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Understanding the Moderators of Physical and Emotional Pain: A Neural Systems-Based Approach

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Zhou and Gao (this issue) put forth an interesting hypothesis, namely, that money, in addition to social support, can reduce the experience of physical pain. Their hypothesis is based on the premise that social support is a "primary pain buffer"—in other words, social support is valued because it reduces the experience of pain—and that money is a secondary pain buffer that can reduce pain experience when one's social support system has failed and is no longer there to act as a buffer. Though the authors' creative analysis is admirable and the hypothesized implications of their research are significant, I propose an alternative theoretical framework for understanding how both social support and money may reduce pain processes. Specifically, I will take a neural systems approach to examine why and how social support and money can alleviate physical pain.

To do this, I outline a theoretical model suggesting that one reason that social support may reduce physical pain is because there is an overlap in the neural systems that support physical and "social pain"—the distressing experience resulting from broken social bonds. (Eisenberger & Lieberman, 2004; Eisenberger, Lieberman, & Williams, 2003). In describing this model, I will also review some of the important differences between experiences of physical and emotional pain. Last, I will propose that money or the desire for money may actually tap into a different neural system than social support and that this separate neural system may produce reductions in physical pain through different neural mechanisms. I will then suggest that if this is the case, other stimuli, in addition to money, that tap into this second system, should also be effective in pain management.

An Overlap in the Neural Systems Underlying Physical and Social Pain

In their target article, Zhou and Gao (this issue) argue that social support is important because it is a primary buffer against physical pain. They defend this argument by noting that in our evolutionary past, social support directly protected individuals from the pain of attacks from predators and thus those who had social support were more likely to evade pain and more likely to survive. In our own work, we have approached the relationship between social support and physical pain differently. Specifically, we have suggested that the fact that social support reduces physical pain is an unintended byproduct of a broader overlap in the neural systems that underlie physical and social pain processes (Eisenberger & Lieberman, 2005). Thus, to the extent that physical and social pain rely on similar neural systems, factors, such as social support, that downregulate one type of pain (social pain) should also downregulate other types of pain (physical pain). In this section, I will review evidence to support the notion that there is an overlap in the neural systems that support physical and social pain and expand on some of the consequences of such an overlap.

The hypothesized overlap in the neural systems underlying physical and social pain is based on the premise that the need for social connection is so critical for survival among mammalian species, that a lack of social connection, like a lack of other basic needs (e.g., food) is experienced as socially "painful" (Eisenberger & Lieberman, 2004). Indeed, most would agree that a lack of social connection or social rejection can "hurt." When individuals describe experiences of social rejection, loss, or abandonment, they often use physical pain words to convey their feelings, complaining of "hurt feelings" and "broken hearts." In fact, the use of physical pain words to describe feelings of social rejection or loss is common to many different languages, not just English (MacDonald & Leary, 2005). However, we have suggested that physical and social pain share more than linguistic similarities; these processes rely on similar neurotransmitters and neural circuitry for their operation (Eisenberger & Lieberman, 2004; see also MacDonald & Leary, 2005).

The first experimental evidence to suggest a possible overlap in the neural systems underlying physical and social pain came from Panksepp's work showing that opioids, known primarily for their analgesic properties, were also effective at reducing separation distress in non-human mammals. Infants treated with opiates demonstrated fewer distress vocalizations when separated from their mothers than those treated with saline (Herman & Panksepp, 1978; Kalin, Shelton, & Barksdale, 1988; Panksepp, 1998; Panksepp, Herman, Conner, Bishop, & Scott, 1978). From these observations,

Panksepp suggested that, over the course of mammalian evolution, the social attachment system, the system that ensures close social bonds, may have piggybacked directly onto the physical pain system to promote survival, borrowing the experience of "pain" to signal social disconnection (Panksepp, 1998). Because Panksepp's studies focused on the effects of opioid-related drugs, he hypothesized that the opioid system was the basis for this physical-social pain overlap (Nelson & Panksepp, 1998).

