

9 A Pain by any other Name (Rejection, Exclusion, Ostracism) still Hurts the Same: The Role of Dorsal Anterior Cingulate Cortex in Social and Physical Pain

Matthew D. Lieberman and Naomi I. Eisenberger

Several chapters in this volume explore whether a particular dimension of social cognition can be reduced to more general cognitive processes by examining whether social and cognitive processes share overlapping neural bases. Some chapters argue for distinct neural processes devoted to social cognition, not shared by more general cognitive processes (Mitchell), and others identify components of social cognition that do share properties with more general cognitive systems as indicated by overlapping neural systems (Phelps, Stone). A social phenomenon that seems an unlikely candidate for this kind of cognitive reduction analysis is social pain, the distress experienced in response to rejection, exclusion, or ostracism. These experiences are profoundly social and, at first glance, there are no obvious cognitive analogues to which they can be reduced.

Nevertheless, we suggest a certain type of reduction. We propose that social pain may be profitably examined by considering its relation to physical pain. More specifically, we suggest that some of the basic neural mechanisms that support the experience of physical pain also support the experience of social pain (although it is doubtful that the overlap is as complete as the extreme position staked out by our Shakespearean title). Evidence from both animal and human research literatures suggest that the dorsal region of the anterior cingulate cortex (dACC) is similarly involved in the distressing component of both forms of pain. Moreover, once a connection is established between the experience of social pain and physical pain, we can explore the underlying computations that connect the processes. In other words, we can examine the computational function of the dACC such that it should be involved in various forms of painful experience. Thus the dACC may function as a neural alarm system, combining both detection of a problem and sounding of an alarm, typically found in any alarm system.

Finally, we reexamine the function of dACC versus rostral anterior cingulate (rACC) to expand on how our model fits with previously held views of the function of the

ACC. The current view is that dACC is involved in cognitive processes and the rACC is involved in affective processes. However, this view does not ultimately hold up to scrutiny when one takes into account pain studies, which typically activate dACC. A different dichotomy of function can account for the previous view, such that both dACC and rACC may be involved in conflict processing, but different forms. The dACC can best be understood as processing *nonsymbolic* conflict in which the conflict is not explicitly represented but is instead best characterized as the tension level in a connectionist constraint-satisfaction network. Alternatively, rACC can best be understood as processing *symbolic* conflict in which the conflict is explicitly represented with symbolic or propositional thought. The capacity to represent conflict symbolically may be a purely human attribute and has implications for how we regulate different types of affective experiences.

We should say from the outset that although we focus on the dACC as a region involved in social and physical pain, we readily admit that we do this because, for the moment, that is where the light is best. An enormous amount of work has been done examining the role of dACC in physical pain and in cognitive processing. Consequently, this region is ripe for consideration. This should not be taken to mean that that is the only region involved in both social and physical pain for it most assuredly is not; right ventral prefrontal cortex is another. Although we do not focus on other regions of the pain matrix (Peyron, Laurent, & Garcia-Larrea, 2000), such as the periaqueductal gray, insula, and somatosensory cortex, the reader should not be surprised if these regions are added in future work. Indeed, some work has already started along these lines (MacDonald & Leary, in press; Panksepp, 1998).

Linguistic Evidence Linking Social and Physical Pain

Whereas a cognitive neuroscientist might bristle at the notion of something as ethereal as social pain being similar to physical pain, nonscientists might think that the truth of this idea is obvious. A layperson might point to the fact that in our culture, we talk about social and physical pain in similar ways so that they should no doubt be related. For instance, we describe physical pain with phrases such as, "I broke my arm," and "my leg hurts." Similarly, we describe social pain with phrases such as, "she broke my heart," and "he hurt my feelings." Indeed, it is difficult to describe social pain without reference to physical pain terminology. In fact, English speakers have no other way to describe the feelings associated with social pain (MacDonald & Leary, in press).

MacDonald and Leary (in press) recently examined whether this linguistic overlap was a feature of only the English language and discovered that it was not. They asked

individuals from fifteen different countries, including a number of non-European countries, to provide typical ways of describing social pain. In each country, social pain descriptions relied on physical pain words. This evidence, at the very least, suggests that social and physical pain may be universally linked in the mental lexica of humans around the world. It does not in itself, however, say much about whether common processes support the experience of the two types of pain. The relationship may simply be metaphorical, although obviously a strong metaphor for it to have spread so widely.

An Evolutionary Story for the Link

The first line of evidence to suggest that the link between social and physical pain might be more than metaphorical came from the work of Panksepp et al. (1978). They were examining the analgesic effects of opiate-based drugs in dogs when they discovered that in addition to altering the amount of pain the dogs could tolerate, opiates diminished the frequency of cries produced while in isolation. The investigators reasoned that the opiate receptor system mitigated the experience of both physical and social pain. Along similar lines, drugs that are typically prescribed to deal with social distress and depression are known to work effectively for chronic pain (Shimodozono et al., 2002). Finally, the "social attachment system" may have piggybacked onto or developed out of the physical pain system, which has older phylogenetic roots than the social pain system (Nelson & Panksepp, 1998).

Unlike other animals that are born relatively mature or have rapid developmental trajectories, infant mammals are unable to care for themselves for an extended period of time and human infants take the longest of all. Thus mammals have unprecedented dependence on their caregivers. Whereas lack of food, water, shelter, and defense against predators will lead to death for any animal, for young mammals, meeting these needs is entirely contingent on the continuing relationship with a caregiver. For mammals, then, social needs supplant all other biological needs in importance, at least in infancy, because meeting them is critical to meeting all other needs.

It is not surprising, therefore, that mammals are among the first to have a social attachment system, a system that monitors for actual or psychological distance from others and elicits distress once distance is detected so that contact can be reestablished. Attachment processes exist primarily in mammalian species and thus as the social attachment system was evolving, the physical pain system was already in place and could serve as a solid foundation for the creation of this attachment system. Whereas the physical pain system produces physical pain in response to physical injuries so

that attention and other biological resources can be mobilized to prevent greater injury and promote survival, the social pain system produces social pain in response to social injuries so that attention and other biological resources can be mobilized to prevent these injuries and promote survival. It is of interest that mammals are also the first species, phylogenetically speaking, to have a cingulate gyrus (MacLean, 1993). Thus, it is plausible that this new structure may be involved in these social attachment processes.

