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Decreased ventral anterior cingulate cortex activity is associated with reduced social pain during emotional support

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People feel psychological pain when they are excluded, and this pain is often attenuated when emotional support is received. It is therefore likely that a specific neural mechanism underlies the detection of social exclusion. Similarly, specific neural mechanisms may underlie the beneficial effects of emotional support. Although neuroimaging researchers have recently examined the neural basis of social pain, there is presently no agreement as to which part of the anterior cingulate cortex (ACC) is involved in the perception and modulation of social pain. We hypothesized that activity in those brain regions that are associated with social pain would be correlated with decrements in social pain induced by emotional support. To examine the effects of emotional support on social pain caused by exclusion, we conducted an fMRI study in which participants played a virtual ball-tossing game. Participants were initially included and later excluded from the game. In the latter half of the session from which participants were excluded, participants received emotionally supportive text messages. We found that emotional support led to increased activity in the left lateral/medial prefrontal cortices and some temporal regions. Those individuals who experienced greater attenuation of social pain exhibited lower ventral ACC and higher left lateral prefrontal cortex activation. These results suggest that the ventral ACC underlies social pain, and that emotional support enhances prefrontal cortex activity, which in turn may lead to a weakened affective response.

Keywords: Social exclusion; Emotional support; Anterior cingulate cortex; Prefrontal cortex; fMRI.

INTRODUCTION

Social pain involves unpleasant affect that is experienced upon social injury, more specifically when social relationships are threatened, damaged, or lost (Eisenberger & Lieberman, 2004). Exclusion may be the result of a number of factors, including rejection, death of a loved one, or forced separation. In daily life, social pain may be experienced as the deep ache of homesickness, grief, abandonment, or longing for a loved one.

Social pain underlies social regulation, in that it serves at least two functions that are crucial for the avoidance of social exclusion (Macdonald & Leary, 2005). First, learning that promotes avoidance of threatening situations is needed to minimize the number of exclusion threats that one faces. Second, quick action in response to potential threat of exclusion is needed to help sustain an inclusionary status. It is necessary to detect signs of social exclusion if useful learning and efficient responding in social relationships are to occur. It is

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likely that the brain has a specific neural mechanism for the detection of social exclusion.

Emotional support subsumes a variety of supportive behaviors, including the provision of compassion, encouragement, and compliments (Berndt & Bridgett, 1986). Emotional support can frequently help to decrease or diminish social pain. Such support may play an important role at different points in the chain of events that begins with a potential stressor and culminates in physiological stress (Cohen & Wills, 1985). First, availability of support may influence a person's ability to resist the effects of stressful events. The perception that others can and will provide necessary aid or resources may beneficially alter a person's appraisal of a potentially stressful event. Second, provision of adequate support may reduce or eliminate the stress reaction itself, or otherwise directly influence underlying physiological processes. Social support may reduce the impact of a stressful appraisal by providing a behavioral or cognitive solution to the problem. Some empirical examinations have emphasized the link between physical pain and emotional support. Pain sensitivity during a cold pressor test decreases when active verbal support or passive support (the presence of another person but no overt communication) is provided, relative to no support (Brown, Sheffield, Leary, & Robinson, 2003). In a functional magnetic resonance imaging (fMRI) study, activation in the neural systems that support emotional and behavioral threat responses to electric shock was attenuated when married women held their husbands' hands (Coan, Schaefer, & Davidson, 2006). In a magnetoencephalography study, fibromyalgia patients reported less thermal pain sensitivity and showed diminished brain activity upon tactile stimulation of a tender point when a significant other was present, as compared with levels when the patients were alone (Montoya, Larbig, Braun, Preissl, & Birbaumer, 2004). Eisenberger and Lieberman (2004) proposed that physical and social pain share a common neural basis. If this is the case, emotional support received during or shortly after social exclusion should lead to observable neural changes in those brain areas that underlie pain perception.

Eisenberger and her colleagues used fMRI to observe which brain regions are active when participants are socially isolated during a virtual game of catch (Eisenberger, Lieberman, & Williams, 2003). A significant increase in dorsal anterior cingulate cortex (dACC) activation was observed during social rejection, and self-reported

social pain was related to this increase in dACC activity. In addition, these changes in dACC activity mediated a correlation between right ventral prefrontal cortex (VPFC) activity and pain. Eisenberger et al. (2003) suggested that the right VPFC might act to regulate social pain by disrupting ACC activity. Moreover, Eisenberger and her colleagues reported that daily availability of support was correlated with dACC activity in those highly supported individuals who showed reduced neurocognitive reactivity (Eisenberger, Taylor, Gable, Hilmert, & Lieberman, 2007). It should also be noted that social pain can motivate people to seek support from others or to pursue new relationships (Leary & Springer, 2001; Maner, DeWall, Baumeister, & Schaller, 2007). We therefore hypothesized that the changes in dACC activity that occur in response to emotional support would be correlated with decreases in self-reported social pain.

