

Empathy for the social suffering of friends and strangers recruits distinct patterns of brain activation

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Humans observe various peoples' social suffering throughout their lives, but it is unknown whether the same brain mechanisms respond to people we are close to and strangers' social suffering. To address this question, we had participant's complete functional magnetic resonance imaging (fMRI) while observing a friend and stranger experience social exclusion. Observing a friend's exclusion activated affective pain regions associated with the direct (i.e. firsthand) experience of exclusion [dorsal anterior cingulate cortex (dACC) and insula], and this activation correlated with self-reported self-other overlap with the friend. Alternatively, observing a stranger's exclusion activated regions associated with thinking about the traits, mental states and intentions of others ['mentalizing'; dorsal medial prefrontal cortex (DMPFC), precuneus, and temporal pole]. Comparing activation from observing friend's vs stranger's exclusion showed increased activation in brain regions associated with the firsthand experience of exclusion (dACC and anterior insula) and with thinking about the self [medial prefrontal cortex (MPFC)]. Finally, functional connectivity analyses demonstrated that MPFC and affective pain regions activated in concert during empathy for friends, but not strangers. These results suggest empathy for friends' social suffering relies on emotion sharing and self-processing mechanisms, whereas empathy for strangers' social suffering may rely more heavily on mentalizing systems.

Keywords: empathy; social pain; anterior cingulate cortex; medial prefrontal cortex

INTRODUCTION

Empathy allows humans to understand and share one another's emotional experiences and is important for successful social interactions (Eisenberg and Miller, 1987; Davis, 1994). According to Hoffman (2000), empathy refers to experiencing an affective response that is more consistent with another person's situation than one's own situation (Hoffman, 2000), which suggests that vicarious emotions are pivotal to empathy. In line with this suggestion, brain imaging studies have shown that observing another person's physical pain corresponds with activation in the dorsal anterior cingulate cortex (dACC) and insula (particularly the anterior insula; Singer *et al.*, 2004; Jackson and Decety, 2005; Gu and Han, 2007), regions that are known to code for the affective distress associated with the firsthand experience of pain (Rainville *et al.*, 1997). It has been suggested that mutual activation in these brain regions during the firsthand experience and observation of physical pain creates an affective link between the observer and target, allowing humans to 'feel' another person's distress (Singer *et al.*, 2004; Jackson *et al.*, 2005; Lamm *et al.*, 2007; Xu *et al.*, 2009).

However, the experience of empathy is not specific to observing another person in physical pain. Many of our daily experiences of empathy occur as part of our everyday social interactions, in which we empathize with others' social emotions and suffering (Masten *et al.*, 2011; Rameson *et al.*, 2012; Zaki *et al.*, 2009). Interestingly, brain imaging studies find increased activity in the dACC and anterior insula among participants who are experiencing social exclusion, suggesting that the distress associated with social exclusion relies on shared neural systems as those coding for the affective component of

pain, a phenomenon referred to as 'social pain' (Eisenberger *et al.*, 2003, 2004; MacDonald and Leary, 2005; DeWall *et al.*, 2010). Given similar activation in the dACC and anterior insula in response to (i) experiencing physical and social pain and (ii) in response to empathizing with experiences of physical pain, it is possible that empathy for social exclusion also activates the dACC and anterior insula.

To date, one study has examined the neural basis of empathy for social exclusion among adults (Masten *et al.*, 2011). While undergoing a functional magnetic resonance imaging (fMRI) scan, participants observed what they believed was a live game of catch ('Cyberball'; Williams *et al.*, 2000) played among strangers over the Internet. The game was in fact preset by the experimenters, and all participants observed the stranger's exclusion during the game. The main effect of observing a stranger's exclusion showed increased activation in the dorsal medial prefrontal cortex (DMPFC) and precuneus, which are associated with mental state attribution (i.e. 'mentalizing'; Gallagher and Frith, 2003; Mitchell *et al.*, 2005; Lieberman, 2010). The brain regions involved in affective pain processing, such as the dACC or anterior insula, however, were not significantly active when observing a stranger's exclusion.

Based on the results reviewed above, it could be the case that empathy for social pain and physical pain rely on distinct neural mechanisms. However, recent findings suggest that the story may be more complicated. That is, the observer's relationship with the victim, specifically whether the observer identifies with the victim, may moderate which neural mechanisms are recruited in empathy for social pain. Behavioral research has shown that people systematically underestimate targets' social pain in response to social exclusion (using the Cyberball paradigm); however, identification with a target increases ratings of the target's social pain (Nordgren *et al.*, 2011). In contrast, research on empathy for physical pain has found increased activation in dACC and insula for both close others (Singer *et al.*, 2004) and strangers (Jackson *et al.*, 2005), although these responses are sensitive to some social factors such as the target's ingroup membership (Xu *et al.*, 2009) and reputation (Singer *et al.*, 2006). By extension, although

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emotion sharing may occur less readily for strangers' social suffering, and may therefore recruit mentalizing regions without recruiting dACC and insula, emotion sharing may occur more readily when there is identification with a close other, corresponding with increased activation in dACC and insula.

An important component of identification, which may increase empathy in social situations, is the degree of overlap between cognitive representations of the self with another—or 'self-other overlap' (Aron et al., 1991). When imagining the emotional state of a target with whom we experience self-other overlap, we may react to the thought of ourselves in a similar situation, and hence, vicarious emotion sharing is probable (Lerner, 1980). This suggestion is consistent with simulation theories of empathy which suggest that humans understand (i.e. 'simulate') others' emotional states by imagining what they themselves would feel in a similar situation (Goldman, 1992; Davies and Stone, 1995; Gallese and Goldman, 1998). In line with this idea, an EEG study found that self-other overlap increases vicarious neural responsiveness to others' errors (Carp et al., 2009). Self-other overlap may facilitate simulation with a close other relative to a stranger given the inclusion of the close other in self-representations. Indeed, neuroimaging studies have shown that representations of close others activate MPFC (BA 10), a region consistently shown to engage during self-processing (Mitchell et al., 2006; Zhu et al., 2007; Wang et al., 2012). Thus, self-other overlap may enhance vicarious emotions in dACC and insula during empathy via simulation processes carried out in the MPFC.