We have chosen to focus on the role of the dACC in both social and physical pain for a number of reasons. First, the ACC has one of the highest densities of opiate receptors in the brain (Vogt, Wiley, & Jensen, 1995), and thus may have been one of the primary sites of action in Panksepp's work on the social and physical pain-alleviating properties of opiates. Second, a large literature shows the dACC to be involved in physical pain processes in humans. Finally, a number of studies with nonhuman mammals suggest that the ACC, and perhaps the dACC specifically, is involved in the experience of separation distress and in the production of distress vocalizations aimed at regaining social contact.

ACC and Physical Pain in Humans

Neural regions involved in physical pain, referred to as the pain matrix, include the dACC, rACC, somatosensory cortex, insula, periaqueductal gray, and right ventral prefrontal cortex. These regions are thought to be differentially involved in the sensory, distressing, and regulatory components of pain. Somatosensory cortex and insula are primarily, although not exclusively, linked with the sensory aspects of pain. Pain-related activity in these regions is associated with being able to identify the region of one's body that is in pain and other sensory features including intensity. Periaqueductal gray, rACC, and right ventral prefrontal cortex are more frequently associated with regulation of pain through opioid release and cognitive processing. Finally, dACC is generally associated with the subjectively distressing component of pain.

Sensory intensity and subjective distress associated with pain are often highly correlated, and thus a few illustrations of their relationship are in order to clarify the difference between the concepts. A useful metaphor is the sound of music on a radio, with sensory intensity likened to the radio's volume and subjective distress likened to the extent to which the music is experienced as unpleasant (Price, 1999). Above a certain threshold, increasing volume will usually be highly correlated with increasing unpleasantness. Nevertheless, the same volume can produce different levels of

unpleasantness depending on the level of ambient noise from being in a quiet room versus outdoors at a barbeque or one's sensitivity to or tolerance of loud noises. Thus, intensity can be distinguished from unpleasantness such that under different conditions or across different people, the same degree of sensory intensity might produce different degrees of unpleasantness.

The consequences of damaging neural structures associated with the sensory and distressing aspects of pain also reveals this dissociation. In the 1960s, patients with chronic pain problems sometimes underwent cingulotomies, a procedure that involves lesioning the anterior cingulate. After the procedure, patients often experienced significant pain relief; however, the relief did not come as a result of all aspects of pain being diminished. Rather, only the subjective distress appears to have abated. Patients would report that the sensory aspects of pain continued, but it no longer seemed to bother them (Foltz & White, 1968). Alternatively, there is a reported case of a patient with damage to somatosensory cortex. When painful stimulation was applied to the body region represented by the damaged part of somatosensory cortex, the patient had difficulty reporting on the location of the stimulation but still experienced the stimulation as distressing (Nagasako, Oaklander, & Dworkin, 2003). So although intensity and distress may feel inextricably linked, they can be separated because they depend on distinct neural processes.

Furthering this conceptual separation, Rainville et al. (1997) conducted a neuroimaging study in which they used hypnotic suggestion to alter the perceived unpleasantness of painful stimulation without changing the perceived intensity. During part of the experiment, subjects were given a suggestion that they would experience the pain as more or less distressing than normal. In fact, subjects reported the pain to be more or less distressing in accord with the suggestion they received. These results were unlikely to be mere demand characteristics, because changes in reports of pain distress were highly correlated with changes in dACC activity. The changes were not correlated with activity in somatosensory cortex, suggesting that this region, unlike dACC, is not a direct contributor to the experience of pain distress.

ACC and Social Pain in Animals

Until recently little research has examined neural correlates of social pain in humans; however, some studies from the animal literature suggest a role for dACC in this regard. Care must be taken in the inferences drawn from the animal literature because similar neural regions in different animals do not always serve the same functions. Along those lines, two issues are worthy of note with respect to the anterior

cingulate across animal and human brains. First, in older animal studies, ACC, which can be subdivided into rostral and dorsal sections, was sometimes referred to as rostral cingulate cortex (Smith, 1945). It is important to note that this designation refers to all of what would now be called anterior cingulate, including dACC. Second, strictly speaking, some primates such as the macaque may not have rACC at all, such that the entire macaque ACC might be functionally analogous to dACC. In humans, dACC and rACC have different morphological properties (i.e., cell layer organization). In the macaque, the entire ACC has morphological properties similar to those in dACC (Smith, 1945). This will be particularly relevant in the final section of this chapter when we suggest that rACC is associated with symbolic processes specific to humans (Lieberman et al., 2002).

One set of animal studies indicating the link between the ACC and social pain comes from work in which lesions were made to various overlapping subregions of the medial prefrontal cortex, including the ACC, in squirrel monkeys (MacLean & Newman, 1988). The only monkeys that ceased to make separation distress vocalizations after the procedure were those for which dACC had been lesioned. It should be noted that these same monkeys also had their rACC lesioned, which may or may not be functionally equivalent to rACC in humans, as rACC homology was examined in macaques, not squirrel monkeys. However, other squirrel monkeys in this study had rACC lesions without dACC lesions and did not show reduced distress vocalizations, whereas none of the monkeys had dACC lesions without reduced distress vocalizations. Moreover, the monkeys were still capable of making different kinds of vocalizations, so it is not the case that the capacity for vocalizing per se was affected by the lesions. This study suggests that dACC may be critical to the experience of social pain that would lead to distress vocalizations.

Electrical stimulation studies support this conclusion as well. Over half a century ago, Smith (1945; Jurgens & Muller-Preuss, 1977) observed that electrical stimulation of dACC produced spontaneous separation distress vocalizations in the absence of social isolation. Thus, these lesion and stimulation studies provide good converging evidence that the dACC plays an important role in social pain.

ACC and Social Pain in Humans

To examine neural correlates of social exclusion in humans, and begin to assess whether the neural basis of social pain is similar to the neural basis of physical pain, it was critical to find a manipulation that would produce a genuine episode of social pain while simultaneously seeming plausible to a subject lying inside a neuroimaging

scanner. Numerous manipulations have been used successfully by social psychologists since the late 1900s to examine cognitive and behavioral responses to social exclusion (see Williams, Forgas, & von Hippel, in press).