There is some evidence that dACC functioning may reflect cognitive processes that do not appear to be directly related to the experience of social pain. Somerville and his colleagues performed an fMRI study in which participants made social judgments, and received positive or negative bogus feedback that was either consistent or inconsistent with their expectations (Somerville, Heatherton, & Kelley, 2006). Observed dACC activity was sensitive to expectancy violations, whereas the ventral anterior cingulate cortex (vACC) was differently responsive to emotional feedback. Bush, Luu, & Posner (2000) suggested that a meaningful distinction be made between the cognitive-dorsal and emotional-ventral parts of the ACC, with the dorsal part being particularly involved in conflict monitoring (Botvinick, Cohen, & Carter, 2004). Somerville et al. (2006) argued that the dACC activity reported in the study of Eisenberger et al. (2003) might reflect violations of the fundamental expectation of social inclusion. However, the question of which portion of the ACC is responsive to social pain remains unsettled. If the ventral portion of the ACC is involved in social pain perception, activity in this area should be related to the changes in social pain that are produced via social exclusion and/or emotional support. One of the goals of the present study was to examine activation changes as a function of the beneficial effects of emotional support, in order to identify which brain regions might operate in the attenuation of negative affect.

The aims of the current experiment were (1) to clarify which portion of the ACC is responsive to

fluctuations in social pain induced by exclusion and emotional support, and (2) to examine which areas of the brain modulate social pain upon receipt of emotional support. We conducted an fMRI study in which participants who were excluded from playing a virtual ball-tossing game were provided with emotional support. Sympathetic, empathetic, and concerned text messages served as the support.

METHOD

Participants

Twenty-six healthy undergraduate students (11 males, 15 females; mean age = 21.7 ± 1.3 years; range = 20–25 years; all right-handed) participated in the experiment. They were paid ¥ 2,000 for their participation.

fMRI task

Participants were initially told that the experimenters were interested in the neural mechanisms that underlie random decision-making, and that they would be playing a virtual ball-tossing game on a computer. Exclusion during a computer game is sufficient to cause subjective social pain (Zadro, Williams, & Richardson, 2004). Participants saw a ball, two virtual computer players on the left and right sides of the screen, an arm representing the participant on the lower center portion of the screen, and either an experimental instruction or a caring message at the top of the screen. The computer players automatically threw the ball to each other or to the participant, waiting 1.0–2.0 s between throws. The participant could return the ball to one of the computer players by pressing one of two keys on a button box.

The fMRI task consisted of nine blocks (with a duration of approximately 50 s per block, and with 20 s rest periods between blocks). The first three blocks constituted the social inclusion (SI) condition, during which participants received six or seven throws per block. The next three blocks constituted the social exclusion (SE) condition, during which participants received just one or two throws. In the SI and SE conditions, the messages provided to participants constituted experimental instructions (for example, “Do not move your head” or “Throw the ball to the left or right player at random”). Two messages per block were presented to the participant, and the message changed

halfway through each block. Twelve different sets of experimental instructions were used, and were counterbalanced across the SI and SE conditions. The last three blocks constituted the emotional support (ES) condition. These blocks were identical to those in the SE condition, except that caring messages were presented instead of instructions (for example, “Sorry, I know it was unpleasant for you to be excluded” or “I also found the task unpleasant when I was a participant”).

On completion of the virtual game, participants completed questionnaires that assessed social pain levels (Williams, Cheung, & Choi, 2000), as well as the extent to which participants thought that the experimenter’s messages reflected genuine caring (ratings on a nine-point scale). Questionnaires were completed separately for each condition. Social pain was measured using a questionnaire that assessed participants’ subjective experiences of self-esteem (“I felt liked”), belongingness (“I felt rejected”), meaningfulness (“I felt invisible”), and control (“I felt powerful”).

fMRI data acquisition

Imaging data were acquired using a Siemens AG 1.5 T scanner. A time course series of 168 volumes per participant was acquired with echo planar imaging sequences (TR = 4000 ms, TE = 48 ms, FOV = 256 mm, matrix size = 128×128 , 38 slices, thickness = 4 mm, flip angle = 90°). Functional scans lasted 11 min and 12 s, including a pre-baseline interval (20 s). After functional scanning, structural scans were acquired using T1-weighted gradient echo pulse sequences (TR = 12 ms, TE = 4.5 ms, FOV = 256 mm, flip angle = 20°).

