doi:10.1093/scan/nsq098 SCAN (2012) 7, 106–114

Time spent with friends in adolescence relates to less neural sensitivity to later peer rejection

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Involvement with friends carries many advantages for adolescents, including protection from the detrimental effects of being rejected by peers. However, little is known about the mechanisms through which friendships may serve their protective role at this age, or the potential benefit of these friendships as adolescents transition to adulthood. As such, this investigation tested whether friend involvement during adolescence related to less neural sensitivity to social threats during young adulthood. Twenty-one adolescents reported the amount of time they spent with friends outside of school using a daily diary. Two years later they underwent an fMRI scan, during which they were ostensibly excluded from an online ball-tossing game by two same-age peers. Findings from region of interest and whole brain analyses revealed that spending more time with friends during adolescence related to less activity in the dorsal anterior cingulate cortex and anterior insula—regions previously linked with negative affect and pain processing—during an experience of peer rejection 2 years later. These findings are consistent with the notion that positive relationships during adolescence may relate to individuals being less sensitive to negative social experiences later on.

Keywords: adolescence; friendship; peer rejection; functional magnetic resonance imaging

During adolescence, peer relationships take on increasing importance and peers begin to play a central role in individuals' social lives. At this age, there is a dramatic increase in the amount of time that adolescents spend with peers (Csikszentmihalyi and Larson, 1984; Brown, 2004), and more time is spent socializing with friends than engaged in any other non-school activity (i.e. studying, working, extra-curricular activities) (Fuligni and Stevenson, 1995). Unfortunately, as more time is spent in peer groups, peer rejection becomes increasingly prevalent (Coie *et al.*, 1990) and yields an array of negative consequences, including compromised mental and physical health outcomes that persist across development (Prinstein and Aikins, 2004; Prinstein *et al.*, 2005; Lev-Wiesel *et al.*, 2006). As a result, increased peer involvement can present social and emotional challenges for youth.

Fortunately, however, adolescents also gain many benefits from these extra hours spent with peers, including companionship, advice and respect (Buhrmester, 1996), and they become reliant on peers as a primary source of social support (Brown, 1990; Buhrmester, 1996; Rubin *et al.*, 2006). While parents might not welcome this change, social support from peers carries with it a host of short- and long-term benefits that may help youth avoid the escalating threat of peer rejection during adolescence. For example, both having high-quality friendships and having a greater number of friends reduce the likelihood of future peer rejection during early adolescence (Hodges and Perry, 1999; Hodges *et al.*, 1999). Moreover, peer rejection is less associated with negative mental health outcomes across time among adolescents with greater social support (Rigby, 2000) and among those who have close friendships (Hodges *et al.*, 1999). Thus, ironically, having closer relationships with peers provides a supportive outlet for adolescents, even as the risk of encountering peer rejection increases.

Despite these positive implications of friend involvement during adolescence, it is unclear what mechanisms yield this positive impact in the face of peer rejection. Furthermore, it is unknown whether the benefits of friends during adolescence remain apparent later, after the transition to young adulthood. In the present investigation, we used a social neuroscience approach to examine the underlying affective processes through which friend involvement during adolescence might be protective in the face of later peer rejection. Specifically, we examined whether spending time with friends during high school was associated with dampened neural sensitivity to peer rejection 2 years later.

Neuroimaging techniques are particularly useful for examining the potential mechanisms through which various types of social support, such as friend involvement, might protect individuals during negative social treatment. For example, one possible mechanism that has recently garnered support is that individuals with more social support perceive social stressors as less threatening, because they feel more supported and cared for in general. As a result, they are less reactive to stressors and display a dampened affective

Received 26 August 2010; Accepted 10 November 2010
Advance Access publication 22 December 2010
The authors wish to thank the Ahmanson-Lovelace Brain Mapping Center. Support for this study was provided to A. J. Fuligni by the Russell Sage Foundation, and the Cousins Center for Psychoneuroimmunology, Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, USA.
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response compared to individuals without social support (Cohen and Wills, 1985; Eisenberger *et al.*, 2007b). Given our growing understanding of the specific neural substrates underlying negative social interactions, we can test how neural affective responses during these negative social interactions relate to varying levels of friend involvement.