The most common manipulation of exclusion involves subjects finding out that no one else in an experimentally created group wants to pair up with them in the upcoming task, so they will be working on their own (Leary et al., 1995; Twenge et al., 2001; see also Gaertner & Iuzzini, in press). Baumeister and colleagues also used a "future alone" manipulation by telling subjects that, on the basis of their answers on questionnaires, they are the kinds of persons who are likely to end up alone in life, even if they have close friends and loved ones now (Baumeister & De Wall, in press). Williams and Sommer (1997) used the most direct and overt manipulation of social exclusion. In their work, a subject is waiting with two same-sex confederates for an experiment to start. One of the confederates picks up a ball from the table between them and begins tossing it to the other confederate and the subject. After being included in the game for a short time, half of the subjects are then excluded by the confederates who never throw the ball to those subjects again. Each of these manipulations proved effective in producing behaviors and self-evaluations that would be expected to result from social exclusion, including lowered self-esteem, increased aggressiveness, and increased conformity to group norms (Leary, in press).

None of these manipulations is easily transferable to the context of a functional neuroimaging study. Fortunately, the ball-tossing manipulation has been converted into a virtual ball-tossing game ("cyberball"), ostensibly played on line with other players, and produces the same effects as the in-person version (Williams, Cheung, & Choi, 2000). In fact, "cyberball" works so well that even when subjects are informed that the other two "players" are really just computer players controlled by the program and that those players will exclude them part way through the game, subjects still report feeling social pain as a result of the experience (Zadro & Williams, 1998). "Cyberball" thus fit the dual constraints of producing a genuine experience of social pain while at the same time making sense in the context of a functional magnetic resonance imaging (fMRI) study.

Subjects in our study of social exclusion (Eisenberger, Lieberman, & Williams, 2003) were informed that we were working out the technical details in a new neuroimaging procedure called hyperscanning. Hyperscanning, which is a real technique being used at Johns Hopkins University, involves scanning many subjects simultaneously while they engage in some kind of coordinated activity so that the relationship between the neural patterns of the different subjects can be analyzed. We showed subjects a write-up of this work that appeared in *Nature Neuroscience* and told subjects that we wanted

to do the same kind of procedure in our laboratory, but that we were still in the technical development stage. Subjects were told that two other subjects were also going to be in scanners at other locations around campus and that we would be having subjects play a simple ball-tossing game so that we would have some basic coordinated neural activity to look at, to see if we were making progress. There was no goal to the ball-tossing game, no points to be won, and no skill involved given that catching occurs automatically and subjects' only decision is whether to throw it to one person or the other (an animation of the game can be seen at www.scn.ucla.edu).

Subjects went through three functional scans. During the first scan (implicit exclusion), they were told that we were having technical difficulties making a full internet link with the other two scanners, so as a result, they would be able to watch the other two players play during the first scan, but they would not be able to receive or throw the ball. This condition is visually identical to the regular exclusion condition; however, our subjects knew that they were not being intentionally excluded. This condition conceptually replicated the study by Zadro and Williams (1998), in which subjects were informed that they were playing a computer game with animated figures and would be automatically excluded part way through the game.

For the second scan (inclusion), subjects were told we had made the full internet link so that they would be able to play. Subjects played with the other two players during this scan and were fully included such that they were thrown the ball with 50 percent probability. In the third and final scan (explicit exclusion), subjects were fully included for about thirty seconds, but then excluded by the other two players for the rest of the scan. After this scan, subjects were removed from the scanner and immediately filled out a questionnaire assessing the degree of social pain experienced during the last scan.

Our primary analysis comparing brain activations showed greater activity in dACC, right insula, and right ventral prefrontal cortex during the explicit exclusion condition, relative to inclusion. Each of these regions is commonly found in neuroimaging studies of physical pain (Petrovic et al., 2000). In a follow-up analysis, we examined the extent to which the individual differences in activity in each of these regions predicted the individual differences in self-reported social pain as measured in the postscanning questionnaire. Insula activity was not correlated with self-reported social pain, however, dACC and right ventral prefrontal activity were both strongly related to social pain. For dACC, greater activity during exclusion relative to inclusion was associated with greater reports of social pain ($r = 0.88$). For right ventral prefrontal cortex, greater activity during exclusion relative to inclusion was associated with diminished reports of social pain ($r = -0.69$).

This pattern of activity is quite similar to results in studies of physical pain. For instance, in a study of visceral pain regulation (Lieberman et al., 2004), dACC, insula, and right ventral prefrontal cortex were all more active during painful stimulation than at baseline. More important, the same pattern of relationships between neural activity and subjective pain reports was found here as in the social pain study; insula activity did not correlate with self-reported pain, dACC activity correlated positively with self-reported pain, and right ventral prefrontal cortex correlated negatively with self-reported pain. In fact, in both studies, dACC activity strongly mediated the relationship between right ventral prefrontal activity and self-reports of pain. These results, consistent with other results (Petrovic et al., 2002; Wager et al., 2004), suggest that although dACC is important in producing the subjective distress of pain, right ventral prefrontal cortex is involved in down-regulating the experience of pain (see Lieberman et al., 2005 for a discussion of the role of right prefrontal cortex in the self-regulation of negative affective states).

In a second set of analyses, we examined brain activations during implicit exclusion. As in the explicit condition, dACC activity was greater during implicit exclusion than during inclusion, and was similar to the explicit exclusion dACC activation in position, cluster size, and intensity. This may be somewhat surprising given that subjects presumably did not consciously believe that they were being excluded during this condition. However, it should be recalled that Zadro and Williams' subjects experienced social pain even when they were told ahead of time that the game was fixed. It may be the case that humans are sufficiently hardwired to respond to exclusion and that the mere appearance of exclusion is sufficient to provoke the response. If so, this would be similar to the way visual illusions function. In most cases, understanding the causes of a visual illusion in no way mitigates the effect; understanding the true shape of an Ames room does not prevent a child from looking as tall as an adult. The reliability of the visual system is either so important or so ancient that evolution has sealed its computations off from intentional modification by the owner of the visual system. Similarly, the need to detect potential exclusion may be so important or ancient that it too resists our conscious beliefs about the true meaning of an episode, in this case that it is not truly exclusionary.

