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Adding insult to injury: neural sensitivity to social exclusion is associated with internalizing symptoms in chronically peer-victimized girls

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Abstract

Despite evidence documenting activation of the social pain network in response to social rejection and its link to temporary distress, far less is known regarding its role in pervasive emotional difficulties. Moreover, research has not considered the intersection between neural activation to experimentally induced social exclusion and naturally occurring social adversity. This study examined an integrated social pain model of internalizing symptoms, which posits that (i) neural sensitivity in the social pain network is associated with internalizing symptoms, (ii) this linkage is more robust in youth with than without a history of social adversity, and (iii) heightened avoidance motivation serves as one pathway linking neural sensitivity and internalizing symptoms. During a functional magnetic resonance imaging scan, 47 adolescent girls (M age = 15.46 years, SD = .35) with well-characterized histories of peer victimization were exposed to social exclusion. Whole-brain analyses revealed that activation to exclusion in the social pain network was associated with internalizing symptoms. As anticipated, this linkage was stronger in chronically victimized than non-victimized girls and was partially accounted for by avoidance motivation. This research indicates the importance of integrating neural, social and psychological systems of development in efforts to elucidate risk for internalizing symptoms among adolescent girls.

Key words: neural sensitivity; internalizing; victimization; avoidance

Introduction

Humans have a fundamental need for social connection, as embodied in concepts such as need for affiliation (McClelland *et al.,* 1953), need to belong (Baumeister and Leary, 1995) and need for approval (Rudolph, Caldwell, & Conley, 2005). Relationships are particularly crucial for development during adolescence, a stage of acute sensitivity to social cues (Rudolph, 2009; Guyer *et al.*, 2012; Rudolph *et al.*, in press). Unfortunately, when social conditions threaten these core needs, individuals experience 'social pain', with neural sequelae akin to those of physical pain (Eisenberger, 2012). Although much research establishes activation of the social pain network in response to social rejection and its association with temporary distress, far less is known regarding its role in more pervasive emotional difficulties, such as internalizing symptoms. Yet, sensitivity in this network is a prime candidate for vulnerability to internalizing symptoms and may even help to explain their dramatic rise in adolescent girls, who show heightened reactivity to social stressors in the form of depression and anxiety (Davila *et al.*, 2010; Rudolph *et al.*, in press).

The present research used functional magnetic resonance imaging (fMRI) to elucidate the role of the social pain network in internalizing symptoms, with a focus on individual differences in vulnerability to these effects and psychological processes

that may explain this vulnerability. In particular, we tested a comprehensive model, which posits that (i) neural sensitivity in the social pain network is associated with internalizing symptoms (depression and social anxiety), (ii) this linkage is more robust in youth with than without a history of social adversity (exposure to chronic peer victimization), and (c) heightened avoidance motivation (psychological sensitivity to social punishment) serves as one pathway linking neural sensitivity and internalizing symptoms.

Social pain network

A growing body of research suggests that exposure to acute social exclusion in the laboratory triggers activation in the same neural circuitry as that underlying the affective component of physical pain (Lieberman and Eisenberger, 2006; Dewall *et al.*, 2010; Eisenberger, 2012). Several regions have been implicated in the social pain network, including the dorsal anterior cingulate cortex (dACC), the subgenual anterior cingulate cortex (sgACC) and the anterior insula (Sebastian, *et al.*, 2001; Masten *et al.*, 2009; Masten *et al.*, 2011; for a review, see Rotge *et al.*, 2014; Eisenberger, 2015). Eisenberger *et al.* (2011) propose that these regions serve as a neural alarm system or 'sociometer', alerting individuals to a discrepancy between their desired social state (social acceptance) and current social conditions (social rejection). This pattern of neural activation is exaggerated in youth exposed to chronic peer stress (Will *et al.*, 2016) and is associated with indicators of temporary distress (for a review, see Rotge *et al.*, 2014), including self-reported distress during exclusion (e.g. Eisenberger, 2012) and greater threat to one's psychological needs (e.g. Eisenberger *et al.*, 2003).

Neural sensitivity to rejection and internalizing symptoms

Given the affective distress accompanying neural sensitivity to social rejection, recent conceptualizations suggest that a heightened social pain response may constitute a risk factor for internalizing symptoms, particularly during adolescence (Masten *et al.*, 2011; Rotge *et al.*, 2014; Silk *et al.*, 2014). Although research linking activation of the social pain network and internalizing symptoms is scarce, two studies provide initial supportive evidence. In one study, adolescents diagnosed with major depressive disorder, relative to healthy adolescents, demonstrated heightened sgACC and left anterior insula activation and more sustained dACC activation in response to rejection during a chatroom task (Silk *et al.*, 2014). In another study, sgACC activation to exclusion during Cyberball (Williams *et al.*, 2000) predicted higher levels of depressive symptoms over a 1-year period in a sample of adolescents (Masten *et al.*, 2011). Adolescents at risk for social anxiety disorder (i.e. those with high early levels of behavioral inhibition) and those with high levels of general and social anxiety also demonstrate differences in neural responses to peer rejection (for a review, see Caouette and Guyer, 2014; Guyer *et al.*, 2015), with one study finding significantly stronger insula activation in anxious than non-anxious youth (Lau *et al.*, 2012). To expand on this research, our first goal was to provide additional evidence that heightened neural sensitivity to exclusion (social pain) is associated with internalizing symptoms, as reflected in symptoms of depression and social anxiety (Hypothesis 1).

Targeted social rejection and internalizing symptoms

Outside of the laboratory, interpersonal theories of internalizing symptoms also highlight social rejection as a mechanism of risk for depression and social anxiety. Slavich and colleagues' 'black sheep' theory of depression (Slavich *et al.*, 2009, 2010) focuses on the role of targeted social rejection, or naturally occurring stressors involving a direct threat to one's sense of belonging. Targeted rejection stressors involve three dimensions: (i) an intent to reject, or stressors characterized by an active and intentional severing of relational ties; (ii) an isolated impact, or stressors directed at, and meant to affect, a single person; and (iii) social demotion, or stressors involving a loss of social status. This theory proposes that targeted rejection stressors play a central role in depression. Because these stressors trigger heightened social-evaluative threat, devaluation of the self, and social avoidance (Slavich *et al.*, 2009, 2010), they also are likely risk factors for social anxiety. Other models of social anxiety also implicate peer rejection as a robust risk factor (Davila *et al.*, 2010; La Greca *et al.*, 2011; Caouette and Guyer, 2014).

Peer victimization is a relatively common form of social stress in childhood (Boivin *et al.*, 2010) that shares the three key features of targeted social rejection. Specifically, peer victimization involves purposeful and direct efforts to reject individuals through physical and/or psychological means (e.g. exposure to hitting, verbal assaults, rumor-spreading, social manipulation and active exclusion; Crick and Grotpeter, 1996); moreover, peer-victimized youth experience a loss of social status over time (Kochel *et al.*, 2012). Consistent with theories of targeted rejection, both early occurring and chronic victimization are robust predictors of depressive symptoms (Rudolph *et al.*, 2011) and social anxiety/avoidance (Siegel *et al.*, 2009; Rudolph *et al.*, 2014).

