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Emotion Reactivity and Regulation in Adolescent Girls Following an Interpersonal Rejection

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Abstract

Failures in emotion regulation, especially as a result of interpersonal stress, are implicated as transdiagnostic risk factors for psychopathology. This study examines the effects of an experimentally-timed targeted interpersonal rejection on emotion reactivity and regulation in typically developing adolescent girls. Girls ($N = 33$, ages 9 – 16, $M = 12.47$, $SD = 2.20$) underwent functional magnetic resonance imaging involving a widely-used emotion regulation task. The emotion task involves looking at negative stimuli and using cognitive reappraisal strategies to decrease reactions to negative stimuli. Participants also engaged in a social evaluation task, which leads participants to believe a pre-selected peer was watching and evaluating the participant. We subsequently told participants they were rejected by this peer and examined emotion reactivity and regulation before and after this rejection. Adolescent girls evidence greater reactivity via higher self-reported emotional intensity and greater amygdala activation to negative stimuli immediately following (compared to before) the rejection. Self-reported emotional intensity differences before and after rejection were not observed during regulation trials. However, on regulation trials, girls exhibited increased prefrontal activation in areas supporting emotion regulation following compared to before the rejection. This study provides evidence that a targeted rejection increases self-report and neural markers of emotion reactivity and that girls increase prefrontal activation to regulate emotions following a targeted rejection.

Keywords

emotion reactivity; emotion regulation; targeted interpersonal rejection; vIPFC; cognitive reappraisal; social feedback

Difficulties with emotion regulation is a transdiagnostic risk mechanism for psychopathology (Aldao et al., 2016; Eisenberg et al., 2001; Gross & Munoz, 1995) and the ability to regulate emotional responses to interpersonal stressors is a fundamental skill that supports positive mental health and well-being (Dahl, 2001). Peer relationships are central to adolescent socioemotional development, and interpersonal stress in peer relationships is expected but contributes risk for maladjustment (Prinstein & Giletta, 2016). Lack of emotion

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regulation during interpersonal interactions predicts peer rejection and subsequent psychopathology in adolescents (Laceulle, Veenstra, Vollebergh, & Ormel, 2017). During the adolescent transition, girls compared to boys, experience more internalizing reactions to interpersonal stress (Rose & Rudolph, 2006), especially targeted interpersonal rejection (i.e., overt social rejection) (Slavich & Irwin, 2014; Slavich, Tartter, Brennan, & Hammen, 2014). Thus, adolescent girls must skillfully apply emotion regulation following interpersonal stress.

Previous research has investigated the neural correlates of emotion reactivity and regulation (Buhle et al., 2014a; Silvers, Shu, Hubbard, Weber, & Ochsner, 2015), but not whether a targeted rejection affects subsequent emotion regulation and associated neural recruitment in areas underlying emotion reactivity to negative stimuli and emotion regulation via cognitive reappraisal. This approach, which we pursue here, is critical for understanding the impact of targeted interpersonal rejection on psychological health. For adolescents, it is not necessarily the immediate impact of targeted interpersonal rejection, but the subsequent impact of dysregulation associated with rejection which drives risk for psychopathology (McLaughlin, Hatzenbuehler, & Hilt, 2009). Importantly, participants were unaware that the social evaluation and the emotion regulation tasks, described below, were linked. We examined whether, following a targeted interpersonal rejection, girls (1) became more reactive to negative stimuli and (2) evidenced altered emotion regulation in an unrelated task.

Functional magnetic resonance imaging (fMRI) studies with adolescent samples consistently implicate the amygdala as a marker of emotional reactivity to negative stimuli (Silvers et al., 2017, 2015) with females showing stronger reactivity than males (Stevens & Hamann, 2012). Cognitive reappraisal represents a form of emotion regulation that decreases negative emotions (Gross, 1998) and reduces biological reactivity to negative stimuli (Buhle et al., 2014; Gross, 1998; Ochsner et al., 2004). Cognitive reappraisal involves reinterpreting the content of an evocative stimulus to reduce emotional intensity. The neural substrates of cognitive reappraisal are well characterized in both typical (Buhle et al., 2014b; McRae et al., 2012; Silvers et al., 2012) and atypical samples (McLaughlin, Peverill, Gold, Alves, & Sheridan, 2015; Pico-Perez, Radua, Steward, Menchon, & Soriano-Mas, 2017). In brief, meta-analytic evidence suggests that cognitive reappraisal reliably activates cognitive control regions, including the dorsomedial prefrontal cortex (dmPFC), dorsolateral PFC (dlPFC), ventrolateral PFC (vlPFC), and posterior parietal lobe in the service of modulating subcortical activation to negative stimuli (Buhle et al., 2014b). The vlPFC in particular plays an important role in cognitive reappraisal due to its facilitation of response selection and inhibition (Braunstein, Gross, & Ochsner, 2017; Buhle et al., 2014a; Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008). However, we have no information about how a targeted rejection affects adolescents' ability to engage cognitive reappraisal to downregulate emotional reactivity.