Still, there ought to be some consequences of whether or not we consciously believe we are being excluded. Individuals ought to be less likely to be thinking about exclusion and its causes if they do not believe they are being excluded, and should also be less likely to try to self-regulate the negative experience. Consistent with this view, no increased right ventral prefrontal activity was evident during implicit exclusion, relative to inclusion, even at very liberal statistical thresholds. Given that right ventral

prefrontal activity has been associated with explicit thought about negative affect and negatively evaluated attitude objects (Crockett, Eisenberger, & Lieberman, 2004; Cunningham et al., 2003) and is also associated with inhibition of negative affective experience, it appears that in our study, subjects were not engaged in these sorts of mental activities. In other words, because subjects had no reason to think they were being excluded, self-regulatory and attributional mechanisms were not engaged. One caveat to this account is that we cannot be sure that implicit exclusion actually produced any distress, because to have assessed social pain after the first scan would have given away our cover story.

What Is the Basic Function of the ACC?

The results thus far, from our own work as well as from the broader physical and social pain literatures, suggest that dACC activity is related to the experience of social and physical pain. The next obvious question to ask is why. What is the function of the dACC such that it should be involved in these forms of pain? It turns out that the answer to this question depends on which end of the psychology department one goes to for an answer.

If clinical and psychopathology researchers are asked, they will probably respond that the function of the dACC is to produce attention-getting affective-motivational states such as pain, anxiety, and distress. Each of these states serves important functions in motivating adaptive and appropriate behavior (Mandler, 1975). Thus, these researchers focus on phenomenological contributions of the ACC.

If cognitive researchers are asked, they will probably respond by saying that the function of the ACC is to monitor for conflict and to detect errors. Numerous studies suggested that dACC is activated when a discrepancy exists between one's goals and one's prepotent responses. For instance, during the Stroop task when a person is shown color words in different color ink (e.g., R-E-D written in blue ink), one's goal is to say the color of the ink that words are written in, but this goal conflicts with the prepotent tendency to read the words themselves. The dACC is activated in this context and "notifies" lateral prefrontal cortex that top-down control processing is necessary to promote contextually appropriate responding (Botvinick et al., 2001). One might expect the same thing to occur when one is required to give responses that appear racially biased when one does not want to appear racist (Amodio et al., 2004). Most researchers in this field agree that the dACC's role is limited to detecting conflict and alerting lateral prefrontal cortex, rather than being involved in resolving conflict directly.

Of interest in this brief tour of the psychology department is that those interested in the cognitive functions of the dACC leave the phenomenological consequences of dACC activity unexamined. At the same time, those interested in the phenomenological consequences of dACC activity have rarely expressed interest in the computations underlying that activity.

The ACC as a Neural Alarm System

We suggest that it might be profitable to consider the possibility that the dACC works as a neural alarm system (Eisenberger & Lieberman, 2004). Such a metaphor might help to bridge the explanations of ACC function that are seemingly in competition with one another. Any alarm system, whether it is a clock alarm or a smoke alarm, must integrate two functions to work effectively. First, it must be able to detect the critical environmental conditions for which it is designed. A clock must be able to detect when there is a match between the current time and the time set for the alarm to go off. A smoke detector must be able to detect when the amount of smoke in the room crosses some threshold for unacceptability. Second, the alarm must be able to notify relevant parties that the critical condition has been met. For most alarms, this means making a loud noise, either to wake people up or let them know a room is filling with smoke and possibly fire. Conceptually, these functions are separable (e.g., a clock alarm with a broken speaker), but they must be integrated and work together for the alarm to function properly.

These two functions of an alarm system sound conspicuously similarly to the two descriptions of ACC function. The cognitive account suggests that the ACC is sensitive to goal conflicts, conditions that are critical to detect. The phenomenological account suggests that the ACC can create attention-getting affective states. If these two processes operate together, they might function as a unitary alarm system, detecting conflicts and "making noise" to attract the person's attention.

There are at least two ways in which this alarm could be instantiated in dACC, and at this point the data are insufficient to differentiate them. In one account, discrepancy detection and distress may go hand in hand, such that the alarm bell sounding may be the phenomenological consequence of the detection of discrepancy. It is possible that previous cognitive studies of the ACC produced distress in their subjects but did not attempt to measure it. The second possibility is that the conflict detector and alarm bell are instantiated in nearby but distinct regions of dACC. The two functions would still be integrated with one another, but this might help explain why performing tasks such as the Stroop or oddball task do not seem to set off major alarm bells, phenomenologically speaking.

As noted, there are no compelling data yet to argue for one or the other of these accounts. However, two studies partially investigated this question by examining neural activity to pain distress and cognitive processing in the same subjects. One study (Derbyshire, Vogt, & Jones, 1998) noted that the regions in dACC activated by a pain and Stroop task were adjacent to one another, but also sometimes overlapping. The ambiguity of these results is only heightened by the small sample—six. A second study (Davis et al., 1997) also found adjacent regions activated by a pain and cognitive task, however, the task did not involve conflict detection and thus is not entirely on point.

Separate from determining whether or not these two potential subcomponents of the alarm system are in the same region of dACC, the more pressing question is whether the two subcomponents actually work together as they should if they really are part of an underlying alarm system. In other words, do phenomenological and conflict-detection processes covary with one another? If so, this would suggest that the overall alarm system is mobilizing its subcomponents en masse, rather than each performing its own process independently. Two studies examined the covariation between these subcomponents.

In a neuroimaging study (Ursu et al., 2003), individuals with obsessive-compulsive disorder (OCD), which is characterized by distress and worry, were scanned while performing a task involving response conflict. Individuals with OCD, compared with healthy controls, showed significantly more dACC activity to high-conflict trials. In addition, a trend was observed, although not significant, such that patients with more severe symptoms of OCD showed more dACC activity to conflict than those with less severe symptoms.

