Chapter 17: Social Communication and Modulation of Pain

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Overview

Within the social environment, pain can serve as a tool used to communicate information about our **status** [position, rank, or standing in relation to others] and well-being. Viewed in this light, it is important to appreciate that pain perception and expression can change depending on our social history, social interactions, and observation of pain within our immediate environment.

Learning Objectives

1. Illustrate how and why pain is communicated in human and nonhuman animals
2. Understand the contribution of the social context to changing pain perception and expression
3. Understand that empathy can influence the pain experience

17.1 Pain and the social environment

The Personal Experience of Pain

Pain is recognized to be a complex perception of unpleasant stimuli that has sensory-discriminative, cognitive-evaluative, and motivational-**affective** [of or relating to feelings or emotions] components (Melzack & Casey, 1968). Pain is often thought of as a highly personal and private experience. When you are injured, individual characteristics such as your sex, gender, ethnic, and cultural identities shape and influence your pain experience (see Chapter 12). It is unreasonable to assume that another individual feels exactly the same sensation as you even though the **stimulus** [a thing or event that evokes a specific functional reaction in an organ or tissue] may be the same. The perception of noxious stimuli, called **nociception,** begins with **nociceptors** [the sensory neurons specific to detection of painful stimuli] that transmit electrical signals along the **neuraxis** [the directional arrangement of the central nervous system] to the brain. The nociceptive pathway in everyone is typically initiated in the periphery and transmitted centrally to the brain. This allows us to perceive pain with unique neurobiology driven by variations in gene expression, development, affective states, and beliefs (Garcia-Larrea & Peyron, 2013).

Image caption: Social contexts can affect pain perception.

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17.1.1 The social environment

Biological targets [receptors, neurochemicals, anatomical structures] for the detection of pain have been a heavy focus for research and treatment, but for pain, especially chronic pain, tissue damage is a poor predictor of whether an injury will heal or turn into a chronic problem. The more we study chronic pain, the more we find that the **social context** [the immediate physical and social setting], including the location we are in, who we are with, and their expressions, heavily influences our actions and perceptions, including the perception of pain. **Social determinants** [conditions in which people are born, grow, live, work, and age and the forces, systems, policies, and social norms that shape daily life] affect an individual's behavior and their experience of pain. Epidemiological studies have revealed associations between various aspects of social determinants (i.e., socioeconomic status, race, age, gender) and an individual's susceptibility to the development of chronic pain. Additionally, in both humans and animals, expressive pain behavior from others has been shown to enhance or suppress pain perception and expression within an individual. However, social determinants are difficult to study in controlled environments. This has led to an emergence of research into the social context, where people (and animals) experience pain in the presence or absence of another individual.

Test Yourself: Social determinants of pain include

A. Genetics, work conditions, and siblings
B. Sex, age, and work conditions
C. Gender, race, age, and socioeconomic status
D. Sex, gender, race, and age

[Social determinants that can affect pain experiences are gender, race, age, and socioeconomic status which can influence how other people interact with us and how we perceive ourselves. Sex is a biological determinant that can influence pain, while gender is a social and cultural determinant because gender is how others perceive our outward presentation of ourselves.]

17.1.2 Sensing pain in others

Pain that is experienced at a personal level is processed by the brain and expressed in the form of pain behavior. Recent research in both humans and other social mammals is building an understanding of pain in terms of the evolutionary benefit of expressions of **affect** [the psychological experience of feelings, attitudes, moods, or emotions which have a spectrum of positive-to-negative values called valence] due to painful experiences and how the social environment impacts medical interventions for pain patients. Affective expressions like a facial grimace or calling out by mammals due to pain serve to externally communicate that individual's pain to others who then perceive the behavioral signal and react. The perception of pain has both **exteroceptive** [sensing stimuli outside of the body] and **interoceptive** [a type of stimulus that comes from within the body, possibly as a result of changes in homeostasis to various bodily systems] sensory elements because pain integrates the sensing of internal stimuli with the affective and motivational state in the body. Similarly, sensing expressions of pain in others and sharing the affective state, a process called **empathy** [the perception and then sharing of affective states of others], also has interoceptive and exteroceptive elements due to the sensing of external stimuli and matching or modulation of affective and motivational state. It is important to recognize that both pain and empathy for pain activate overlapping brain regions and serve as tools for communication to assess threats to bodily integrity or needed resources like social connections. Taken together, individual and social contexts play a large part in the biopsychosocial model of pain.

Image caption: While observing someone in distress or pain, people often experience empathy and can subsequently be motivated to act by consoling the person in pain. The cues from one individual can influence the behavior of pairs or groups of people.

Source: Shutterstock ID 483282583

17.1.3 Pain in others can affect my pain

Experiencing pain along with a social partner compared to when alone can **modulate** [change, e.g. increase or decrease] how unpleasant a stimulus is. In varying social contexts, individuals may differ both in their perception of painful stimuli and in their perception of pain expressions. You may rate a pain stimulus as two (out of 10), but your friend may rate the same stimulus as an eight. Your friend may not notice Jodie wincing, but you saw she was in a lot of pain and may feel more empathy for her than your friend. When we express behaviors that indicate pain in a social environment, the people around us decode our pain and make decisions about what to do: Should they run away? Do they choose to help or engage in some other action? These simple actions may then feedback to the individual and change the perception and expression of pain. In the social environment, pain may be used or changed for different reasons including:

- The communication of pain to members of your group to elicit caregiving actions
- To increase pain in bystanders so that dangerous situations can be avoided
- To reduce pain and suffering when comforted by a caregiver

This chapter will focus on all the above points through the illustration of different theories within the **social dynamic framework** [a means of examining behavior through consideration and analysis of social interactions] and compare the usefulness of understanding these perspectives from the point of human and nonhuman animals.

17.2 Social communication of model of pain

Different factors at any given point in time create the social context we experience. For people, cultural expectations and religion can influence the social context, as well as the place they are living (rural or urban, dense apartment or gated community), educational experiences, economic background, age, family members, and all of the different people we come into contact with on a daily basis. For example, an unwelcoming atmosphere and a rude waiter at a new restaurant might cause you to perceive that the food tastes bad and you may never choose that dish or restaurant again. But a fun and relaxing environment may lead you to perceive that the new food tastes great and you would be happy to choose it again. We can also extrapolate the social context based on cues that we see, and this can influence how we act. As an illustration, if everyone you see is solemn, sad, and wearing black, you may assume that they are attending (or recently attended) a funeral, and this may influence you to speak respectfully and act solemnly. Similarly, if you see someone rubbing their arm and making an upset face, you may think this person is in pain and choose to come near to see if you can help. Conversely, if you see someone that looks like they are sick (e.g., red nose, tired expression), you may choose to avoid contact for fear of contagion. We extract information about individuals around us through our social context, and the actions and expressions of individuals can influence our behavior and perceptions.

Image caption: A mother comforts her daughter, an example of the "magic mommy kiss."