Here, we test whether self-other overlap enhances vicarious affect sharing during empathy for social pain. We predicted that participants would show activation in the affective pain regions when observing a friend (someone with a high-degree of self-other overlap) experience social exclusion and those greater self-reported feelings of self-other overlap with the friend would be associated with this activation. Moreover, consistent with the idea that self-other overlap with a target engages self-processing, we predicted that empathy for a friend's social exclusion relative to a stranger's social exclusion would be associated with stronger activation in regions that have been previously linked with self-processing (e.g. the MPFC; Gusnard et al., 2001; Kelley et al., 2002; Mitchell et al., 2005, 2006; Northoff et al., 2006; Zhu et al., 2007; Ma and Han, 2011) in addition to increased activation in affective pain regions. Finally, to the extent that some degree of self-relevant processing (e.g. the target is tied to 'me') is necessary for an individual to show affective empathy for another's social pain, we hypothesized that activation in the MPFC would be functionally coupled with

activation in affective pain regions while participants observed a friend's social exclusion and that this functional connectivity would be stronger than when observing a stranger's social exclusion.

METHODS

Participants

Sixteen, right-handed, native Chinese university students (12 females/4 males), ages, $M=21.69$, $s.d.=2.12$, participated in the study. Participants completed written consent in accordance with the local ethics committee and were paid for their participation.

Procedure

Participants came to the scanner with their gender-matched best friend and were told that the study examined how the brain responds to watching live, coordinated interactions (i.e. they were blind to the purpose of the study). Participants and their friends were told that they would first each play separate games of Cyberball with two real strangers over the Internet in a room adjacent to the scanner and that they would then watch their friend's game of Cyberball live while undergoing an fMRI scan. The reason why participants played their own Cyberball game outside of the scanner first was to that participants believed that their friend would view their own game during the friend's scan. While playing 'Cyberball', each participant tossed a computerized ball back and forth with the two other 'players,' who were actually computer controlled. Importantly, when the participant played the initial game of 'Cyberball' in the room adjacent to the scanner (prior to the scan), the participant was not excluded, contrary to previously used versions of Cyberball. Instead, they were included by the other two 'players' equally throughout the game.

After participating in this initial game of Cyberball, each participant was then asked to observe while: (i) their friend plays a round of Cyberball with two strangers and (ii) a stranger plays a round of Cyberball with those same two strangers while undergoing an fMRI scan (Figure 1). Participants were verbally instructed as to whose Cyberball game they were observing and a photograph of their friend and stranger was shown at the bottom of the screen. All friends' photos showed a neutral facial expression and all participants observed the same gender-matched stranger photograph. In reality, these Cyberball games were pre-recorded videos that were the same for all participants, and not actually their friend (or strangers) playing. Each round lasted 2 min, 45 s. During both of these scans, participants observed Cyberball games in which the supposed friend in one game

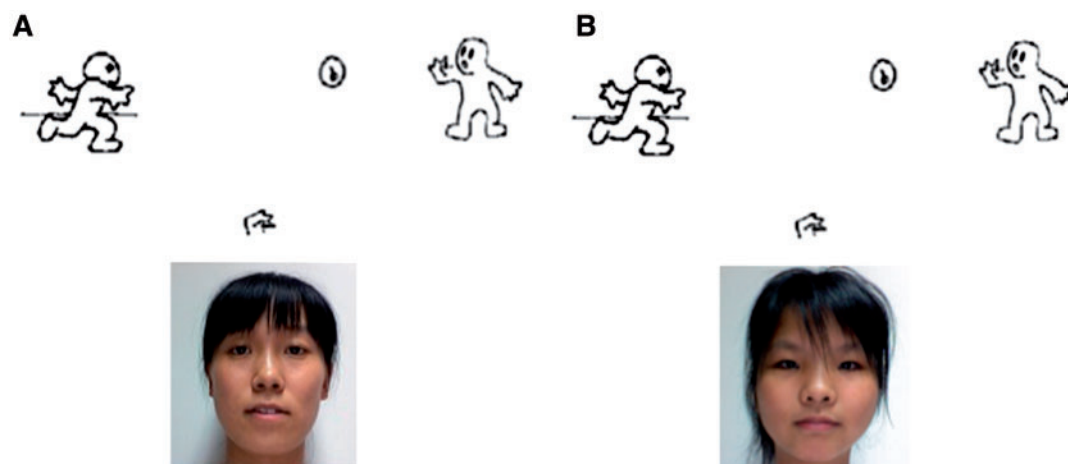


Fig. 1 Pictorial representation of Cyberball task for observing a (A) stranger's Cyberball game and (B) friend's Cyberball game. Actual Cyberball games were video recordings, not static images.

and stranger in another game were systematically excluded—they stopped receiving the ball from players after an initial 10 throws (24s) during which all players were included. This paradigm has been shown to reliably evoke the experience of social exclusion and produce feelings of distress during the firsthand experience of Cyberball exclusion (Eisenberger *et al.*, 2003, 2007; Zadro *et al.*, 2004; Van Beest and Williams, 2006; Taylor *et al.*, 2007) and similar feelings during the observation of another person's Cyberball exclusion (Masten *et al.*, 2011). Consistent with this, funneled debriefing responses with participants after scanning indicate that they believed the games were real. Scan order (friend's Cyberball game *vs* stranger's Cyberball game) was counterbalanced across participants to control for order effects of watching either target before the other.