In particular, both the dorsal anterior cingulate cortex (dACC) and the anterior insula have been consistently linked with individuals' affective responses to negative social treatment. The dACC has been linked to social exclusion among young adults (Eisenberger *et al.*, 2003; Eisenberger *et al.*, 2007a, b, c; Kross *et al.*, 2007; DeWall *et al.*, 2010; Masten *et al.*, 2010b) and among adolescents and adults high in rejection sensitivity (Burklund *et al.*, 2007; Masten *et al.*, 2009). The anterior insula has also been linked with social exclusion among both young adults (Eisenberger *et al.*, 2003; Kross *et al.*, 2007; DeWall *et al.*, 2010; Masten *et al.*, 2010a, b) and adolescents (Crowley *et al.*, 2010; Masten *et al.*, 2009, 2010a), as well as negative affective states more generally (e.g. Phan *et al.*, 2004). Thus, to the extent that friend involvement leads individuals to perceive negative social interactions as less threatening, those who are more involved with friends should display less activity in the dACC and anterior insula during these interactions.

In support of this, one recent study demonstrated that daily involvement with close others was associated with dampened threat responses to social exclusion. Specifically, young adults who reported more frequent interactions with supportive others on a daily basis demonstrated reduced activity in the dACC during social exclusion (Eisenberger *et al.*, 2007b). Given this concurrent link between daily social support and reduced responses to social exclusion in early adulthood, we aimed to extend this research by examining whether involvement with friends during adolescence—when peer relationships are particularly important—would lead to similar dampened responses to social exclusion during young adulthood. In particular, given that friends are considered a primary source of social support during adolescence (Rubin *et al.*, 2006), we expected that adolescents who reported more involvement with friends would show less neural evidence of sensitivity to social exclusion 2 years later.

In order to examine friendship involvement during adolescence, we measured the amount of time that individuals spent with their friends outside of school using a daily diary. The amount of time spent with friends was considered a useful index of adolescents' involvement in supportive peer relationships because both friendship quality (Mathur and Berndt, 2006) and friendship intimacy (Berndt and Perry, 1990) increase as more time is spent with friends at this age. Also, we were interested in examining time spent with friends during adolescence specifically, because of the heightened importance placed on maintaining peer acceptance at this particular stage of development (Brown, 2004).

Furthermore, given that social support and close friendships during adolescence are thought to provide long-term protection from the negative effects of peer rejection across time (Hodges *et al.*, 1999; Rigby, 2000), we assessed whether time spent with friends during adolescence would relate to neural responses to peer rejection at a later time point. To assess this, 2 years after completing the daily diary, participants underwent an fMRI scan during which they were ostensibly excluded by two same-age peers. We examined social exclusion both because its neural substrates have been established in prior research (e.g. Eisenberger *et al.*, 2003; Masten *et al.*, 2009), and because excluding peers is one of the most dominant forms of peer rejection during adolescence (Coie *et al.*, 1990). We predicted that, to the extent that individuals spent more time with their friends during high school—when peer relationships are particularly important—they would be less sensitive to social exclusion 2 years later and thus show less neural activity in regions typically associated with negative affective processing (e.g. dACC and anterior insula), compared to individuals who spent less time with friends.

METHODS

Participants

Participants included 21 individuals in their 12th grade year of high school (13 females; mean age = 17.77, s.d. = 0.43). They were 52% White ($n = 11$; seven females) and 48% Latino ($n = 10$; six females), which is representative of the geographic region in which participants were recruited. Participants reported no MRI contraindications (i.e. metal in their bodies, claustrophobia, pregnancy) and were fluent in English. All participants provided written consent in accordance with UCLA's Institutional Review Board.

Procedures

During the spring of 12th grade, participants completed a daily diary every night for 2 weeks, in which they indicated the amount of time that they had spent with friends outside of school that day. This variable was coded as the number of hours reported each day, and a summary variable was created by averaging the time reported across each of the 14 days. The daily diary method is a particularly useful way of examining how individuals spend their time each day that is less dependent on retrospective reporting (Bolger *et al.*, 2003). Participants were given a 14-day supply of daily diary checklists, 14 envelopes and a small electronic time stamper (with a security code to prevent tampering) to help monitor diary completion. Participants completed each daily checklist before going to bed for 14 consecutive nights. They were instructed to place each completed checklist in an envelope and to stamp the seal with the electronic time stamper to indicate the time and date they completed each diary.