More recent work has provided additional support for the notion that physical and social pain processes overlap by showing that these processes rely on shared neural circuitry. For example, one neural region, the dorsal anterior cingulate cortex (dACC), a large structure on the medial wall of the frontal lobe, has been shown to play a role in physical and social pain processes in both humans and non-human mammals.

Neuropsychological and neuroimaging studies have shown that the dACC is involved in the affective or "distressing" component of physically painful experience. Before expanding on the role of the dACC in the distress of physical pain, it is important to note that physically painful experience can be divided into two subcomponents: the sensory and affective components (Price, 2000). The sensory component of pain relates to the intensity of the painful stimulus, which can be likened to asking: "How loud is the volume on the radio?" The affective component relates to the perceived unpleasantness of the painful stimulus and can be likened to asking: "How much does the volume of the radio bother you?" The answers to these questions will often be correlated, but each addresses distinct features of experience.

As an example of dACC involvement in the affective component of pain, chronic pain patients who have undergone cingulotomy, a surgical procedure in which a portion of the dACC is removed, often report that while they can still identify the source location of the painful stimuli, the pain "no longer bothers" them (Foltz & White, 1968). Such evidence highlights the unique role that the dACC plays in the distressing or what is sometimes referred to as the "suffering" component of pain experience. In a similar vein, neuroimaging studies have shown that dACC activity tracks the affective component of pain experience (Rainville, Duncan, Price, Carrier, & Bushnell, 1997) and correlates specifically with self-reports of pain unpleasantness (Peyron, Laurent, & Garcia-Larrea, 2000; Ploghaus et al., 1999; Sawamoto et al., 2000). Thus, it is important to note that we have suggested that it is this distressing component of painful experience, rather than the sensory component, that is shared by both physical and social pain (Eisenberger & Lieberman, 2004).

In addition to its role in the unpleasant experience of physical pain, the dACC is also involved in social pain processes as evidenced by its role in separation distress vocalizations in non-human mammals. Across many mammalian species, infants emit distress vocalizations when separated from their mothers. These vocalizations are thought to reflect separation distress in the infants and serve the purpose of cueing the mother to retrieve the infant in order to prevent prolonged separation between the two. To demonstrate the unique role that the dACC plays in the production of distress vocalizations, it has been shown that ablation of the dACC in squirrel monkeys leads to decreases in distress vocalizations but not other kinds of vocalizations (Kirzinger & Jurgens, 1982; MacLean & Newman, 1988), whereas electrical stimulation of the dACC in rhesus monkeys leads to the spontaneous production of distress vocalizations (Jurgens & Ploog, 1970; Ploog, 1981; Smith, 1945). In addition, highlighting the specific role of the dACC, rather than other neural regions, in producing distress vocalizations, stimulation of the area corresponding to Broca's area, an area known to be involved in speech production, elicits movement of the vocal chords but no distress vocalizations in monkeys and apes (Leyton & Sherrington, 1917; Ploog, 1981).

Based on the involvement of the dACC in physical pain in humans and separation distress behaviors in non-human mammals, we examined whether this neural region was also involved in social pain experience in a human sample. In this neuroimaging study of social exclusion in humans (Eisenberger et al., 2003), participants were led to believe that they would be scanned while playing an interactive ball-tossing game, over the Internet, with two other individuals who were also in fMRI scanners. Unbeknownst to participants, they were actually playing with a preset computer program. Participants completed one round of the ball-tossing game in which they were included for the entire game and a second round in which they were excluded by the other players, partway through the game. After completing the game, participants exited the scanner and filled out self-report measures of how much social distress they felt in response to being left out (e.g., "I felt rejected," "I felt meaningless.")