Integrating laboratory and naturalistic research on targeted rejection

Typically, social rejection has been conceptualized and studied either in terms of the neural effects of acute social exclusion in the laboratory or the psychological effects of naturally occurring targeted rejection. The present study represents one of the first efforts to integrate these two lines of research to provide a comprehensive picture regarding the joint role of neural sensitivity and targeted rejection in risk for internalizing symptoms. Specifically, we anticipated that exposure to chronic peer victimization would impart a social 'bruise' that intensifies the effect of subsequent social insults, thereby amplifying the association between acute neural sensitivity to rejection and internalizing symptoms. Thus, our second goal was to investigate whether heightened neural sensitivity to exclusion (social pain) is more strongly associated with internalizing symptoms among youth with a history of chronic peer victimization than among youth with minimal exposure to peer victimization (Hypothesis 2).

Avoidance motivation as an explanatory pathway

A third goal of this study was to better understand the psychological pathway linking neural sensitivity to exclusion with internalizing symptoms. Although it is clear why heightened activation in the social pain network might lead to temporary increases in emotional distress, why would this acute sensitivity foster pervasive and persistent emotional difficulties such as

depressive symptoms and social anxiety? To answer this question, we focused on avoidance motivation as one explanatory process. Avoidance motivation can be conceptualized as a psychological sensitivity to aversive aspects of the social environment. In this study, we incorporated three aspects of avoidance motivation: general avoidance motivation, construed as a drive to avoid exposure to threat, punishment, and loss (Gray, 1991; Carver and White, 1994); performance-avoidance goals, construed as a drive to avoid negative judgments and loss of status in the peer group (Rudolph *et al.*, 2013; Llewellyn and Rudolph, 2014); and avoidance-oriented need for approval, construed as a depletion of one's self-worth in the face of social disapproval (Rudolph *et al.*, 2005; Rudolph and Bohn, 2014).

An enhanced social pain response (i.e. greater neural activation in response to rejection) may be reflected in an accompanying psychological sensitivity to aversive social cues in the form of avoidance motivation. Indeed, individuals who show heightened dACC activation in response to acute social exclusion also demonstrate pro-inflammatory responses to social evaluation (Slavich *et al.*, 2010), suggesting that social pain is associated with activation of the stress response system in the context of social evaluation. Heightened social pain responses also are linked to self-reported rejection sensitivity (Burklund *et al.*, 2007; Masten *et al.*, 2009) and an anxious attachment style marked by vigilance to rejection cues (DeWall *et al.*, 2012). Thus, youth who show a heightened social pain response may become sensitive to social cues of evaluation and potential rejection, may formulate social goals aimed at avoiding such adverse social judgments, and may develop a sense of worth that is threatened by disapproval. Chronically victimized youth with a heightened social pain response may be especially prone to developing these forms of persistent psychological sensitivity given their history of social maltreatment. In turn, heightened avoidance motivation predicts depressive symptoms (Coplan *et al.*, 2006; Rudolph *et al.*, 2013; Llewellyn and Rudolph, 2014) and social anxiety/withdrawal (Coplan *et al.*, 2006; Rudolph and Bohn, 2014; for a review, see Caouette and Guyer, 2014). We therefore hypothesized that avoidance motivation would serve as one pathway linking neural sensitivity to exclusion with internalizing symptoms among victimized youth (Hypothesis 3).

Study overview

To address these research questions, we recruited adolescent girls who had well-characterized histories of victimization through the school years (2nd–8th grades). We focused on this group because adolescence is a stage of heightened neural sensitivity (i.e. heightened affective processing during peer evaluation) and psychological sensitivity (i.e. anxiety about peer acceptance and evaluation) to social threat, particularly in girls (Nelson *et al.*, 2005; Guyer *et al.*, 2009; Guyer *et al.*, 2012). Moreover, relative to boys, girls show a dramatic rise in depressive symptoms (Hankin and Abramson, 2001) and social anxiety (Nelemans *et al.*, 2014) during adolescence as well as a stronger contribution of interpersonal stress and social sensitivity to internalizing symptoms (Gunnar *et al.*, 2009; Rudolph, 2009; Davila *et al.*, 2010).

Materials and methods

Participants and procedures

Participants included 47 adolescent girls who were recruited from a longitudinal study tracking youth from 2nd–8th grade

(M_{age} second grade = 7.91 years, s.d. = 0.95 years; for details about the longitudinal study, see Rudolph, Lansford *et al*, 2014; Rudolph, Troop-Gordon *et al.*, 2014; Troop-Gordon *et al.*, 2015). Four additional girls were scanned but not included due to either a malfunction in the Cyberball program or missing data on key measures. Based on youths' annual reports of victimization across the 7 years, we recruited 24 chronically victimized girls (M_{age} = 15.46 years, s.d. = 0.35) and 23 non-victimized girls (M_{age} = 15.35 years, s.d. = 0.37). Chronically victimized girls scored ≥ 0.75 s.d. above the mean on victimization for at least 3 of 7 years (average = 4.33 years, range = 3–7 years), with an average victimization score of 1.22 s.d. above the mean. Non-victimized girls scored ≤ -0.75 s.d. below the mean on victimization for at least 3 of 7 years (average = 4.83 years, range = 3–7 years), with an average victimization score of 0.82 s.d. below the mean. Parents provided written consent and adolescents provided written assent in accordance with the University of Illinois' Institutional Review Board. During the summer following ninth grade, participants completed a functional brain scan while playing Cyberball (Williams *et al.*, 2000), a well-established laboratory manipulation of acute social exclusion. Following the scan, they completed measures of depressive symptoms and social anxiety. The participants received a monetary incentive for their participation.

Self-report measures

Peer victimization. During the 2nd–8th grades, participants completed a 21-item revised version (for details, see Rudolph *et al.*, 2014) of the Social Experiences Questionnaire (Crick and Grotpeter, 1996) to assess exposure to peer victimization. This measure assesses overt victimization (being the target of behaviors intended to harm others through physical damage, threat of such damage, or verbal aggression; 11 items; e.g. 'How often do you get hit by another kid?', 'How often does another kid insult you or put you down?') and relational victimization (being the target of behaviors intended to harm others through manipulation of relationships; 10 items; e.g. 'How often does another kid say they won't like you unless you do what they want you to do?'). Youth checked a box indicating how often they experienced each type of victimization on a 5-point scale. Scores were computed as the mean of the 21 items.

Internalizing symptoms. Two measures were used to assess internalizing symptoms at the time of the scan. First, youth completed the Short Mood and Feelings Questionnaire (Angold *et al.*, 1995) to assess depressive symptoms (e.g. 'I felt unhappy or miserable'). Youth indicated how much they experienced each symptom on a 4-point scale. Scores were computed as the mean of the 13 items. Second, youth completed the Social Anxiety Scale for Adolescents (La Greca and Lopez, 1998) to assess social anxiety (e.g. 'I'm afraid to invite peers to do things with me because they might say no'). Youth indicated how much they experienced each symptom on a 5-point scale. Scores were computed as the mean of the 18 items. Because we had similar hypotheses for depressive symptoms and social anxiety and the measures were strongly correlated ($r = 0.42$, $P = 0.004$), a composite variable was formed by standardizing and averaging the two measures.

