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Identifying the Neural Correlates Underlying Social Pain: Implications for Developmental Processes

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Abstract
Although the need for social connection is critical for early social development as well as for psychological well-being throughout the lifespan, relatively little is known about the neural processes involved in maintaining social connections. The following review summarizes what is known regarding the neural correlates underlying feeling of 'social pain', the painful experiences associated with social estrangement or loss, which may be critical for motivating social connection. Using this general framework, the review then specifies the ways in which neuroimaging may provide insight into the development of these neural systems in humans. To this end, the review elaborates on the specific types of questions that are best addressed using neuroimaging techniques and examines several lines of inquiry within the developmental literature that may be aided by these methods.

> We need others. We need others to love and we need to be loved by them. There is no doubt that without it, we too, like the infant left alone, would cease to grow, cease to develop...
> *Leo Buscaglia*

Few would question the assertion that children need care and affection for successful growth and development. Although this statement seems self-evident today, psychologists long thought otherwise. Until 50 years ago, it was believed that a child's bond to his or her caregiver was based solely on the child's need for food and the

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caregiver's ability to fulfill that basic need [Dollard & Miller, 1950; Mussen & Conger, 1956]. In one of the most profound demonstrations to the contrary, Harlow [1958] and Harlow and Zimmermann [1959] showed that infant rhesus monkeys 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 for social connection, over and above the need for food.

As further evidence of the profound importance of social connection, individuals who lack social connection early in life are likely to show disrupted social and emotional development. For example, in Harlow's classic studies, infant rhesus monkeys, raised without the companionship of a real or a cloth mother, exhibited significant behavioral and emotional problems [Harlow, 1958; Harlow & Zimmerman, 1959]. Although the initial reason for raising infant monkeys in isolation was to investigate the development of specific learning skills without the distraction of mother-infant interactions, the extreme emotional disturbances seen among these isolated infants soon led Harlow and others to focus their investigations on the emotional consequences of early maternal separation instead [Harlow, Harlow, & Suomi, 1971; Pollak, 2005].

Paralleling Harlow's work in primates, Bowlby's [1969] influential theory of attachment, which outlined the adaptive significance of the mother-infant relationship, was built upon observations that children who were separated from their primary caregivers early in life exhibited severe distress during the separation episode as well as continued psychological disturbance following reunion. From these observations, Bowlby suggested that prolonged separation from a caregiver in early life was likely to lead to various forms of psychopathology in later life. Indeed, recent observations from Eastern European orphanages support this claim; orphans lacking early social ties do not develop normal social or emotional skills and have long-lasting problems maintaining social relationships [Wismer Fries & Pollak, 2004].

Despite the well-known importance of early social ties for normal growth and development, relatively little is known about the underlying neural systems that regulate these attachment-related processes in humans or how these systems may be altered by early negative experiences. Given the profound influence that social ties have on psychological function, both in childhood and throughout the lifespan [Repetti, Taylor, & Seeman, 2002], it is important to investigate how the systems involved in maintaining social connection develop, how they may influence or interact with the activity and function of other systems and how they may become altered through negative experiences.

The following review will begin by summarizing what is known regarding the neural correlates underlying feelings of social estrangement in adult humans (for a comprehensive review of the neural correlates underlying feelings of social connection and affiliative motivation, see Depue & Morrone-Strupinsky [2005]). Although little is known about the neural underpinnings of human social attachment processes per se (however, see Gillath, Bunge, Shaver, Wendelken, & Mikulincer [2005], Schore [2000]), recent research has begun to elucidate some of the neurocognitive correlates underlying feelings of 'social pain' [Eisenberger & Lieberman, 2004], the hurt feelings following social rejection [Eisenberger, Lieberman, & Williams, 2003] or social loss [Gundel, O'Connor, Littrell, Fort, & Lane, 2003; Najib, Lorberbaum, Kose, Bohning, & George, 2004]. Experiences of social pain may be critical in maintaining attachment relationships, as the pain of social distance may motivate dis-

tress-related behaviors in infants and young children (e.g., crying) as well as maternal behaviors (e.g., retrieval of infants), both of which are aimed at preventing social estrangement. Moreover, the neural circuitry supporting socially painful experience may be critically important during early development when individuals cannot fully take care of themselves and are almost exclusively dependent upon others for survival. This review will outline some of the work that has investigated the neurocognitive correlates of social pain in humans as well as related work that has investigated attachment-related behaviors in animals.

Using this general framework for understanding some of the neural structures involved in avoiding social distance and maintaining social connection, this review will then specify the ways in which neuroimaging may provide insight into the development of these neural systems in humans. In the past decade, functional magnetic resonance imaging has been increasingly used as a noninvasive technique for investigating the neural underpinnings of specific social processes, such as those that underlie emotion regulation, person perception and empathy [Adolphs, 2003; Blakemore, Winston, & Frith, 2004; Lieberman, in press; Ochsner, 2004]. However, despite the fact that one of the primary goals of most of these psychological processes is to establish, navigate and maintain social relationships, relatively little work has focused on the neural correlates associated with feelings of social connection or social estrangement. Moreover, at this point, no work in humans has investigated the *development* of the neural structures that underlie feelings of social connection or estrangement or how early social experiences may alter the functioning of this neural circuitry. Given the importance of social relationships for social development and long-term psychological health, developmental psychologists and developmental neuroscientists are poised to play a critical role in helping to understand the developing social brain. To this end, this review will elaborate on the specific types of questions that are best addressed using neuroimaging and will examine several lines of inquiry within the developmental literature that may be significantly illuminated by these methods.