Approximately 2 years later, participants came to UCLA's campus and underwent a simulated experience of social

exclusion during an fMRI scan (see details below). They were told that the goal of the study was to examine neural activity as they engaged in a social interaction with two other 'participants' their age; however, in reality they interacted with a preset computer program. In order to enhance ecological validity, participants met two confederates (one male, one female) prior to scanning, who acted as these other 'participants'. The participant and confederates completed consents and were given instructions together. They introduced themselves by stating their name, current employment or major in college, and something interesting about themselves. They were then told that they would each be escorted to their assigned scanner, at which point the participant began the fMRI scan and the confederates were discretely escorted to the exit.

fMRI paradigms

Cyberball

To simulate a real, interactive experience of social exclusion, participants completed an experimental paradigm called 'Cyberball' (Williams *et al.*, 2000, 2002). Cyberball is a staged computer program during which participants believed they were playing a computerized ball-tossing game via the Internet with the two confederates that they met prior to the scan. Throughout the game of Cyberball, the ball was thrown back and forth among the three players, with the participant choosing the recipient of their own throws, and the throws of the other two 'players' determined by the pre-set program. Participants could see the images representing the other two players on a computer screen, as well as their own 'hand' that they controlled using a button-box. After being included for 10 throws, participants were excluded for the duration of the game. This paradigm has been used previously in several behavioral and neuroimaging studies to successfully simulate an experience of social exclusion and examine links between responses to social exclusion and a range of socio-emotional indices (e.g. social distress, rejection sensitivity, interpersonal competence, aggression; trust, social support; see Eisenberger *et al.*, 2003, 2007a, b, c; Williams, 2007; Gross, 2009; Masten *et al.*, 2009, 2010b; Sebastian *et al.*, 2009; Crowley *et al.*, 2010; DeWall *et al.*, 2010; Hillebrandt *et al.*, 2010).

Control task

Prior to playing the Cyberball game, participants completed a control task, which experimenters explained was necessary for 'visual calibration' of the goggles. For 1 min, participants passively watched a small star shape move around the screen in a triangular pattern that was similar to the movements of the ball's path during the Cyberball game (although the star did not exactly mimic 'exclusion', so as not to prime participants' expectations about the Cyberball game). The goal of this control task was to obtain a baseline that was visually similar to the game, but non-social in nature, in order to help isolate activity involved in social exclusion. To avoid the possibility that residual feelings of distress from Cyberball would contaminate this baseline, the control task was always administered prior to Cyberball.

fMRI data acquisition

Images were collected using a Siemens Trio 3-Tesla MRI scanner. Extensive instructions and foam padding were provided to decrease motion. For each participant, an initial 2D spin-echo image (TR = 4000 ms, TE = 40 ms, matrix size 256 × 256, 4-mm thick, 1-mm gap) in the sagittal plane was acquired in order to enable prescription of slices obtained in structural and functional scans. In addition, a high-resolution structural scan (echo planar T2-weighted spin-echo, TR = 4000 ms, TE = 54 ms, matrix size 128 × 128, FOV = 20 cm, 36 slices, 1.56-mm in-plane resolution, 3-mm thick) coplanar with the functional scans was obtained for functional image registration during fMRI analysis preprocessing. The functional tasks were presented on a computer screen through MR-compatible goggles. The control task was completed during a functional scan lasting 1 min, and the Cyberball game was completed during a functional scan lasting 2 min, 48 s (parameters for both scans: echo planar T2*-weighted gradient-echo, TR = 2000 ms, TE = 25 ms, flip angle = 90°, matrix size 64 × 64, 36 axial slices, FOV = 20-cm; 3-mm thick, skip 1-mm). Collection of structural data and functional data for both the control task and Cyberball took ~10 min.

fMRI data analysis

Neuroimaging data were preprocessed and analyzed using Statistical Parametric Mapping (SPM5; Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK), and ROI extraction was performed using the MARsBaR toolbox within SPM (MARSeille Boîte À Région d'Intérêt; Brett *et al.*, 2002). Preprocessing included image realignment to correct for head motion (no participant exceeded 2 mm), normalization into a standard stereotactic space defined by the Montreal Neurological Institute and the International Consortium for Brain Mapping, and spatial smoothing using an 8-mm Gaussian kernel, full-width at half maximum, to increase signal-to-noise ratio.

Modeling of contrasts

Cyberball and the control task were modeled using a block design. The control task comprised one block (lasting 1 min), and the portion of Cyberball during which the participant no longer received the ball comprised one exclusion block (lasting 1 min). Linear contrasts comparing the exclusion block to the control block were calculated for each participant. These individual contrast images (exclusion *vs* the control task) were then used in all group-level analyses.

