocal recognition in free-ranging vervet monkeys. Animal Behavior, 28, 362-367.

Chua, P., Krams, M., Toni, I. Passingham, R., & Dolan, R. (1999). A functional anatomy of anticipatory anxiety. NeuroImage, 9, 563-571.

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.

Coghill, R.C., McHaffie, J.G., & Yen, Y. (2003). Neural correlates of interindividual differences in the subjective experience of pain. Proceedings of the National Academy of Sciences, 100, 8538-8542.

Cohen S, Doyle WJ, Skoner DP, Rabin BS, Gwaltney JM Jr. (1997). Social ties and susceptibility to the common cold. Journal of the American Medical Association, 227, 1940-1944.

Costa P.T. (1987). Influence of the normal personality dimension of neuroticism on chest pain symptoms and coronary artery disease. American Journal of Cardiology, 60, 20-26.

Costa, P.T., Jr., & McCrae, R.R. (1985). Hypochondriasis, neuroticism, and aging: When are somatic complaints unfounded? American Psychologist, 40, 19-28.

Costa, P.T., Jr., & McCrae, R.R. (1987). Neuroticism, somatic complaints, and disease: Is the bark worse than the bite? Journal of Personality, 55, 299-316.

Costa, P.T., Zonderman, A.B., Engel, B.T., Baile, W.F., Brimlow, D.L. & Brinker, J. (1985). The relation of chest pain symptoms to angiographic findings of coronary artery stenosis and neuroticism. Psychosomatic Medicine, 47, 285-293.

Crombez, G., Vlaeyen, J.W.S., Heuts, P.H.T.G., & Lysens, R. (1999). Pain-related fear is more disabling than pain itself: Evidence on the role of pain-related fear in chronic back pain disability. Pain, 80, 329-339.

Damasio, A.R. (1994). Descartes' Error: Emotion, Reason, and the Human Brain. G.P. Putnam's Sons: New York.

Davis, K.D., Hutchison, W.D., Lozano, A.M., & Dostrovsky, J.O. (1994). Altered pain and temperature perception following cingulotomy and capsulotomy in a patient with schizoaffective disorder. Pain, 59, 189-199.

Darbonne, A.R. (1969). Study of psychological content in the communication of suicidal individuals. Journal of Consulting and Clinical Psychology, 33, 590-596.

Davitz, J.R. & Mason, D.J. (1955). Socially facilitated reduction of a fear response in rats. Journal of Comparative and Physiological Psychology, 48, 149-151.

de Wied, M. & Verbaten, M.N. (2001). Affective pictures processing, attention, and pain tolerance. Pain, 90, 163-172.

Dollard, J., & Miller, N.E. (1950). Personality and Psychotherapy. McGraw-Hill, New York, p. 133.

Dougherty D.D., Baer, L., Cosgrove, G.R., Cassem, E.H., Price, B.H., Nierenberg, A.A., Jenike, M.A., & Rauch, S.L., (2002). Prospective long-term follow-up of 44 patients who

received cingulotomy for treatment-refractory obsessive-compulsive disorder. American Journal of Psychiatry, 159, 269-275.

Durkheim, E. (1951). Suicide: a study in sociology. (G. Simpson, Ed. and J.A. Spaulding & G. Simpson, Trans.). Glencoe: The Free Press. (Original work published 1897).

Duval, S. & Wicklund, R. A. (1972). *A Theory of Objective Self-Awareness*. Oxford: Academic Press.

Eisenberger, N.I. & Gable, S.L. (2004). Individual differences in social distress cognitions following conflict. Unpublished data.

Eisenberger, N.I. & Lieberman, M.D. (under review). Why rejection hurts: The neurocognitive overlap between physical and social pain. Submitted to Trends in Cognitive Sciences.

Eisenberger, N.I., Satpute, A.B., & Lieberman, M.L. (2003). Self-awareness of arousal states and the anterior cingulate cortex: An fMRI study of personality. Poster presented at the 10th Annual Cognitive Neuroscience Society conference, New York, NY.

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

Epley, S.W. (1974). Reduction of the behavioral effects of aversive stimulation by the presence of companions. Psychological Bulletin, 81, 271-283.

Eysenck, H. J. (1967). The biological basis of personality. Springfield, IL: Charles C. Thomas.

Eysenck, S. B. G. & Eysenck, H. J. (1975). *Manual of the Eysenck Personality Questionnaire*. London: Hodder & Stoughton.