Social Pain and Its Neural Underpinnings

> 'A condition that makes being a mammal so painful is separation from a sustaining member or members of a group' [MacLean, 1985b, p. 220].

As noted by MacLean, one of the consequences of being human, or of being a mammal more generally, is the profound experience of pain when separated from loved ones. Indeed, the English language is replete with phrases that denote the pain associated with broken social bonds. We complain of '*hurt* feelings' and '*broken* hearts' to describe feelings of social pain and, notably, we have few ways to express these feelings other than with words denoting physical pain [MacDonald & Leary, 2005]. Why is it that broken social ties have the capacity to 'wound' us so deeply?

One mechanism that could explain why social separation is experienced as painful follows from the importance of close social ties for survival in mammalian species [Eisenberger & Lieberman, 2004; MacDonald & Leary, 2005]. Mammals are unique in their need for prolonged attention from a caregiver. Unlike our reptilian

ancestors, who are born almost completely mature and self-sufficient [MacLean, 1985a], mammals require close contact with a caregiver in order to acquire the appropriate nourishment and protection to survive. Because of this, separation of the infant from the caregiver is a dangerous proposition that may result in death for the infant. Consequently, it has been hypothesized that the social attachment system, the system that keeps us near close others, may have piggybacked onto the physical pain system to promote survival in mammalian species [Panksepp, 1998]. Thus, to the extent that being separated from a caregiver is dangerous, feeling pain in response to this separation may be an adaptive way to prevent it.

This hypothesized overlap in the systems underlying physical and social pain was first proposed by Panksepp [1998] based on some work examining the effect of exogenous opiates on pain tolerance in puppies. Panksepp noted that, in addition to reducing pain experience, opiate administration also reduced crying behavior in puppies that were socially isolated [Panksepp, Herman, Conner, Bishop, & Scott, 1978]. Others have found similar effects, showing that morphine, an opiate-based drug, reduced separation-induced distress vocalizations in nonhuman primates as well [Kalin, Shelton, & Barksdale, 1988]. From this, it has been suggested that opioid mechanisms may be one neural substrate common to both physical and social pain [Nelson & Panksepp, 1998; reviewed in Panksepp, 1998].

Recent evidence from neuroimaging studies provides further support for this hypothesized overlap by showing that some of the same neural structures involved in the experience of physical pain are also involved in the distressing experience associated with social rejection or social loss. Moreover, animal studies have shown that this same neural circuitry also plays a role in specific behaviors that are critical for maintaining mother-infant contact such as maternal care as well as distress vocalizations, emitted by infants when separated from the mother to reestablish social contact. Thus, there may be certain neural structures that are involved both in feelings of social distress upon social separation and in initiating behaviors aimed at reestablishing contact with close others.

I will first review some evidence linking activity in the dorsal portion of the anterior cingulate cortex (dACC) to feelings of physical and social pain in humans. (In the second half of the paper, I will review another account of the function of this neural region, namely its role in conflict monitoring [Botvinick, Cohen, & Carter, 2004].) I will also review other studies in adult humans that have explored the neural correlates underlying feelings of social pain. These studies will reveal the involvement of other neural structures in the experience and regulation of social pain, including the insula, involved in the processing of visceral sensation as well as negative affective experience [Aziz, Schnitzler, & Enck, 2000; Cechetto & Saper, 1987; Lane, Reiman, Ahern, Schwartz, & Davidson, 1997; Phan, Wager, Taylor, & Liberzon, 2004; Philips et al., 1997], the periaqueductal gray (PAG), involved in pain processing and attachment-related behaviors [Bandler & Shipley, 1994; Dunckley et al., 2005], and the right ventral prefrontal cortex (RVPFC), involved in regulating the distress of physical pain or negative affect more generally [Hariri, Bookheimer, & Mazziota, 2000; Lieberman, Hariri, Jarcho, Eisenberger, & Bookheimer, 2005; Petrovic & Ingvar, 2002]. Lastly, I will review some of the animal literature linking the anterior cingulate gyrus and the PAG to attachment-related behaviors more generally.

Defining Social Pain

Throughout this review, the term 'social pain' will be used broadly to refer to the distressing experience that results from perceived social separation. In the same manner that 'separation distress' can be defined as the distressing experience resulting from perceived distance from a caregiver [Bowlby, 1969], social pain can be defined as *the distressing experience arising from the perception of psychological distance from close others or from the social group*. In this case, psychological distance can include perceptions of rejection, exclusion, noninclusion, loss or any socially relevant cue that makes an individual feel disconnected from or disregarded by relationship partners. Whereas infants may only be capable of detecting actual physical distance from a caregiver, emergent cognitive capacities soon enable young children 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 sociorelational information.

Based on expanding cognitive capacities that allow adults to represent, manipulate, imagine and predict complex social information, many more cues may be capable of eliciting social pain in adults 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 in later stages of development with the emergence of enhanced cognitive resources that allow symbolic and propositional representations [Brothers, 1990; Deacon, 1997; Lieberman, Gaunt, Gilbert, & Trope, 2002].

It should also be noted that the social pain resulting from perceived distance from a caregiver, attachment figure or significant other (e.g., separation distress) may be phenomenologically and neurocognitively different from the social pain resulting from perceived distance from one's social group or peers (e.g., social rejection). For example, it has been shown that the neural systems underlying separation-induced distress vocalizations are dissociable from the neural systems underlying threat-induced (e.g., perception of novel stimuli) freezing behavior in primates [A.S. Fox et al., 2005; Kalin & Shelton, 1998]. Thus, it is possible that being rejected by one's peers may be processed as a threatening environmental stressor rather than as a separation-related stressor and should therefore recruit neural systems related to threat perception rather than separation perception. However, based on similar neural activations to social rejection from peers and to the loss of significant others in adult humans [Eisenberger et al., 2003; Gundel et al., 2003; Najib et al., 2004], the term 'social pain' will be used to refer to both types of experiences for the purposes of the present review. Further research will be needed to better understand the extent to which experiences of social rejection and experiences of social loss rely on similar or distinct neural systems and whether there are developmental changes in the neural systems that underlie these experiences.