Upon being excluded from the game, compared to when being included, participants reported feeling significant levels of social distress and showed increased activity in a region of the dACC, very similar to the region associated with the unpleasantness of physical pain. Moreover, the magnitude of dACC activity correlated strongly with self-reports of social distress felt during the exclusion episode, 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, Schnitzler, &

Enck, 2000; Cechetto & Saper, 1987; Lane, Reiman, Ahern, Schwartz, & Davidson, 1997; Phan, Wager, Taylor, & Liberzon, 2004; Phillips et al., 1997). Finally, in response to social exclusion relative to inclusion, participants showed significant activity in the right ventral prefrontal cortex (RVPFC), a neural region typically associated with regulating physical pain experience or negative affect (Hariri, Bookheimer, Mazziotta, 2000; Lieberman et al., 2007, 2004; Ochsner & Gross, 2005; Petrovic & Ingvar, 2002; Wager et al., 2004). Consistent with this region's role in emotion regulatory processes, greater RVPFC activity was associated with lower levels of self-reported social distress in response to social exclusion, suggesting that this region may be involved in regulating the distress of being socially excluded.

Thus, neural responses to an episode of social exclusion recruited some of the same neural regions that are involved in the distress and regulation of physical pain experience. Several follow-up studies have further supported the role of physical pain-related neural circuitry in the experience of social pain by showing that (a) the finding that social distress correlates positively with dACC activity and negatively with RVPFC activity has been replicated (Eisenberger, Taylor, Gable, Hilmert, & Lieberman, 2007); (b) individuals who tend to feel more rejected in their everyday social interactions also show greater dACC activity to a scanner-based episode of rejection (Eisenberger, Gable, & Lieberman, 2007); (c) individuals who are more rejection sensitive show greater dACC activity to disapproving faces, which are thought to be cues of social rejection (Burklund, Eisenberger, & Lieberman, 2007); and (d) bereaved individuals show increased dACC activity to pictures of a lost loved one compared to pictures of a stranger (Gündel, O'Connor, Littrell, Fort, & Lane, 2003; O'Connor et al., 2008).

An overlap in the neural circuitry that underlies physical and social pain should have several functional consequences. First, as mentioned earlier, factors that regulate or potentiate one kind of pain should have a similar effect on the other. Thus, social support, which typically regulates or reduces feelings of social pain, should also be able to regulate or reduce physical pain experience—a finding that has been shown in both correlational and experimental studies (Brown, Sheffield, Leary, & Robinson, 2003; Kennell, Klaus, McGrath, Robertson, & Hinkley, 1991; King, Reis, Porter, & Norsen, 1993; Kulik & Mahler, 1989; Zaza & Baine, 2002). Thus, according to this overlap model, the fact that social support reduces physical pain is a functional byproduct of the overlapping physical and social pain systems.

A second consequence of this overlap is that individual difference factors that relate to one type of pain should relate to the other as well; thus, individuals who are more sensitive to one type of pain should be more sensitive to the other as well. Indeed, we have shown that individuals who reported greater pain sensitivity to a heat pain stimulus also rated a separate social rejection experience as being more distressing (Eisenberger, Jarcho, Lieberman, & Naliboff, 2006). Moreover, we have found that individual differences in a μ-opioid receptor gene polymorphism (OPRM1; A118G), known for its role in physical pain processes, were also associated with individual differences in social pain sensitivity (Way, Taylor, & Eisenberger, 2008).

In addition to the stated functional consequences of this physical-social pain overlap, we can use our understanding of this overlap to help make sense of some potentially odd findings observed in the literature. For example, it has been consistently shown that experiences of rejection can lead individuals to behave more aggressively toward others (Buckley, Winkel, & Leary, 2003; Leary, Twenge, & Quinlivan, 2006; Twenge, 2005; Twenge, Baumeister, Tice, & Stucke, 2001); however, aggression following rejection does not seem like a promising coping strategy. If social connection is valued and important, it would make more sense for an individual to try to reestablish social connections after a rejection episode rather than to try to act aggressively toward others. However, to the extent that social pain processes co-opted physical pain circuitry, aggressive action following rejection makes more sense, as one of the consequences of painful stimulation in animals is aggressive attacks on conspecifics (Berkowitz, 1993). Thus, aggression following the "pain" of social rejection may represent a conservation of behaviors resulting from this physical-social pain overlap and not something that is adaptive in its own right.