A second neuroimaging study (Eisenberger, Lieberman, & Satpute, in press) investigated this issue by correlating dACC activity on a conflict-detection task with neuroticism scores. Neuroticism is typically defined as a heightened tendency to experience negative affect frequently and/or intensely (Costa & McCrae, 1985). Thus, we can safely assume that neurotics tend to have alarm bells that ring louder and/or more often than in nonneurotics. The question of interest was whether they also have more sensitive conflict-detection systems, even for conflicts that are generally nondistressing to detect. The results suggested that indeed such was the case. The magnitude of activations to conflict relative to nonconflict trials correlated strongly ($r = 0.76$) with neuroticism.

Dorsal versus Rostral ACC

Evidence presented thus far supports the notion of the dACC functioning as a neural alarm system involved both in the cognitive detection of critical conditions and the

affective sounding of a phenomenological alarm. On the face of it, this characterization conflicts with an influential account of the distinct functions of dACC and rACC. Bush, Luu, and Posner (2000) reviewed various cognitive and affective task paradigms that activated the ACC. The major conclusion was that cognitive tasks tended to activate dACC and deactivate rACC, whereas affective tasks tended to activate rACC and deactivate dACC. Thus, our conclusion that one function of dACC is to sound an affective alarm conflicts with this conceptual organization of ACC function.

One limitation of that review is that it included no pain imaging studies. Once these studies are taken into account, the affective-cognitive distinction becomes muddled, because the emotional distress of pain was reliably linked to dACC rather than rACC activity in numerous studies (Rainville et al., 1997).

The fact that the affective-cognitive distinction seems insufficient to capture functional differences associated with the dorsal and rostral regions of the ACC led us to consider an alternative formulation. After a search of the literature, although admittedly not an exhaustive one, we developed the hypothesis that dACC and rACC may both be involved in conflict processing but differ with regard to the extent to which the conflict is represented symbolically or nonsymbolically.

Symbolically and nonsymbolically represented conflict should vary in a number of ways. The most critical is whether there is an explicit Intentional representation of the conflict or of the source of the conflict.¹ According to this view, when conflict is symbolic, there is not merely conflict in the system (e.g., in the ACC), rather there is awareness of the conflict as a conflict (Lieberman et al., 2002).

These two kinds of conflict processing should also vary in the kind of computational mechanisms that could support them. Nonsymbolic conflict can be thought of as tension between two or more competing representations or responses. Connectionist networks representing the combined outputs of multiple interconnected inputs naturally produce conflict maps that represent the total level of tension or conflict among various inputs. When inputs are coherent and consistent with one another, the network has a low level of tension, whereas when these inputs conflict, the network has a high level of tension (Hopfield, 1982, 1984). An elegant model of this process suggests that when the tension level in dACC is high, it automatically triggers a signal to lateral prefrontal cortex, which then exerts top-down control over the competing inputs (Botvinick et al., 2001). Nowhere in this model is conflict itself or the decision to resolve conflict modeled. Indeed, its authors value the model, in part, because it has no "ghost in the machine" regress in which an intelligent agent must be posited but left unexplained.

Although little or nothing is known about the process by which conflicts or anything else are represented symbolically (Lieberman et al., 2002), symbolic

representations do have a number of features that are known. Symbolic processes involve conscious awareness of and attention to a specific symbolic representation. The resources of awareness and attention are limited (Miller, 1956) such that only a handful of symbolic representations can be attended to and processed at any one time (Schneider & Shiffrin, 1977). These representations are typically thought to be processed serially. Thus, although many conflicts may be nonsymbolically processed, only a single symbolic conflict can be processed at any one time.

We propose that symbolically represented conflict is processed primarily in rACC, whereas nonsymbolically represented conflict is processed primarily in dACC. With respect to cognitive conflict, both symbolic and nonsymbolic forms exist. For instance, connectionist networks in which tension effects naturally emerge out of competing inputs can nicely model standard oddball, go-no-go, and Stroop effects. Alternatively, error-detection tasks involve overt awareness that a particular error has been made and the nature of the error. Using a Talaraich y-coordinate of 30 to divide rostral from dorsal ACC activations, we find that most nonsymbolic forms of cognitive conflict activate dACC (Braver et al., 2001; Bush et al., 2003; Carter et al., 2000; Weissman et al., 2003). Alternatively, error-detection tasks, which involve symbolic conflict representations, tend to activate rACC (Garavan et al., 2003; Kiehl, Liddle, & Hopfinger, 2000; Rubia et al., 2003).

Emotion can also be construed within a conflict model. Appraisal models of emotion suggest that negative emotions are the result of a conflict between desired or expected outcomes and what actually occurs (Frijda, 1986; Lazarus, 1991; Mandler, 1975). Most negative emotions (anger, fear, sadness) are thought to have a specific Intentional object such that they are, symbolically speaking, about something. When someone is afraid, he or she is afraid of something in particular and knows what that something is. Anxiety, however, is a negative affect that is distinguished from fear in that it lacks an Intentional object (Kierkegaard, 1844/1981). Although anxiety may have a specific cause (e.g., someone in the room who makes us uncomfortable), it does not involve the anxious individual knowing this specific cause. Considering neuroimaging studies of anxiety-provocation versus the induction of other emotions conforms to our symbolic-nonsymbolic theory of the ACC. Sadness, anger, and fear reliably activate rACC (Damasio et al., 2000; Dougherty et al., 1999; George et al., 1995; Kimbrell et al., 1999; Liotti et al., 2000; Mayberg et al., 1999; Shin et al., 2000). Anxiety, however, tends to activate dACC (Kimbrell et al., 1999; Liotti et al., 2000). Along similar lines, perception of discrete emotional expressions activates rACC (Ueda et al., 2003) whereas perception of ambiguous emotional expressions activates dACC (Nomura et al., 2003).

Finally, pain distress can also be divided along symbolic and nonsymbolic lines. Typically, pain is a nonsymbolic bottom-up process (animals without symbolic capacities presumably experience pain). Consistent with this, the experience of pain is most often associated with dACC activation (Hsieh, Stone-Elander, & Ingvar, 1999; Ploghaus et al., 1999; Sawamoto et al., 2000; Tolle et al., 1999). However, when pain is anticipated or expected it becomes more symbolic and tends to be processed in rACC (Buchel et al., 1998; Chua et al., 1999; Ploghaus et al., 1999, 2003).