Avoidance motivation. Three measures were used to assess avoidance motivation at the time of the scan. First, youth completed a slightly revised version (for details, see Rudolph *et al.*, 2013) of the Behavioral Inhibition Scale (BIS) (Carver and White,

1994; Muris *et al.*, 2005). The BIS subscale assesses general sensitivity to aversive stimuli, although some items include a social focus (e.g. 'I feel hurt when people scold me or tell me that I did something wrong'). Youth indicated how true each item was on a 4-point scale. Scores were computed as the mean of the seven items. Second, youth completed the performance-avoidance subscale of the Social Achievement Goals Survey (Rudolph and Abaied *et al.*, 2011), which assesses goals that focus on demonstrating competence by avoiding negative social judgments (e.g. 'My main goal is to make sure I don't look like a loser'). Youth received the prompt: 'When I am around other kids…' and indicated how true each item was on a 5-point scale. Scores were computed as the mean of the seven items. Third, youth completed the avoidance subscale of the Need for Approval Questionnaire (Rudolph *et al.*, 2005), which assesses sensitivity to peer disapproval (the extent to which peer disapproval weakens one's sense of self-worth; e.g. 'I feel like I am a bad person when other kids don't like me'). Youth indicated how true each item was on a 5-point scale. Scores were computed as the mean of the four items. Because the three indexes of avoidance motivation assessed similar constructs and were strongly correlated (r's ranged from 0.39 to 0.70, all P's < 0.001), a composite variable was formed by standardizing and averaging the three measures. Similar composites have established validity (e.g. Rudolph *et al.*, 2013; Llewellyn and Rudolph, 2014).

fMRI task

While completing the scan, participants were exposed to social rejection using Cyberball (Williams *et al.*, 2000), which creates a subjective experience of being excluded. Participants were told they would be playing an on-line ball-throwing game with two peers (ostensibly in another room) also completing the same study and connected via the Internet. Participants could see the photographs of the other two players on a computer screen as well as their own 'hand' that they controlled using a button-box. Throughout the game, the ball is thrown back and forth among the three players. When the participant received the ball, she returned it to either player by pushing one of two buttons. The throws of the other two 'players' were determined by the pre-set program. Each participant completed two rounds. In the inclusion round, she was equally included in the tosses. In the exclusion round, she was excluded after 10 tosses. Providing validity for the exclusion experience, chronically victimized girls ($M = 3.18$, s.d. $= 0.85$) reported feeling significantly more threat to their need to belong following Cyberball than non-victimized girls [$M = 2.63$, s.d. $= 0.58$, $t(45) = 2.54$, $P = 0.02$; $d = 0.74$], measured by the Need-Threat Scale (Williams *et al.*, 2000), a 12-item self-report measure (higher scores reflect more threat to one's needs) assessing feelings of rejection (e.g. 'I felt rejected'), belongingness (e.g. 'I felt disconnected'), self-esteem (e.g. 'I felt good about myself') and social control (e.g. 'I felt powerful').

fMRI data acquisition and analysis

fMRI data acquisition. Imaging data were collected using a 3 Tesla Siemens Trio MRI scanner. The Cyberball task included T2*-weighted echoplanar images (EPI) (slice thickness $= 3$ mm; 38 slices; TR (temporal resolution) $= 2$ s; TE (echo time) $= 25$ ms; matrix $= 92 \times 92$; FOV (field of view) $= 230$ mm; voxel size $2.5 \times 2.5 \times 3$ mm^3). Structural scans consisted of a T2*weighted, matched-bandwidth (MBW), high-resolution, anatomical scan (TR $= 4$ s; TE $= 64$ ms; FOV $= 230$; matrix $= 192 \times 192$; slice thickness $= 3$ mm; 38 slices) and a T1* magnetization-prepared rapid-

acquisition gradient echo (MPRAGE; TR $= 1.9$ s; TE $= 2.3$ ms; FOV $= 230$; matrix $= 256 \times 256$; sagittal plane; slice thickness $= 1$ mm; 192 slices). The orientation for the MBW and EPI scans was oblique axial to maximize brain coverage.

fMRI data preprocessing and analysis. Neuroimaging data were preprocessed and analyzed using Statistical Parametric Mapping (SPM8; Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK). Preprocessing for each participant's images included spatial realignment to correct for head motion (no participant exceeded 2 mm of maximum image-to-image motion in any direction). The realigned functional data were coregistered to the high resolution MPRAGE, which was then segmented into cerebrospinal fluid, gray matter and white matter. The normalization transformation matrix from the segmentation step was then applied to the functional and T2 structural images, thus transforming them into standard stereotactic space as defined by the Montreal Neurological Institute and the International Consortium for Brain Mapping. The normalized functional data were smoothed using an 8 mm Gaussian kernel, full-width-at-half maximum, to increase the signal-to-noise ratio.

Statistical analyses were performed using the general linear model (GLM) in SPM8. The task was modeled as a block design, with two blocks: inclusion and exclusion. High-pass temporal filtering with a cutoff of 128 s was applied to remove low-frequency drift in the time series. Serial autocorrelations were estimated with a restricted maximum-likelihood algorithm with an autoregressive model order of 1. The parameter estimates resulting from the GLM were used to create linear contrast images comparing exclusion to inclusion. Random effects, group-level analyses were performed on all individual subject contrasts.

To correct for multiple comparisons, we conducted a Monte Carlo simulation implemented using 3dClustSim in the software package AFNI (Ward, 2000). We used our group-level brain mask, which included only gray matter. Results of the simulation indicated a voxel-wise threshold of $P < 0.005$ combined with a minimum cluster size of 42 voxels for the whole brain, corresponding to $P < 0.05$, False Wise Error corrected.

Overview of analyses

At the group level, our primary analysis examined neural activation for the contrast exclusion–inclusion. To examine the association between neural activation during exclusion and internalizing symptoms (Hypothesis 1), we conducted whole-brain regression analyses in which we regressed internalizing symptoms for the whole sample ($N = 47$) onto neural activation during exclusion–inclusion. We then extracted parameter estimates of signal intensity from the clusters of activation for *a priori* regions of interest (ROIs; i.e. dACC, sgACC and bilateral insula) that showed significant correlations with internalizing symptoms. These values were used in a series of path analyses to test whether (i) heightened neural activation to exclusion (specifically in regions linked to social pain) would be more strongly associated with internalizing symptoms in victimized than non-victimized girls (Hypothesis 2); and (ii) higher levels of avoidance motivation would account, in part, for the link between neural activation and internalizing symptoms in victimized girls (Hypothesis 3). These analyses were conducted in Mplus (Muthén and Muthén, 1998–2007) using full information maximum likelihood (Enders and Bandalos, 2001).

Figure 2 presents the integrated conceptual model. For each index of neural sensitivity (dACC, sgACC and insula activation),

a separate path model was estimated. We conducted model-testing in two steps. To test Hypothesis 2, Step 1 examined the total effect of neural sensitivity on internalizing symptoms and its moderation by victimization status by setting the paths to and from avoidance motivation to 0. This step allowed us to estimate the total effect of neural sensitivity on internalizing symptoms for victimized and non-victimized girls. To test Hypothesis 3, Step 2 examined the extent to which this total effect could be accounted for by an indirect effect through avoidance motivation. Specifically, we freely estimated the path from neural sensitivity to avoidance motivation (Path *b*) and the path from avoidance motivation to internalizing symptoms (Path *c*). To determine whether moderation of the total effect of neural sensitivity on internalizing symptoms could be accounted for by a difference in the neural sensitivity–avoidance motivation link among victimized *vs* non-victimized girls, victimization status served as moderator of Path *b*. Path *a* and its moderation by victimization status also were estimated in Step 2, providing an estimate of the remaining direct effect of neural sensitivity on internalizing symptoms after taking into account the indirect effect (i.e. whether neural sensitivity was linked to internalizing symptoms above and beyond the path through avoidance motivation).