fMRI data analysis

Imaging data were analyzed using SPM5 software (Wellcome Department of Cognitive Neurology, London, UK). The first three volumes of each fMRI run were discarded because the MRI signal was unsteady. Slice timing correction was performed for each set of functional volumes. Each set was realigned to the first volume, spatially normalized to a standard template based on the Montreal Neurological Institute (MNI) reference brain, and finally smoothed using an 8 mm FWHM Gaussian kernel. A mixed design was modeled, with the regressors of (block-designed) SI, SE, ES, and (event-related designed) response movement

(deciding which character to throw the ball toward). The durations of SI, SE, and ES were set at approximately 50 s, and those of the response movements were 0 s. Because the numbers of the responses were different among the three conditions, the activation related with the response movements was independently separated.

Random effects analyses of group were conducted using the contrast images generated for each participant. Comparisons of “SI vs. SE” and “SE vs. ES” were performed via whole-brain paired *t*-tests. The statistical threshold for these *t*-tests was set at uncorrected $p < .001$ and voxel size > 50 . Regression analyses were used to detect possible relationships between changes in social pain and brain activation. The threshold of these analyses was set at uncorrected $p < .005$ and voxel size > 10 . All coordinates are reported in MNI coordinate space.

Psychophysiological interaction (PPI) analysis (Friston et al., 1997) captures correlations between brain regions in relation to the experimental paradigm. The seed region was a 6 mm sphere in the ACC, which was the peak area of activation identified in preceding analyses. The first eigenvariate time series for the seed region was extracted for each participant. The contrast of “ES minus SE” was used in the PPI analysis, and the individual images were used to perform a random effect analysis using whole-brain one-sample *t*-tests. The threshold of the PPI analysis was set at uncorrected $p < .001$ and voxel size > 30 .

RESULTS

Figure 1 shows self-reported social pain and message supportiveness ratings for each condition. Repeated measures one-way ANOVAs were used

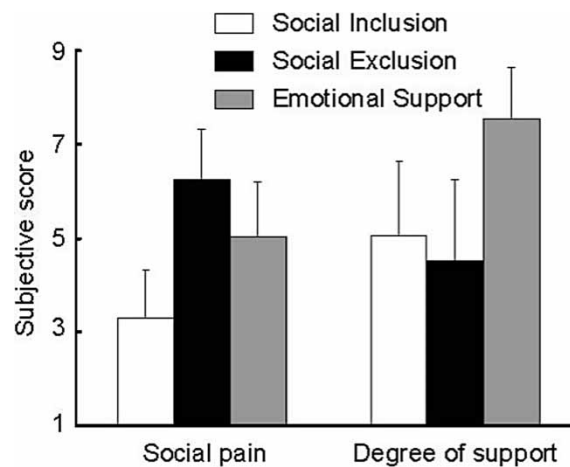


Figure 1. Subjective social pain and emotional support scores for each condition.

for statistical analysis of the behavioral data, and Greenhouse Geisser adjustments were applied. Behavioral results indicated that participants felt more social pain during the SE condition than during the SI condition, and less pain during the ES condition compared to the SE condition, $F(2, 50) = 61.3$, $\epsilon = 0.90$, $p < .001$, all comparisons: $p < .001$. The participants felt that the messages were more emotionally supportive in the ES as compared with the SI and SE conditions, $F(2, 50) = 35.7$, $\epsilon = 0.96$, $p < .001$; multiple comparison: $ES > SI$ and $ES > SE$, $p < .001$.

Table 1 shows brain activation comparisons between the SI and SE conditions. The SE condition produced activation in the insula and posterior cingulate cortex, relative to the SI condition. Activation of the somatosensory area was greater in the SI than in the SE condition. Table 2 summarizes comparisons between the SE and ES conditions. The ES condition gave rise to activation in the dorsal/ventral medial prefrontal

TABLE 1
Comparison of brain activations between social inclusion and exclusion

	MNI coordinates				
Brain region (Brodmann areas)	x	y	z	Size	T
Social exclusion > social inclusion					
R. insula (13)	44	−28	−4	72	4.27
R. PCC	6	−40	38	140	4.32
Social inclusion > social exclusion					
L. SSA	−46	−30	48	283	5.22

Notes: L: left, R: right, PCC: posterior cingulate cortex, SSA: somatosensory area, size: activation voxels, T: *t*-value.