Source: Shutterstock ID 1047352294

Humans communicate their experience of pain through several different behaviors including rubbing a wound, expressing affect through facial grimaces, and by using vocal outcries, and interjections such as "ouch" in the English language. Rubbing of a limb is typically discussed in terms of the gate control theory of pain, where rubbing activates somatosensory receptors near the active nociceptor and silences the nociceptive response (see Chapter 6). However, rubbing is also an external signal that can be viewed by other individuals who can potentially elicit empathy, **consolation** [the physical and/or psychological comfort given to someone after a loss or injury], and helping behavior. In the human social communication model of pain (Craig, 2008), the person in pain encodes signals through expressions, while observers must interpret what the person in pain is experiencing; this causes observers to make judgments on what care to perform or actions to take (**Figure 17.1**). In this model, the person in pain elicits help through successful encoding using behavioral expressions, but many **intrapersonal** [existing within a person] and **interpersonal** [existing between people] influences (see **Table 17.1**) can disrupt a successfully transmitted message and prevent proper care from occurring. The person in pain displays behavioral expressions that serve to communicate distress to bystanders, who then react to the situation, and provide caregiving actions that may impact the sufferer's pain experience. The classical example of this is the "magic mommy kiss." Young children are notoriously susceptible to an endless barrage of scrapes, knocks, and bruises, leaving countless numbers of children crying and screaming for their mommy. For most of these minor injuries, the kiss of their mother is all it takes to make the pain go away. From birth, the gentle touch of our mothers' hands has been the source of calm and healing. There is a lot to unpack in this scenario, but it portrays the social aspects of the **biopsychosocial model** [a model that incorporates the connection between biology, psychology, and sociological factors to understand behaviors or disease]—the pain expression of the child combined with the socialization and comfort offered by the mom. The caregiving actions evoked by the pain communication of the child are thought of as the typical result of human empathy, but animals have been shown to perform similar actions after observing other species members in pain.

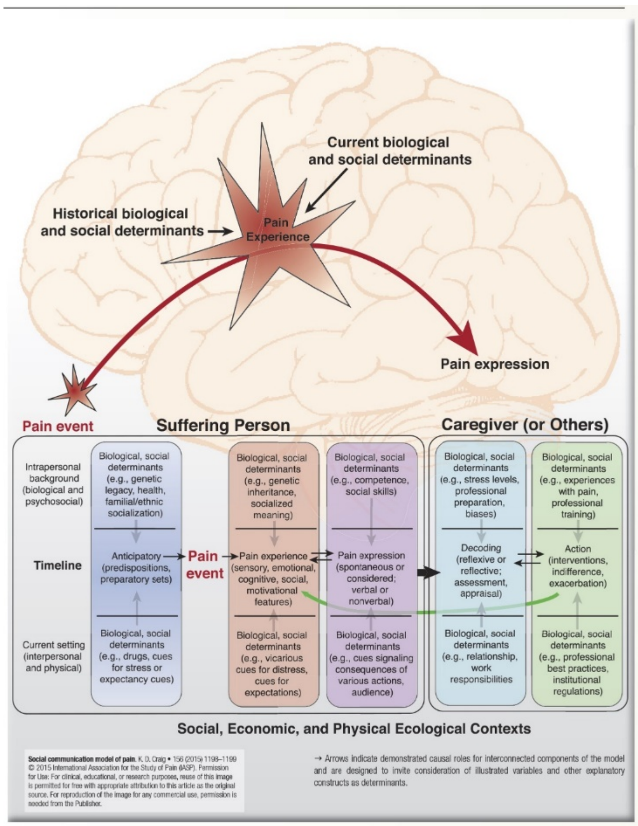


Figure 17.1. The pain social communications cycle. All stages (1) operate within causal, social, and ecological contexts, (2) have biological substrates, (3) are amenable to change through social and biological interventions. The process is recursive, reciprocal, and dynamic.

Source: Craig, 2015.

Influences on Pain

Intrapersonal (within)	Interpersonal (between)
• Personal history	• Physical setting, e.g. clinic, home
• Genetics	• Social context
• Biological makeup	• Perception of responsibility
• Biases	• Relationships
• Knowledge	• Ease of solicitation

Adapted from (Craig, 2008)

Table 17.1. The social context of the biopsychosocial model of pain consists of numerous intrapersonal and interpersonal influences on our perception.

Source: Adapted from Craig, 2008.

Test Yourself: See whether pain serves an intrapersonal or interpersonal influence in the following examples:

A. Warns of real or potential biological threat **= intrapersonal**
B. Motivates the individual to escape **= intrapersonal**
C. Alarm to warn against personal danger **= interpersonal**
D. Influences how others may respond **= interpersonal**
E. Instigates empathy or caretaking behavior **= interpersonal**

[A and B: Intrapersonal influences are within an individual. C, D, and E: Interpersonal influences are between two or more individuals.]

Observing another person in pain can elicit caregiving behaviors, but these caregiving behaviors have been shown to have the opposite result than intended. In a landmark study, Flor and colleagues (Flor et al., 1987) used the West Haven-Yale Multidimensional Pain Inventory (WHYMPI) to examine the impact of chronic pain on patients' lives, the response of the spouse to the patients' communication of pain, and the extent to which patients participate in common daily activities. The perception of the spouse was recorded through a daily spouse diary, which captured the influence that the spouse was having on the patient from their own perspective. In brief, this study showed that patients' pain reports were best predicted by the **solicitousness** [characterized by or showing interest or concern] of the spouse toward the patient. The best predictor of the patients' pain experience was spouse reinforcement as perceived by the patient, not the spouse's perception of their own effectiveness in the spouse diary (**Table 17.2**). Intriguingly, spouses who were more generous with support, attention, and encouragement exacerbated pain, while spouses who ignored the patients' pain or responded negatively to the feedback diminished pain as measured by an increase in activity levels in pain patients. This finding is consistent with Fordyce's operant conditioning model in that positive and negative reinforcement of pain behavior such as moaning or inactivity may alter the development of chronic pain (Fordyce, 1976).

TABLE II —CORRELATION COEFFICIENTS FOR THE PAIN SEVERITY, ACTIVITY AND THE REINFORCEMENT VARIABLES

	Composite pain score r	Total activity score r
WHYMPI		
Punishment	−0.19	0.36*
Solicitousness	0.48†	−0.10
Distraction	0.01	−0.12
Spouse diary		
Punishment	−0.03	0.32*
Solicitousness	0.31*	−0.35*
Distraction	−0.38*	−0.03

*$p < 0.05$ †$p < 0.01$

Table 17.2: The patient related WHYMPI scales are scored from 0 (low magnitude) to 6 (high magnitude), which spouse responses were combined into a total score. Positive values indicate that the measure increased pain or activity, negative values indicate a reduction in pain or activity. Only the most prominent variables are shown.

Source: Flor et al., 1987.

Test Yourself: The punishment scale on the WHYMPI was associated with:

A. Increased pain outcomes in chronic pain patients
B. Reduced pain outcomes in chronic pain patients
C. Increased activity levels in chronic pain patients
D. Reduced activity levels in chronic pain patients

[The punishment scale was associated with increased activity levels.]

The phenomenon in which empathetic responses enhance pain is important to pay attention to for medical practitioners because the social environment could enhance as opposed to diminish pain. Environmental cues may indicate that a person is experiencing pain, such as lowered daily motion (as in the Flor et al., 1987 study) or willingness to participate in activities that the person normally enjoys. Previous nociceptive activation from an injury or previous social experiences with other caregivers can influence the willingness of that person to express pain or the anticipation of pain. Additionally, the expressions of one individual can influence others in social surroundings, lending to unintentional enhanced pain perception in those that see the expressions. Thus, caregivers must be aware that the social context influences the pain experience in order to consider individual treatment for pain conditions.