This two-step model-testing approach allowed us to test the significance of (i) the conditional total effect of neural sensitivity on internalizing symptoms (i.e. the effect for victimized and non-victimized girls; Step 1), (ii) the conditional indirect effect of neural sensitivity on internalizing symptoms through avoidance motivation (i.e. Path *b* estimated separately for victimized and non-victimized girls * Path *c*; Step 2), and (iii) the conditional direct effect of neural sensitivity on internalizing symptoms (i.e. the direct effect for victimized and non-victimized girls after accounting for the indirect effect in Step 2). In sum, this analysis examined the total effect (i.e. direct + indirect effects) of neural sensitivity on internalizing symptoms, the indirect effect via avoidance motivation, and the remaining direct effect as well as whether these effects were significant for victimized and non-victimized girls (Preacher *et al.*, 2007).

Results

Descriptive statistics

Table 1 presents descriptive data and group comparisons for 2nd–8th grade peer victimization in the longitudinal study as well as depressive symptoms, social anxiety and the three indexes of avoidance motivation at the time of the scan. Victimized girls reported more 2nd–8th grade peer victimization, all d's > 1.55, as well as higher levels of depressive symptoms, $d = 1.37$, social anxiety, $d = 0.89$, behavioral inhibition, $d = 0.95$, and avoidance-oriented need for approval, $d = 0.62$, at the time of the scan than did non-victimized girls. They did not report more performance avoidance than did non-victimized girls, $d = 0.12$. As shown in Supplementary Figure S1, victimized girls showed greater activation in the dACC during exclusion relative to inclusion than non-victimized girls, as well as greater activation in the amygdala and inferior fusiform gyrus (Supplementary Table S1).

Association between neural activation and internalizing symptoms

In whole-brain regression analyses, we regressed internalizing symptoms onto neural activation during exclusion–inclusion.

Consistent with Hypothesis 1, greater activation in the social pain network, including the dACC, sgACC and anterior insula, was associated with heightened internalizing symptoms (Table 2). For descriptive purposes, we extracted parameter estimates of signal intensity from these regions and plotted the association for neural activation and internalizing symptoms in the total sample as well as within victimized and non-victimized girls (Figure 1). As reflected in Table 2, regions outside of the social pain network also showed heightened activation in relation to internalizing symptoms. For parsimony, follow-up analyses were conducted only with the three *a priori* ROIs.

Tests of the full model

To test the model depicted in Figure 2 (Hypotheses 2 and 3), we extracted parameter estimates of signal intensity from each of the three ROIs that showed a significant correlation with internalizing symptoms for the whole sample. For parsimony, we took an average of the standardized values for the two regions of activation in the dACC and sgACC, respectively, creating a single score for each region. We then conducted a separate path analysis for each ROI. In Step 1, only paths reflecting the main and interactive effects of neural sensitivity and victimization status on internalizing symptoms were estimated. Moderation of the effect of neural sensitivity on internalizing symptoms by victimization status was tested by including a Neural Sensitivity × Victimization Status interaction term. This step provided an estimate of the conditional total effect of neural sensitivity on internalizing symptoms for victimized and non-victimized girls. In Step 2, the paths reflecting the indirect effects of neural sensitivity, victimization status and their interaction on avoidance motivation also were estimated. Moderation of the effect of neural sensitivity on avoidance motivation by victimization status was tested by including a Neural Sensitivity × Victimization Status interaction term. This step provided an estimate of the extent to which the conditional total effect was accounted for by a conditional indirect effect through avoidance motivation (for additional detail, see Overview of Analyses). Table 3 presents results of these analyses.

Model 1: DACC activation. To determine whether dACC activation was significantly associated with internalizing symptoms and whether victimization status moderated this association (Step 1), we first tested the model setting Path *b*, Path *c* and moderation of Path *b* by Victimization Status equal to 0 (Figure 2). This provided a test of the conditional total effect (i.e. the conditional effect of dACC activation on internalizing symptoms without considering avoidance). The analysis yielded a significant main effect for victimization status, $b = 0.77$, SE = 0.14, P < 0.001, and a significant dACC × Victimization Status interaction, $b = 0.54$, SE = 0.17, P = 0.002. The total effect of dACC activation on internalizing symptoms was significant for victimized girls, $b = 0.70$, SE = 0.12, P < 0.001, but not for non-victimized girls, $b = 0.16$, SE = 0.12, P = 0.20 (Figure 3A).

In Step 2, we tested the extent to which the conditional total effect of dACC activation on internalizing symptoms could be accounted for by a conditional indirect effect through avoidance. The paths from dACC activation to avoidance (Path *b*) and from avoidance to internalizing symptoms (Path *c*) were estimated, as was the path from the dACC × Victimization Status interaction to avoidance. The left column in Table 3 presents the results of this analysis. A significant dACC × Victimization Status interaction emerged in the prediction of avoidance,

Table 1. Descriptive statistics and psychometrics for victimized and non-victimized girls

Variable	Victimized girls		Non-victimized girls		t-test (df)	α
	M	s.d.	M	s.d.		
Second grade peer victimization	2.98	0.92	1.87	0.48	5.07*** (42)	0.93
Third grade peer victimization	2.94	0.87	1.47	0.45	7.15*** (44)	0.96
Fourth grade peer victimization	2.67	0.71	1.31	0.30	8.28*** (42)	0.95
Fifth grade peer victimization	2.54	0.68	1.22	0.28	8.66*** (45)	0.95
Sixth grade peer victimization	2.45	0.68	1.17	0.21	8.59*** (45)	0.95
Seventh grade peer victimization	2.45	0.55	1.07	0.08	11.80*** (45)	0.96
Eighth grade peer victimization	2.44	0.58	1.10	0.14	10.95*** (45)	0.96
Depressive symptoms	2.03	0.71	1.21	0.51	4.54*** (44)	0.95
Social anxiety	2.53	0.91	1.84	0.64	2.99** (45)	0.96
Behavioral inhibition	2.63	0.72	2.03	0.54	3.19** (45)	0.83
Performance avoidance	2.08	1.10	1.98	0.60	.39 (44)	0.90
Avoidance-oriented NFA	1.86	1.09	1.35	0.49	2.07* (45)	0.89

Note. NFA, need for approval.
*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

$b = 0.55$, SE $= 0.19$, $P = 0.004$, showing that the effect of dACC activation on avoidance (Path b) was significantly moderated by victimization status. The effect of dACC activation on avoidance was significant for victimized girls, $b = 0.75$, SE $= 0.14$, $P < 0.001$, but not for non-victimized girls, $b = 0.19$, SE $= 0.14$, $P = 0.17$. Moreover, avoidance significantly predicted internalizing symptoms, $b = 0.34$, SE $= 0.12$, $P = 0.005$. This resulted in a significant conditional indirect effect of dACC activation on internalizing symptoms through avoidance for victimized girls, $b = 0.25$, SE $= 0.10$, $P = 0.01$, but not for non-victimized girls, $b = 0.06$, SE $= 0.05$, $P = 0.22$. The dACC × Victimization Status interaction predicting internalizing symptoms was smaller after accounting for the conditional indirect effect, but remained significant, $b = 0.36$, SE $= 0.17$, $P = 0.04$. The direct effect of dACC activation on internalizing symptoms was significant for victimized girls, $b = 0.45$, SE $= 0.14$, $P < 0.001$, but not for non-victimized girls, $b = 0.09$, SE $= 0.12$, $P = 0.42$.