TABLE 2
Comparison of brain activations between social exclusion and support

	MNI coordinates				
Brain region (Brodmann areas)	x	y	z	Size	T
<i>Emotional support > social inclusion</i>					
MPFC (9/10)	−4	56	32	1490	5.63
L. VLPFC (45)	−54	22	14	237	4.84
L. VLPFC (47)	−28	20	−14	126	5.59
L. TP (38)/STS (21/22)	−52	−28	−2	1693	7.35
L. STS (39)	−56	−54	16	379	4.95
R. TP (38)/STS (21/22)	54	12	−22	695	6.79
L. precuneus (31)	−6	−56	32	184	4.81
<i>Social inclusion > emotional support</i>					
R. DLPFC (10)/VLPFC (46)	44	40	28	339	5.49
R. VLPFC (9/44)	54	12	26	258	4.95
R. insula (13)	34	20	0	84	5.24
R. premotor area (6)	32	10	62	1111	5.27
L. premotor area (6)	−30	−8	68	507	5.86
R. IPL (40)	50	−44	56	1455	5.22
L. IPL (41)	−36	−50	54	135	4.84
R. precuneus (7)	10	−68	52	121	4.49
R. precuneus (7)	−10	−70	52	82	4.21
R. ITS (37)	58	−52	−6	103	4.29

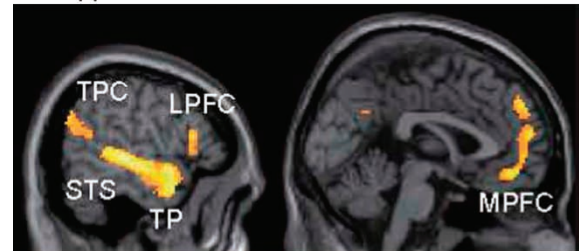
Notes: L: left, R: right, MPFC: medial prefrontal cortex, VLPFC: ventrolateral prefrontal cortex, DLPFC: dorsolateral prefrontal cortex, TP: temporal pole, STS: superior temporal sulcus, ITS: inferior temporal sulcus, IPL: inferior parietal lobule, size: activation voxels, T: t-value.

cortex (MPFC), left dorsolateral prefrontal cortex (DLPFC), VLPFC, bilateral superior temporal sulcus, bilateral temporal pole, left temporal-parietal conjunction, and precuneus, compared with the SE condition (Figure 2A). In contrast, the right DLPFC, VLPFC, insula, bilateral premotor area, inferior parietal lobule, precuneus, and right inferior temporal sulcus showed decreased activation during the ES as compared with the SE condition (Figure 2B).

We performed regression analyses to determine the brain regions involved in the perception and modulation of social pain. Increases in self-reported pain upon exclusion (the value of SE – SI) were positively correlated with increases in dorsal and ventral ACC activity (Figure 3; dACC: $t = 3.27$, $r = .56$, $p = .002$; vACC: $t = 4.98$, $r = .71$, $p < .001$). Furthermore, the right DLPFC, right superior temporal sulcus, bilateral precuneus, left fusiform gyrus, left visual cortex, left medial globus pallidus, and pons also showed similar positive correlations (each peak: $t > 3.73$, $r > .61$, $p < .001$, summarized in Table 3). There were no significant negative correlations between changes in brain activation and social pain.

On the contrary, decreases in social pain as a result of support (the value of ES – SE) were

A Support > Exclusion



B Exclusion > Support

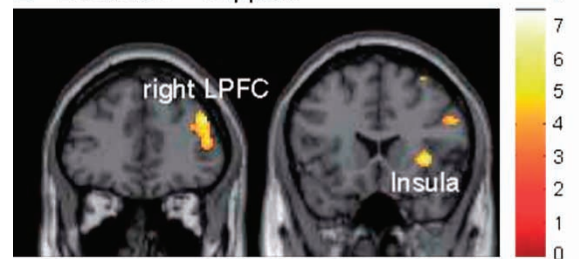


Figure 2. Activated areas: (A) emotional support > social exclusion and (B) social exclusion > emotional support. The threshold for the whole-brain paired t -tests was set at uncorrected $p < .001$ at voxel level and voxels > 50 . TPC: temporal-parietal conjunction, STS: superior temporal sulcus, TP: temporal pole, LPFC: lateral prefrontal cortex, MPFC: medial prefrontal cortex.