As a second example, the authors note the seemingly contradictory findings that (a) social support can reduce perceptions of physical pain (Brown et al., 2003) and (b) social exclusion (using the virtual ball-tossing game paradigm) can lead to decreased pain sensitivity for those who are most rejection-sensitive (MacDonald, Kingsbury, & Shaw, 2005). How is it possible for both social support and social exclusion, two polar opposites, to reduce physical pain? Although these findings seem contradictory, they actually make some sense in light of what is known about the physical pain system. Specifically, the pain system comes with its own "shut-off valve" and there are several factors that can naturally trigger this self-protective mechanism. For example, under extreme stress, when pain perception could disrupt effective coping and pain inhibition would be more adaptive, stressors can lead to temporary analgesia and numbness (Gear, Aley, & Levine, 1999; Terman, Shavit, Lewis, Cannon, & Liebeskind, 1984). Thus, in the study showing that rejection-sensitive individuals evidenced reduced pain sensitivity following social exclusion, it is possible that for rejection-sensitive individuals, exposure to social exclusion may represent a serious enough stressor that

these self-protective, antinociceptive mechanisms were engaged to reduce pain experience. Obviously this is speculative; however, it is simply meant to highlight the possibility that the nuances of the pain system itself may be able to more parsimoniously account for some of these seemingly contradictory findings without resorting to other psychological explanations (e.g., thoughts of money may reduce pain for those who are excluded).

How Might Money Manage Pain?

In a creative analysis, the authors suggest that money may be able to substitute for social support in reducing physical pain experience. The authors do not propose a specific mechanism for how this might occur; however, one could suppose several different possibilities. One way that money might be able to reduce physical pain is if thoughts about money, like social support, also relied on the computations of the physical pain system. In other words, to the extent that the need for money acts like any other basic need, a lack of money would be experienced as psychologically painful and could be hypothesized to also utilize this "pain-related" neural circuitry to ensure the presence of money. Indeed, the authors cite a study showing that the possible loss of money can activate neural structures involved in negative affect and visceral pain (insula; Knutson, Rick, Wimmer, Prelec, & Loewenstein, 2007). Based on this possibility, factors that reduce the pain of losing money (e.g., obtaining more money) should also reduce physical pain in a manner similar to the way in which factors that reduce social pain (e.g., social support) can reduce physical pain. Obviously, unlike social support, an overlap in the systems underlying physical pain processes and money would not likely be one that was selected for over the course of our evolutionary history but rather one that would be learned in the course of a lifetime. This seems plausible, however, as there are other psychological constructs that operate in a similar way; race-related prejudice is something that is not innate but learned yet still relies on primitive fear-related neural circuitry for its operation (Hart et al., 2000; Lieberman, Hariri, Jarcho, Eisenberger, & Bookheimer, 2005; Phelps et al., 2000).

However, money not only shares features with other basic human needs, it also seems to have addictive qualities; in other words, individuals can crave money (even when they already have it) in a way that they do not seem to crave social support or freedom from physical pain (when they already have it). Indeed, most neuroimaging work that has examined the characteristics of processing money show not only that the prospect of losing money is distressing, but that the prospect of gaining money is very, very rewarding (Knutson & Cooper, 2005). For example, studies that examine the brain's response to the anticipation of increasing monetary rewards consistently demonstrate activity in the nucleus accumbens (NA), a neural region known to respond specifically to the magnitude of anticipated rewards (Knutson, Adams, Fong, & Hommer, 2001; Knutson, Fong, Adams, Varner, & Hommer, 2001; Knutson, Westdorp, Kaiser, & Hommer, 2000). Moreover, this reward-related neural activity appears to be dopamine-mediated as dopaminergic projections to the NA fire selectively in response to the presentation of reward cues (Schultz, Apicella, Scarnati, & Ljungberg, 1992).