Physical and Social Pain in Humans

In humans, the dACC plays a role both in the unpleasantness of physical pain as well as in the distress associated with social estrangement. With regard to physical pain, the dACC seems to be involved in the *affective* as opposed to the *sensory* component of pain. For example, following cingulotomy for chronic pain, a procedure in which a portion of the anterior cingulate cortex is removed, patients report still being able to feel the intensity of pain but report that the pain no longer bothers them [Foltz & White, 1968], highlighting the role that this structure plays in registering the distressing, rather than the purely sensory, component of the pain experience. In line with this, several neuroimaging studies have shown that the activity of the dACC corresponds to perceived pain unpleasantness, whereas the activity of the primary somatosensory cortex corresponds to perceived pain intensity from cutaneous stimulation [Peyron, Laurent, & Garcia-Larrea, 2000; Ploghaus et al., 1999; Rainville, Duncan, Price, Carrier, & Bushnell, 1997; Sawamoto et al., 2000]. The insula, another neural region involved in pain experience, processes visceral rather than cutaneous sensation; its specific role in the affective versus sensory dimension of pain is not yet clear [Aziz et al., 2000].

More recent research has begun to reveal the role of the dACC in the distress of social pain as well. In a study investigating the neural correlates of social exclusion [Eisenberger et al., 2003], participants were led to believe that they would be playing a virtual ball-tossing game called Cyberball [Williams, Cheung, & Choi, 2000], with two other players over the internet while in the functional magnetic resonance imaging scanner. Upon being excluded from the game, compared to when being included, participants showed increased activity in a region of the dACC, very similar to the region of the dACC associated with the unpleasantness of physical pain. Moreover, the magnitude of dACC activity correlated strongly ($r = 0.88$) with self-reports of social distress felt during the exclusion episode (e.g., 'I felt rejected,' 'I felt invisible'), such that individuals who showed greater dACC activity in response to social rejection also reported feeling more distressed by the rejection episode. Participants also showed increased activity in the insula, a region known to be involved in processing visceral sensation (e.g., visceral pain) as well as negative affective states [Aziz et al., 2000; Cechetto & Saper, 1987; Lane et al., 1997; Phan et al., 2004; Philips et al., 1997]; however, insular activity did not correlate significantly with self-reported social distress in this study.

Lastly, participants also showed increased activity in the RVPFC, a region of the brain typically associated with regulating feelings of pain or negative affect [Hariri et al., 2000; Lieberman et al., 2005; Petrovic & Ingvar, 2002]. Moreover, greater activity in the RVPFC was associated with lower levels of self-reported social distress in response to the ball-tossing game ($r = -0.69$), suggesting that this region may have been playing a role in regulating the distress of being socially excluded.

A similar study investigated how neural responses to social rejection (using the same exclusion paradigm described in the previous study) related to real-world feelings of social connection or estrangement in daily social interactions. It was found that individuals who showed greater activity in the dACC, PAG and amygdala in response to a single episode of social rejection in the scanner were more likely to report feeling socially disconnected during their daily social interactions across a 10-day period [Eisenberger, Gable, & Lieberman, 2006]. Thus, in addition to the dACC, ac-

tivity in the PAG and amygdala may also relate to socially painful experience in humans.

Although the role of the PAG in social pain processing fits with previous work relating this neural region to pain processing as well as attachment-related behaviors in nonhuman mammals (distress vocalizations; nursing behavior [Bandler & Shipley, 1994; Dunckley et al., 2005; Lonstein & Stern, 1998]), the role of the amygdala in social pain processes has not yet been clearly established. Animal research has demonstrated that amygdala lesions consistently reduce fearfulness to innate fear stimuli (e.g., replicas of snakes), but have no clear effects on social fears [Amaral, 2003]. Amygdala lesions can either produce no changes in social behavior, decreases in social fear or increases in social fear, depending on the age at which the lesion occurred (i.e., lesions during infancy lead to increased social fear, lesions during adulthood lead to reduced social fear [Amaral, 2003]). In addition, increased amygdala activity in nonhuman primates correlates negatively with separation-induced distress vocalizations, thought to be indicative of social pain processes [A.S. Fox et al., 2005; Kalin & Shelton, 1998], suggesting that amygdala activation may be associated with reduced social pain experience. Thus, it is possible that the amygdala is more involved in signaling when a social situation might be threatening or socially painful than in the actual experience of social pain per se. Future work is needed to determine the extent to which the amygdala plays a role in social pain processes.

Other studies have investigated the neural correlates associated with more personally relevant forms of social pain. In one study, bereaved participants were scanned while viewing pictures of their deceased first-degree relative or a stranger. In response to viewing pictures of the deceased, compared to pictures of a stranger, the participants showed greater activity in regions of the dACC and insula [Gundel et al., 2003]. Similarly, in a study investigating the neural responses associated with grieving a romantic relationship, women whose romantic relationship had ended within the preceding 4 months showed greater activity in several neural regions when thinking about their relationship, compared to when thinking about another individual, including the dACC [Najib et al., 2004]. However, there were many neural regions activated in response to thinking about the former partner, and thus it is difficult to clearly identify which neural activations are specifically related to feelings of social pain.