Image Caption: Spouse Pain Cartoon.

Source: www.cartoonstock.com search ID CX903185

17.3 Social communication of pain in animals

Verbal cues, rubbing a limb, and facial expressions all signal pain in humans, but many other mammals express some of these same gestures highlighting the evolutionary continuity of pain behavior and communication. Yet for many animals, displaying injury is a liability because it could signal an easy target for predators. For these expressive behaviors to exist despite potential predation, a benefit toward **reproductive fitness** [the ability of individuals to pass on their genes to subsequent generations] must arise for the species. Sending signals like facial expressions due to pain and having fellow group members perceive those signals benefits the species by either signaling other members to assist the individual or steer clear of the danger. Thus, while pain perception acts as an internal signal to warn the individual of bodily injury, external affective expression due to pain serves as a communication mechanism between social animals to gain assistance or alert others of danger.

Image caption: Animals including mice produce species-specific facial expressions that indicate affect. Facial expressions can consist of ear position, eye openness, nose scrunching, cheek protrusions, or other species-specific feature movement.

Source: Shutterstock ID 207253459

The human model for the social communication of pain can be simplified and applied to a number of social animals (see **Figure 17.2**). In this model, pain sensations lead to external expressions encoded by the animal in pain, while those expressions must be decoded by members of the social group. Through perception and activation of similar neural processes, affective states and experiences may become shared between individuals (i.e., those in pain and those merely observing). In this section, we'll discuss instances of pain communication within social groups as measured in nonhuman animals—mostly rodent species.

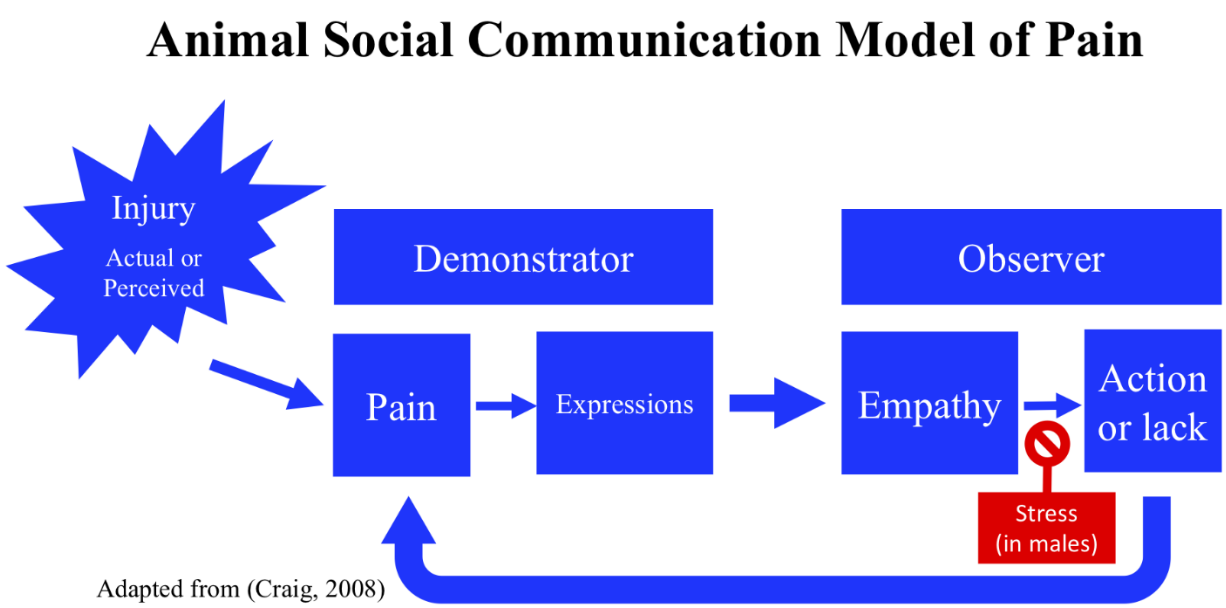


Figure 17.2. In the simplified Animal Social Communication Model of Pain, the demonstrator perceives pain from injury, then encodes expressions of pain like facial grimace, vocal expressions, favoring a limb or olfactory cues. The observer decodes the expressions using empathy to sense the pain expressions and match the affective state of the demonstrator, which can (but does not always) motivate action. This action can be blocked through a stress response (data from male rodents). The actions or inaction of observers can feed back to demonstrators and affect the pain response.

Source: Adapted from Craig, 2008.

Animals in pain display a combination of clearly visible pain behaviors including changes in body position, licking afflicted areas, and altered facial expressions (Langford, Bailey, et al., 2010; Martin, Hathaway, et al., 2015; Martin, Piltonen, et al., 2015). In fact, facial expressions to communicate affect are common among several species and have been thoroughly described using a taxonomy of facial movements in humans (Ekman et al., 2002; Ekman & Wallace, 1978; Hjortsjö, 1969), chimpanzees (Vick et al., 2007), and horses (Wathan et al., 2015). In response to noxious stimuli, numerous studies have reported that facial grimacing is present in mice (Langford, Bailey, et al., 2010), rats (Sotocinal et al., 2011), rabbits (Keating et al., 2012), horses (Dalla Costa et al., 2014), sheep (Guesgen et al., 2016; Häger et al., 2017; McLennan et al., 2016), piglets (Di Giminiani et al., 2016; Viscardi et al., 2017), ferrets (Reijgwart et al., 2017), and cats (Finka et al., 2019; Holden et al., 2014) with each animal displaying features that are unique to that species (i.e., ear position will change in mice, while humans are not able to change this feature of their face).

In rodents, much like people, the observation of another in pain affects how the observer responds to the pain of the other. Male rats will avoid the image of a rat in pain, but only when the face and body of the rat in pain are clearly visible (Nakashima et al., 2015). In contrast, female, but not male, mice will approach a familiar mouse in pain more frequently than an unaffected **cagemate** [an animal that shares the same cage, often of the same sex] or a stranger in pain (Langford, Tuttle, et al., 2010). Further, approach and avoidance behavior is dependent on the age or familiarity of the other rodent. In a study of adult rats of both sexes, rats avoided a stressed adult rat of the same sex but approach a stressed juvenile rat (Rogers-Carter, Varela, et al., 2018). In a follow-up study that examined familiarity using the same choice paradigm, male and female rats both avoided a stressed stranger rat. Male rats also avoided a stressed familiar rat, but female rats approached stressed familiar rats (Rogers-Carter, Djerdjaj, et al., 2018). Increased social approach to pain or distress in females is explicitly predicted by the “tend and befriend” model (Taylor et al., 2000), which suggests that conditions of stress cause females to respond by tending to offspring, which in turn decreases their stress levels.