Thus, cognitive, affective, and pain processes are each distributed across dACC and rACC. They do, however, seem to be organized such that more symbolic forms of cognition, emotion, and pain are processed in rACC with less symbolic forms processed in dACC. It is worth returning to a point made earlier regarding the homology of function between human and primate ACC. Smith (1945) pointed that though macaques have ACCs that correspond in location to the human dACC and rACC, the morphology of both their rACC and dACC is consistent with the morphology of human dACC. Smith concluded that macaques do not, functionally speaking, have an equivalent to human rACC. This conclusion takes on new meaning in light of our claim that rACC is involved in symbolic representations of conflict, a capacity that humans have and may not share with any other animal (Deacon, 1997). Symbolic representations of conflict allow for unparalleled consideration of contextual factors such as time and place. If one is aware of the source of one's distress, one may choose to delay responding (one may choose to ignore the distress caused by one's boss while the boss is still in the room) or consider complex strategies of response ("I'll settle this when I have lunch with my boss's boss next week"). Nonsymbolic conflict simply produces tension and anxiety until it is resolved or a symbolic representation is generated.

Conclusion

We suggest that because of the role of social attachment in mammals, the social pain system may have piggybacked onto the physical pain system during our evolution. In addition, the dACC may have been one of the primary sites in which this overlap evolved, such that today, this region produces similar experiences of distress in response to both physical and social injuries. More generally, we propose that the dACC may be thought of as a neural alarm system that is involved both in detection of actual or potential threats as well as in sounding a phenomenological alarm that redirects our attention and motivation toward dealing with the source of the threat. Finally, we attempted to integrate our model with what previously was hypothesized regarding the function of the ACC by proposing a new conceptual distinction for the

contribution of rACC versus dACC to psychological processes. Specifically, we propose that the dACC is involved in detecting nonsymbolic conflict whereas rACC is involved in detecting symbolic conflict. In future work, we hope to explore more fully the ways in which physical and social pain processes are intertwined, as well as distinct, in order to understand better in what ways "pains by any name" really do "hurt the same."

Note

1. In philosophy, when the word "Intentional" is capitalized it refers to the quality of Intentionality, which includes, but is not limited to, mental acts such as beliefs and desires. Intentionality, first described by Aristotle in *De Anima* and later by Brentano (1874/1995) and Husserl (1913) as one of the cornerstones of continental phenomenology, refers to the fact that certain reflective acts of mental life are irreducibly *directed at* or *about* something else. Physical objects are never intrinsically about anything else, serving only as representations to the extent that they are designated as such by the Intentional acts of humans. Although mental acts can possess the quality of Intentionality, many do not. For instance, most visual information that is processed by the brain at any moment is not overtly attended to. Parafoveal priming works, in part, because it is cognitively processed but not Intentionally; the individual has no thought about the primes.

References

- Amodio, D. M., Harmon-Jones, E., Devine, P. G., Curtin, J. J., Hartley, S. L., & Covert, A. E. (2004). Neural signals for the detection of unintentional race bias. *Psychological Science*, *15*, 88–93.
- Baumeister, R. F. & De Wall, C. N. (in press). The inner dimension of social exclusion: Intelligent thought and self-regulation among rejected persons. In K. D. Williams, J. P. Forgas, & W. von Hippel (Eds.), *The Social Outcast: Ostracism, Social Exclusion, Rejection, and Bullying*. New York: Psychology Press.
- Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. *Psychological Review*, *108*, 624–652.
- Braver, T. S., Barch, D. M., Gray, J. R., Molfese, D. L., & Snyder, A. (2001). Anterior cingulate cortex and response conflict: Effects of frequency, inhibition and errors. *Cerebral Cortex*, *11*, 825–836.
- Brentano, F. (1874/1995). *Psychology from an Empirical Standpoint*. London: Routledge.
- Buchel, C., Morris, J., Dolan, R. J., & Friston, K. J. (1998). Brain systems mediating aversive conditioning: An event-related fMRI study. *Neuron*, *20*, 947–957.
- Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences*, *4*, 215–222.
- Bush, G., Shin, L. M., Holmes, J., Rosen, B. R., & Vogt, B. A. (2003). The multi-source interference task: Validation study with fMRI in individual subjects. *Molecular Psychiatry*, *8*, 60–70.

- Carter, C. S., MacDonald, A. W., Botvinick, M. M., Ross, L. L., Stenger, V. A., Noll, D., et al. (2000). Parsing executive processes: Strategic vs. evaluative functions of the anterior cingulate cortex. *Proceedings of the National Academy of Sciences of The United States of America*, *97*, 1944–1948.
- Chua, P., Krams, M., Toni, I., Passingham, R., & Dolan, R. (1999). A functional anatomy of anticipatory anxiety. *Neuroimage*, *9*, 563–571.
- Costa, P. T., Jr. & McCrae, R. R. (1985). Hypochondriasis, neuroticism, and aging: When are somatic complaints unfounded? *American Psychologist*, *40*, 19–28.
- Crockett, M. J., Eisenberger, N. I., & Lieberman, M. D. (2004). Stereotype activation or behavior regulation? An fMRI study of automatic behavior effects. Proceedings of the 11th annual meeting of the Cognitive Neuroscience Society, San Francisco, April 16.
- Cunningham, W. A., Johnson, M. K., Gatenby, J. C., Gore, J. C., & Banaji, M. R. (2003). Neural components of social evaluation. *Journal of Personality and Social Psychology*, *85*, 639–649.
- Damasio, A. R., Grabowski, T. J., Bechara, A., Damasio, H., Ponto, L. L., Parvizi, J., et al. (2000). Subcortical and cortical brain activity during the feeling of self-generated emotions. *Nature Neuroscience*, *3*, 1049–1056.
- Davis, K. D., Taylor, S. J., Crawley, A. P., Wood, M. L., & Mikulis, D. J. (1997). Functional MRI of pain- and attention-related activations in the human cingulate cortex. *Journal of Neurophysiology*, *77*, 3370–3380.
- Deacon, T. W. (1997). *The Symbolic Species: The Co-evolution of Language and the Brain*. New York: Norton.
- Derbyshire, S. W., Vogt, B. A., & Jones, A. K. (1998). Pain and Stroop interference tasks activate separate processing modules in anterior cingulate cortex. *Experimental Brain Research*, *118*, 52–60.
- Dougherty, D. D., Shin, L. M., Alpert, N. M., Pitman, R. K., Orr, S. P., Lasko, M., et al. (1999). Anger in healthy men: A PET study using script-driven imagery. *Biological Psychiatry*, *46*, 466–472.
- Eisenberger, N. I., Lieberman, M. D., & Satpute, A. B. (in press). Personality from a controlled processing perspective: an fMRI study of neuroticism, extraversion, and self-consciousness. *Cognitive, Affective, and Behavioral Neuroscience*.
- Eisenberger, N. I., Lieberman, M. D., & Williams, K. D. (2003). Does rejection hurt: An fMRI study of social exclusion. *Science*, *302*, 290–292.
- Foltz, E. L. & White, L. E., (1968). The role of rostral cingulotomy in “pain” relief. *International Journal of Neurology*, *6*, 353–373.
- Frijda, N. H. (1986). *The Emotions*. New York: Cambridge University Press.
- Gaertner, L. & Iuzzini, J. (in press). Rejection and entitativity: A synergistic model of mass violence. In K. D. Williams, J. P. Forgas, & W. von Hippel (Eds.), *The Social Outcast: Ostracism, Social Exclusion, Rejection, and Bullying*. New York: Psychology Press.