Lastly, several studies have examined the neural structures involved in human parental behavior. Two of these studies scanned mothers while they listened to baby cries versus control sounds (white noise), a contrast which might lead to greater feelings of social distress and more attachment-related behaviors (e.g., attempts at soothing the infant). Results indicated that mothers had more dACC 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; Stamm, 1955]. Mothers also showed greater activity across several different prefrontal cortical regions in response to hearing baby cries as well, including the medial prefrontal cortex, RVPFC and dorsolateral prefrontal cortex. Given previous work showing the involvement of the RVPFC as well as the medial prefrontal cortex [Quirk, Likhtik, Pelletier, & Pare, 2003] in regulating limbic activity or negative affective processes, it is possible that these activations were associated with mothers' attempts to regulate their own distress at hearing infant cries; however, this account

is only speculative. Additional studies are needed to more carefully determine the types of emotional experiences that are associated with these neural activations.

An additional study scanned mothers and fathers of young children as well as men and women without children while they listened to infant crying and laughing [Seifritz et al., 2003]. When comparing neural activity while listening to infant cries versus infant laughing, parents (mothers and fathers) showed greater activity in the right amygdala, middle cingulate cortex, bilateral insulae and the left ventral prefrontal cortex than nonparents. This study extends previous findings by showing that similar patterns of neural activity are found for mothers as well as fathers while hearing infant cries.

Based on a prior, influential review suggesting that the dACC is involved in cognitive processing, whereas the rostral-ventral division of the ACC is involved in affective processing [Bush, Luu, & Posner, 2000], it may be surprising that many of the studies that have examined social pain processes in adult humans have found activity in the dorsal, rather than the rostral, ACC. It should be noted that at the time that this prior review was conducted, no studies of social pain processes had been conducted. Moreover, this review did not include or integrate any of the studies showing that physical pain, which seems more affective than cognitive in nature, primarily activates regions of the dACC [Peyron et al, 2000]. Thus, this proposed distinction between dACC and rostral division of the ACC may need some updating and reformulation based on the addition of the physical pain studies as well as the new studies of affective processes that have been conducted since that time (for a possible alternative account, see Eisenberger & Lieberman [2004]).

Attachment-Related Behaviors in Nonhuman Mammals

Animal work has focused less on the painful experiences associated with social separation and more on the behaviors involved in preventing social separation and promoting social contact. Mammals, unique in their profound need for social contact, engage in certain behaviors aimed at maintaining social bonds, including maternal care (e.g., nursing, pup retrieval) and audiovocal communication for maintaining mother-offspring contact [MacLean, 1985a, 1993]. Both of these behaviors aid in maintaining mother-infant contact, either by mother-initiated behaviors, such as pup retrieval, or by infant-initiated behaviors, such as the production of distress vocalizations, emitted by separated infants to motivate retrieval by the mother.

The cingulate gyrus, which has no clear counterpart in the reptilian brain, appears for the first time, phylogenetically, in mammalian species [MacLean, 1985a, 1993] and thus may play a role in these uniquely mammalian social behaviors. Research from the animal literature supports this claim. Ablation of the cingulate gyrus in adult female rats results in deficits in maternal behavior, including the nursing and retrieval of pups [Stamm, 1955]. Following cingulate ablation in females, rat mothers become less responsive to the distress vocalizations of their pups. The survival rate of rat pups, whose mothers have cingulate lesions, is only 12%, compared to 95% among healthy controls. This rather dismal survival rate highlights the importance of this structure in maintaining mother-infant contact and promoting the survival of mammalian infants.

In addition to maternal care, the cingulate gyrus also plays a role in the production of distress vocalizations, which are considered to be the most primitive and basic mammalian vocalizations with the original purpose of maintaining mother-infant contact [Lorberbaum et al., 1999, 2002; MacLean, 1985a]. Thus, ablation of the ACC in squirrel monkeys leads to decreased distress vocalizations [Kirzinger & Jurgens, 1982; MacLean & Newman, 1988], whereas electrical stimulation of the ACC leads to the spontaneous production of distress vocalizations in rhesus monkeys [Jurgens & Ploog, 1970; Ploog, 1981; Smith, 1945].

In addition to playing a role in behaviors aimed at maintaining social connection, the dACC also seems to be affected by early social experiences and thus may play a role in the developmental consequences of early negative social experience. For example, maternal separation among newborn rodents changes various neurotransmitter fiber systems in the dACC of these rodents, which can then have consequences for the function of these neural systems [Braun, Lange, Metzger, & Poeggel, 2000]. Conversely, hearing the sound of the mother's voice while being separated buffers against these changes [Braun & Poeggel, 2001; Ziabreva, Schnabel, Poeggel, & Braun, 2003]. Thus, social separation may have the capacity to alter the structural makeup of the neural systems involved in maintaining social bonds, thus enhancing the risk for later socioemotional problems.

Another neural region that has been shown to play a role in attachment-related behaviors in nonhuman mammals is the PAG. The PAG is a small brainstem structure involved in pain processing, maternal behavior and distress vocalizations in nonhuman mammals [Bandler & Shipley, 1994; Dunckley et al., 2005]. In addition, the PAG receives dense projections from the dACC and insular cortex, both of which are activated in response to physical and social pain in humans. Animal studies have shown that lesions to specific regions of the PAG disrupt the nursing posture of rat mothers, resulting in 10% less weight gain in pups of lesioned compared to nonlesioned mothers [Lonstein & Stern, 1998]. Moreover, lesioning the PAG decreases distress vocalizations in pups separated from their mothers, whereas electrically stimulating this region can lead to the spontaneous production of these vocalizations [Panksepp, 1998].