In sum, these results confirm the hypothesis that dACC activation predicts internalizing symptoms in victimized but not non-victimized girls. As expected, the effect of dACC activation on internalizing symptoms was partly explained by a link between dACC activation and avoidance motivation for victimized but not non-victimized girls. However, there remained a direct effect of dACC activation on internalizing symptoms for victimized girls that was not accounted for by avoidance motivation.

Model 2: sgACC activation. To determine whether sgACC was significantly associated with internalizing symptoms and whether victimization status moderated this association (Step 1), we first tested the model setting Path b, Path c and moderation of Path b by Victimization Status equal to 0 (Figure 2). This provided a test of the conditional total effect. The analysis yielded a significant main effect for victimization status, $b = 0.77$, SE $= 0.16$, $P < 0.001$, and a significant sgACC × Victimization Status interaction, $b = 0.48$, SE $= 0.20$, $P = 0.02$. The total effect of sgACC activation on internalizing symptoms was significant for victimized girls, $b = 0.51$, SE $= 0.11$, $P < 0.001$, but not for non-victimized girls, $b = 0.03$, SE $= 0.17$, $P = 0.84$ (Figure 3B).

In Step 2, we tested the extent to which the conditional total effect of sgACC activation on internalizing symptoms could be accounted for by a conditional indirect effect through avoidance. The paths from sgACC activation to avoidance (Path b) and from avoidance to internalizing symptoms (Path c) were estimated, as was the path from the sgACC × Victimization Status interaction to avoidance. The middle column in Table 3 presents the results of this analysis. Although the sgACC × Victimization Status interaction did not significantly predict avoidance, $b = 0.33$, SE $= 0.25$, $P = 0.20$, the conditional effect of sgACC activation on avoidance (Path b) was significant for victimized girls, $b = 0.38$, SE $= 0.13$, $P = 0.004$, but not for non-victimized girls, $b = 0.06$, SE $= 0.22$, $P = 0.79$. Moreover, avoidance significantly predicted internalizing symptoms, $b = 0.44$, SE $= 0.10$, $P < 0.001$. This resulted in a significant conditional indirect effect of sgACC activation on internalizing symptoms through avoidance for victimized girls, $b = 0.17$, SE $= 0.07$, $P = 0.01$, but not for non-victimized girls, $b = 0.03$, SE $= 0.10$, $P = 0.79$. The sgACC × Victimization Status interaction predicting internalizing symptoms was smaller after accounting for the conditional indirect effect, but remained significant, $b = 0.33$, SE $= 0.17$, $P = 0.05$. The direct effect of sgACC activation on internalizing symptoms was significant for victimized girls, 0.34, SE $= 0.10$, $P < 0.001$, but not for non-victimized girls, 0.01, SE $= 0.14$, $P = 0.95$.

In sum, these results confirm the hypothesis that sgACC activation predicts internalizing symptoms in victimized but not non-victimized girls. As expected, the effect of sgACC activation on internalizing symptoms was partly explained by a link between sgACC activation and avoidance motivation for victimized but not non-victimized girls. However, there remained a direct effect of sgACC activation on internalizing symptoms for victimized girls that was not accounted for by avoidance motivation.

Model 3: Insula activation. To determine whether insula activation was significantly associated with internalizing symptoms and whether victimization status moderated this association (Step 1), we first tested the model setting Path b, Path c and moderation of Path b by Victimization Status equal to 0 (Figure 2). This provided a test of the conditional total effect. The analysis yielded a significant main effect for victimization status, $b = 0.67$, SE $= 0.19$, $P < 0.001$, and a marginally significant
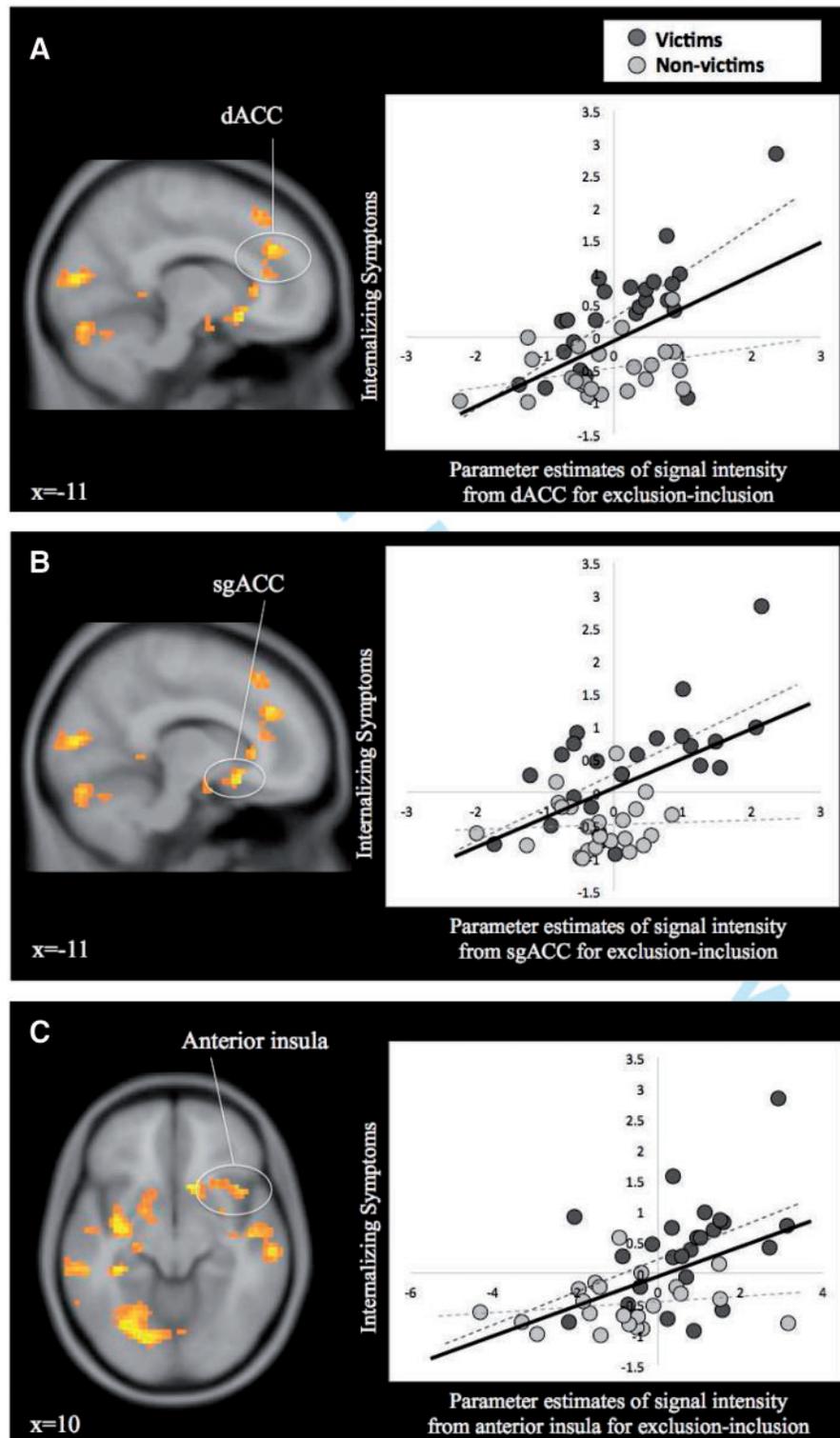
Fig. 1. Greater activation in the dACC, sgACC and anterior insula predicts higher levels of internalizing symptoms: (A) dACC activation during the exclusion condition compared with the inclusion condition that was positively correlated with internalizing symptoms; (B) sgACC activation during the exclusion condition compared with the inclusion condition that was positively correlated with internalizing symptoms; (C) anterior insula activation during the exclusion condition compared with the inclusion condition that was positively correlated with internalizing symptoms. *Note.* In the scatterplots, the solid black line indicates the trend line for the entire sample, the dashed black line indicates the trend line for victims, and the dashed gray line indicates the trend line for non-victims.
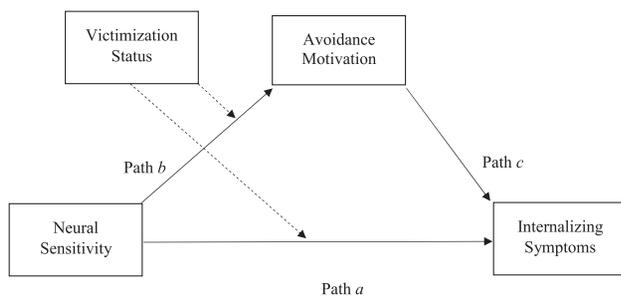
Fig. 2. Conceptual model showing conditional direct effects of neural sensitivity on internalizing symptoms and conditional indirect effects of neural sensitivity on internalizing symptoms through avoidance motivation. Dotted lines represent moderation of Path *a* and Path *b*.