It is also well known that perceiving that others are expressing pain can elicit consolation behavior. Following a paw injection of bee venom or formalin, rats display obvious pain behaviors such as paw lifting (**Figure 17.3 panel A**) and attending (C.-L. Li et al., 2018). When observer rats are paired with a cagemate demonstrating pain, observers have been shown to follow, sniff and groom (**Figure 17.3 panel B**), and body support (**Figure 17.3 panels C and D**) the cagemate (C.-L. Li et al., 2018). Further, a painful foot shock of a cagemate will cause pair-bonded prairie voles to groom and lick the shocked cagemate more frequently than a shocked stranger. This social interaction increased activity in the anterior cingulate cortex (ACC), and infusion of an oxytocin receptor **antagonist** [a substance that blocks the physiological action of another] into this region disrupted the cagemate-directed licking/grooming (Burkett et al., 2016). Oxytocin is thought to be involved in social bonding, so one might expect that disruption of this system would affect social interactions. In another model of empathy, rats learn to open a container to release a trapped and distressed cagemate (Ben-Ami Bartal et al., 2011). This empathy behavior (i.e., opening the restrainer) is impaired by midazolam, a drug prescribed to reduce anxiety, an indicator that this behavior may be driven by negative affect (Ben-Ami Bartal et al., 2016). Additionally, pain due to chronic nerve injury has been shown to change social dynamics and disrupt social relationships in mice (Tansley et al., 2018). The specific response to pain or distress in a social partner may likely be dependent on the social context including sex, familiarity, and social relationships within the species.

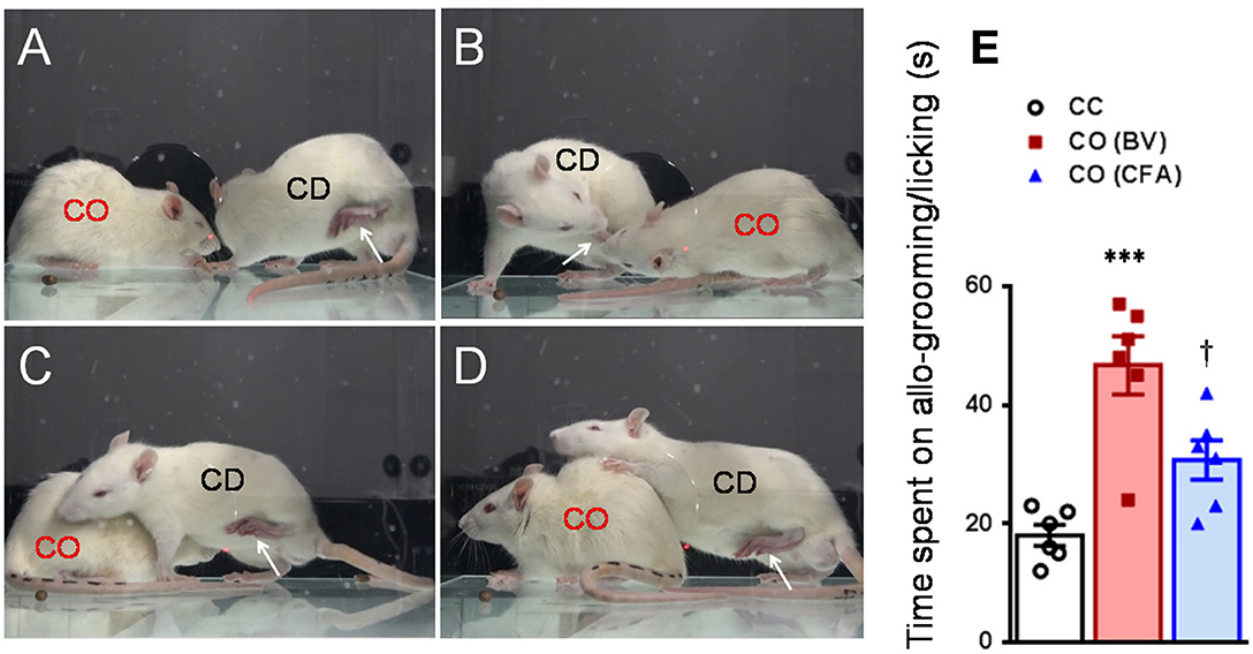


Figure 17.3. Observation of pain behaviors in rats. CO is the cagemate observer while CD is the cagemate demonstrator of pain—a paw injection of bee venom produces obvious paw lifting while a paw injection of complete Freund's adjuvant (CFA) produces little paw lifting. (A) CD displaying paw lifting (B) CO sniffing and licking the affected paw (C) and (D) examples of body supporting of the CD in pain by the CO. (E) Authors measured amount of time the CO spent grooming the CD and found increased behavior in both pain conditioned but exaggerated grooming when displayed pain behaviors were more obvious with a bee venom paw injection.

Source: C.-L. Li et al., 2018.

17.4 Empathy in humans

We have seen that the social context can influence our own pain experience when we see others expressing behaviors that indicate they are in pain. Yet our ability to perceive those expressions not only serve to inform us of danger in the social setting but also serve to strengthen our social ties. Accurately perceiving and responding to social cues can serve to maintain social connection, which helps humans and other social animals gain much needed resources like food, shelter, and access to mates. Behavioral responses to social cues include **mirroring** [mimicking, matching or replicating] a gesture, posture, or vocal cue of the observed individual, which has been shown to increase rapport in both humans and other animals, and **emotional contagion** [the phenomenon of affective state and the associated expressions being triggered by subconsciously observing that state in others; for example, when you see someone smile, without realizing it you may also smile and are in a pleasant mood]. These behaviors in reaction to cues in others, whether rudimentary mimicry or cognitive and complex, are considered a form of empathy and are thought to establish and preserve social bonds.

Image caption: Seeing a child in distress often elicits an emotional empathetic response in the person observing the expressions.

Source: Shutterstock ID 723470008

Empathy is the perception and then sharing of affective states of others, which occurs through observing the behaviors of others within our environment. It is difficult to explain how one individual can share the affective state of another, but it is through the species-specific expressions of internal states and the neurological interpretation of those expressions by observers that elicit physiological responding in those engaged in observation. The mere observation and perception of pain causes similar patterns of brain activation as the firsthand experience of pain. When observers experience empathy for pain, empathy is the mechanism through which pain expressions are detected and subsequently understood to alter pain responses. During perception, brain regions active in the observer elicit mirroring behavior or emotional contagion. The mirror system was initially implicated as the cortical mechanism through which understanding in others occurs (Cattaneo & Rizzolatti, 2009; Gerbella et al., 2019; Preston & de Waal, 2017). The mirror system, originally found in monkeys, consists of a class of neurons in the premotor and posterior parietal cortices that are appropriately referred to as mirror neurons. It is thought that activation of these neurons allows observers to not only understand and respond to movements from those around us, but mirror neurons give us the ability to understand affective expressions and complex behaviors. This is a well-known phenomenon where the person in pain causes the activation of brain regions corresponding to a similar experience in observing individuals, which may cause activation of the **somatic** [sensory and motor neuron system that gives voluntary control of muscles] and **autonomic** [unconscious systems like threat response, digestion, and sexual attraction] nervous systems of observers such that appropriate responses are elicited (Preston & de Waal, 2002).

Image caption: Mirror neurons.

Source: Shutterstock ID 1254890389

Brain regions believed to be associated with affective aspects of perceiving signals from noxious stimuli in the body have been shown to be active when individuals observe others expressing pain behavior. In human participants, observing pain expressions in others has been found to activate the anterior insular cortex (AI) and the ACC, regions that are also active during the firsthand experience of pain (**Figure 17.4**) (Botvinick et al., 2005; Singer et al., 2004). Additional human imaging studies implicate the primary (SI) and secondary (SII) somatosensory cortices, specifically the Brodmann Area 2 of the anterior parietal cortex in SI along with SII, when attention is directed at the somatic source of another person's pain (Costantini et al., 2008; Keysers et al., 2010). Current imaging study data indicates that when the source of the pain in others is known, the somatosensory cortex is activated, but when the source of pain is not known, affective motivation regions including the AI cortex and the rostral cingulate cortex are activated when perceiving that another person is experiencing pain (Keysers et al., 2010). Put simply, when the source is known, the empathetic response may be similar to experiencing that kind of pain ("I know how you feel"), whereas, when the source is not known, the response is a general empathetic response ("I imagine that hurts").