Together, these findings from the human and animal literature suggest that the ACC and PAG are involved in the experience of separation distress as well as in some of the behaviors needed to maintain close social contact with a caregiver or the social group.

In humans, activity in the dACC in response to social estrangement can be thought to index the magnitude of distress felt in response to social estrangement. Activity of the PAG may be indexing a similar type of experience. Moreover, activity in the RVPFC, involved in regulating feelings of social distress or negative affect more generally, can be thought to index regulatory processes. Activity in the insula seems to occur, in some cases, to socially painful experience; however, its role in social pain experience is not yet clear as it has not yet been shown to correlate with the distress of social estrangement. The role of the amygdala in social pain processes is not yet clear either, showing, in some cases, a negative correlation with separation distress (distress vocalizations [A.S. Fox et al., 2005; Kalin & Shelton, 1998]) and in other cases a positive correlation with social pain experience (feelings of social distress during real-world social interactions [Eisenberger et al., 2006]). Although there are undoubtedly many other neural structures involved in maintaining social connections,

this review will focus primarily on how activity in these particular neural structures may underlie or contribute to specific developmental issues. In the next section, I will specify the general types of questions that are best addressed using neuroimaging techniques. To illustrate these questions, I will use examples that are based on the neural structures reviewed above and will explore several developmental questions, which may be better understood through the use of neuroimaging techniques.

What Is Neuroimaging Good for?

In the past decade, the field of psychology has witnessed a surge in the number of studies using neuroimaging techniques to elucidate the neural underpinnings of various psychological phenomena. These efforts, however, have been met with varied responses. Some have applauded these techniques, deeming them necessary for generating new ways of understanding psychological experience and treating psychological disorders. These proponents have suggested that neuroimaging techniques afford researchers a better sense of the computational subcomponents that comprise certain psychological experiences and thus may be helpful in determining the specific processes that are altered as a function of psychological disorders. Others have remained more skeptical, arguing that these methods are no better than the ones that researchers have been using for years. These skeptics have suggested that neuroimaging techniques do not provide any additional information that cannot be gleaned from carefully planned behavioral studies and that the scanner itself constrains what can actually be examined with these techniques, as subjects in these studies are limited in what they can physically do within the scanner (e.g., subjects cannot talk or move). In truth, both of these perspectives are valid.

Neuroimaging techniques, like any of the other tools employed for investigating psychological phenomena, are useful for investigating some aspects of psychological experience and not as useful for investigating others [Kosslyn, 1999]. However, within the time span that neuroimaging techniques have been utilized, most researchers have agreed on at least a few very powerful uses for this machinery. These recognized uses for neuroimaging techniques include: (1) determining to what extent seemingly different psychological processes recruit *common* neurocognitive substrates, (2) determining to what extent seemingly similar psychological processes recruit *distinct* neurocognitive substrates and (3) identifying the specific neurocognitive mechanisms underlying complex behavioral and emotional outcomes. In addition, using neuroimaging techniques for examining psychological phenomena moves researchers one step closer to a common language (e.g., neural activity) for understanding psychological experience across disparate levels of analysis (e.g., human, primate, rodent). This use of a common language may promote translational advances that bridge across various disciplines of psychology.

In the next section, I will examine each of these uses for neuroimaging in turn and will elaborate on some developmental questions that may be addressed using these techniques. I will also expand on the ways in which research on social development can be shaped based on recent findings from the neuroimaging literature.

Different Psychological Processes, Similar Neural Substrates

One of the most significant uses for neuroimaging techniques is in determining whether certain psychological phenomena rely on similar neural substrates. Showing that two seemingly different psychological processes activate similar neural regions suggests that these two processes share at least some similar computational mechanisms. Moreover, demonstrating that certain psychological processes share computational similarities may highlight new ways of understanding these processes and may provide new testable hypotheses regarding this shared circuitry.

Physical Pain and Social Pain. Showing that social pain activates some of the same neural regions that are activated by physical pain suggests real, rather than merely metaphorical, similarities between these two processes. For example, in a recent behavioral study examining some potential consequences of this physical-social pain overlap, we investigated whether individuals who are more sensitive to physical pain are also more sensitive to social pain, based on a lower threshold for activity in this same neural system [Eisenberger, Jarcho, Lieberman, & Naliboff, in press]. We found that individuals who at baseline were more sensitive to physical pain (e.g., heat stimulation applied to the forearm) also reported feeling more social distress in response to being socially rejected during a Cyberball game. Moreover, this relationship remained significant after controlling for neuroticism, suggesting that this relationship cannot be easily explained by a general tendency to experience anxiety and thus report higher levels of both types of pain.

Findings such as these may have important implications for understanding the relationships between negative social experiences and physical pain experience. For example, a recent meta-analysis revealed that adults with chronic pain conditions are more likely to have been abused or neglected as children [Davis, Luecken, & Zautra, 2005], pointing to the possibility of a pain-distress system that has become sensitized in part, due to early negative social experience. Moreover, adults with chronic pain disorders, compared to healthy controls, 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], again highlighting the relationship between heightened physical pain experience and a heightened sensitivity to some forms of social pain. Based on these findings, it is possible that treatments for pain disorders may be improved by focusing, not only on the pain symptoms themselves, but also on the social stressors that may exacerbate painful experience.