Table 2. Regions of activation to exclusion condition *vs* inclusion condition that correlated significantly with internalizing symptoms

Region name	x	y	z	t	k
Fusiform gyrus	−36	−34	−14	5.98	779[a]
Hippocampus	−21	−16	−20	3.92	[a]
Subgenual ACC	−15	11	−14	3.18	[a]
Amygdala	−15	−4	−14	3.34	[a]
Fusiform gyrus	−30	−67	−11	4.38	858
Posterior insula	51	−1	1	3.55	419
IFG	−36	23	28	4.27	200[b]
Middle frontal gyrus	−27	44	34	3.55	[b]
Superior medial gyrus	0	44	40	2.98	[b]
Subgenual ACC	12	17	−11	4.26	194[c]
Anterior insula	42	14	−14	3.90	[c]
Amygdala	17	−3	−17	4.14	[c]
TPJ	−42	−52	19	4.24	106
Dorsolateral ACC	3	35	31	3.46	642[d]
Dorsolateral ACC	−3	20	37	3.81	[d]
Cerebellar vermis	6	−46	1	3.68	51
Precentral gyrus	45	−10	49	3.38	49

Notes. x, y and z refer to MNI (Montreal Neurological Institute) coordinates; t refers to the t-score at those coordinates (local maxima); k refers to the number of voxels in each significant cluster. Clusters that share the same superscript are part of the same cluster of activation. IFG, inferior fusiform gyrus; TPJ, temporal parietal junction.

Insula × Victimization Status interaction, $b = 0.36$, $SE = 0.20$, $P = 0.07$. As expected, the total effect of insula activation on internalizing symptoms was significant for victimized girls, $b = 0.43$, $SE = 0.15$, $P < 0.004$, but not for non-victimized girls, $b = 0.07$, $SE = 0.13$, $P = 0.57$ (Figure 3C).

In Step 2, we tested the extent to which the conditional total effect of insula activation on internalizing symptoms could be accounted for by a conditional indirect effect through avoidance. The paths from insula activation to avoidance (Path *b*) and from avoidance to internalizing symptoms (Path *c*) were estimated, as was the path from the Insula × Victimization Status interaction to avoidance. The right column in Table 3 presents the results of this analysis. Although the Insula × Victimization Status interaction did not significantly predict avoidance, $b = 0.29$, $SE = 0.21$, ns, the conditional effect of insula activation on avoidance (Path *b*) was significant for victimized girls, $b = 0.54$, $SE = 0.16$, $P < 0.001$, and marginally significant for non-victimized girls, $b = 0.25$, $SE = 0.13$, $P = 0.06$. Moreover, avoidance significantly predicted internalizing symptoms, $b = 0.55$, $SE = 0.12$, $P < 0.001$. This resulted in a significant conditional indirect effect of insula activation on internalizing symptoms through avoidance for victimized girls,

$b = 0.30$, $SE = 0.11$, $P = 0.005$, and a marginally significant conditional indirect effect for non-victimized girls, $b = 0.14$, $SE = 0.08$, $P = 0.08$. After accounting for the conditional indirect effect, the Insula × Victimization Status interaction did not significantly predict internalizing symptoms, $b = 0.20$, $SE = 0.17$, $P = 0.22$, and the direct effect of insula activation on internalizing symptoms was nonsignificant for victimized girls, $b = 0.14$, $SE = 0.14$, $P = 0.32$, and for non-victimized girls, $b = −0.06$, $SE = 0.11$, $P = 0.55$.

In sum, these results confirm the hypothesis that insula activation predicts internalizing symptoms, and this effect was explained by avoidance motivation. Although the difference between the effects for the victimization groups (i.e. the interactions) tended not to be significant, the within-group effects suggested a more robust effect of insula activation on internalizing symptoms (via avoidance motivation) for victimized than non-victimized girls.

Discussion

Theory and research implicate challenges to the human need to belong as a risk factor for emotional distress (Rudolph *et al.*, 2005; Slavich *et al.*, 2010). Previous support for this idea has emerged from two distinct lines of investigation. One set of studies focuses on neural sensitivity to experimentally induced acute social exclusion (e.g. Masten *et al.*, 2011; Eisenberger, 2012; for a review, see Rotge *et al.* 2014), whereas a second set of studies focuses on emotional sensitivity to naturally occurring social rejection (e.g. Slavich *et al.*, 2009; Rudolph *et al.*, 2011). The present study makes a novel contribution by integrating these two lines of theory and research to examine (i) whether neural sensitivity to exclusion is associated with internalizing symptoms, (ii) whether this link is contingent on adolescent girls' naturally occurring social experiences, and (iii) what psychological processes are involved in this process.

Association between neural sensitivity and internalizing symptoms

Social pain theory suggests that threats to social bonds activate neural regions associated with physical pain, including the dACC, sgACC and insula. Although this theory highlights the emotional distress associated with exposure to social pain, most research has examined distress immediately following an experimental manipulation of social rejection (for exceptions, see Masten *et al.* 2011; Lau *et al.*, 2012; Silk *et al.*, 2014). Our first goal was to examine whether neural activation in the social pain network is associated with indexes of more pervasive and enduring distress, as reflected in internalizing symptoms, in a sample of adolescent girls. Consistent with our hypothesis and a few prior studies, whole-brain regression analyses revealed that activation in the dACC, sgACC and insula was significantly associated with higher levels of internalizing symptoms.