Behavioral measures

Manipulation check

Following the scan, participants completed a manipulation check which asked the following yes/no questions about the interactions they observed in both scans: 'one player was treated unfairly by the other players', 'one player seemed left out by the others' and 'all the players got the ball the same amount'. Next, participants completed a questionnaire used by Masten *et al.* (2011), which asked participants a series of questions concerning how they thought the rejected participant felt during the game, or 'imagined negative emotion' (i.e. he/she felt like an outsider; Cronbach's $\alpha = 0.89$), as well as how the participant felt for the rejected participant, or 'shared negative emotion' (i.e. it hurt to watch him/her play; Cronbach's $\alpha = 0.82$). Participants filled out this set of questionnaires for both their friend and the stranger separately. All questionnaires were presented in Chinese.

Self-other overlap questionnaire

Participants also completed the Inclusion of Other in the Self Scale (Aron *et al.*, 1992), a reliable and valid measure of incorporating close others into the self-concept (Aron *et al.*, 1992) to measure the extent of self-other overlap participants felt towards the specific friend they observed during their scan. The scale measures self-other overlap with a close other via a pictorial display of seven Venn diagrams that indicate no to extreme self-other overlap. Each Venn diagram corresponds with numbers 1 through 7, with 7 being the most overlapping circles. Each participant therefore receives a 1–7 score representing the degree to which they conceptually associate the friend as included in their self-view. This scale is designed to measure degree of self-other overlaps with close others. Thus, it was not included to measure self-other overlap with a stranger.

fMRI data acquisition

fMRI data were collected using a Siemens Trio 3-Tesla head-only MRI scanner at the Chinese Academy of Sciences Institute of Biophysics. The task was presented to participants on an LCD screen in the scanner. Whole-brain blood oxygenation-level-dependent (BOLD) functional scans were acquired during the 2 min 45 s task (echo-planar T2-weighted gradient-echo, TR = 2000 ms, TE = 30 ms, flip angle = 90°, matrix size = 64 × 64 × 32 axial slices, FOV = 24 × 24 cm; 4 mm thick, voxel size = 3.44 × 3.44 × 5 mm). In addition to the functional images acquired during the tasks, a set of high-resolution T1-weighted structural images were acquired coplanar with the functional scans (matrix size 256 × 256 × 176 matrix with a spatial resolution of 1 × 1 × 1 mm, TR = 2600 ms, TE = 3.02 ms, inversion time (TI) = 900 ms, flip angle = 8°, thickness = 1 mm).

fMRI data analysis

Neuroimaging data were preprocessed and analyzed with SPM5 (the Wellcome Trust Centre for Neuroimaging, London, UK). Preprocessing for each participant's images included skull-stripping using Brain Extraction Tool (BET; Smith, 2002) to enhance preprocessing accuracy, spatial realignment to correct for head motion, normalization into a standard stereotactic space as defined by the Montreal Neurological Institute and spatial smoothing using an 8-mm Gaussian kernel, full-width at half-maximum, to increase the signal-to-noise ratio.

Each round of Cyberball was modeled at the first (individual subject) level as a run with a period of inclusion and exclusion modeled as blocks within the run. Although inclusion occurred for 24 s and the remaining of the block was exclusion, we only contrasted the first 24 s of the inclusion period with 24 s of the exclusion period. The remaining exclusion time was coded with a zero in the contrast in order for variance associated with this portion of the task to be modeled in our design, but not included in the contrast. This ensures that effects associated with exclusion are not influenced by longer exclusion periods in the 2 min 45 s runs. Linear contrasts among these conditions were computed for each participant as a measure of differential BOLD activation, and then entered into random effects analyses at the group level for statistical inference. All figures display activation on participants' mean anatomical images calculated in SPM5.

Group-level, whole-brain analyses

All whole-brain contrasts used a voxel-wise threshold of $P < 0.005$ with a 25-voxel extent threshold. We used this joint voxelwise and cluster-size threshold because these parameters provide a balance between Types I and II errors and are a conservative parallel of false-detection rates in social psychological behavioral studies (Lieberman and Cunningham, 2009). First, group-level analyses were computed across the whole brain first for 1) activation while observing a friend's exclusion compared to inclusion and 2) activation while observing a stranger's exclusion compared to inclusion. Second, to examine whether the degree of self-reported self-other overlap with the friend correlated with brain activation while observing the friend's exclusion, a whole-brain regression analysis was computed using the whole-brain simple effect contrast of observing the friend's exclusion and adding participants' self-other overlap scores as a regressor. We chose to look at the friend's exclusion period only for this correlation because any relationship between friend inclusion and self-other overlap would complicate interpreting the correlation coefficient. Third, to narrow in on what activation was unique to empathizing with a friend (someone with a high degree of self-other overlap) compared to a stranger (someone with a low degree of self-other overlap), we also compared activation in the interaction between exclusion and identification: [exclusion > inclusion during a friend's Cyberball game] > [exclusion > inclusion during a stranger's Cyberball game]. This interaction was modeled at the first-level of analysis and then compared as a *t*-test at the group level.

Psychophysiological interactions

Finally, we conducted psychophysiological interaction (PPI) analyses to test whether self-other overlap modulated the relationship between MPFC and affective pain regions during empathy for social exclusion. PPI measures functional connectivity between the time series of a seed voxel of interest (VOI) and the time series of the rest of the voxels in the brain (Friston *et al.*, 1997; Gitelman *et al.*, 2003). As a seed VOI, we used the peak voxel within the MPFC that was associated with the friend' exclusion relative to inclusion contrast

($x = -4$, $y = 46$, $z = 0$). We chose this seed voxel because we predict that self-processing corresponds with vicariously feeling the pain of exclusion in the friend condition. Given that the MPFC region has been associated with self-other overlap, we hypothesized that it should be a cluster that shows this relationship with the dACC and insula.