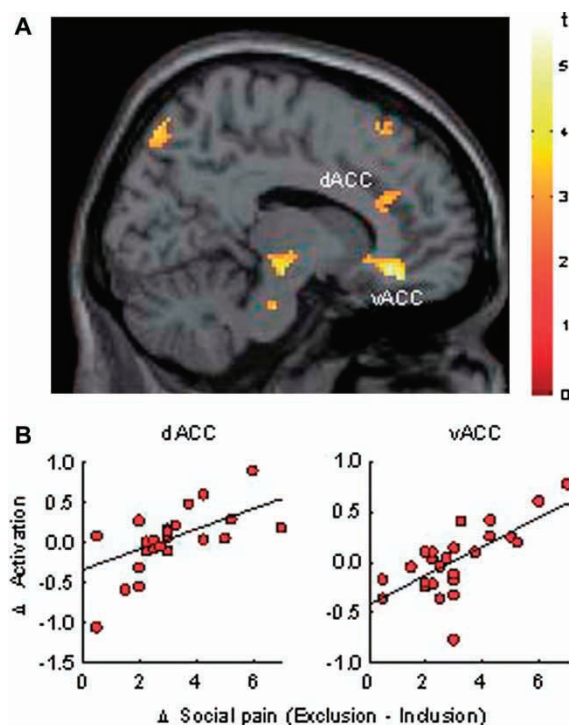


Figure 3. Relationship between changes in blood-oxygen-level dependent (BOLD) signal and subjective social pain during social exclusion. (A) Sagittal section ($x=12$) and (B) scatter plots of dACC and vACC. The threshold for these analyses was set at uncorrected $p < .005$ at voxel level and voxels > 10 . The peaks of correlation coefficients were .56 ($p = .002$) in the dACC, and 0.71 ($p < .001$) in the vACC.

positively correlated with decreases in vACC activity, as opposed to dACC activity (Figure 4; $t = 3.22$, $r = .55$, $p = .002$). Activation in the right superior parietal lobule and left visual cortex also showed positive correlations with social pain (each peak: $t > 3.53$, $r > .58$, $p < .002$). Reductions in social pain were negatively correlated with the left DLPFC, left superior temporal sulcus, and right caudate activation (each peak: $t > 3.73$, $r < -.61$, $p < .002$, summarized in Table 3).

The vACC activity we observed was positively correlated with both the degree of social pain experienced and the decrease in social pain produced by support. We therefore defined the 6 mm sphere with the peak in vACC activation [$10, 32, -10$] as the seed region of the PPI analysis. This analysis was conducted to estimate functional integration in the ES minus SE subtraction condition. The left DLPFC, postcentral gyrus, posterior cingulate cortex, visual cortex, and cerebellum showed negative coupling with the vACC for the ES compared with the SE

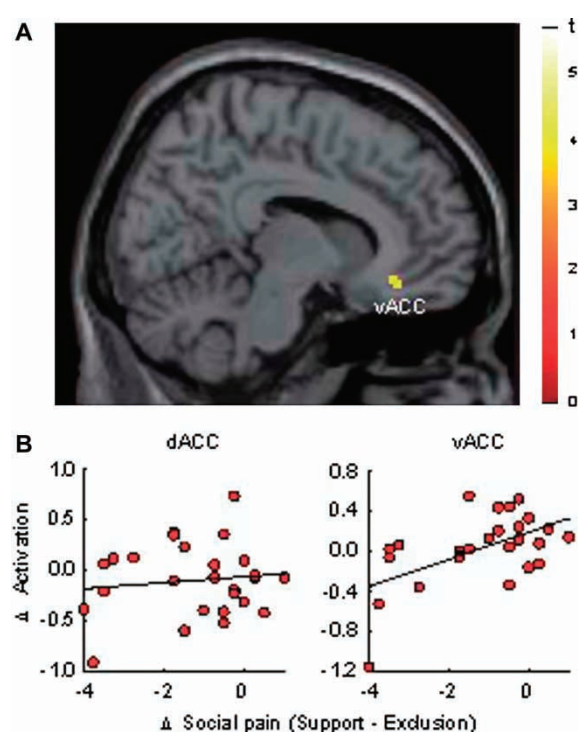


Figure 4. Relationship between changes in BOLD signal and subjective social pain during receipt of emotional support. (A) Sagittal section ($x=10$) and (B) scatter plots of dACC and vACC. The coordinate of dACC in the scatter plot is the same as in Figure 3. The correlation coefficients were .10 (ns) in the dACC, and .55 ($p = .002$) in the vACC.

condition, and there was no positive connectivity with the vACC (Table 4).

DISCUSSION

The main goal of the current study was to identify brain regions involved in the perception and modulation of social pain, by examining the effects of both social exclusion and support. Participants were excluded during a virtual ball-tossing game, and they then received emotionally supportive messages. Social pain increased during social exclusion and decreased when emotional support was provided. vACC activation was strongly correlated with changes in social pain levels, as a function of both social exclusion and support. Left DLPFC activity was negatively correlated with social pain levels and dACC activity during the receipt of emotional support. These results suggest that the vACC may be involved in the perception of social pain and is regulated by the functioning of the left DLPFC.