Fenigstein, A., Scheier, M. F. & Buss, A. H. (1975). Public and private self-consciousness: Assessment and theory. *J. Consult. Clin. Psychol.* **43**, 522-527.

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

Gillespie, N.A., Johnstone, S.J., Boyce, P., Heath, A.C., & Martin, N.G. (2001). The genetic and environmental relationship between interpersonal sensitivity measure (IPSM) and the personality dimensions of Eysenck and Cloninger. Personality and Individual Differences, 31, 1039-1051.

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.

Harlow, H.F. (1958). The nature of love. American Psychologist, 13, 673-685.

Harlow, H.F. & Zimmermann, R.R. (1959). Affectional responses in the infant monkey. Science, 130, 421-432.

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.

Hoogendoorn, W.E., van Poppel, M.N.M., Bongers, P.M., Koes, B.W., & Bouter, L.M. (2000). Systematic review of psychosocial factors at work and private life as risk factors for back pain. Spine, 25, 2114-2125.

International Association for the Study of Pain Task Force On Taxonomy (1994). Classification of Chronic Pain: Description of Chronic Pain Syndromes and Definition of Pain Terms, edn. 2, Merskey, H. & Bogduk, N. (Eds.), Seattle, IASP Press.

Jenike, M.A., Baer, L., Ballantine, T., Martuza, R.L., Tynes, S., Firiunas, I., Buttolph, L., & Cassem, N.H. (1991). Cingulotomy for refractory obsessive-compulsive disorder: A long-term follow-up of 33 patients. Archives of General Psychiatry, 48, 548-555.

Jueptner, M. et al. (1997). Anatomy of motor learning. I. Frontal cortex and attention to action. *J. Neurophysio.,* **77**, 1313-1324.

Jurgens U. & Ploog, D.W. (1970). Cerebral representation of vocalization in the squirrel monkey. Experimental Brain Research, 10, 532-554.

Katon W, Sullivan M, Walker E. (2001). Medical symptoms without identified pathology: relationship to psychiatric disorders, childhood and adult trauma, and personality traits. Annals of Internal Medicine, 134, 917-925.

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.

Kim, C.H., Chang, J.W., Koo, M.S., Kim, J.W., Suh, H.S., Park, I.H., & Lee, H.S. (2003). Anterior cingulotomy for refractory obsessive-compulsive disorder. Acta Psychiatry Scandinavia, 107, 283-290.

Kimbrell, T. A., George, M. S., Parekh, P. I., Ketter, T. A., Podell, D. M., Danielson, A. L., Repella, J. D., Benson, B. E., Willis, M. W., Herscovitch, P., & Post, R. M. (1999). Regional brain activity during transient self-induced anxiety and anger in healthy adults. Biological Psychiatry, 46, 454-465.

Kjaer, K. W., Nowak, M. & Lou, H. C. (2002). Reflective self-awareness and conscious states: PET evidence for a common midline parietofrontal core. *NeuroImage,* **17**, 1080-1086.

Kummer, H. (1967). Tripartate relations in hamadryas baboons. In Social Communication Among Primates, Ed. Altmann S.A. University of Chicago Press: Chicago. (OR USE REF BELOW)

Kummer, H. (1967). Tripartate relations in hamadryas baboons. Reprinted in R. Byrne & A. Whiten, (Eds.) (1988). Machiavellian Intelligence: Social Expertise and the Evolution of Intellect in Monkeys, Apes, and Humans. Clarendon Press: Oxford, pp. 113-121.

Kummer, H. (1981). Social knowledge in free-ranging primates. In Animal Mind-Human Mind. Ed. Griffin, D.R., Springer-Verlag: Berlin.

Lane R. D., Fink G. R., Chau P. M. & Dolan R. J. (1997). Neural activation during selective attention to subjective emotional responses. *Neuroreport* **8**, 3969-3972.

Lang, P.J., Bradley, MM., Cuthbert, B.N. (1995). International affective picture system (IAPS): technical manual and affective ratings, Gainesville, FL: Center for Research in Psychophysiology, University of Florida, 1995.

Laplane, D., Talairach, J., Meininger, v., Bancaud, J., & Orgogozo, M. (1977). Clinical consequences of corticectomies involgin the supplementary motor area in man. Journal of the Neurological Sciences, 34, 301-316.

Leary, M.R. (2003). Emotional reactions to interpersonal rejection: Why do hurt feelings hurt? Talk presented at the Society for Personality and Social Psychology conference, Los Angeles, CA.