- Garavan, H., Ross, T. J., Kaufman, J., & Stein, E. A. (2003). A midline dissociation between error-processing and response-conflict monitoring. *Neuroimage*, *20*, 1132–1139.
- George, M. S., Ketter, T. A., Parekh, P. I., & Horwitz, B. (1995). Brain activity during transient sadness and happiness in healthy women. *American Journal of Psychiatry*, *152*, 341–351.
- Hopfield, J. J. (1982). Neural networks and physical systems with emergent collective computational abilities. *Proceedings of the National Academy of Sciences of the United States of America*, *79*, 2554–2558.
- Hopfield, J. J. (1984). Neurons with graded response have collective computational properties like those of two-state neurons. *Proceedings of the National Academy of Sciences of the United States of America*, *81*, 3088–3092.
- Hsieh, J., Stone-Elender, S., & Ingvar, M. (1999). Anticipatory coping of pain expressed in the human anterior cingulate cortex: A positron emission tomography study. *Neuroscience Letters*, *262*, 61–64.
- Husserl, E. (1913/1962). *Ideas: General Introduction to Pure Phenomenology*. New York: Collier Press.
- Jurgens, U. & Muller-Preuss, P. (1977). Convergent projections of different limbic vocalization areas in the squirrel monkey. *Experimental Brain Research*, *8*, 75–83.
- Kiehl, K. A., Liddle, P. F., & Hopfinger, J. B. (2000). Error processing and the rostral anterior cingulate: An event-related fMRI study. *Psychophysiology*, *37*, 216–223.
- Kierkegaard, S. (1844/1981). *The Concept of Anxiety*. Princeton, NJ: Princeton University Press.
- Kimbrell, T. A., George, M. S., Parekh, P. I., Ketter, T. A., Podell, D. M., Danielson, A. L., et al. (1999). Regional brain activity during transient self-induced anxiety and anger in healthy adults. *Biological Psychiatry*, *46*, 454–465.
- Lazarus, R. S. (1991). *Emotion and Adaptation*. New York: Oxford University Press.
- Leary, M. R. (in press). Varieties of interpersonal rejection. In K. D. Williams, J. P. Forgas, & W. von Hippel (Eds.), *The Social Outcast: Ostracism, Social Exclusion, Rejection, and Bullying*. New York: Psychology Press.
- Leary, M. R., Tambor, E. S., Terdal, S. K., & Downs, D. L. (1995). Self-esteem as an interpersonal monitor: The sociometer hypothesis. *Journal of Personality and Social Psychology*, *68*, 518–530.
- Lieberman, M. D., Gaunt, R., Gilbert, D. T., & Trope, Y. (2002). Reflection and reflexion: A social cognitive neuroscience approach to attributional inference. In M. Zanna (Ed.), *Advances in Experimental Social Psychology* (pp. 199–249). New York: Academic Press.
- Lieberman, M. D., Hariri, A., Jarcho, J. M., Eisenberger, N. I., & Bookheimer, S. Y. (2005). An fMRI investigation of race-related amygdala activity in African-American and Caucasian-American individuals. *Nature Neuroscience*, *8*, 720–722.
- Lieberman, M. D., Jarcho, J. M., Berman, S., Naliboff, B., Suyenobu, B. Y., Mandelkern, M., et al. (2004). The neural correlates of placebo effects: A disruption account. *NeuroImage*, *22*, 447–455.