TABLE 3
Regression analyses between brain activation and social pain

	MNI coordinates					
Brain region (Brodmann areas)	x	y	z	Size	T	r
Positive correlation between changes of brain activation and social pain in $\Delta SE - SI$						
R. DLPFC (8)	18	30	52	103	4.48	0.67
dACC (8)	16	36	26	88	3.55	0.59
vACC (32)	12	34	-10	339	4.98	0.71
L. MGP	-10	0	2	96	4.71	0.69
R. STS (21)	58	-8	-14	133	4.57	0.68
R. STS (22/39)	60	-62	14	82	5.13	0.72
L. FG (37)	-26	-38	-18	143	5.63	0.75
Negative correlation between changes of brain activation and social pain in $\Delta SE - SI$						
No region						
Positive correlation between changes of brain activation and social pain in $\Delta ES - SE$						
vACC (32)	10	32	-10	16	3.22	0.55
R. SPL (7)	30	-58	46	24	3.53	0.59
L. VC (18/19)	-40	-82	-12	125	4.54	0.68
Negative correlation between changes of brain activation and social pain in $\Delta ES - SE$						
L. DLPFC (46)	-34	24	22	44	4.12	0.64
L. STS (22)	-50	4	-8	65	3.75	0.61
R. caudate	12	2	22	49	3.72	0.61

Notes: L: left, R: right, vACC: ventral anterior cingulate cortex, MGP: medial globus pallidus, STS: superior temporal sulcus, FG: fusiform gyrus, SPL: superior parietal lobule, VC: visual cortex DLPFC: dorsolateral prefrontal cortex, size: activation voxels, T: t-value, r: correlation coefficient.

Subjective effects of social exclusion and emotional support

The participants in the present study felt social pain during exclusion, even though they recognized that their partners during the virtual game were not real people. In a psychological study, Zadro et al. (2004) reported that participants who were excluded during a computer-based task felt

social pain that was comparable to that felt by participants who were excluded by actual people. For primates and many other species, social exclusion is highly detrimental, and members of these species are therefore quite attuned to its possible effects. In human society, exclusion can herald various difficulties, including loss of contact with important others or loss of other resources. Zadro and her colleagues interpreted their results

TABLE 4
Psychophysiological interaction analysis under contrast of "social support minus social exclusion" subtraction condition

Brain region (Brodmann areas)	MNI coordinates			Size	T
	x	y	z		
Positive connectivity					
No region					
Negative connectivity					
L. DLPFC (9)	−26	36	18	31	4.49
L. postcentral gyrus (6)	−46	−18	28	36	4.78
R. posterior central gyrus (30)	20	−64	6	96	5.81
R. visual cortex (19)	4	−86	30	49	4.22
L. cerebellum	−24	−62	−24	141	5.07

Notes: L: left, R: right, DLPFC: dorsolateral prefrontal cortex, size: activation voxels, T: t-value.

as strong evidence for a very primitive and automatic adaptive sensitivity to even the slightest hint of social exclusion (Zadro et al., 2004).

Emotional support alleviated self-reported social pain in the present study. Surprisingly, however, experimental studies in social psychology have failed to show that receiving emotional support is consistently beneficial in social exclusion situations (Bolger, Zuckerman, & Kessler, 2000). For example, perceived availability of emotional support has a beneficial effect on adjustment to heart attacks, whereas support received from significant others actually appears to have harmful effects (Vicki, 1993). One of a few studies that demonstrated a beneficial effect of received support was an experiment conducted by Bolger and Amarel (2007). In their study, participants were led to expect a stressful speech task, and a confederate peer provided support in a way that was either visible (explicit) or invisible (unnoticed, not interpreted as support). Invisible support reduced emotional reactivity; however, visible support was ineffective. Supportive behavior that occurred outside of the recipients' awareness was effective in lowering emotional reactivity to a significant stressor (Bolger & Amarel, 2007). Of course, the support used in the current study should be considered explicit. It is necessary to further examine which type of social support is more effective under different conditions.