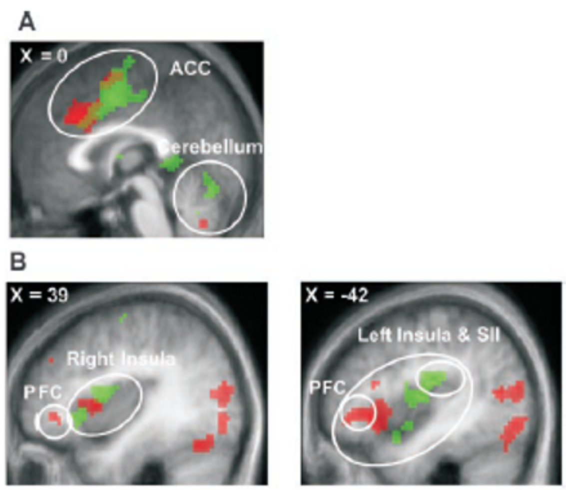
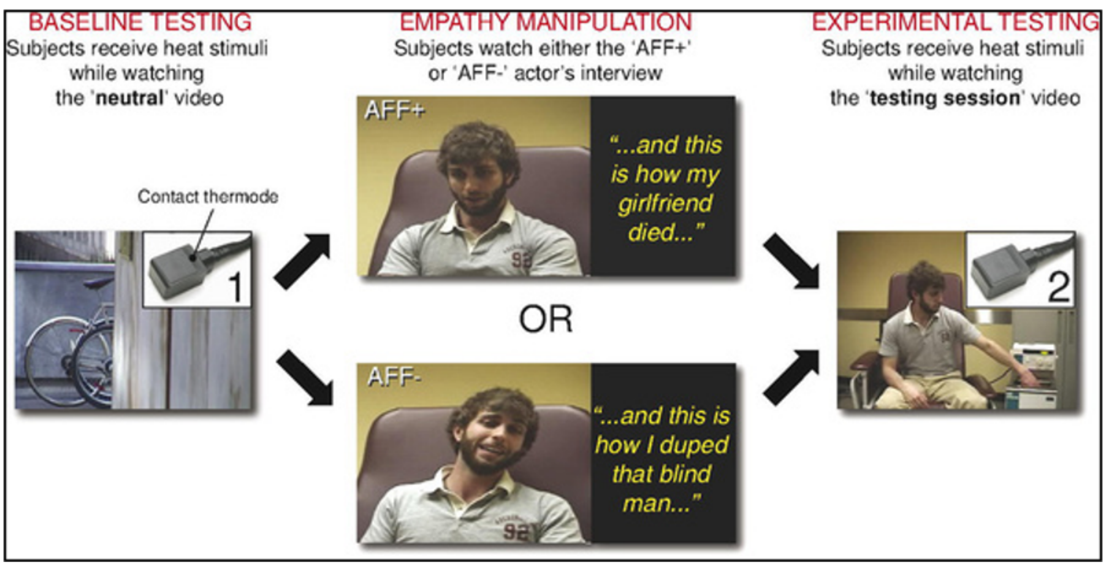


Figure 17.4. Pain-related activation associated with either experiencing pain in oneself or observing one's partner feeling pain. Areas in green represent significant activation for the "self" condition and areas in red the "observing" condition. (A) Activation in anterior cingulate cortex and cerebellum. (B). Bilateral insula cortex extending into the lateral prefrontal cortex and somatosensory cortex (SII).

Source: Adapted from Singer et al., 2004.

The observation of pain increases the activation of pain-associated brain regions, which may act to increase pain perception, but this may be dependent on whether a previously-formed positive empathic bond has been established. We have investigated whether sharing a brief social experience with a stranger was sufficient to induce a state of empathy. Participants who played 15 minutes of the video game Rock Band together and then experienced pain, demonstrated more pain—as measured by the cold pressor test—than when tested alone or compared with participants who had played the video game alone (Martin, Hathaway, et al., 2015). Similarly, in an experimental study where viewing a video of a **confederate** [an experimenter posing as a participant] undergoing pain testing lead participants to report more pain in response to a nociceptive stimulus, but only if they watched a video of the confederate telling a sad story about how his girlfriend died (Loggia et al., 2008). The story was created to evoke an emotional reaction in the participants and create a positive bond between them and the confederate. Another group of participants watched the same confederate tell a story about how he once cheated a blind man out of some money. Both sensory and affective pain ratings were increased by the positive empathy bond. The effects were observed even when the confederate received nonpainful stimuli, suggesting that it is the empathy itself that alters pain perception, not merely the observation of pain behaviors (**Figure 17.5**). Thus, a shared experience through social bonding or similar adverse experiences may prepare cortical region in the context of observing social signals.

Does this mean that somatic pain and perceiving pain in others both constitute as pain? This question is still discussed today (Riečanský & Lamm, 2019; Zaki et al., 2016), but what may make sense is that multiple methods of perception of different stimuli use a network of brain regions that monitor the body and environment constantly in order to watch for actual or potential harm. The regions that overlap in nociception and empathy for pain expressions are also found among the frontal-parietal-cingulate **salience network** [a large brain network involved in detection and filtering salient stimuli]. The salience network that has been proposed to perform a broad appraisal of incoming stimuli from multiple sources of sensory inputs including pain (Bilevicius et al., 2018; Davis & Moayedi, 2013; Downar et al., 2002; Legrain et al., 2011; Seeley et al., 2007; Torta & Cauda, 2011). This evidence together bolsters the idea of the brain being sensitive to multiple inputs and responding to different types of threats so that appropriate responses can serve to maintain health.



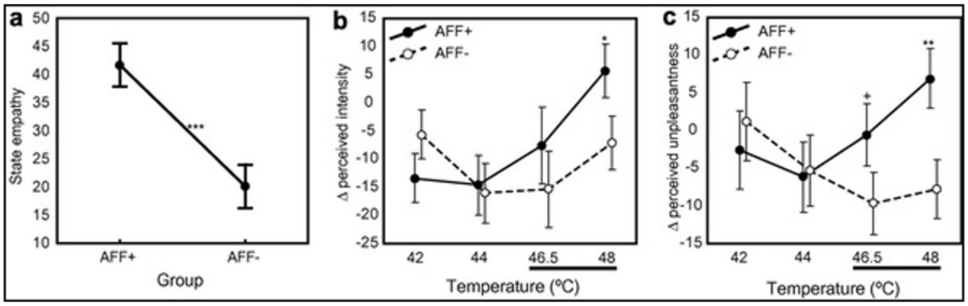


Figure 17.5. **Top panels:** Study design in the Loggia et al., 2008 study. Participants' thermal responses were measured while watching a neutral video. An interview with a confederate was then shown (after introducing the confederate as another study participant), followed by the second thermal testing session (which was performed while participants watched the "testing video"). **Bottom panels:** Effects of empathy on pain perception. Overall, the two groups reported different levels of empathy toward the actor (p < 0.01). Both graphs show the average rating for each temperature (intensity and unpleasantness) while the participants watched the "testing video" minus the baseline rating recorded while the participants watched the neutral video.