Main-effect analysis

To examine neural activity during social exclusion, we performed a group-level contrast comparing activity during the Cyberball exclusion to activity during the control task. Clusters of activity were considered significant at $P < 0.005$, with a 10-voxel minimum cluster size, for *a priori* defined regions known to be involved in affective processing during social exclusion (e.g. dACC, anterior insula; Lieberman and Cunningham, 2009). All other brain regions not defined a priori were examined at a threshold corrected for multiple comparisons (corrected for false-discovery rate in SPM5; $P < 0.05$, 10-voxel minimum cluster size). All coordinates are reported in Montreal Neurological Institute (MNI) format.

Regression analyses

To examine how time spent with friends during high school related to neural activity during social exclusion 2 years later, we performed two sets of regression analyses: (i) region of interest (ROI) analyses that tested how the amount of time spent with friends during high school related to activity during social exclusion (*vs* the control task) in our specific dACC and anterior insula ROIs (see details of ROI definition below), and (ii) a follow-up whole brain analysis that tested how time spent with friends during high school related to activity during social exclusion (*vs* the control task) across the entire brain volume.

Regions of interest were functionally defined (using the MARsBaR toolbox) as the clusters in the dACC and anterior insula that were found to show greater activation to social exclusion than to the control task in the current study. There were three ROIs defined in total: one in the dACC [peak voxel: (0 15 27)], one in the right anterior insula [peak voxel: (42 27 −9)], and the other in the left anterior insula [peak voxel: (−45 18 −15)]. Mean cluster-level parameter estimates for each participant (that model the amplitude of the BOLD response during exclusion *vs* control) were then extracted and averaged across all voxels in each ROI. Standard statistical software (SPSS 16.0, Chicago, IL, USA) was used to conduct correlations to determine whether these parameter estimates were correlated with the amount of time that participants spent daily with their friends during high school. A standard statistical threshold of $P < 0.05$ was used for these correlational ROI analyses.

In order to supplement these ROI analyses, whole brain regression analyses were run in SPM5 to test whether time spent with friends (entered as a regressor) related to the difference in activity during exclusion compared to the control task, at each voxel across the entire brain volume. Thus, findings from these whole-brain regressions reflect the regions of the brain in which time spent with friends was significantly associated with activity during exclusion (*vs* the control task). The statistical threshold was the same as that used in the whole-brain, main effect analysis that examined which regions were more active during exclusion *vs* the control task (i.e. $P < 0.005$, 10 voxels for a priori regions, and FDR-corrected, $P < 0.05$, 10 voxels for other regions; see detailed description above).

RESULTS

Behavioral analyses

Participants' average daily reports of how much time they spent outside of school with their friends during high school ranged from 0 to 4.75 h ($M = 1.78$, s.d. $= 1.26$). The amount of time spent with friends did not significantly differ by gender ($F = 1.24$, $P = 0.28$); however, there was a marginal effect of ethnicity such that Whites reported spending marginally more time with friends ($M = 2.26$, s.d. $= 1.08$) than Latinos ($M = 1.26$, s.d. $= 1.27$; $F = 3.86$, $P = 0.06$). Thus, we controlled for ethnicity in all analyses.

Whole brain, main effect analysis

During social exclusion compared to the control task, participants displayed heightened activity in the dACC, as well as in the right and left anterior insula (details in Table 1), which is consistent with previous work examining affective activity during social exclusion (Eisenberger *et al.*, 2003, 2007a; 2007b; 2007c; DeWall *et al.*, 2010). In addition, they displayed greater activity in several regions previously linked with emotion regulation during social exclusion (e.g. ventrolateral and dorsolateral prefrontal cortices, rostral anterior cingulate cortex; Eisenberger *et al.*, 2003; Masten *et al.*, 2009, 2010b). See Table 1 for a complete list of activations.

ROI analyses

Next we examined how the amount of time that participants spent with their friends in high school related to their neural activity during social exclusion (*vs* the control task) in the specific areas of the dACC and anterior insula that showed heightened activity during social exclusion compared to the control task across the whole sample. Time spent with friends in high school was negatively associated with activity in the left anterior insula during social exclusion ($r = -0.44$, $P < 0.05$; Figure 1), although it was not related to dACC activity. Thus, to the extent that young adults spent more time with their friends during high school, they displayed less activity in the anterior insula—a region associated with social pain and negative affect—2 years later.