PPI analyses were first performed for the effect of observing exclusion to inclusion separately for friends and strangers. Then, first-level contrast estimates from each subject's PPI analysis from friend (exclusion–inclusion) and stranger (exclusion–inclusion) were compared as a paired-samples t -test at the group level of analysis to examine what regions were more functionally connected with MPFC during empathizing for friends relative to strangers.

RESULTS

Behavioral measures

Manipulation checks

Perceived exclusion. Responses to the manipulation check questions showed that all participants (except one who did not complete the form) believed that both their friend and the stranger were excluded during the 'Cyberball' games.

Imagined negative emotions and shared negative emotions for target. Participants were equally likely to report that a friend and stranger's feelings were hurt from the exclusion [‘imagined negative emotions’; M friend = 3.81, $s.d.$ = 0.68; M stranger = 3.78, $s.d.$ = 0.62, $t(14) = 0.32$, $P = 0.76$]. However, when reporting their own feelings, participants reported feeling significantly more negatively for the excluded friend ('shared negative emotion'; $M = 3.77$, $s.d.$ = 0.47) than the excluded stranger [$M = 3.48$, $s.d.$ = 0.50; $t(14) = 4.04$, $P < 0.001$]. One participant who did not complete all of the questions about how the stranger felt in the scanner was not included in these analyses.

Inclusion of other in the self scores

All participants selected some to a high degree of self-other overlap with their friend, $M = 4.25$, $S.D. = 1.34$, range = 2–7, which is consistent with previous studies measuring self-other overlap with friends using this measure (Wauugh and Fredrickson, 2007; Kang et al., 2010).

fMRI results

Whole-brain main effects. To examine brain activation during the observation of a stranger's social exclusion, we compared activation during the observation of a stranger's social exclusion to social inclusion. Replicating the prior work (Masten et al., 2011), this contrast showed significantly greater activation in DMPFC, precuneus, and temporal poles (TP; Table 1 and Figure 2).

We also examined brain activation during the observation of a friend's social exclusion vs inclusion. The main effect of observing a friend's social exclusion compared to social inclusion showed increased activity in dACC and left insula and MPFC (Table 1 and Figure 2).

Neural activity during friend's exclusion that correlated with self-reported self-other overlap. We hypothesized that self-reported self-other overlap with the friend would correspond with increased activation in affective pain regions when empathizing with a friend. Consistent with this prediction, a whole-brain regression analysis examining how self-reported self-other overlap related to neural activity while watching a friend's exclusion (vs inclusion) showed significant activity in dACC and anterior insula, which are associated with

Table 1. Brain regions showing increased activity while observing a (i) stranger's social exclusion compared to inclusion and (ii) friend's social exclusion compared to inclusion

Region	Laterality	x	y	z	t	Voxels
Stranger						
DMPFC	L	-14	52	18	4.52	164
	L	-16	34	36	5.48	104
Precuneus	L	-6	-48	36	4.31	537
		-2	-66	30	3.72	26
TP	L	-50	-6	-26	8.14	672
	R	50	-4	-32	4.63	57
Friend						
MPFC	L	-4	46	0	3.41	32
dACC	R	11	23	34	4.39	309
pgACC	L	-14	43	12	4.8	237
Insula	L	-34	-18	22	4.72	26
OFC	L	-26	40	-10	5.21	70
Putamen	R	28	6	12	4.11	62
Calcarine	R	22	-56	14	3.68	28

All activations are significant at $P < 0.005$, 25 voxels.

the firsthand experience of social exclusion (e.g. Eisenberger et al., 2003, 2004). Details of these activations are provided in Table 2 and displayed in Figure 3.

Whole-brain interaction effects. The main hypothesis of our study was that greater self-other overlap with a target (i.e. a friend vs a stranger) should enhance vicarious emotion sharing during empathy for a target's social exclusion. Although the main effect analyses support this suggestion, we wanted to more specifically examine whether this hypothesis is supported when directly comparing the observation of a friend's social exclusion compared to a stranger's social exclusion. Specifically, we searched for neural regions that were differentially active while viewing a friend vs a stranger who experienced social exclusion (vs inclusion), using the contrast: [exclusion > inclusion during a friend's Cyberball game] > [exclusion > inclusion during a stranger's Cyberball game]. Whole-brain analyses of this contrast showed significant activations in dACC and left anterior insula. In addition, this contrast showed significant activation in MPFC (Figure 4). For a complete list of activations, see Table 3. Importantly, the reverse contrast: stranger (exclusion–inclusion) – friend (exclusion–inclusion) did not show any significant activation.

Functional connectivity between the MPFC and affective pain regions during empathy for friends. PPI analyses further support the suggestion that self-other overlap affects empathy for social suffering through self-processing and emotion sharing mechanisms. The MPFC activity showed increased functional connectivity with bilateral anterior insula and dACC in the contrast comparing the friends' exclusion to inclusion (Table 4 and Figure 4). However, the same analysis in the contrast comparing the stranger's exclusion to inclusion showed no significant activation. Moreover, when comparing functional connectivity between these two contrasts, we found significantly stronger connectivity between MPFC and both the dACC and bilateral insula for the friend's exclusion compared to the stranger's exclusion (Table 4 and Figure 5).