Leary, M.R. & Springer, C.A. (2001). Hurt feelings: The neglected emotion, in R.M. Kowalski (Ed). Behaving Badly: Aversive Behaviors in Interpersonal Relationships, pp. 151-175. Washington, DC, US: American Psychological Association.

Leenaars, A., Lester, D., & Wenckstern, S. (1999). Suicide notes in alcoholism. Psychological Reports, 85, 363-364.

Leung HC, Skudlarski P, Gatenby JC, Peterson BS, Gore JC. (2000). An event-related functional MRI study of the stroop color word interference task. Cerebral Cortex, 10, 552-560.

Levine, F.M., Krass, S.M., Padawer, W.J. (1993). Failure hurts: the effects of stress due to difficult tasks and failure feedback on pain report. Pain, 54, 335-340.

Leyton, A.S.F., & Sherrington, C.S. (1917). Observations of the excitable cortex of the chimpanzee, orangutan, and gorilla. Quantitative Journal of Experimental Physiology, 11, 135-222.

Liddell, H.S. (1954). Conditioning and emotions. Scientific American, 190, 48,57.

Lieberman, M. D., Gaunt, R., Gilbert, D. T. & Trope, Y. (2002). Reflection and reflexion: A social cognitive neuroscience approach to attributional inference. M. Zanna (Ed.), *Advances in Experimental Social Psychology* **34**, 199-249. New York: Academic Press.

Lorberbaum, J. P., Newman, J. D., Dubno, J. R., Horwitz, A. R., Nahas, Z., Teneback, C.C., Bloomer, C. W., Bohning, D. E., Vincent, D., Johnson, M. R., Emmanuel, N., Brawman-Mintzer, O., Book, S. W., Lydiard, R. B., Ballenger, J., & George, M. S. (1999). Feasibility of using fMRI to study mothers responding to infant cries. Depression and Anxiety, 10, 99-104.

Lorberbaum JP, Newman JD, Horwitz AR, Dubno JR, Lydiard RB, Hamner MB, Bohning DE, George MS. (2002). A potential role for thalamocingulate circuitry in human maternal behavior. Biological Psychiatry, 51, 431-445.

Luty, S.E., Joyce, P.R., Mulder, R.T., Sullivan, P.F., McKenzie, J.M. (2002). The interpersonal sensitivity measure in depression: associations with temperament and character. Journal of Affective Disorders, 70, 307-312.

MacDonald A.W., Cohen J.D., Stenger, V.A., & Carter C.S. (2000). Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science, 288*, 1835-1838.

MacLean, P.D. (1977). The triune brain in conflict. Psychotherapy and Psychosomatics, 28, 207-220.

MacLean, P.D. (1985a). Brain evolution relating to family, play, and the separation call. Archives of General Psychiatry, 42, 405-417.

MacLean, P.D. (1985b). Evolutionary psychiatry and the triune brain. Psychological Medicine, 15, 219-221.

MacLean, P.D. (1993). Perspectives on cingulate cortex in the limbic system. In B.A. Vogt & M.Gabriel (Eds.) Neurobiology of Cingulate Cortex and Limbic Thalamus: A Comprehensive Handbook. Birkhauser: Boston.

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.

McCormick, R.A., Dowd, E.T., Quirk, S., & Zegarra, J.H. (1998). The relationship of NEO-PI performance to coping styles, patterns of use, and triggers for use among substance abusers. Addictive Behaviors, 23, 497-507.

Metee, D. R., Taylor, S. E., & Fisher, S. (1971). The effect of being shunned upon the desire to affiliate. Psychonomic Science, 23, 429-431.

Miller, G. A., Galanter, E. & Pribram, K. H. (1960). *Plans and the Structure of Behavior*. Oxford: Holt.

Mussen, P.H. & Conger, J.J. (1956). Child Development and Personality. Harper: New York, p. 137-138.

Nagasako, E.M., Oaklander, A.L. & Dworkin, R.H. (2003). Congenital insensitivity to pain: an update. Pain, 101, 213-219.

Neeleman J., Wessely S., & Wadsworth M. (1998). Predictors of suicide, accidental death, and premature natural death in a general-population birth cohort. Lance, 351, 93-97.

Nelson, E.E. & Panksepp, J. (1998). Brain substrates of infant-mother attachment: Contributions of opioids, oxytocin, and norepinephrine. Neuroscience and Biobehavioral Reviews, 22, 437-452.