Whole brain analyses

Participants who reported spending more time with friends displayed less activity during social exclusion (*vs* the control task) in two areas of the left anterior insula [(−42 12 −12), $r = -0.69$, $P < 0.0005$, $k = 125$ voxels; Figure 2a; (−48 0 9), $r = -0.66$, $P < 0.001$, $k = 20$ voxels]—consistent with ROI analyses, and in an area of the dACC that was slightly posterior to the dACC ROI [(−6 −6 57), $r = -0.63$, $P < 0.005$, $k = 40$ voxels; Figure 2b], during social exclusion (*vs* the control task). There were no other regions in which time

Table 1 Regions active during social exclusion *vs* the control task (controlling for ethnicity)

Anatomical Region	BA		*x*	*y*	*z*	*t*	*k*	*P*
Anterior insula		R	42	27	−9	6.67	2518	<0.0001
Anterior insula		L	−45	18	−15	4.28	139	<0.0005
dACC	24		0	15	27	4.59	16	<0.0001
Lateral occ. cortex	37	R	54	−69	3	12.86	3235	<0.0001
TPJ	40	R	63	−42	24	9.34	3235	<0.0001
Fusiform gyrus	37	R	39	−51	−15	8.41	3235	<0.0001
Precuneus	7	R	9	−54	60	5.27	3235	<0.0001
Lateral occ. cortex	39	L	−48	−72	12	11.29	780	<0.0001
TPJ	40	L	−57	−48	27	6.34	780	<0.0001
SFG	6	R	42	3	54	7.26	2848	<0.0001
MPFC	10		0	54	15	5.89	2848	<0.0001
DLPFC	45	R	45	24	24	4.87	2848	<0.0001
DMPFC	9	R	3	54	39	4.43	2848	<0.0005
Striatum		R	6	6	9	7.07	313	<0.0001
Brainstem		L	−3	−30	−3	5.40	140	<0.0001
Cerebellum		L	−15	−78	−30	5.40	426	<0.0001
Temporal pole	28	L	−30	9	−24	5.12	160	<0.0001
SFG	6	L	−24	0	69	5.03	187	<0.0001
Fusiform gyrus	37	L	−39	−60	−12	4.93	132	<0.0001
Cerebellum		R	6	−42	−36	4.53	55	<0.0005
SPL	19	L	−24	−72	36	4.44	70	<0.0005
DLPFC	45	L	−42	15	24	4.43	64	<0.0005
Amygdala		R	15	−3	−15	3.88	27	<0.001
VLPFC	10	R	27	54	9	3.18	13	<0.005
rACC	24	R	12	27	21	3.17	13	<0.005

Note: Regions identified *a priori* (e.g. dACC, anterior insula) are listed if they were significant at $P < 0.005$, 10 voxels or greater (*k*-values listed for these regions were taken from this thresholding map). Other regions listed were not the primary focus of this investigation but were still significant after correction for multiple comparisons (*k*-values listed for these regions were taken from the thresholding map at $P < 0.05$, 10 voxels, FDR-corrected). The individual *P*-values listed indicate the level of significance that each particular region met. BA refers to putative Brodmann's Area; L and R refer to left and right hemispheres; *x*, *y* and *z* refer to MNI coordinates; *t* refers to the *t*-score at those coordinates (local maxima); *k* refers to the number of voxels in each significant cluster. The following abbreviations are used for the names of specific regions: dorsal anterior cingulate cortex (dACC), occipital (Occ.), temporoparietal junction (TPJ), superior frontal gyrus (SFG), medial prefrontal cortex (MPFC), dorsolateral prefrontal cortex (DLPFC), dorsomedial prefrontal cortex (DMPFC), superior parietal lobule (SPL), ventrolateral prefrontal cortex (VLPFC) and rostral anterior cingulate cortex (rACC).

spent with friends was negatively or positively related to neural activity.[1]

DISCUSSION

Overall, the current investigation provides evidence that spending more time with friends during adolescence is associated with less sensitivity to future social exclusion, as evidenced by dampened neural activity during social exclusion two years later in regions known to be involved in negative affective processing. These findings contribute to our understanding of how friendships may protect adolescents who experience peer rejection and are consistent with the notion that a high level of friend involvement during adolescence may contribute to beneficial outcomes later on.