In the case of social pain, the source is some social entity. Trying to exert control over the source of social pain may therefore be tantamount to attempting to control another person. The participants in the current study could not exert control over the source of their social pain, and thus the beneficial effects that our participants experienced could not be due to control of the source. Other possible causes of the decrease could include reappraisal and suppression. Reappraisal is a form of cognitive change that involves construing an emotion-eliciting situation in a way that changes its emotional impact (Lazarus & Alfert, 1964), whereas suppression is a form of response modulation that involves inhibiting ongoing emotion-expressive behavior (Gross & Levenson, 1993). Reappraisal and suppression appear to have different effects on negative emotionality elicited by film clips (Gross, 1998), in that suppression decreases behavioral expression of negative emotions but not subjective experience, whereas reappraisal decreases both the subjective experience of negative emotions

and the behavioral expression of them. Reappraisal may be generally more effective for emotional regulation, but it is necessary to examine this process in social contexts.

Neural effects of social exclusion and emotional support

We predicted that social exclusion would activate the ACC, and that this area might be deactivated upon receipt of emotional support. However, significant changes in ACC activity were not observed in the direct comparisons among the SI, SE, and SS conditions, which was not the case for subjective social pain ratings. In the ball-tossing game of Eisenberger et al. (2003), the dorsal portion of the ACC was activated during social exclusion. While it was explained to the participants in our study that the other players in the game were computerized, the participants in Eisenberger et al. (2003) believed that the other players were real persons playing over a network. The degree of ACC activity during social scenarios may be influenced by whether the relevant parties are real humans. Some studies suggest that neural responses differ according to whether the opponent in an economic trust game is human or a computer (McCabe, Houser, Ryan, Smith, & Trouard, 2001). Similar findings pertain to the rock-paper-scissors game (Gallagher, Jack, Roepstorff, & Frith, 2002), prisoner's dilemma game (Rilling, Sanfey, Aronson, Nystrom, & Cohen, 2004), and "chicken" game (Fukui et al., 2006). Whether an opponent is human or not may be an important factor in social interaction scenarios even if there is no competitive element, and this factor may account for differences between our findings and those of Eisenberger et al. (2003).

The most important finding of the current study is that ventral ACC activity appears to reflect changes in subjective social pain that accompany both social exclusion and support. Our findings favor a general role for the vACC in social and emotional evaluation. As opposed to the case of the vACC, dACC activity appears to reflect the effects of exclusion alone, with no significant correlation between dACC activity and the support effect. In the study of Eisenberger and her colleagues, activation of the dorsal ACC was associated with increased pain during a social exclusion task (Eisenberger et al., 2003). Their results are not consistent with the prevalent theory

of a dorsal–cognitive/ventral–emotional functional dissociation within the ACC (Bush, Luu, & Posner, 2000; Mohanty et al., 2007). dACC activity appears to signal the occurrence of cognitive conflicts during a variety of tasks (Carter et al., 1998). Somerville and his colleagues demonstrated that the dACC is sensitive to social expectancy violations, with the vACC being differentially responsive to social feedback (Somerville et al., 2006). Our findings also suggest that the ventral part of the ACC may be more responsive to social pain than the dorsal part. vACC activation during social support subsequent to social pain may be related to positive effects of support on physical pain. The findings of an fMRI study by Coan et al. (2006) are consistent with our results. In their study, married women were subjected to the threat of electric shock while holding their husband's hand, the hand of an anonymous male experimenter, or no hand at all. vACC activation was attenuated in the spouse and stranger hand-holding conditions, compared with no hand-holding. Evidence suggests that the vACC may be sensitive to the beneficial effects of support on both physical and social pain.

The left lateral prefrontal cortex was activated during the emotional support condition, and activity in the dorsolateral portion was correlated with the beneficial effects of support on subjective pain and vACC activity. Activity in this region is associated with emotional regulation through reappraisal (i.e., the reinterpretation of a stimulus so that it no longer elicits a negative response) (Ochsner et al., 2004; Phan et al., 2005), and also with cognitive control processes that are engaged in the generation and maintenance of reappraisal strategies (Smith & Jonides, 1999). The DLPFC seems to be involved in the regulation of the vACC activity that underlies social pain, and our finding of an LPFC–vACC connection appears to be novel. The medial frontal area (including the vACC) has intrinsic corticocortical connections with the orbital prefrontal area (Ongur & Price, 2000), and a connectivity analysis of a cognitive task has reported that vACC activity is negatively correlated with orbitofrontal cortex activity (Butler et al., 2007). Further studies are needed to examine whether the regulatory functions of the DLPFC are direct or indirect, perhaps occurring via other frontal areas such as the orbitofrontal cortex.