DISCUSSION

We present the first brain imaging evidence that self-other overlap with a target enhances vicarious emotions during empathy for an experience

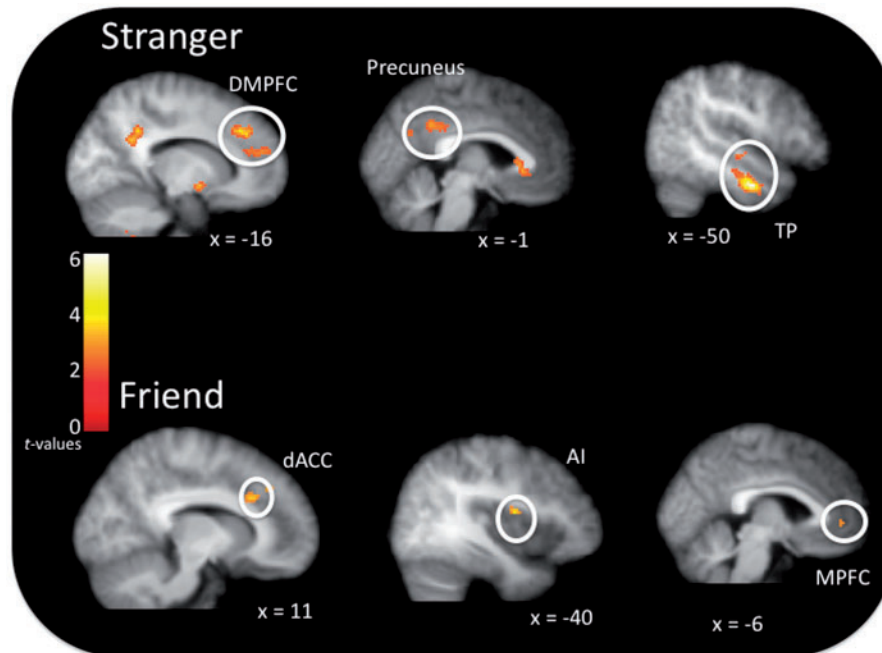


Fig. 2 Main effects of observing a friend and stranger's social exclusion. Regions associated with empathizing for a friend and stranger's social exclusion. *T*-values are represented by the intensity of the activation, with lighter activations representing larger *t*-values. Coordinates shown demonstrate the extent of activation for friend: dACC: 11 24 33; Insula: -40 0 16; MPFC: -6 45 0 and stranger: DMPFC: -16 35 36; precuneus: -1 -46 36; TP: -50 -6 -26.

Table 2. Brain regions during the observation of a friend's social exclusion that correlated positively with self-other overlap scores

Region	Laterality	<i>x</i>	<i>y</i>	<i>z</i>	<i>t</i>	Voxels
dACC	R	6	18	28	3.87	205
Anterior insula	R	40	2	-2	3.91	55
Insula	L	-34	-14	14	3.78	129
Middle temporal lobe	L	-62	-18	2	3.58	30
TPJ	L	-56	-40	14	3.84	67

All activations are significant at $P < 0.005$, 25 voxels.

of social pain. Specifically, comparisons between observing a friend's exclusion and a stranger's exclusion showed increased activation in the dACC and anterior insula which have been implicated in the firsthand experience of social exclusion (Eisenberger *et al.*, 2003, 2004), as well as the MPFC, which has been associated with self-related processing (Gusnard *et al.*, 2001; Kelley *et al.*, 2002).

Similarities and differences between empathy for physical and social pain

Importantly, our findings converge with certain findings on empathy for physical pain. Although empathy for the physical pain of close others and strangers both correspond with dACC and insula activation, the observers' feelings for, and identification with, the target moderates the degree of affective pain activation during empathic experiences. Singer *et al.* (2006) found that when participants played an economic game with an unfair confederate prior to scanning, male participants subsequently showed less dACC and insula in response to viewing the confederate in physical pain. Additionally, Xu *et al.* (2009) found that participants showed increased dACC activation when observing the physical pain of racial ingroup members, but not outgroup members. Importantly, the location of the dACC and insula

clusters reported in response to a friend's exclusion and the friend's exclusion relative to the stranger's exclusion not only overlap with one another (overlapping coordinates for dACC: $x = 12$, $y = 20$, $z = 34$; overlapping coordinates for insula: $x = 32$, $y = 6$, $z = 14$) but are also similar to those reported previously in empathy for pain studies (Jackson *et al.*, 2006), as well as those reported in the firsthand experience of social pain (Eisenberger *et al.*, 2003; 2004). Thus, this data may be interpreted similarly to those previously reported in empathy for pain studies—namely, through simulation theories of empathy. Simulation theories of empathy suggest that individuals empathize with targets by imagining what they would feel if they were the target (Goldman, 1992; Gallese, 2001). In other words, we understand another's mental experience by simulating their experience as though it were happening to ourselves. Results from our study and others support simulation theories, however, with the additional twist that one's feelings for, and relationship with, the target may affect how readily one simulates that person's suffering as if it were one's own.

Although our findings are consistent with past research on empathy for physical pain, they also point to potential differences in empathizing for social, rather than physical, pain. While people have previously been shown to recruit dACC and insula for the physical pain of close others (Singer *et al.*, 2004) and strangers (Jackson *et al.*, 2005), in this study, this activation only occurred to observation of social pain for a close other (close friend) and the self-reported degree of self-other overlap with the friend corresponded with more activation in these regions. This distinction in affective pain activation may reflect the unique importance of self-other overlap in enhancing negative emotion sharing for others' social pain.