To examine how daily reports of time spent with friends during high school related to neural affective responses to social exclusion two years later, we performed both ROI regression analyses focused on the specific regions of the dACC and anterior insula that were more active during exclusion (*vs* the control task), as well as a regression analysis across the whole brain. Together, these findings indicated that time spent with friends during adolescence was negatively associated with activity in the anterior insula and dACC during social exclusion. This is consistent with research indicating that interacting with supportive others relates to reduced social pain-related neural responses to social exclusion among adults (Eisenberger *et al*., 2007b), and with developmental research indicating that friend involvement during adolescence is protective in the face of peer rejection (e.g. Hodges and Perry, 1999; Hodges *et al*., 1999; Rigby, 2000; Kochenderfer-Ladd and Skinner, 2002). Notably, the current findings also support the possibility that the protective role of friends during adolescence might have a lasting impact.

[1]Similar to prior studies employing the Cyberball task (e.g. Eisenberger *et al*., 2003; Masten *et al*., 2009; Sebastian *et al*., 2009; Crowley *et al*., 2010; DeWall *et al*., 2010), we measured participants' self-reported distress (using the 12-item Need Threat Scale, NTS; Williams *et al*., 2000) following exclusion, to examine whether NTS scores related to greater activity in dACC and anterior insula. However, we did not find expected correlations between distress and brain activity at our specified threshold. This may have been due to the fact that the NTS was administered after completion of the fMRI scan, which, in addition to Cyberball, included another task in which participants received monetary rewards. Thus, subjective feelings of distress related to Cyberball may have been altered by the time the NTS was ultimately completed due to feelings induced during this other task. Nevertheless, lowering the whole-brain analysis threshold to $P < 0.05$ for exploratory purposes, revealed expected positive correlations between NTS scores and activity in regions previously linked with distress (dACC: [18 18 51], $t = 2.95$, $r = 0.56$, $P < 0.005$, $k = 24$ voxels; [−15 6 54], $t = 2.73$, $r = 0.53$, $P < 0.01$, $k = 24$ voxels; anterior insula: [−36 12 9], $t = 1.97$, $r = 0.41$, $P < 0.05$, $k = 3$ voxels; [36 15 3], $t = 1.89$, $r = 0.40$, $P < 0.05$, $k = 9$ voxels).

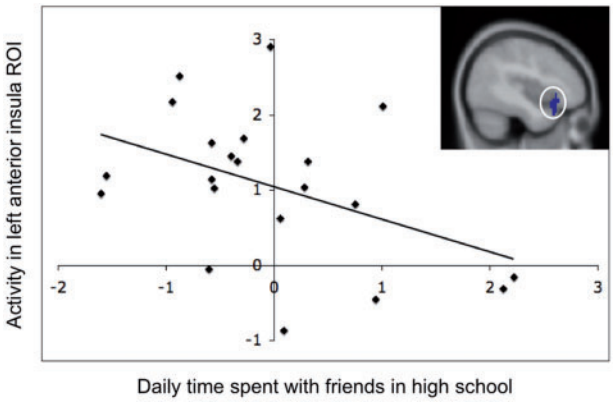

Fig. 1 Activity during social exclusion vs the control task in the left anterior insula ROI [functionally defined as the cluster that displayed greater activity during exclusion vs the control task across the whole sample, controlling for ethnicity; peak voxel: (−45 18 −15)], that is negatively associated with the amount of time that participants reported spending with their friends during high school. The values for 'daily time spent with friends during high school' represent residualized scores reflecting the variance in the amount of hours spent per day with friends, after having removed the variance due ethnicity.

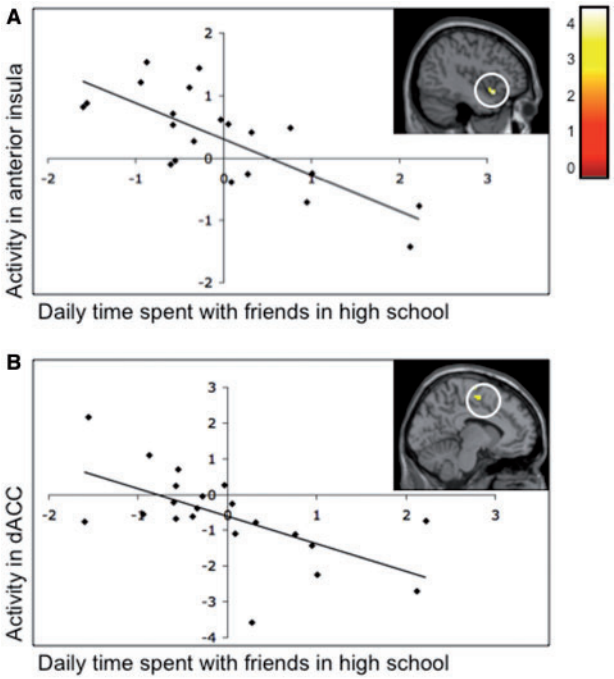

Fig. 2 Activity during social exclusion *vs* the control task identified through a whole-brain regression to be negatively associated with the amount of time that participants reported spending with their friends during high school in: (**A**) the left anterior insula (−42 12 −12), and (**B**) the dACC (−6 −6 57). The values for 'daily time spent with friends during high school' represent residualized scores reflecting the variance in the amount of hours spent per day with friends, after having removed the variance due ethnicity.