The fact that the anticipation of money recruits dopamine-related reward systems fits nicely with the notion that dopamine is primarily related to "wanting" as opposed to "liking" (Berridge, 2007). Thus, as most would agree, the rewarding properties of money seem to be due to individuals' desire for money (wanting) rather than their enjoyment of money once they have it (liking). In contrast, "liking" is thought to be mediated by opioid-related processes that code for the pleasure that an individual experiences in response to a reward stimulus. Opioid-related "liking" processes have been proposed to underlie the pleasurable experiences engendered in social relationships (e.g., social support; Depue & Morrone-Strupinsky, 2005). Thus, money-related processes (which are likely to rely on dopaminergic processes associated with "wanting") and social support-related processes (which are likely to rely on opioidergic processes associated with "liking") may rely on dissociable neural systems.

The fact that the desire for money relies on dopamine-related reward circuitry is interesting in light of the authors' hypothesis that money can reduce pain, because dopaminergic processes, like opioid-related processes, have pain-reducing properties. Specifically, dopamine activity in certain reward-related neural regions has been associated with pain suppression (Altier & Stewart, 1999); dopamine agonists, which increase dopaminergic activity, have been shown to reduce pain ratings in humans (Ertas, Sagduyu, Arac, Uludag, & Ertekin, 1998); and dopamine-related NA activity to a monetary reward task was associated with the magnitude of placebo analgesia (Scott et al., 2007). Thus, as the authors suggested, the desire for money may have pain-relieving properties. However, based on the analysis of the separate neural and neurotransmitter systems involved in the desire for money vs. social support, it is possible that the pain-relieving properties of money rely on different neural processes than the pain-relieving properties of social support.

Implications of Linking Desire for Money With Dopaminergic Reward-Related Neural Circuitry

One of the implications of the hypothesis that money can reduce pain through dopamine-related neural circuitry is that other reward-related stimuli that also

utilize this circuitry should be able to reduce physical pain as well. Thus, it would be interesting to examine whether there is something special about money that reduces physical pain or whether other dopamine-dependent reward processes, such as the desire for food or sexual behavior, would also be capable of reducing painful experience. Along these lines, it has been shown that other opioid-related reward processes, besides social support, can reduce physical pain experience; indeed, pleasant odors, images, music, and food have all been shown to lessen pain experience in animal and human subjects (Kenntner-Mabiala & Pauli, 2005; Reboucas et al., 2005; Roy, Peretz, & Rainville, 2008; Villemure, Slotnick, & Bushnell, 2003). Based on this, it seems likely that dopamine-related reward processes, besides the desire for money, could have pain-relieving properties as well.

Another follow-up question that might be more central to the authors' primary interest in the pain-relieving properties of money is whether other rewarding monetary processes could alleviate physical pain as well. The authors suggest that the reliance on money as a pain buffer is a negative coping strategy because it focuses individuals on selfish concerns and prevents them from developing supportive, empathic, loving relationships. For the most part, this seems like an accurate depiction. However, there are certain reward-related monetary processes that are less selfish. For example, as the authors mention, recent research has shown that spending money on others has the potential to increase happiness (Dunn, Aknin, & Norton, 2008). Along these lines, a recent neuroimaging study demonstrated that giving to charity activated reward-related neural circuitry (NA) to a greater degree than did receiving pure monetary rewards (Moll et al., 2006), and this finding has been replicated in subsequent work (Harbaugh, Mayr, & Burghart, 2007). Thus, not all money-related coping strategies are negative and this one in particular, giving money to charity, might also reduce physical pain.

In conclusion, the authors' account of the pain-reducing properties of social support and money is an interesting one that sparks important new questions and will likely lead to novel empirical findings. The purpose of this commentary was to suggest that the authors' analysis of social support and money as pain management mechanisms may benefit from a neural systems approach. This approach attempts to highlight the underlying neural systems that may play a role in the pain-relieving effects of social support and money and to use what is known about these underlying systems to better understand these phenomena. Conceptualizing the desire for money as a dopamine-based reward process allows us to tap into the rich literature that already exists to understand how these processes operate as well as how they relate to physical pain.

Note

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