These findings suggest that challenges to social bonds not only result in temporary emotional perturbations but also may create pervasive emotional difficulties. It is reasonable that at the time of a social rejection, many youth feel a sense of social pain and, accordingly, report more emotional distress. Moreover, enhanced social pain responses co-occur with increasing age (Guyer *et al.*, 2009) and puberty (Silk *et al.*, 2014), suggesting that adolescence may be a time of particular neural sensitivity to rejection. But not all girls develop internalizing symptoms during adolescence—for whom might this heightened neural sensitivity foster more pervasive internalizing symptoms and how does this process unfold? We sought to address these two questions by testing an integrated model of

Table 3. Path analyses testing the indirect, direct and total effects of neural sensitivity (dACC, sgACC and insula activation) on internalizing symptoms

| | Model 1: dACC | | Model 2: sgACC | | Model 3: Insula | |
| | | | Unstandardized path coefficients | | | |
	b (SE)		b (SE)		b (SE)	
Neural sensitivity to internalizing symptoms (Path a)	0.09 (0.12)		0.01 (0.14)		−0.06 (0.11)	
Victimization status to internalizing symptoms	0.65*** (0.14)		0.60*** (0.14)		0.60*** (0.16)	
Neural Sensitivity × Victimization Status to Internalizing symptoms (i.e. moderation of Path a by victimization status)	0.36* (0.17)		0.33† (0.17)		0.20 (0.17)	
Neural sensitivity to avoidance (Path b)	0.19 (0.14)		0.06 (0.22)		0.25† (0.13)	
Victimization status to avoidance	0.35* (0.16)		0.39* (0.20)		0.15 (0.20)	
Neural Sensitivity × Victimization Status to Avoidance (i.e. moderation of Path b by victimization status)	0.55** (0.19)		0.33 (0.25)		0.29 (0.21)	
Avoidance to internalizing symptoms (Path c)	0.34** (0.12)		0.44*** (0.10)		0.55*** (0.12)	
	Conditional Effects on Avoidance for Victimized and Non-Victimized Girls					
	Vic. Girls	Non-Vic. Girls	Vic. Girls	Non-Vic. Girls	Vic. Girls	Non-Vic. Girls
Neural sensitivity to avoidance	0.75*** (0.14)	0.19 (0.14)	0.38** (0.13)	0.06 (0.22)	0.54*** (0.16)	0.25† (0.13)
	Decomposition of Effect of Neural Sensitivity on Internalizing Symptoms					
	Vic. Girls	Non-Vic. Girls	Vic. Girls	Non-Vic. Girls	Vic. Girls	Non-Vic. Girls
Total effect (estimated at Step 1)	0.70*** (0.12)	0.16 (0.12)	0.51*** (0.11)	0.03 (0.17)	0.43** (0.15)	0.07 (0.13)
Indirect effect (estimated at Step 2)	0.25* (0.10)	0.06 (0.05)	0.17* (0.07)	0.03 (0.10)	0.30** (0.11)	0.14† (0.08)
Direct effect (estimated at Step 2)	0.45*** (0.14)	0.09 (0.12)	0.34*** (0.09)	0.01 (0.14)	0.14 (0.14)	−0.06 (0.11)

Note. Non-vic., non-victimized; Vic., victimized.
†$P < 0.10$; *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

internalizing symptoms that places neural sensitivity within the context of girls' everyday social lives and considers one possible explanatory pathway through which neural sensitivity is associated with internalizing symptoms.

## Individual differences in the neural sensitivity–internalizing symptoms link

To better understand whether some adolescents are more vulnerable than others to the pervasive emotional effects of a heightened social pain response, we examined whether neural sensitivity to social exclusion has particularly robust implications for emotional well-being among adolescents with a history of chronic social rejection in the form of peer victimization. Supporting this hypothesis, heightened activation in each of the three social pain regions was associated with internalizing symptoms among adolescent girls with a history of peer victimization but not among those without a history of peer victimization, with a particularly strong interactive effect for the dACC. Being exposed to negative social feedback across the school years may leave a social bruise that intensifies the meaning of subsequent painful social experiences, such that a heightened social pain response is linked to more pervasive and lasting emotional difficulties, such as depressive symptoms and social anxiety, in victimized than non-victimized girls. Consistent with the idea that exclusion has more aversive implications for victimized girls, this group reported higher levels of threat to their social needs after exposure to acute social exclusion than did non-victimized girls. This research suggests the need to consider how individual differences in youths' neural responses to social cues of rejection help to determine their emotional vulnerability in the face of victimization or similar social stressors.

In a supplementary analysis (Supplementary Data), we also examined whether victimized and non-victimized girls differed in their level of neural activation (rather than the link between activation and internalizing symptoms). In one prior study, Will *et al.* (2016) found heightened dACC activation to exclusion relative to inclusion in chronically rejected youth compared with stably accepted youth. The present study yielded a similar pattern: chronically victimized girls compared with non-victimized girls showed greater dACC activation to exclusion relative to inclusion. It is noteworthy that this pattern replicated across groups with a different gender and age composition as well as across different operationalizations of social rejection. The Will *et al.* (2016) study classified children according to peer sociometric nominations of social preference; from this perspective, social rejection is operationalized as an attitude of the peer group (feelings of dislike toward others). In contrast, our study classified youth according to self-reports of peer victimization; from this perspective, social rejection is operationalized as exposure to specific threatening behaviors from peers (e.g. physical harm, verbal abuse, manipulation of relationships). The similar pattern of results may reflect the co-occurrence of attitudes of rejection and behavioral manifestations of these attitudes—that is, youth who are rejected by their peers often are exposed to victimization and/or peers may develop negative attitudes toward victimized youth (Kochel *et al.*, 2014). Collectively, the Will *et al.* (2016) findings along with the present research suggest a 2-fold risk in youth exposed to early social adversity: these youth show more neural sensitivity to exclusion and this sensitivity is more strongly associated with internalizing symptoms compared with youth exposed to low levels of social adversity.

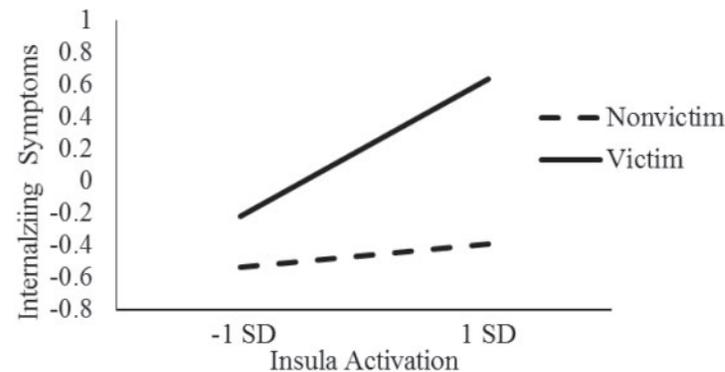## Psychological pathway from neural sensitivity to internalizing symptoms

To better understand why neural sensitivity in the social pain network might be associated with internalizing symptoms, we
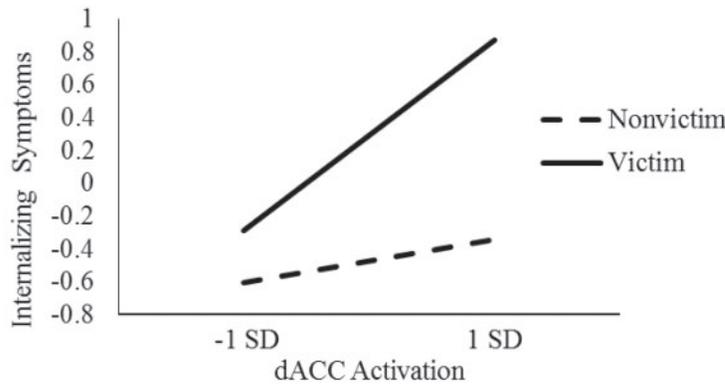
A dACC Activation × Victimization Status predicting internalizing symptoms
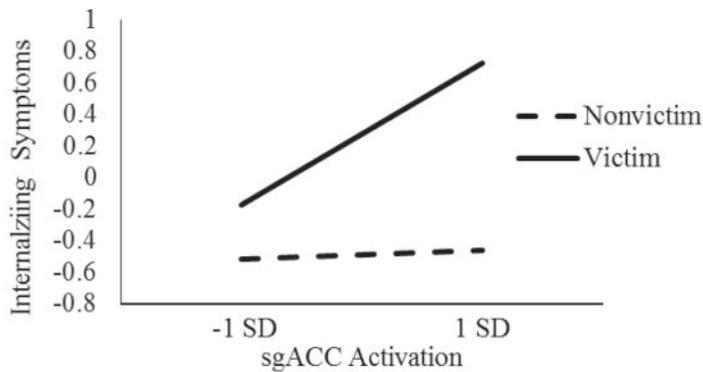
B sgACC Activation × Victimization Status predicting internalizing symptoms