Nemeth, G., Hegedus, K., & Molnar, L. (1988). Akinetic mutism associated with bicingular lesions: Clinicopathological and functional anatomical correlates. European Archives of Neurological Sciences, 237, 218-222.

Nemoto H, Toda H, Nakajima T, Hosokawa S, Okada Y, Yamamoto K, Horiuchi R, Endo K, Ida I, Mikuni M, & Goto F. (2003). Fluvoxamine modulates pain sensation and affective processing of pain in human brain. Neuroreport, 14, 791-797.

Newman, J.D., Murphy, M.R., & Harbaugh, C.R. (1982). Naloxone-reversible suppression of isolation call production after morphine injections in squirrel monkeys. Society for Neuroscience Abstracts, 233, 299-315.

Norton, G.R., Cox, B.J., Hewitt, P.L, McLeod, L. (1997). Personaltiy factors associated with generalized and non-generalized social anxiety. Personality and Individual Differences, 22, 655-660.

Ogrodniczuk, J.S., Piper,W.E., Joyce, A.S., McCallum, M., Rosie, J.S. (2003). NEO-five factor personality traits as predictors of response to two forms of group psychotherapy. Internal Journal of Group Psychotherapy, 53, 417-442.

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.

Panksepp, J., Vilberg, T., Bean, N.J., Coy, D.H., & Kastin, A.J. (1978). Reduction of distress vocalization in chicks by opiate-like peptides. Brain Research Bulletin, 3, 663-667.

Papez, J.W. (1937). A proposed mechanism of emotion. Archives of Neurology and Psychiatry, 38, 725-743.

Pauli P, Wiedemann G, Nickola M. (1999). Pain sensitivity, cerebral laterality, and negative affect. Pain, 80, 359-364.

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.

Ploghaus, A., Tracey, I., Gati, J.S., Clare, S., Menon, R.S., Matthews, P.M., & Rawlins, J.N.P. (1999). Dissociating pain from its anticipation in the human brain. Science, 284, 1979-1981.

Ploog, D. (1981). Neurobiology of primate audio-vocal behavior. Brain Research, 3, 35-61.

Porro CA, Baraldi P, Pagnoni G, Serafini M, Facchin P, Maieron M, & Nichelli P. (2002). Does anticipation of pain affect cortical nociceptive systems? Journal of Neuroscience, 3206-3214.

Premack, D. 'Does the chimpanzee have a theory of mind?' revisited. In R. Byrne & a. Whiten (Eds.), Machiavellian intelligence: social expertise and the evolution of intellect in monkeys, apes, and humans. Oxford, England: Clarendon Press.

Price DD. (2000). Psychological and neural mechanisms of the affective dimension of pain. Science, 288, 1769-1772.

Price DD, Harkins SW, Baker C. (1987). Sensory-affective relationships among different types of clinical and experimental pain. Pain, 28, 297-307.

Pujol J, Lopez A, Deus J, Cardoner N, Vallejo J, Capdevila A, Paus T. (2002). Anatomical variability of the anterior cingulate gyrus and basic dimensions of human personality. Neuroimage, 15, 847-855.

Rainville P. (2002). Brain mechanisms of pain affect and pain modulation. Current Opinions 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.

Rasmussen, E.W. (1939). Social facilitation. Acta Psychologica, 4, 275-291.

Rauch et al. (1994) Regional CBF measured during symptom provocation in OCD using 15-O-labeled CO2 and PET. Archives of General Psychiatry, 150, 713-719.

Sawamoto, N., Honda, M., Okada, T., Hanakawa, T., Kanda, M., Fukuyama, H., Konishi, J., & Shibasaki, H. (2000). Expectation of pain enhances responses to nonpainful somatosensory stimulation in the anterior cingulate cortex and parietal operculum/posterior insula: An event-related functional magnetic resonance imaging study. Journal of Neuroscience, 20(7438-7445).

Schore, A.N. (2001). Effects of secure attachment relationship on right brain development, affect regulation, and infant mental health. Infant Mental Health Journal, 22, 7-66.

Seidman, D., Bensen, S.B., Miller, I., & Meeland, T. (1957). Influence of a partner on tolerance for a self-administered electric shock. Journal of Abnormal and Social Psychology, 54, 210-212.

Shallice, T. (1988). *From Neuropsychology to Mental Structure*. New York: Cambridge 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.

Shiomi, K. (1978). Relations of pain threshold and pain tolerance in cold water with scores on Maudsley Personality Inventory and Manifest Anxiety Scale. Perceptual & Motor Skills, 47, 1155-1158.

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.