One could argue that the differences in empathy for social and physical pain findings may be attributed to the abstract nature of Cyberball. Cyberball represents the players with cartoon stick figures rather than actual human displays of exclusion (e.g. pictures and videos). Previous research on empathy for physical pain, however, shows that cartoon displays of pain elicit activation in affective pain

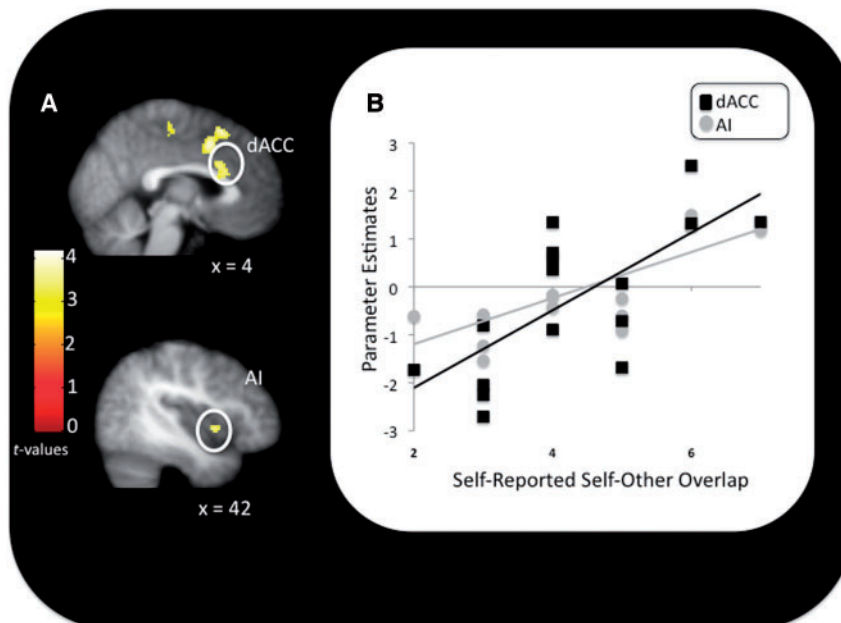


Fig. 3 Brain regions during a friend's exclusion predicted by self-other overlap scores. (A) Affective pain regions (coordinates shown demonstrate the extent of activation for dACC: 4 18 27 and anterior insula: 42 6 -3) observed in the contrast regressing self-other overlap scores with the friend's exclusion contrast. *T*-values are represented by the intensity of the activation, with lighter activations representing larger *t*-values. (B) Mean parameter estimates of most significant voxels (sphere centered around peak voxel with 3 mm extent) in these regions are plotted on the *y*-axis of the graphs and self-other overlap scores are plotted on the *x*-axis.

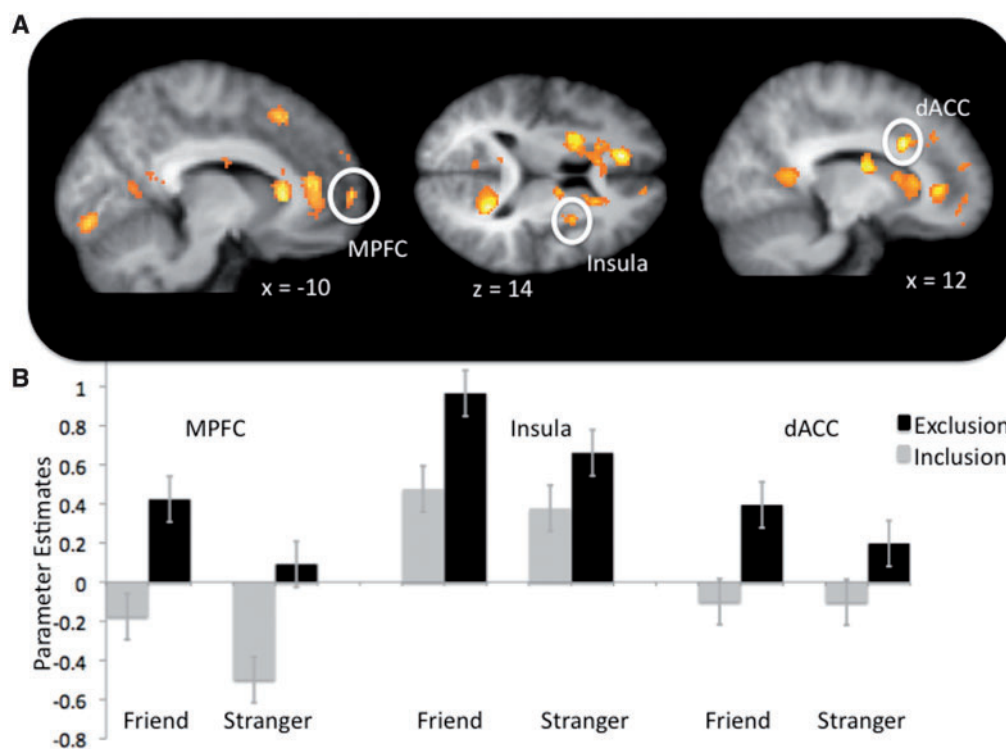


Fig. 4 Brain regions significantly active in the interaction contrast comparing a friend's exclusion > inclusion to a stranger's exclusion > inclusion. (A) Brain activations during the observation of a friend compared to stranger's social exclusion. Coordinates shown demonstrate the extent of activation for MPFC: -10 63 3; dACC: 12 22 34; and Insula: 33 5 14. *T*-values are represented by the intensity of the activation, with lighter activations representing larger *t*-values. (B) Mean parameter estimates of most significant voxels (sphere centered around peak voxel with 3 mm extent) in the dACC, insula and MPFC.

processing regions, although this activation is reduced compared to activation in response to human photographs of pain (Gu and Han, 2007). Since no affective pain activation was observed for stranger's Cyberball exclusion (even at liberal thresholds), it is possible that the

effects are not specific to the abstract format of Cyberball, but rather something unique to social pain. Interestingly, a recent meta-analysis of empathy for physical pain found that empathy for pain paradigms that show participants cues indicating when a confederate receives

Table 3. Brain regions showing increased activity while observing a friend's social exclusion > inclusion compared to a stranger's social exclusion > inclusion

Region	Laterality	x	y	z	t	Voxels
MPFC	L	-6	46	4	4.8	269
	L	-10	64	6	4.45	49
dACC	L	-14	42	14	6.98	5014
Anterior insula ^a	L	-30	8	14	3.82	261
Posterior cingulate ^b	R	16	-54	12	6.99	287
Putamen	L	-28	6	12	5.95	238
OFC	L	-30	22	-20	4.38	135
Supplementary motor area	L	-8	20	54	4.53	332
Superior frontal gyrus	L	-20	32	48	6.92	1025
Fusiform gyrus	R	40	-18	-18	5.45	203
TP	L	-56	4	-30	5.3	105
Superior occipital cortex	L	-18	-88	-10	7.24	955

All activations are significant at $P < 0.005$, 25 voxels.