It must also be noted that right prefrontal cortex activity was decreased in the emotional support condition as compared to the exclusion

condition. There is an influential brain model of hemispheric asymmetry in emotional processing, such that negative emotions appear to be lateralized in the right prefrontal cortex, as shown by functional brain imaging studies (Canli, Desmond, Zhao, Glover, & Gabrieli, 1998). Given that activity in the right prefrontal cortex is involved in negative emotional processing, the attenuation of such activity via emotional support would appear to be a likely possibility.

The MPFC and some temporal lobe regions showed robust activation during the emotional support condition as compared with the social exclusion condition. The MPFC, superior temporal sulcus, and temporal pole are consistently active in imaging studies of “theory of mind”, which is the ability to explain and predict other people's behavior by attributing to them independent mental states such as beliefs and desires (Gallagher & Frith, 2003). Our results suggest that accepting emotional support may be accompanied by an understanding of the supporter's feeling state. Some studies suggest that the MPFC is the key region involved in mentalizing (Gallagher et al., 2002; McCabe et al., 2001), and it is proposed that MPFC activity occurs during the determination of another's mental state (Gallagher & Frith, 2003). The precise role played by the temporal regions in our findings is still unclear. It has been reported that some temporal regions are associated with understanding the meaning of stories and cartoons involving people, with or without the requirement to mentalize (Gallagher et al., 2000). The functions of these temporal regions might relate to abilities that aid mentalizing, and it could be from these pre-existing abilities that mentalizing has evolved (Gallagher & Frith, 2003).

Shared pain system

Some researchers have argued that the aversive emotional state of social pain is the same unpleasantness that is experienced in response to physical pain (Eisenberger & Lieberman, 2004; Macdonald & Leary, 2005). The existence of nonphysical pain has already been proposed, and it is suggested that functional analogous, nonphysical pain focuses attention on significant social events and promotes correction and avoidance of such events in the future (Thornhill & Thornhill, 1989). The ACC is involved in social pain during exclusion. Because ACC activation appears to be related to the

affective or distressing component of physical pain, Eisenberger et al. (2003) proposed that social and physical pain share a common neural mechanism. They proposed that this shared system is responsible for detecting cues that might be harmful to survival, as well as for recruiting attention and coping resources to minimize threat. Such overlap would be evolutionarily adaptive. Because of the need for maternal care of mammalian infants, it has been suggested that the pain mechanisms involved in detecting and preventing physical danger were co-opted by a more recently evolved social attachment system for the detection and prevention of social separation (Panksepp, 1998).

This shared system may constitute one important component of a cognitive architecture underlying empathy (Decety & Jackson, 2004). Some studies suggest that the perception of pain in others elicits the affective processing of pain through activation of the ACC and insula (Jackson, Meltzoff, & Decety, 2005; Singer et al., 2004). A meta-analysis revealed that activation sites in the ACC follow a clear caudo-rostral organization base on the target (self or other) of pain (Jackson, Rainville, & Decety, 2006). Perception of pain in the self is associated with more caudal regions of the ACC, while perception of pain in others is represented in more rostral ACC regions. Furthermore, imagining oneself in pain maps onto the more caudal cluster of the ACC, consistent with the proposed self-other distinction (Jackson, Brunet, Meltzoff, & Decety, 2006). Jackson et al. (2006) proposed a functional model of the ACC based on subject of experience (self or other) and consequently the experimental proximity, tangibility or self-embodiment of pain. There is a proximo-distal continuum of triggers for the representation of pain, with somatic inputs producing the more robust activation of pain representations along with a correspondingly vivid pain experience, and pain-related cues producing a weaker activation of pain representations. The social pain in Eisenberger et al.'s (2003) study was localized in a more caudal part of the ACC than the social pain observed in the current study. Participants in Eisenberger et al. (2003) believed that their partners in the ball-tossing game were real persons, and thus they may have felt more intense pain than our participants.

Lamm and his colleagues suggested that the shared pain system is affected by cognitive appraisals (Lamm, Batson, & Decety, 2007). In their study, the participants observed painful facial expressions on a video clip of a medical treatment. Cognitive appraisals were manipulated by indicating to participants that the depicted medical treatment had or had not been successful. Activation of the ACC was greater when treatment was thought not to be effective than when it was thought to be effective. It appears that cognitive appraisal processes play an important role in the perception of pain in others, such that they enable us to evince supportive behavior even in potentially dangerous or harmful situations.

CONCLUSION

The current study revealed that vACC activity might represent a neurocognitive index of social pain, and a possible mechanism that underlies the beneficial effects of emotional support. Emotional support could engage the regulatory processes of the left prefrontal area, which in turn work to attenuate the social pain that is generated in the vACC. This mechanism can be considered to be one possible foundation of the relationship between emotional support and mental/physiological health.

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