Of course, longitudinal neuroimaging studies are needed to test the benefits of friend involvement over time. However, our findings indicate that youth who spend a lot of time with friends are less neurally sensitive to negative social treatment as they enter early adulthood, and it is possible that this pattern reflects long-term advantages of friend involvement.

The current findings also support the notion that friend involvement may yield protective benefits among adolescents specifically by decreasing the degree to which social stressors are initially perceived as threatening. Some theorists have alternatively suggested that social support might reduce stress via enhanced emotional regulatory processes that attenuate affective stress responses (Cohen and Wills, 1985). However, the current findings provided little evidence of enhanced regulation associated with friend involvement (i.e. no positive correlations between time spent with friends and regulatory neural activity), despite heightened activity in regulatory regions during exclusion overall (Table 1),[2] and despite previous evidence that activity in these regulatory regions (i.e. prefrontal cortices) relates to less sensitivity to peer rejection (Masten *et al.*, 2009), and relational aggression (Baird *et al.*, 2010). Thus, one long-term outcome of friend involvement during adolescence may be desensitization to negative social treatment, rather than a heightened ability to regulate affective responses to social stressors.

There are several reasons why being rejected by peers might be perceived as less threatening among adolescents who spend more time with their friends. One possibility is that these individuals are simply less bothered by peer rejection because they know that they have reliable friends who care about them. For example, there is some evidence that peer rejection is particularly threatening during adolescence because of the heightened importance that these youth place on maintaining peer acceptance (Parkhurst and Hopmeyer, 1998). Thus, youth who spend a lot of time with friends may feel a strong sense of belonging and acceptance in relation to their particular group of friends, and be less concerned that negative interactions with others will threaten this acceptance. Over time, this feeling of acceptance may become internalized and continue to reduce the degree to which social stressors are perceived as threatening, even years later. On a related note, to the extent that social rejection increases the desire to reconnect with others (Maner *et al.*, 2007), individuals with more friends may be somewhat buffered by the negative consequences of rejection because they have greater opportunities to reconnect with others after the rejection episode.

Alternatively, one recent study provided another interesting possibility. Nishina and Bellmore (2010) demonstrated that when adolescents witness others being rejected by peers, friends of the victim are the most likely witnesses to interfere with the rejection and provide help. Thus, adolescents who

[2]Although not the primary focus of this investigation, we also examined whether time spent with friends was associated with activity in any known regulatory regions (e.g. ventrolateral prefrontal cortex, dorsolateral prefrontal cortex, rostral ACC) using the same ROI approach used to examine the dACC and anterior insula. Consistent with the whole-brain findings, these analyses yielded no evidence of heightened regulatory activity during exclusion (*vs* the control task) among individuals who spent more time with friends during high school.

spend a lot of time with friends may have learned that more often than not, encounters with peer rejection are often resolved quickly due to the interference of a friend. Across adolescence, if these individuals were 'rescued' by their friends whenever the threat of peer rejection arose, they may have developed the belief that these encounters are 'not that bad', and thus, react less strongly to future instances of peer rejection even when there are no friends present. Although these possibilities cannot be explored with the current data, it would be useful for future research to examine how neural activity during social exclusion relates to feelings of belonging and acceptance, as well as support seeking and friend interactions immediately following the exclusion.

Future research should also examine other indices of friend involvement and social support during adolescence that might yield positive benefits in the face of peer rejection. For example, while time spent with friends outside of school is one useful measure of friend involvement at this age, it would also be interesting to examine how neural responses to social exclusion are impacted by the number of friends that adolescents have and the quality of their friendships (i.e. 'best' friends and reciprocal friends), given that each of these measures is known to be protective in the context of peer rejection (e.g. Hodges and Perry, 1999; Hodges *et al.*, 1999). Furthermore, longitudinal studies examining these qualitative aspects of adolescents' friendships could also explore the stability of these characteristics (i.e. adolescents' ability to maintain high-quality friendships and peer acceptance) over time, in relation to neural responses to peer rejection. This work could examine the possibility that lower neural sensitivity to peer rejection is a general characteristic of individuals with more friends (and/or the reverse—that hyperactivation in dACC and anterior insula characterizes individuals with fewer or low-quality friendships), rather than a consequence of friend involvement during adolescence as we suggest here.