With regard to developmental issues, the relationship between physical and social pain may have implications for understanding some recent work showing that children who are victimized by their peers report greater levels of physical symptoms, such as headaches and upset stomaches [Nishina, Juvonen, & Witkow, 2005; Williams, Chambers, Logan, & Robinson, 1996]. Although it is possible that peer victimization may increase the risk for physical illness through traditional stress-related physiological processes, such as increases in stress-related hormones that make physical illness more likely [McEwen, 2000], it is also possible that social pain experience can heighten sensitivity to physical pain directly by sensitizing the underlying neural system that supports both types of pain experience. Thus, to the extent that physical and social pain experiences rely on some of the same neural structures for their operation, experiences of social pain may have direct implications for physical pain experience.

Conflict Monitoring and Social Pain. Many studies have suggested that the dACC is involved in 'conflict monitoring', the process of detecting conflicts or discrepancies in incoming information (for a broader review of this account as well as other accounts of dACC function, see Botvinick et al. [2004]). Although conflict monitoring was originally conceptualized as pertaining primarily to behavioral response conflict (when two behavioral tendencies are simultaneously activated), it has now been expanded to include other forms of conflict as well, such as discrepancies between automatic responses and current goals, between actual and expected events, or between new stimuli and preexisting representations that do not map onto each other [Barch et al., 2001; Botvinick, Braver, Barch, Carter, & Cohen, 2001; Botvinick et al., 2004; Braver, Barch, Gray, Molfese, & Snyder, 2001; Hajcak, Holroyd, Moser, & Simons, 2005; Inui et al., 2000; MacLeod & MacDonald, 2000]. Once a conflict has been detected, regions of the lateral prefrontal cortex, including, in some cases, the RVPFC, are recruited in order to exert top-down controlled processes to resolve the conflict [Carter et al., 2000; MacDonald, Cohen, Stenger, & Carter, 2000].

Notably, our own research has shown that dACC activity in response to errors, one form of conflict (when behavioral responses conflict with current goals), during a simple cognitive task (go/no-go), overlapped with dACC activity in response to social rejection [Eisenberger & Lieberman, 2006], suggesting that conflict detection and social pain processes may rely on some of the same computational substrates. Based on this possible functional overlap in the neural substrates underlying conflict detection and social pain processes, as well as the suggestion that this neurocognitive loop is critical for the development of affect and behavioral regulation in children [Casey et al., 1997], it is important to understand how these processes, which seem quite distinct, relate to one another.

Research has suggested that conflict monitoring processes become more efficient with increasing age [Casey et al., 1997]. Based on the overlap in the neural structures underlying conflict detection processes and social distress responses, several questions can be asked. For example, if it is the case that conflict detection processes show increasing efficiency during adolescence [Davies, Segalowitz, & Gavin, 2004; Ladouceur, Dahl, & Carter, 2004], it is interesting to note that this increasing efficiency seems to parallel the heightened sensitivity to peer evaluation that accompanies this time period. Does the development of more efficient conflict detection processes make individuals more sensitive to rejection? Are individuals who are less concerned with social connection also less sensitive to conflict more generally? Furthermore, does the ability to regulate negative emotional responses to social rejection relate to the capacity to resolve conflict? What would such findings imply for the development of affect and behavioral regulatory processes?

While these findings open up many more questions than answers, they also provide some novel ways of thinking about the complex relationships between the development of cognitive and social skills and the ways in which these processes may influence one another. In response to some of the questions listed above, preliminary evidence suggests that individuals who are unconcerned with social relationships show reduced neural activity in response to errors [Santesso, Segalowitz, & Schmidt, 2005], suggesting that reduced social sensitivity may relate to less efficient conflict or error detection processes. Another study has shown that experimentally manipulating social pressures can alter neural responses to errors, specifically the error-related negativity [Hajcak, Moser, Yeung, & Simons, 2005], an event-related brain po-

tential observed when errors are committed, which has been localized to the ACC [Holroyd, Dien, & Coles, 1998]. In this study, participants performed a conflict detection task while either being evaluated (e.g., told that a research assistant was viewing their responses and comparing them to how others did at the same task) or while not being evaluated. Results showed that subjects showed larger error-related negativities to errors when they were being evaluated than when they were not, suggesting that social stressors may influence sensitivity to certain forms of conflict detection as well.

Another interesting avenue for exploration would be to examine the consequences of peer victimization or rejection on the development of cognitive performance on conflict detection tasks. Thus, for a child who is continually regulating the distress associated with being victimized, do these constant efforts compromise the child's ability to engage these same neural systems to successfully complete other types of school-related cognitive tasks? Moreover, does the impact that victimization has on cognitive abilities change as a function of developmental status, perhaps affecting younger children more than older children? Questions such as these may shed new light on developmental issues and further our understanding of the complex relationships between social and cognitive development.

Similar Psychological Processes, Different Neural Substrates

Another use for neuroimaging techniques is in determining whether distinct neural systems are involved in seemingly similar psychological processes. Showing that certain psychological processes with similar behavioral or experiential characteristics activate distinct neural regions suggests that these processes rely on separate computations and may provide insight into the ways in which these processes can be dissociated.

For example, basic behavioral research demonstrates that social estrangement can lead to emotional distress and that social connection can ameliorate these negative feelings. However, it is less clear if the negative feelings associated with social estrangement and the positive feelings associated with social connection are the product of a single system or tap into distinct underlying systems. In other words, are feelings of social estrangement and social connection two ends of the same continuum, such that feeling socially connected is the opposite of feeling socially estranged, or do these processes rely on the computations of separate underlying systems, such as has been observed with positive and negative emotions? Moreover, could there be more than one neural substrate underlying feelings of social connection, perhaps one underlying feelings of relief at not being separated and one underlying feelings of joy at being connected?