C Insula Activation × Victimization Status predicting internalizing symptoms

Fig. 3. (A) dACC activation, (B) sgACC activation and (C) insula activation interact with victimization status to predict internalizing symptoms.

examined avoidance motivation as one possible underlying psychological process. Across all three social pain regions, we found a significant indirect effect from neural sensitivity through avoidance motivation to internalizing symptoms in victimized girls. For girls who have been exposed to chronic victimization, heightened neural sensitivity to exclusion translated into a generalized psychological sensitivity to aversive social cues, as reflected in a drive to avoid negative judgments, peer disapproval and loss of social status. Thus, chronically victimized adolescent girls with heightened neural sensitivity to exclusion not only may experience more adverse reactions to actual rejection experiences but also may show constant

vigilance to potential social threats and a tendency to avoid the possibility of future rejection. Having a sense of self and a set of social goals that is contingent on the judgments and approval of peers may set these youth up for the development of critical self-appraisals, helplessness, and negative emotions characteristic of depression and social anxiety. These findings are consistent with conceptualizations of targeted rejection, which emphasize its role in triggering social-evaluative threat, negative self-appraisals, social withdrawal and depression (Slavich *et al.*, 2009, 2010).

Future research will need to continue exploring why neural sensitivity to exclusion serves as a more robust predictor of

avoidance motivation and internalizing symptoms among victimized than non-victimized girls. Prior research shows that victimization predicts negative self-appraisals (Cole *et al.*, 2010), emotion dysregulation (McLaughlin *et al.*, 2009; Rudolph *et al.*, 2009) and maladaptive responses to social stressors (Troop-Gordon *et al.*, 2015), suggesting that perhaps non-victimized girls can recover more quickly from social rejection experiences by engaging in effective regulation of their cognitive and emotional reactions. Thus, it would be beneficial to explore various explanations for why neural sensitivity to exclusion has fewer adverse psychological and emotional effects on non-victimized than victimized youth.

Study strengths, limitations and future directions

This study is among the first to establish an association between neural sensitivity in the social pain network and internalizing symptoms (see also Masten *et al.*, 2011; Silk *et al.*, 2014) and is the first to reveal individual differences in this association that are contingent on naturally occurring exposure to social stress. In particular, these findings suggest that sensitivity to social exclusion may serve as a neural marker of vulnerability for internalizing symptoms only in youth who have a history of chronic rejection (e.g. frequent exclusion from the peer group, rejection by friends, or romantic break-ups). Moreover, we identify one pathway explaining the association between neural sensitivity and internalizing symptoms, thereby addressing the need to better understand psychological and emotional processes linked to the social pain response (Eisenberger, 2015). More broadly, this research unites social pain theory with interpersonal theories of depression and social anxiety, providing a multi-level perspective on the increasing risk for internalizing symptoms that emerges in girls over the course of adolescence.

Despite these contributions, further investigation is warranted to clarify the precise role of various regions of the social pain network in risk for internalizing symptoms. The most robust findings in the present study involve the dACC, although similar patterns of effects were observed in the sgACC and insula. Despite the existing data base linking dACC and sgACC activation to social pain (Eisenberger *et al.*, 2003; Dewall *et al.*, 2010; Masten *et al.*, 2011; Eisenberger, 2012; for a review, see Rotge *et al.*, 2014), the anterior cingulate cortex (ACC) may be involved in a variety of processes of potential relevance to Cyberball, including violation of expectations (Somerville *et al.*, 2006; Bolling *et al.*, 2011) and conflict monitoring (Botvinick *et al.*, 2004). Thus, it is possible that ACC activation during Cyberball also is linked to processes other than the social pain response. One study using Cyberball to distinguish social pain from neural activation in response to violation of expectations found evidence linking dACC activation specifically to social exclusion (but not overinclusion; Kawamoto *et al.*, 2012). Moreover, recent findings from a large-scale quantitative reverse inference analysis (Lieberman and Eisenberger, 2015) indicate preferential activation of certain parts of the dACC in response to pain. However, consistent with the conceptualization of ACC activation as a 'neural alarm system' (Eisenberger *et al.*, 2011), it is possible that heightened ACC activation in the context of Cyberball reflects in part greater conflict monitoring as youth react to the discrepancy between their desired social state and current social conditions. Of note, recent evidence also suggests distinctions between the neural representation of physical and social pain, despite some overlap (Woo *et al.*, 2014). Additional research is therefore needed to clarify the particular role of these regions in pain processing as well as the extent of overlap *vs* distinctiveness between the neural networks involved in physical and social pain.

Future research also will need to determine whether this pattern of findings is specific to neural sensitivity to social rejection or whether it would extend to other types of stress reactivity. Because of our focus on victimized youth, we anticipated that social exclusion would be a particularly salient stressor. However, we did not include a task measuring neural activation to other types of interpersonal stressors (e.g. family conflict) or noninterpersonal stressors (e.g. physical threat, academic failure). It will be important to directly examine whether neural reactivity to other forms of stress also is linked to internalizing symptoms in victimized youth or whether they are particularly sensitized to exclusion-related stressors.

Finally, although our study involved a prospective assessment of victimization, providing unique data about girls' long-term history of social adversity, we used concurrent assessments of neural processing, avoidance motivation and internalizing symptoms. Thus, we cannot draw firm conclusions about the direction of effects. Elucidating the interactive contribution of early social adversity and neural processing to girls' emotional development will require longitudinal designs that track changes in neural activation, exposure to social stress and internalizing symptoms over the course of adolescence. Results from the present study therefore can serve as a basis for designing prospective studies that examine the dynamic interconnections among these processes over time.

Conclusions and implications

In conclusion, this research makes a novel contribution both to social pain theory (Eisenberger *et al.*, 2003) and to interpersonal theories of internalizing symptoms (Rudolph, 2009; Davila *et al.*, 2010; Rudolph *et al.*, in press) by providing evidence for the interactive influence of neural sensitivity and social context on internalizing symptoms, highlighting the need for integrative multi-level theoretical models that consider the joint influence of biological, social and psychological systems of development when elucidating the processes underlying heightened risk for internalizing symptoms in adolescent girls. Given the debilitating and persistent burden associated with adolescent internalizing symptoms (Rudolph and Flynn, 2014), it is critical to identify effective targets of prevention. These results suggest that in addition to the development and implementation of effective anti-bullying programs (Williford *et al.*, 2012), altering victimized girls' neural reactivity to social exclusion in ways that reduce their heightened focus on peer judgments and approval may help prevent the onset of internalizing symptoms during adolescence in girls with a history of social vulnerability.

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Supplementary data

Supplementary data are available at *SCAN* online.

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