Slotnick, B.M. (1967). Disturbances of maternal behavior in the rat following lesions of the cingulate cortex. Behaviour, 24, 204-236.

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.

Smith, B.W. & Zautra, A.J. (2002). The role of personality in exposure and reactivity to interpersonal stress in relation to arthritis disease activity and negative affect in women. Health Psychology, 21, 81-88.

Stamm, J.S. (1955). The function of the medial cerebral cortex in maternal behavior of rats. Journal of Comparative Physiological Psychology, 47, 21-27.

Staub, E., Tursky, B., & Schwartz, G.E. (1971). Self-control and predictability: their effects on reactions to aversive stimulation. Journal of Personality and Social Psychology, 18, 157-162.

Strazielle, C., Lalonde, R., Hebert, C., & Reader, T. A (1999). Regional brain distribution of noradrenaline uptake sites, and of alpha-1, alpha-2 and beta-adrenergic receptors in PCD mutant mice: A quantitative autoradiographic study. Neuroscience, 94, 287-304.

Talbot JD, Marrett S, Evans AC, Meyer E, Bushnell MC, Duncan GH. (1991). Multiple representations of pain in human cerebral cortex. Science, 251, 1355-1358.

Tashiro M, Itoh M, Kubota K, Kumano H, Masud MM, Moser E, Arai H, Sasaki H. (2001). Relationship between trait anxiety, brain activity and natural killer cell activity in cancer patients: a preliminary PET study. Psychooncology, 10, 541-546.

Taylor, S.E. (in press). Social support. In: H.S. Friedman & R.C. Silver (Eds.), Oxford Handbook of Health Psychology. New York: Oxford University Press.

Tow, P.M. & Whitty, C.W.M. (1953). Personality changes after operations of the cingulate gyrus in man. Journal of Neurology, Neurosurgery, and Psychiatry, 16, 186-193.

Trapnell, P. D. & Campbell, J. D. (1999). Private self-consciousness and the five-factor model of personality: Distinguishing rumination from reflection. *J. Pers. Soc. Psychol.* **76**, 284-304.

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 & Social Psychology, 81, 1058-1069.

Twenge, J. M. & Campbell, W. K. (2003) "Isn't it fun to get the respect that we're going to deserve?" Narcissism, social rejection, and aggression. Personality & Social Psychology Bulletin, 29, 261-272.

Twenge, J. M., Catanese, K. R., & Baumeister, R. F. (2003). Social Exclusion and the Deconstructed State: Time Perception, Meaninglessness, Lethargy, Lack of Emotion, and Self-Awareness. Journal of Personality & Social Psychology, 85, 409-423.

Ursu, S., Stenger, V.A., Shear, M.K., Jones, M.R., & Carter, C.S. (2003). Overactive action monitoring in OCD: Evidence from functional magnetic resonance imaging. Psychological Science, 14, 347-353.

van den Hout, J.H.C., Vlaeyen, J.W.S., Ruud, M.A.H., Soeters, A.P.M., & Peters, M.L. (2001). The effects of failure feedback and pain-related fear on pain report, pain tolerance, and pain avoidance in chronic low back pain patients. Pain, 92, 247-257.

van den Hout, J.H.C., Vlaeyen, J.W.S., Peters, M.L., Engelhard, I.M., & van den Hout, M.A. (2000). Does failure hurt? The effects of failure feedback on pain report, pain tolerance and pain avoidance. European Journal of Pain, 4, 335-346.

Vogeley, K. et al. (2001). Mind reading: Neural mechanisms of theory of mind and self-perspective. *NeuroImage,* **14,** 170-181.

Vogt, B. A., Wiley, R. G., & Jensen, E. L. (1995). Localization of Mu and delta opioid receptors to anterior cingulate afferents and projection neurons and input/output model of Mu regulation. Experimental Neurology, 135, 83-92.

Wall, P.D. (1999). Pain: The Science of Suffering. Weidenfeld & Nicolson: London.

Watson D, Pennebaker JW. (1989). Health complaints, stress, and distress: exploring the central role of negative affectivity. Psychological Review, 96, 234-254.

Weissman, D. H., Giesbrecht B., Song A. W., Mangun G. R. & Woldorff M. G. (2003). Conflict monitoring in the human anterior cingulate cortex during selective attention to global and local object features. Neuroimage, 19, 1361-1368.

Williams, A.C. (2002). Facial expression of pain: An evolutionary account. Behavioral and Brain Sciences, 25, 439-488.

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.