Using a parallel example from emotion research, although it was first thought that positive and negative emotion were two ends of the same spectrum, it has now been shown that positive and negative emotions rely on the computations of two dissociable systems [Cacioppo & Berntson, 1994]. This finding has led to greater specificity in understanding the ways in which these two systems can become dysregulated and how best to treat these problems. For example, it has been demonstrated that depression relates, not only to increased negative affect, but to a disturbance in the system that is implicated in positive affective experience as well [Clark & Watson,

1991]. Understanding this distinction and recognizing that certain disorders (e.g., depression) relate to altered functioning in a specific underlying system (e.g., the system that regulates positive affect) provides a more targeted way of treating specific disorders.

The extent to which feelings of social connection and feelings of social estrangement rely on common or distinct neural processes has important implications. If we assume that feelings socially connected and socially estranged rely on the same computational substrates, then the capacity to feel socially connected would be a direct correlate of one's capacity to feel socially estranged, such that those with the capacity to feel the most socially estranged would also receive the most benefit from social support. In other words, social support might only be rewarding to the extent that one is feeling socially distant. On the other hand, if feelings of social connection and social estrangement rely on the computational substrates of two separate systems, then sensitivity to social ties or a lack thereof should be dissociable, such that individuals who feel the most socially connected can also either be low or high in sensitivity to rejection or social estrangement. Moreover, this two-system approach also suggests that psychological well-being may depend not only on the absence of negative social interactions, but also on the presence of positive social interactions.

In addition, identifying the basic neural architecture that responds to social connection and estrangement may be critical for understanding how early social ties influence later social development. For example, it has been shown that the presence of abuse during childhood leads to very different psychological outcomes than does neglect or the absence of affection. Children who have been exposed to early abuse seem to show a heightened sensitivity to negative emotional cues that signify harm or aggression (such as angry faces) [Pollak & Kistler, 2002], whereas neglected children tend to show a different psychological profile characterized by avoiding social interactions altogether or showing indiscriminate friendliness towards all [Wismer Fries & Pollak, 2004]. Part of the reason for these different behavioral profiles may be due to the fact that these early experiences shape the sensitivity of separate neural systems, and thus may have different consequences for psychological function.

Clarifying Neurocognitive Mechanisms

Neuroimaging can also be used to elucidate the types of neurocognitive mechanisms underlying complex behaviors. Because behavior is the final output of the functioning of several underlying neural systems, the causes of that behavior can be multiply determined. Neuroimaging techniques allow researchers to investigate the types of computational processes that give rise to certain psychological experiences or behaviors and can be especially useful when examining the predictors of certain behaviors that are difficult to examine with self-report or behavioral measures alone.

For example, it is difficult to determine if greater emotional reactivity among children is due to: (a) a heightened sensitivity to emotional cues and thus a more intense emotional experience, (b) a diminished capacity to successfully regulate emotional states or (c) some combination of both [Fox, 2004; Posner & Rothbart, 1998]. While these processes can be difficult to disentangle with traditional behavioral methods, they may be more easily dissociated with neuroimaging methods. If emotional reactivity is due to a greater sensitivity to negative emotional stimuli, emotionally reactive children, compared to less emotionally reactive children, should show

greater activity in emotion-related neural regions (such as the dACC, insula or PAG in response to social rejection or the amygdala in response to viewing negative emotional faces). Conversely, if emotional reactivity is due, not to a greater sensitivity to emotional stimuli, but rather to poorer regulatory ability, then emotionally reactive children, compared to less emotionally reactive children, should show reduced activity in prefrontal regions like the RVPFC, typically associated with emotion-regulatory processes, in response to negative emotional stimuli [Hariri et al., 2000; Lieberman et al., 2005; Petrovic & Ingvar, 2002].

Predictors of Aggression. Similar types of distinctions can be made with regard to aggressive behavior in children. A large amount of developmental work has shown that negative social experiences early on, such as abuse or rejection, can increase an individual's risk for later behavioral problems such as aggression or antisocial behavior [Dodge & Pettit, 2003]. However, a complete understanding of how these early experiences influence later behavioral problems or what neurocognitive sensitivities are being altered has not been well specified. For example, when children act aggressively, what are the underlying neurocognitive sensitivities that lead to these specific behavioral outputs?

Researchers have identified several different subtypes of aggression-related disorders, such as conduct disorder, psychopathy and antisocial personality disorder (for comprehensive reviews on the development of aggressive behavior and psychopathy, see Dodge & Pettit [2003] and Blair, Peschardt, Budhani, Mitchell, & Pine [2006], respectively). Although all of these disorders involve antisocial or aggressive behavior as a functional outcome, the experiential predictors of this behavior can vary. For example, a core feature of psychopathy is a lack of empathy, anxiety and guilt [Frick, O'Brien, Wootton, & McBurnett, 1994]. This stands in contrast to reactive aggression, which is triggered by a negative event and is associated with greater emotional reactivity to the event [Crick & Dodge, 1996]. Thus, it has been suggested [Blair et al., 2006] that some subtypes of aggression-related behavior, such as psychopathy, may be best characterized by reduced reactivity in emotion-related neural regions (e.g., amygdala [Birbaumer et al., 2005]), whereas other subtypes of aggression-related behavior, such as those related to reactive aggression, may be best characterized by either enhanced reactivity of emotion-related neural regions (e.g., amygdala [Meyer-Lindenberg et al., 2006]) or by reduced activity of prefrontal regions involved in inhibiting emotional responses (e.g., orbital and ventrolateral prefrontal cortex [Anderson, Bechara, Damasio, Tranel, & Damasio, 1999; Grafman, Schwab, Warden, Pridgen, & Brown, 1996]). These experiential predictors of aggressive behavior may be differentiated using neuroimaging techniques.