^aActivation extends into part of a larger cluster in putamen, maximally active voxel: -28 6 12.

^bActivation extends into part of a larger cluster in the calcarine/precuneus, maximally active voxel: 22 -56 12.

Table 4. Brain regions showing functional connectivity with MPFC for (i) the friend's exclusion and (ii) the friend's exclusion compared to stranger's exclusion

Region	Laterality	x	y	z	t	Voxels
Friend's Exclusion						
dACC	R	6	16	26	4.2	145
Anterior insula	R	46	14	-2	5.26	692
	L	-38	12	-2	5.46	711
Supplementary motor area	L	-2	6	52	3.88	191
Medial frontal gyrus	R	26	4	52	3.97	42
Precentral gyrus	R	28	-18	60	4.5	167
Postcentral gyrus	R	26	-36	60	3.67	34
Lingual gyrus	R	26	-74	0	3.61	638
Friend's exclusion compared to Stranger's exclusion						
dACC	R	8	16	26	3.45	80
Anterior insula	L	-36	20	0	3.55	33
		-34	6	14	4.14	70
VMPFC	L	-12	50	-4	5.09	156

All activations are significant at $P < 0.005$, 25 voxels.

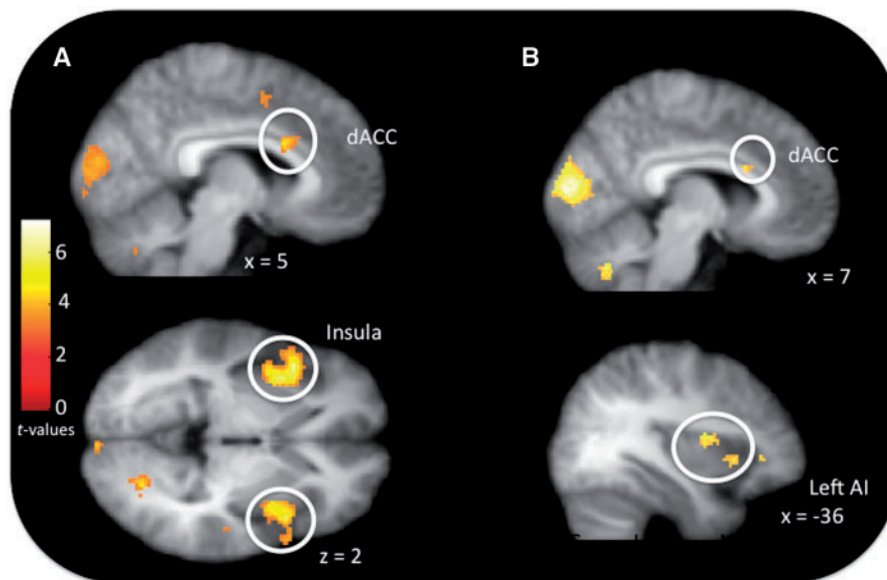


Fig. 5 Brain regions showing functional connectivity with MPFC for the friend's exclusion and the friend's exclusion compared to stranger's exclusion. (A) Affective pain regions (Coordinates shown demonstrate the extent of activation for dACC: 5 18 26; bilateral anterior insula: L -38 17 0; R 40 14 0) that showed increased functional connectivity with the MPFC during observation of a friend's exclusion. *T*-values are represented by the intensity of the activation, with lighter activations representing larger *t*-values. (B) Comparing the functional connectivity activation with the MPFC seed for the friend's exclusion and the stranger's exclusion showed significantly more connectivity with the dACC (coordinate showing extent of activation: 7 17 26) and anterior insula (coordinate showing extent of activation: L -36 1 31) for the friend's exclusion relative to the stranger's exclusion.

pain, rather than displaying images of physical pain, elicit activation in DMPFC, precuneus and TP in addition to dACC and insula (Lamm *et al.*, 2011). However, it is unclear whether activation in regions associated with mentalizing reflects the abstract nature of the pain paradigm or the social nature of a live confederate engaged in the paradigm. Future research should tease out the similarities and differences between abstract and live empathy for physical and social pain.

Distinctions between empathizing for the social pain of friends and strangers

While emotion sharing is considered a 'bottom-up' component of empathy, 'top-down,' cognitive factors also contribute to empathy (Lamm *et al.*, 2007, 2011; Fan and Han, 2008; Decety and Meyer, 2008), and different cognitive mechanisms involved in empathy may

engage when observing close others (e.g. friends) and strangers' social pain. Here, we replicated the findings reported by Masten *et al.* (2011), showing that observation of a stranger's social exclusion compared to inclusion corresponded with significantly increased activation in DMPFC, precuneus and TP, regions that consistently engage during mentalizing (Mitchell *et al.*, 2006; Lieberman, 2010). However, empathizing with a friend, compared to a stranger, led to significantly more activation in MPFC which has been previously implicated in self-processing (e.g. Mitchell *et al.*, 2005). Thus, empathizing with friends may activate self-related processes as a top-down mechanism that elicits empathy for social suffering.