- Liotti, M., Mayberg, H. S., Branna, S. K., McGinnis, S., Jerabek, P., & Fox, P. T. (2000). Differential limbic-cortical correlates of sadness and anxiety in healthy subjects: Implications for affective disorders. *Biological Psychiatry*, *48*, 30–42.
- MacDonald, G. & Leary, M. R. (in press). Why does social exclusion hurt? The relationship between social and physical pain. *Psychological Bulletin*.
- MacLean, P. D. (1993). Perspectives on cingulate cortex in the limbic system. In B. A. Vogt & M. Gabriel (Eds.), *Neurobiology of Cingulate Cortex and Limbic Thalamus: A Comprehensive Handbook* (pp. 1–23). Boston: Birkhauser.
- MacLean P. D. & Newman, J. D. (1988). Role of midline frontolimbic cortex in production of the isolation call of squirrel monkeys. *Brain Research*, *45*, 111–123.
- Mandler, G. (1975). *Mind and Emotion*. New York: Krieger.
- Mayberg, H. S., Liotti, M., Brannan, S. K., McGinnis, S., Mahurin, R. K., Jerabek, P. A., et al. (1999). Reciprocal limbic-cortical function and negative mood: Converging PET findings in depression and normal sadness. *American Journal of Psychiatry*, *156*, 675–682.
- Miller, G. A. (1956). The magical number seven, plus or minus two: Some limits on our capacity for processing information. *Psychological Review*, *63*, 81–97.
- Nagasako, E. M., Oaklander, A. L., & Dworkin, R. H. (2003). Congenital insensitivity to pain: An update. *Pain*, *101*, 213–219.
- Nelson, E. E. & Panksepp, J. (1998). Brain substrates of infant-mother attachment: Contributions of opioids, oxytocin, and norepinephrine. *Neuroscience and Biobehavioral Reviews*, *22*, 437–452.
- Nomura, M., Iidaka, T., Kakehi, K., Tsukiura, T., Hasegawa, T., Maeda, Y., et al. (2003). Frontal lobe networks for effective processing of ambiguously expressed emotions in humans. *Neuroscience Letters*, *348*, 113–116.
- Panksepp, J. (1998). *Affective Neuroscience*. New York: Oxford University Press.
- Panksepp, J., Herman, B., Conner, R., Bishop, P., & Scott, J. P. (1978). The biology of social attachments: Opiates alleviate separation distress. *Biological Psychiatry*, *13*, 607–618.
- Petrovic, P., Petersson, K. M., Ghatan, P. H., Stone-Elander, S., & Ingvar, M. (2000). Pain-related cerebral activation is altered by a distracting cognitive task. *Pain*, *85*, 19–30.
- Peyron, R., Laurent, B., & Garcia-Larrea, L. (2000). Functional imaging of brain responses to pain. A review and meta-analysis. *Neurophysiological Clinics*, *30*, 263–288.
- Ploghaus, A., Becerra, L., Borras, C., & Borsook, D. (2003). Neural circuitry underlying pain modulation: Expectation, hypnosis, placebo. *Trends in Cognitive Sciences*, *7*, 197–200.
- Ploghaus, A., Tracey, I., Gati, J. S., Clare, S., Menon, R. S., Matthews, P. M., et al. (1999). Dissociating pain from its anticipation in the human brain. *Science*, *284*, 1979–1981.
- Price, D. D. (1999). *Psychological Mechanisms of Pain and Analgesia*. Seattle: IASP Press.

- Rainville, P., Duncan, G. H., Price, D. D., Carrier, B., & Bushnell, M. D. (1997). Pain affect encoded in human anterior cingulate but not somatosensory cortex. *Science*, *277*, 968–971.
- Rubia, K., Smith, A. B., Brammer, M. J., & Taylor, E. (2003). Right inferior prefrontal cortex mediates response inhibition while mesial prefrontal cortex is responsible for error detection. *Neuroimage*, *20*, 351–358.
- Sawamoto, N., Honda, M., Okada, T., Hanakawa, T., Kanda, M., Fukuyama, H., et al. (2000). Expectation of pain enhances responses to nonpainful somatosensory stimulation in the anterior cingulate cortex and parietal operculum/posterior insula: An event-related functional magnetic resonance imaging study. *Journal of Neuroscience*, *20*, 7438–7445.
- Schneider, W. & Shiffrin, R. M. (1977). Controlled and automatic human information processing. I. Detection, search, and attention. *Psychological Review*, *84*, 1–66.
- Shimodozono, M., Kawahira, K., Kamishita, T., Ogata, A., Tohgo, S., & Tanaka, N. (2002). Reduction of central poststroke pain with the selective reuptake inhibitor fluvoxamine. *International Journal of Neuroscience*, *112*, 1173–1181.
- Shin, L. M., Dougherty, D. D., Orr, S. P., Pitman, R. K., Lasko, M., Macklin, M. L., et al. (2000). Activation of anterior paralimbic structures during guilt-related script-driven imagery. *Biological Psychiatry*, *48*, 43–50.
- Smith, W. (1945). The functional significance of the rostral cingulate cortex as revealed by its responses to electrical excitation. *Journal of Neurophysiology*, *8*, 241–255.
- Tolle, T. R., Kaufmann, T., Siessmeier, T., Lautenbacher, S., Berthele, A., Munz, F., et al. (1999). Region-specific encoding of sensory and affective components of pain in the human brain: A positron emission tomography correlation analysis. *Annals of Neurology*, *45*, 40–47.
- Twenge, J. M., Baumeister, R. F., Tice, D. M., & Stucke, T. S. (2001). If you can't join them, beat them: Effects of social exclusion on aggressive behavior. *Journal of Personality and Social Psychology*, *81*, 1058–1069.
- Ueda, K., Okamoto, Y., Okada, G., Yamashita, H., Hori, T., & Yamawaki, S. (2003). Brain activity during expectancy of emotional stimuli: An fMRI study. *Neuroreport*, *14*, 41–44.
- Ursu, S., Stenger, V. A., Shear, M. K., Jones, M. R., & Carter, C. S. (2003). Overactive action monitoring in obsessive-compulsive disorder: Evidence from functional magnetic resonance imaging. *Psychological Science*, *14*, 347–353.
- Vogt, B. A., Wiley, R. G., & Jensen, E. L. (1995). Localization of mu and delta opioid receptors to anterior cingulate afferents and projection neurons and input/output model of mu regulation. *Experimental Neurology*, *135*, 83–92.
- Wager, T. D., Rilling, J. K., Smith, E. E., Sokolik, A., Casey, K. L., Davidson, R. J., et al. (2004). Placebo-induced changes in fMRI in the anticipation and experience of pain. *Science*, *303*, 1162–1167.

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

Williams, K. D. & Sommer, K. L. (1997). Social ostracism by coworkers: Does rejection lead to loafing or compensation? *Personality and Social Psychology Bulletin*, *23*, 693–706.

Williams, K. D., Cheung, C. K. T., & Choi, W. (2000). Cyberostracism: Effects of being ignored over the Internet. *Journal of Personality and Social Psychology*, *79*, 748–762.

Williams, K. D., Forgas, J. P., & von Hippel, W. (in press). *The Social Outcast: Ostracism, Social Exclusion, Rejection, and Bullying*. New York: Psychology Press.

Zadro, L. & Williams, K. D. (1998). Impact of ostracism on social judgments and decisions: Explicit and implicit responses. In J. P. Forgas, K. D. Williams, & W. von Hippel (Eds.), *Social Judgments: Implicit and Explicit Processes* (pp. 325–342). Cambridge: Cambridge University Press.