As an example of this strategy, we have recently completed a study investigating the neurocognitive mediators underlying a well-established connection between a genetic polymorphism and aggressive behavior. Recent research has suggested that a functional polymorphism in the monoamine oxidase A (MAOA) gene is associated with aggressive or antisocial behavior, especially among those individuals with early adverse experience [Caspi et al., 2002]. Individuals with the low expression version of the MAOA allele ($MAOA_{LE}$), who were exposed to early adversity, were more likely to have committed violent crimes. However, while there seems to be a relationship between MAOA and aggressive behavior [Brunner, Nelen, Breakefield, Ropers, & van Oost, 1993], it is not clear how this genetic polymorphism predisposes individuals to aggression. For example, it is not clear if the $MAOA_{LE}$ is related to aggres-

sion through reduced emotional reactivity, more characteristic of psychopathy, or through increased emotional reactivity or reduced inhibitory control, more characteristic of reactive aggression.

To examine the neurocognitive mechanisms associated with this genetic profile, we investigated how different allelic variants of the MAOA gene related to neural responses to social rejection [Eisenberger, Way, Taylor, Welch, & Lieberman, in press]. If $MAOA_{LE}$ is related to aggressive behavior through reduced emotional reactivity or reduced social concern, then $MAOA_{LE}$ individuals should show reduced dACC reactivity to social rejection as they presumably care less about social relationships or being socially included. This reduced social concern may then lead to aggressive behavior because these individuals care less about harming others or the consequences of doing so. If, however, $MAOA_{LE}$ is related to aggressive behavior through a heightened sensitivity to negative emotional experiences like social rejection, then $MAOA_{LE}$ individuals should show greater dACC activity and/or reduced RVPFC activity to social rejection as these individuals should be hypersensitive to these types of negative social experiences and unable to regulate these responses. This heightened sensitivity to negative social experiences may then result in defensively aggressive behavior (e.g., reactive aggression). Indeed, a large literature has shown that being rejected can trigger aggressive responses [Dodge & Pettit, 2003; Dodge et al., 2003; Twenge, 2005].

Results indicated that $MAOA_{LE}$ individuals, compared to those with the high expression allele ($MAOA_{HE}$), showed higher levels of self-reported trait aggression as well as greater dACC activity to social rejection [Eisenberger et al., 2006], suggesting that the relationship between this genetic polymorphism and aggressive behavior may be due to heightened, rather than reduced, emotional reactivity to negative social cues like rejection. The MAOA polymorphism was not associated with RVPFC activity or other regulatory-related prefrontal activity, suggesting that the MAOA gene may be more closely tied to emotional reactivity than to regulatory capacity. In addition, dACC reactivity to social rejection mediated the relationship between the MAOA gene and trait aggression.

Thus, it is possible that the MAOA polymorphism is related to a heightened sensitivity to negative social cues and that aggressive behavior is the functional output of this heightened sensitivity, rather than the direct consequence of this polymorphism. Obviously, future studies will need to include a measure of aggressive behavior to more clearly investigate whether individuals with the low expression allele who show greater dACC activity to social rejection are also more likely to show aggressive tendencies following rejection episodes. However, this study provides a first step in understanding the neurocognitive and experiential correlates of specific genetic profiles and thus how these genetic profiles may contribute to behavioral outcomes, like aggression. Showing that this aggressive behavior is due to heightened social sensitivity rather than reduced social sensitivity has important implications for the types of interventions that could be developed to treat these aggressive problems.

As illustrated here, one additional use of neuroimaging techniques is in elucidating the neurocognitive mechanisms that mediate genetic contributions to affect, behavior and cognition [Hariri & Weinberger, 2003]. This area may be of particular interest to developmental psychologists as a great deal of work has now shown that early social experiences can impact the expression of certain genes, thus contributing to different neurocognitive reactivities and thus to different behavioral outcomes

[Caspi et al., 2002; Fox et al., 2005]. Exploring gene-by-environment interactions may be a powerful way to understand which individuals are most likely to be negatively affected by early negative social experiences and which individuals may be spared.

Conclusion

Although research examining the neural substrates of different types of social experiences is expanding at an increasingly rapid rate, we still have much to learn. Developmental psychologists are needed in this endeavor to help elucidate how these social and emotional skills develop and the ways in which these processes can go awry. The present review has attempted to briefly outline some of the neural structures involved in the painful experience associated with broken social bonds and then to suggest some of the ways in which neuroimaging techniques can be useful in investigating how these neural systems mature, how they interact with other neural systems and how early experience may shape their development.

While some developmental questions have been posed here (e.g., what are the consequences of the same neural structures being involved in both social pain and conflict detection processes?), there are many more questions that can be asked and hopefully answered. For example, do the patterns of neural activation to social rejection look the same in children as they do in adults? Do children have more difficulty regulating the negative feelings associated with socially painful experience, and does this make the experience more distressing? Are there gender differences in neural responses to social pain? If so, are they altered as a function of puberty?

It is important that the growing amount of research on the neural correlates of adult social experience is balanced by research exploring the development of these same psychological processes in children. Through interdisciplinary research that examines psychological development at different levels of analysis, we may be able to better understand the critical impact that social ties have on normal human development. Techniques such as neuroimaging may provide new ways of understanding the developing social brain.

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