Source: Adapted from Loggia et al., 2008.

Test Yourself: When observing pain in another individual, if the source of the pain is not known, affective motivation regions including the _______ are activated when perceiving that another person is experiencing pain

- **A. Anterior insula and the rostral cingulate cortex**
- **B.** Cerebellum and basal ganglia
- **C.** Somatosensory cortices SI and SII
- **D.** Prefrontal cortex and cerebellum

[When the source of pain is not known, affective motivation regions including the anterior insular cortex and the rostral cingulate cortex are activated when perceiving that another person is experiencing pain.]

17.5 Pain modulation due to empathy in rodents

As we have seen, empathy serves as a basic method of socially communicating states in others. Like in humans, empathy has been observed in many social mammals suggesting conserved behavior through evolution and a shared neurobiology driving the behavior. Empathy can lead to behavioral responses in the form of rudimentary mimicry or can drive more complex actions like consolation, targeted helping, and perspective-taking, which has been observed in a number of different mammals from rodents to canines to apes (de Waal & Preston, 2017; Sivaselvachandran et al., 2018). Increased pain sensitivity by observing another in pain is a fundamental finding associated with human empathy and as such has been adopted for nonhuman animals, particularly rodents, to better understand the neural mechanisms (Sivaselvachandran et al., 2018).

Image caption: Mice are social animals that display emotional contagion, a form of empathy.

Source: Shutterstock ID 765224923

When mice are tested in the presence of a familiar mouse also in pain, the pain behavior observed by experimenters increases. This was first reported in 2006 and provided comprehensive evidence that mice are capable of emotional contagion. Mice were given a weak vinegar injection in the stomach, which induces twisting of the abdomen, or writhing, like a tummy ache, and were placed in pairs (cagemates or strangers) or alone in an arena (see Chapter 5). The number of writhing episodes evoked by the vinegar were greater in cagemate pairs compared with stranger pairs or mice tested alone. Mice seemed to experience more pain when with another mouse that they were familiar with, who was also in pain. However, this enhancement was blocked by placing an opaque barrier between the cagemate pair of mice, suggesting that pain behavior within the social environment is facilitated by visual stimuli—removing other sensory input did not block pain facilitation (Langford et al., 2006). In the same study, when the target mouse was placed together with a mouse given a higher concentration of formalin, the target mouse licked the paw more compared to when paired with a mouse given the same concentration; in the reverse direction, when the target mouse was placed with a mouse given a weaker concentration of formalin, the target mouse licked the paw less. This study showed a bidirectional modulation of a painful experience when the social partner was given a stronger or weaker concentration, suggesting that the behavior of social partners directly altered pain expression (**Figure 17.6**)

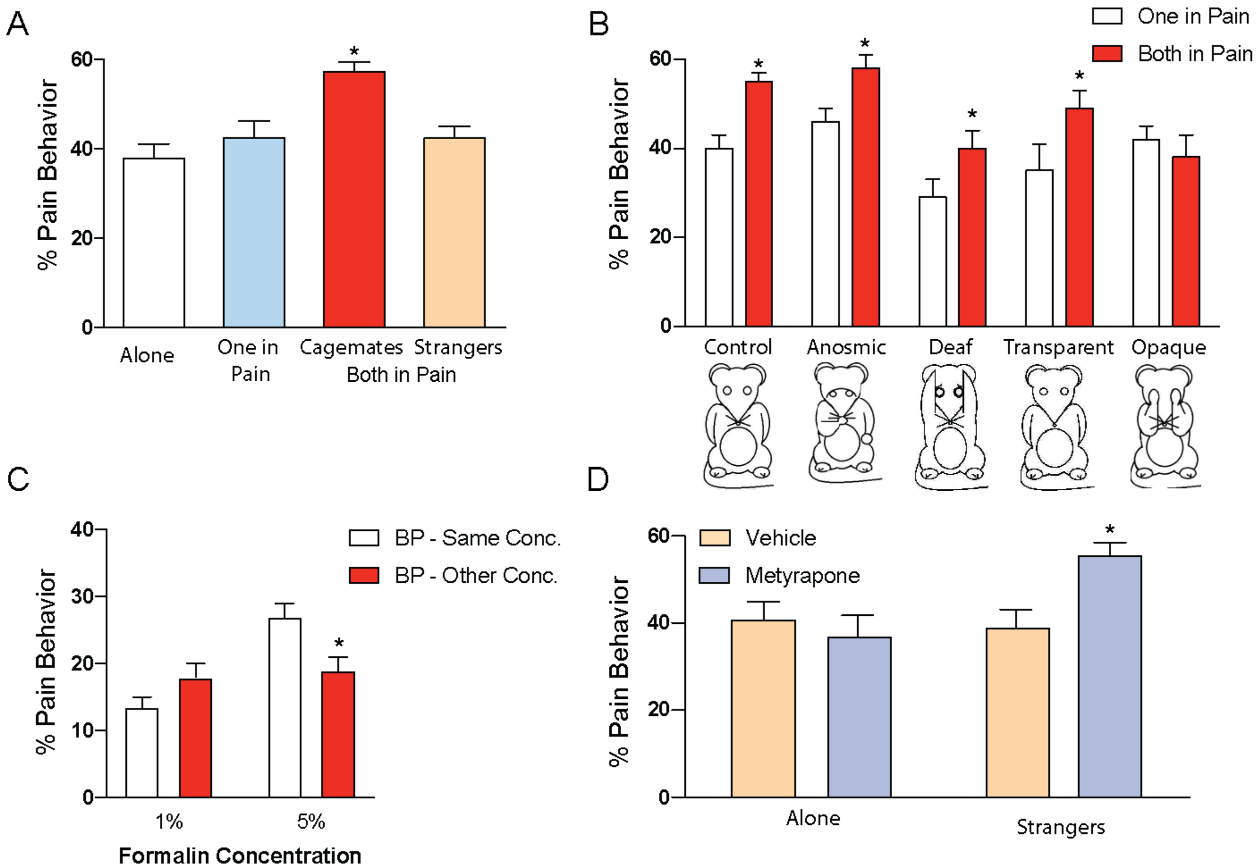


Figure 17.6. Social modulation of pain as a model of empathy in mice. Mice were tested for pain on the acetic acid abdominal constriction test (graphs **A**, **B**, and **D**) or the formalin test (graph **C**) either alone or with a social partner where either one mouse was injected (one in pain) or both mice were injected (both in pain; BP). (**A**) Increased pain behavior in cagemates (but not strangers) both injected with acetic acid. (**B**) Social facilitation of pain in BP cagemates was blocked by placing an opaque (as opposed to transparent) Plexiglas barrier between the mice. Occluding the sense of smell (anosmic mice) or hearing (deaf mice) had no effect. (**C**) Alteration in formalin (1% or 5 %) pain behavior caused by co-testing with a cagemate injected with the same concentration (Same Conc.) of formalin or the other concentration (Other Conc.). (**D**) Blocking the stress response with metyrapone promoted the social facilitation of pain when paired with a stranger mouse. Metyrapone did not alter pain behavior in mice tested alone. Bars represent mean ± SEM percentage of video samples containing pain behavior. *p < 0.05, ***p < 0.001 compared to Isolated.