A related issue in the current study is that time spent with friends and neural sensitivity to peer rejection were each measured at only one time point. Thus, it will be particularly important for future studies to examine how these variables change across time, which could reveal directionality and causal links between friendship and sensitivity to peer rejection across adolescence as well as the long-term stability of these associations. As alluded to above, the correlational nature of this study cannot rule out the possibility that stable, trait-level factors not examined in the current study (e.g. social status, self-esteem, or the long-term maintenance of quality friendships) might lead some individuals to be both more involved with friends and less sensitive to peer rejection more generally. Additionally, while we suggest that friend involvement during adolescence may be particularly crucial—given the heightened reliance on friends at this age—measuring friend involvement both during adolescence and at the time of the peer rejection experience 2 years later could reveal whether friend relationships in adolescence are particularly important as a buffer against future rejection, or whether friend involvement at the time of a rejection experience might be equally beneficial. Thus, while the current findings are consistent with the notion that friend involvement during adolescence may reduce neural sensitivity to peer rejection, longitudinal research directly examining the long-term effects of friend involvement on neural sensitivity is needed to confirm this possibility and rule out other explanations.

In this study, it is also important to note that we make some inferences based on previous research linking brain activity with specific emotional processes, when interpreting the meaning of our findings. In other words, we suggest that the dampened brain activity in dACC and anterior insula among individuals who spent more time with friends during adolescence may be an indicator of lower levels of distress following rejection. However, we cannot be certain that the dACC and anterior insula activity observed in this study were in fact indexing feelings of distress—particularly given that activity in any particular brain region at any given time is likely indicative of multiple brain functions (Poldrack, 2006), and given our inability to obtain high-quality, subjective reports of distress to relate to this observed brain activity (note 2). Thus, while we believe that making these kinds of theoretically-grounded inferences is informative for both data interpretation and for formation of new research questions, additional work is needed to further investigate the meaning and directionality of the present findings.

Finally, future work should continue to explore other biological and neurochemical processes through which positive social relationships might yield long-term positive benefits. For instance, given recently discovered links between specific genetic polymorphisms and neural responses to social exclusion (e.g. MAOA and μ-opioid receptor-related polymorphisms; see Eisenberger *et al.*, 2007c; Way *et al.*, 2009; Sebastian *et al.*, 2010), it would be useful to examine other neurochemical, as well as structural, brain processes that might be impacted by social interactions during adolescence. For example, social contact results in the release of endogenous opioids in the brain, which are known to have stress-reducing effects (Panksepp, 1998), and the dACC in particular has a large density of opioid-receptors (Vogt *et al.*, 1995; Schlaepfer *et al.*, 1998). Thus, one possibility is that repeated exposure to supportive others triggers the frequent release of opioids in the dACC and other threat-processing regions, and reduces threat sensitivity over time. Alternatively, interacting with supportive others may also impact the development of brain structures relevant for threat-processing. For example, animal research has indicated that when newborn rodents are separated from their mothers, neurotransmitter fiber systems in some brain regions (e.g. dACC) can be structurally altered in ways that may impact the function in these regions

(Braun *et al.*, 2000). However, cues indicating close proximity of the mother (i.e. hearing the mother's voice) can prevent these changes (Ziabreva *et al.*, 2003), suggesting that social connection may impact structural development of threat-processing regions over time. As such, examining how adolescent friend involvement affects μ-opioid-related and other neurochemical processes, as well as structural changes in specific brain regions, might reveal mechanistic pathways that mediate the link between positive social interactions and neural desensitization to social stressors.

As a whole, the findings presented here indicate that spending more time with friends during adolescence relates to dampened affective neural responses to later social exclusion, and supports the possibility that greater friend involvement may result in individuals feeling less threatened when they encounter future negative social treatment. This work extends the developmental literature on the positive role of friendships during adolescence, and contributes to our understanding of potential mechanisms through which interactions with close others may yield positive benefits. Our hope is that these findings will help shape future behavioral and neuroimaging studies that continue to examine the interplay of social connection and responses to peer rejection during adolescence, in order to increase understanding of adolescents' daily social interactions and the implications of these interactions over time.

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