Interestingly, in brain imaging studies of mentalizing, participants recruit more dorsal portions of the medial prefrontal cortex (dMPFC; BA 8/9) when mentalizing about strangers, whereas they recruit more ventral regions of the medial prefrontal cortex (BA 10), similar to the MPFC activation reported in the current study, when mentalizing

about close others with whom participants experience self-other overlap (Mitchell et al., 2006; Krienen et al., 2010). In fact, while Mitchell et al. refer to this region as ventral MPFC (in relation to the more dorsal MPFC activation observed for mentalizing with nonsimilar others), it is nearly identical to the activation observed in our study (labeled 'MPFC'), as can be seen by the location of the clusters (in the z -plane) of MPFC observed in our study ($z=4$) relative to those reported by Mitchell et al. (2006; $z=9$). Indeed, it has been suggested that this more ventral MPFC activation (BA 10) observed while mentalizing about close others might reflect participants' simulating the close other's experience from their own perspective (Mitchell et al., 2006). Thus, in the context of empathy, recruiting more ventral (BA 10), rather than dorsal (BA 8/9), portions of MPFC may indicate a similar distinction in simulating a close other's experience from one's own perspective.

Consistent with this suggestion, functional connectivity analyses showed that MPFC activation was more strongly associated with affective pain region activation while observing a friend's exclusion relative to a stranger's exclusion. The MPFC has been associated with trait empathy (Shamay-Tsoory et al., 2003; Singer et al., 2004; Rankin et al., 2006), emotional perspective taking (Hynes et al., 2006) and may mediate the relationship between emotion sharing and pro-social behaviors (Masten et al., 2011; Rameson et al., 2012). In empathizing with stranger's social pain, recruiting the dorsal MPFC may correspond with mentalizing without bringing emotion-sharing online, whereas recruiting the more ventral MPFC more effectively acts as a top-down initiator of emotion sharing, leading to a full-blown empathic response (i.e. sharing and understanding another's emotional experience).

It is worth noting that an alternative interpretation to our findings is that observing the social exclusion of close others induces attachment-related processing, as the ACC is known to be involved in attachment-related behaviors in animals (MacLean and Newman, 1988), and activates in humans in response to viewing a loved one (e.g. child, romantic partner; Bartels and Zeki, 2004). Indeed, attachment processing and empathy for close others may be correlated and may be useful to explore in conjunction in the future to tease apart their overlapping and unique variance in the response to close others' social (and physical) pain.

While MPFC activation in response to close others' exclusion may reflect simulating a close other's experience from one's own perspective, what cognitive mechanisms DMPFC and other mentalizing regions observed in response to a stranger's exclusion represent qualitatively, in terms of the 'kind of mentalizing' engaged, remains an open question. On the one hand, recruiting these regions may reflect the use of a cognitive, rather than emotional, mentalizing mechanism. A distinction between cognitive and affective mentalizing has been suggested in the empathy literature (Shamay-Tsoory et al., 2008; Jenkins and Mitchell, 2009), and given that we did not observe activation in limbic regions along with mentalizing network activation, this seems like a possible interpretation. On the other hand, it is possible that recruiting the mentalizing system reflects thinking about people that we have no prior information and assumptions about. It has been suggested that activating DMPFC in conjunction with other mentalizing regions may reflect cognition about 'people in general,' and applying rules and norms about how the average person is likely to think and feel (Lieberman, 2010). Future research should investigate whether one or both of these interpretations are valid.

LIMITATIONS, FUTURE DIRECTIONS AND CONCLUSIONS

This study is not without potential limitations. For example, our fMRI results could reflect an attentional bias towards friends' situations.

However, participants rated being equally aware of friends' and strangers' feelings of social exclusion even though they reported sharing significantly more negative emotions during their friends' social exclusion. Thus, we doubt that this potential bias in attention directed toward the friend significantly impacted the results. Rather, self-reports suggest that participants were aware of both targets' negative emotions, but experienced shared negative emotions to a greater extent when their friend was the target.

It is also worth noting that all of the subjects in this study were Chinese, and there is a cultural difference in the extent to which people tend to view close others as connected to their own identity (Markus and Kitayama, 1991). In Western cultures, individuals tend to possess highly developed independent self-construals, where they see themselves as unique entities (Markus and Kitayama, 1991). In Eastern cultures, however, individuals tend to possess highly developed interdependent self-construals, where they view themselves in relation to other people with whom they are emotionally close (i.e. friends and family; Bond and Cheung, 1983; Cousins, 1989; Markus and Kitayama, 1991). In fact, recent brain imaging studies find that East Asian compared to Western participants show more MPFC activity in response to close others (Zhu et al., 2007; Chiao et al., 2009; Wang et al., 2012). On a related note, most of the subjects in our study were female and there are known gender differences in empathic neural responses between genders (Singer et al., 2006; Han et al., 2008). An interesting future direction would be to explore whether cultural and gender differences in self-construal affect the role of self-other overlap in empathy for social pain.

Limitations aside, our findings offer interesting insight into everyday experiences of empathy for social pain. Evolutionary theories suggest that empathy facilitates the survival of ourselves and close others (DeWall, 2008) and that self-other overlap mediates the relationship between empathy and helping (Cialdini et al., 1997). However, contemporary society increasingly demands the ability to empathize with and help nonclose others (i.e. when learning about a socially disconnected war victim in a foreign country). Future research should examine how perspective taking, which has been shown to increase self-referential processing (Ames et al., 2008) and increase empathy for physical pain (Lamm et al., 2008), may increase activation in affective pain and self-processing networks during empathy for social pain.

Taken together, our results provide the first neuroimaging evidence that self-other overlap with a target enhances vicarious emotion sharing during empathy for social pain. These findings support the idea that self-other overlap with a target may allow us to recruit brain mechanisms that indicate that we ourselves are experiencing the target's situation.

Conflict of Interest

None declared.

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