Source: Panels A, B, and C adapted from Langford et al., 2006.

Panel D adapted from Martin et al., 2015.

Pain facilitation in socially-familiar rats has also been reported and is dependent on the medial prefrontal cortex (mPFC) (Z. Li et al., 2014). Rats were paired for 30 minutes with a cagemate that received a paw injection of bee venom or formalin. Rats that observed cagemates in pain had higher sensitivity to mechanical pressure compared to baseline sensitivity before the observation session. Interestingly, this effect was absent in rats with a brain lesion in the mPFC. In rats, cells in the ACC have been identified that respond both to when the rat experienced shock and when the rat observed social partner receive shock (Carrillo et al., 2019). These experiments in mice and rats demonstrate that the social environment can enhance pain behavior compared to when measured alone. They also indicate that comparable brain structures between humans and rodents may be responsible for these effects.

To add to this complexity, the social environment may work to suppress pain behavior. We have followed-up on the Langford et al. (2006) paper to understand why pain is not facilitated in the presence of a stranger mouse. We showed that administration of metyrapone, an inhibitor of the stress-response, enhanced pain behavior but only when a stranger mouse—also in pain—was present (Martin, Hathaway, et al., 2015). It should be noted that, although the pain behavior of mice in the presence of strangers was less than when paired with cagemates, they are not **hypoalgesic** [a decreased sensitivity to painful stimuli] because the pain behavior is similar to control mice (i.e., those tested alone). However, pain sensitivity may vary with respect to the degree of social threat with more severe social threat producing hypoalgesia. When confined near a stranger male mouse—that is not in pain—prominent hypoalgesia/analgesia is observed in mice injected with acetic acid (Langford et al., 2011). Social threat is increased in this scenario because the mouse that is not in pain is perceived as healthy with a physical advantage over the mouse in pain should a fight occur. This phenomenon is dependent on testosterone as demonstrated via castration and testosterone replacement (Langford et al., 2011) and it represents a form of social stress-induced analgesia that is blocked by the opioid antagonist **naloxone** [an opioid antagonist that blocks the effects of opioid drugs, as well as endorphins or the endogenous opioids that your body produces] (Pitcher et al., 2017).

In addition, social proximity enhances pain sensitivity in the absence of injury. Mice housed in the same room as mice injected with complete Freund's adjuvant (CFA) or exposed to morphine or alcohol withdrawal became sensitive to mechanical, thermal, and chemical pain stimuli for multiple weeks (Smith et al., 2016). The induction of pain in one group of mice—either through CFA, morphine, or alcohol withdrawal caused pain sensitivity in another group of mice, even though this second group had never been exposed to any pain stimulus nor directly interacted with the "pain" mice. Using the **olfactory preference test** [a test in rodents wherein two scents are presented (often on cotton swabs) and the time spent sniffing/investigating is measured as preference for one odor over another], cues associated with **hyperalgesia** [an enhanced painful response to a painful stimuli] were aversive to mice, confirming the negative affective valence of the experience was mediated by olfactory communication (Smith et al., 2016). Experiments testing brain region activation of this hyperalgesia showed increased activation of ACC and AI in the mice. Inhibition of the ACC using **chemogenetic** [a modern neuroscience technique used to insert receptor proteins into neurons that interact with administered chemical compounds that then change the activity of the neurons, e.g., hM4Di is a man-made receptor that silences neurons when the chemical clozapine-N-oxide is injected into the body and crosses the blood–brain barrier] approaches blocked social transfer– and alcohol withdrawal–induced hyperalgesia, indicating a crucial role for this brain region in this phenomenon (Smith et al., 2017). These findings not only highlight the different modes of pain communication in animals, but also demonstrate the need for critical evaluation of control conditions in preclinical studies. They may also provide evidence for importance of social environment in the development of chronic pain.

Test Yourself: When two mice are together in an arena, and the pain behavior of one mouse increases the pain behavior of the other mouse, this is used a model of ______ in rodents.

A. Social threat
B. Hypoalgesia
C. Social stress
D. Empathy
E. Social buffering

[Empathy is the perception and then sharing of affective states of others, which serves as a method of social communication, e.g., ouch! I'm in pain!]

17.6 Analgesia and buffering of pain by social interactions

The social context can modify pain experiences both by enhancing experienced pain and by decreasing experienced pain. The mammalian body has an **endogenous** [produced within the body] system that releases protein signals to decrease signaling between neurons to diminish the experience of pain. One category of protein signals and the associated receptors of these signals that has been well-studied in this role is the opioid system, including endorphins and their receptors, the μ-opioid receptors. More recently, the role of the opioid system has been studied with respect to the effect of the social context on endorphin release and pain modulation.

Image caption: Endorphin molecules (red) binding to their receptors (purple).

Source: Getty Images 973901260

When the body is injured or experiences stress, the opioid system can be activated to release endorphins as a mechanism to allow a mammal to endure physical activity, escape and survive. Interestingly, the opioid system is also activated during pleasant social encounters and can act to dampen subsequent pain experiences. In humans, rewarding social experiences such as social acceptance (Hsu et al., 2013), social support (Heinrichs et al., 2003), and social laughter (Manninen et al., 2017) have been shown to reduce pain. Reunion—following a long period of separation—between male mice, which may be akin to a pleasant encounter resulted in profound **analgesia** [pain reduction, or the state of pain relief] that was blocked by naloxone [(D'Amato & Pavone, 1996). The analgesia evoked through reunion interactions was related to physical affiliative contact since there was a correlation between **huddling behavior** [aggregation of animals into a close group, often for warmth] and pain sensitivity (D'Amato & Pavone, 1996). Intriguingly, there was a sex-specificity to this effect because female siblings separated at **weaning** [the process whereby a young animal no longer is dependent on its mother's milk for sustenance] did not display any behavioral signs indicating recognition of separated siblings and did not display analgesia upon reunion. However, female mice did display opioid-mediated analgesia when reunited with unrelated cagemates; this was presumably because the length of separation was shorter and they were able to socially recognize former cagemates (D'Amato, 1997).

Image caption: Snow monkeys (Japanese macaques) huddling for warmth.

Source: Shutterstock ID 1667906029

Different forms of **social support** [the friends or family that are available in times of need] can affect the pain experience by altering the autonomic and neurophysiological response to the threatening quality of noxious stimuli. As we discussed earlier, presence of others in the social context is not always beneficial toward dampening pain perception such as when solicitous partners worsen pain experienced by chronic pain patients (Flor et al., 1987). But the presence of others can be supportive like in **social buffering** [a phenomenon where the presence and availability of one or more social partners during times of threat reduces activity of stress-mediating physiological systems], which acts to dampen the effects of stress or the experience of pain. Buffering can take place through the presence of other individuals, or through social touch, another form of perception that transmits pleasant and socially salient information to the brain. Specific somatosensory receptors have been studied that respond explicitly to gentle touch (Liu et al., 2007; Vrontou et al., 2013) and have been shown to produce behavior indicating the sensation carries a positive affective quality leading the animal to develop wanting or preference (McGlone et al., 2012, 2014; Pawling et al., 2017; Perini et al., 2015; Triscoli et al., 2014). Recent brain imaging shows evidence of synchronization of cortical brain activity between two adults when touching in humans (Goldstein et al., 2017, 2018) and mice (Bolaños et al., 2018), indicating that touch has a role in harmonizing brain activity to foster social relationships. Thus, social touch may reduce pain perception. As in humans, laboratory animals also demonstrate social buffering, but past studies have focused on the buffering of nonpainful environmental threats. Lower levels of stress-related behaviors and plasma **corticosterone** [a cholesterol-based steroid produced by the adrenal gland during stress, as the rodent equivalent of cortisol in humans] have been measured when rats were placed in a novel environment with a social partner compared with rats placed in the same environment by themselves (Latané, 1969; Leshem & Sherman, 2006). Interestingly, these effects are not necessarily dependent on physical touch because the social buffering effect is present when rats were paired with a physically separated (caged) rat (Latané, 1969) or an anaesthetized rat (Latané & Glass, 1968). These examples show that the pleasant effect of social interactions can lessen pain and stress experiences by interacting with neurological and physiological mechanisms that influence behavior.

Test Yourself: The reduction of pain by social interactions is known as

A. Social support
B. Social buffering
C. Social touch
D. Social reunion

[Social buffering is the effect where nearby social partners decrease the experience of pain or physiological stress]

17.7 Summary

In this chapter, we discussed a complex relationship between pain and the social environment where the social environment can both enhance or decrease the experience of pain. This relationship is best described by the U-shaped curve shown in **Figure 17.7** where a low level of social interaction or, conversely, high solicitous behavior may work to increase pain, while a high level of social support may work to decrease pain. Like humans, other animals have been shown to exhibit the effects of social interactions on pain responses. Rodents are thoroughly capable of performing elaborate social behaviors, and pain responsiveness in rodents has been shown to be affected by the social environment (Fanselow, 1985; Raber & Devor, 2002; Sorge et al., 2014). Rodents and other animal models offer avenues for experiments that do not exist in human research. Modern neuroscience tools, including ***in vivo*** [in live animals] imaging and genetic manipulation of specific cell types in rodent models, will build an in-depth understanding of the mechanisms of empathy and social modulation of pain. Research using these tools will continue to build understanding of the mechanisms through which neural activation in the salience network drive appropriate responses, which warn us of bodily damage or help us maintain social connections and will give us insight into therapies when these systems are disrupted in neurological disorders.

On a final note, the social context as a determinant and modifier of pain—including chronic pain—has garnered a lot of recent attention. Notably, Craig and Williams (Williams & Craig, 2016) proposed that the **International Association for the Study of Pain (IASP)** [a multidisciplinary organization of over 7,200 members around the world. Based in Washington, DC; its mission is to promote research, education, policies for understanding, prevention, and treatment of pain] definition of pain be updated to acknowledge its social components. They specifically proposed the definition be revised to "*Pain is a distressing experience associated with actual or potential tissue damage with sensory, emotional, cognitive, and social components.*" While IASP has recently updated their definition, it did not specifically incorporate the social aspect, but acknowledged social well-being in the accompanying notes (IASP, 2019). With respect to the rest of the pain field, this area is in its infancy, but great strides will only be made through the acknowledgment that *social* is an important aspect of the biopsychosocial model.

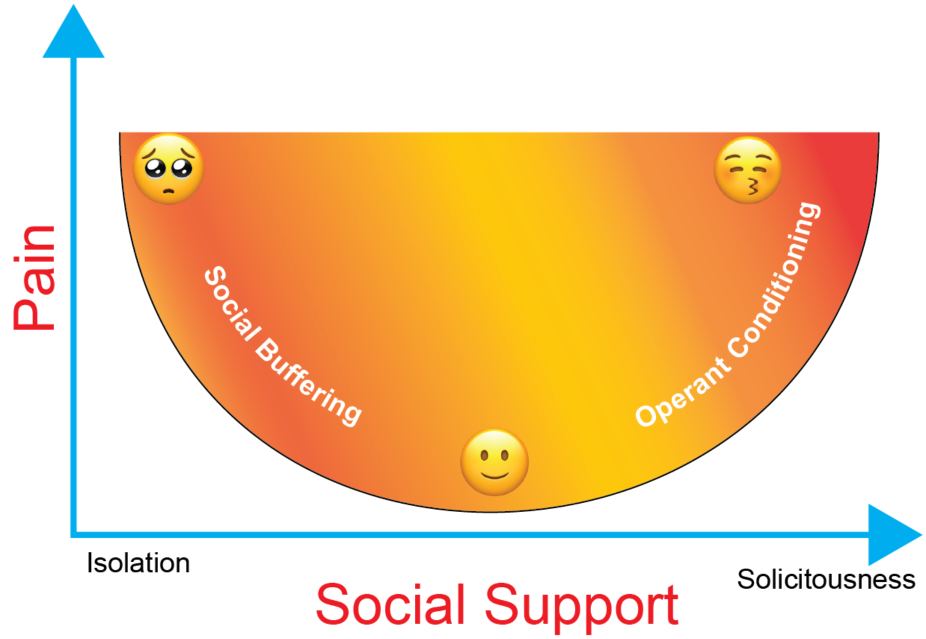


Figure 17.7. The influence of social buffering on pain perception can be described by a U-shaped curve. Social isolation—usually perceived as negative—and solicitousness—usually perceived as positive—may work to enhance pain perception. An intermediary is achieved where optimal social support decreases pain perception through social buffering.

Figure originally produced by J. Mogil (McGill University), adapted and modified by L. Martin.

17.8. Chapter Quiz

Test Yourself: In the human social communication model of pain, the person in pain encodes signals through expressions, while observers must

- **A. Interpret what the person in pain is experiencing**
- B. Run away
- C. Help
- D. Ignore them

[The observing person must interpret or decode the pain signals encoded by the person experiencing pain.]

Test Yourself: An animal may communicate pain to group members through

- A. Facial expressions
- B. Vocalizations

C. Olfactory cues
D. All of the above

[Animals can communicate pain they experience through a change in facial positions, expressing vocalizations indicating distress, and emitting organic compounds into the air that other animals perceive through olfaction, or the sense of smell.]

Test Yourself: When administered systemically, an antagonist of which receptor type disrupted social grooming in pair-bonded prairie voles?

A. Oxytocin receptor
B. Mu-opioid receptor
C. Corticosterone receptor
D. hM4Di receptor

[When administered an antagonist for oxytocin receptors, prairie voles that observed cagemates after a shock experience groomed their social partner less than without the antagonist.]

Test Yourself: The social context can influence social approach or social avoidance toward a rodent in distress, including:

A. Age
B. Familiarity
C. Sex
D. All of the above

[Age, Familiarity, and Sex of the rodents can be social context factors in approach toward distress.]

Test Yourself: When given a dose of ______, dyads of male mice experiencing pain increased pain behaviors, showing increased emotional contagion when the stress response was reduced.

A. Corticosterone
B. Metyrapone
C. Naloxone
D. Oxytocin

[When administered Metyrapone, the stress response was reduced, and the pain behavior increased when mice experienced pain in a dyad.]

Test Yourself: Which level of social support influences increased pain experiences in people living with chronic pain?

A. Low level of social interaction
B. High level of social support
C. High solicitous behavior
D. A and C

[Described in a U-shaped curve, low level of social interaction and high solicitous behavior both increase pain experiences, while a high level of social support can lower experience pain.]

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