Research from the peer literature distinguishes targeted interpersonal rejections from social exclusion suggesting that targeted rejections may have more immediate effects on adolescents' subsequent ability to regulate emotions (Prinstein and Giletta, 2016). Previous research has investigated neural correlates of social exclusion (Bolling et al., 2011; Chester & DeWall, 2014; Eisenberger, Lieberman, & Williams, 2003; Fowler, Miernicki, Rudolph,

& Telzer, 2017; Masten et al., 2011; Sebastian et al., 2011; Somerville, Heatherton, & Kelley, 2006; van der Meulen et al., 2017), and social evaluation (Somerville et al., 2013). Many of these studies use the Cyberball task (Bolling et al., 2011; Chester & DeWall, 2014; Eisenberger et al., 2003; Fowler et al., 2017; Sebastian et al., 2011; van der Meulen et al., 2017), chatroom tasks, or similar (Guyer et al., 2008; Silk et al., 2013) to elicit feelings of social exclusion. Somerville and colleagues (2013) developed a task where adolescents are lead to believe that a potential peer is watching them to elicit feelings of social evaluation. Broadly, these tasks have been shown to activate the vIPFC (Guyer et al., 2008; Sebastian et al., 2011), the mPFC (Somerville et al., 2013), and the bilateral amygdala (Guyer et al., 2008; Silk et al., 2013). While these tasks elicit a temporary negative or heightened emotional state, there is little information about how this temporary emotion state affects near term emotions and related neural activation to negative stimuli and ability regulate these emotions. For female adolescents in particular, this ability to regulate emotions following a targeted rejection is central to mental health and well-being.

One previous study in adults has investigated the effects of psychosocial stress on cognitive reappraisal. Shermohammed and colleagues (2017) found that individuals exposed to stress exhibited increased activation in the left amygdala and right middle frontal gyrus (MFG) during regulation trials; however, these observations did not survive correction for multiple comparisons. The authors conclude that for adults the stress manipulation, which was not a targeted rejection, had little effect on neural recruitment during either reactivity or regulation trials. As we review above, adolescent girls have stronger emotion dysregulation reactions to interpersonal rejection. Thus, in the current study, we expect different effects—both because the effects of a targeted rejection may be stronger than general interpersonal stress and because we assess these processes in adolescents.

Given previous work documenting increased amygdala activation in the context of negative emotion reactivity (Buhle et al., 2014b; Silvers et al., 2017), we hypothesized that girls would exhibit a temporary increase in amygdala activation when passively viewing negative stimuli following a targeted rejection. Based on previous work demonstrating that typically developing children and adolescents are able to effectively use cognitive reappraisal techniques to down regulate emotion reactivity (Buhle et al., 2014b), we hypothesized that these typically developing girls would effectively regulate their emotional responses to negative stimuli following targeted rejection. However, as in Shermohammed and colleagues (2017), we expected this regulation to be accompanied by a temporary increase in recruitment in frontal control regions implicated in cognitive reappraisal during these attempts. Specifically, we expected the vIPFC to be recruited to a greater extent immediately following targeted rejection. The vIPFC is commonly observed during cognitive reappraisal, and activation of the vIPFC and vIPFC/amygdala functional connectivity is associated with the degree of reduction in self-reported emotion following reappraisal (Braunstein et al., 2017; Buhle et al., 2014b; Silvers et al., 2016, 2017).

Method

Participants

Participants included 33 girls (ages 9 – 16, $M = 12.47$, $SD = 2.20$, 81% 9–14) who completed a baseline assessment and participated in the scanning procedures described below. Participants identified as African American ($n = 14$, 42.4%), Asian ($n = 1$, 3%), Caucasian ($n = 15$, 45.5%), and mixed race ($n = 2$, 6.1%). One participant preferred not to answer. Three individuals (9.7%) identified as Hispanic or Latinx. Participants were recruited from a variety of sources including internet ads, flyers, listserv emails, and medical chart reviews. Exclusion criteria were any history of diagnosed mental health issues, psychiatric medications¹, braces, claustrophobia, left handedness, active substance dependence or use on the day of the scan, pervasive developmental disorders, and lack of ability to speak/read English. All procedures approved by the institutional review board.

Functional Magnetic Resonance Imaging (fMRI) Tasks

Emotion reactivity and regulation task—During the fMRI scan, participants completed an event-related task assessing neural markers of emotion reactivity and regulation (Ochsner et al., 2004), which has been used with children and adolescents (McLaughlin et al., 2015; Silvers et al., 2012). Design and contrasts of this task were based on extensive previous literature (Ochsner et al., 2004; Silvers et al., 2012). Participants viewed neutral and negative images from the International Affective Picture System (Lang, Bradley, & Cuthbert, 1999) and from a normed sample of images for youth (available here: <https://osf.io/43hfq/>) (Jenness et al., 2018). Neutral pictures were always preceded by a “look” cue. Before each negative picture, participants saw a cue to either “look” or “decrease.” During look trials, participants simply looked at the image and allowed emotions to unfold naturally without altering their emotional reaction. During decrease trials, participants used specific cognitive reappraisal strategies to reduce emotional reaction to the negative stimuli. Prior to scanning, participants were trained with specific cognitive reappraisal strategies to use in the scanner for “decrease” trials. They observed examples completed out loud by the experimenter and completed practice trials using stimuli different than those used in the scanner. Participants were instructed to think about the image as more psychologically distant by either imagining the scene as further away, not involving them, or simply involving actors. Further, participants were instructed to decide on a strategy that worked well for them prior to the scan. These strategies have been used successfully in previous studies (McRae et al., 2012; Miller et al., 2018; Ochsner et al., 2004; Silvers et al., 2012). After each stimulus, participants rated the strength of their emotional reaction on a 5-point scale. Participants were extensively trained on how to use the self-reported emotional intensity scale. During training, participants were given explicit anchors for the emotion ratings ranging from a minimum of 0 “I experienced almost no emotion” to a maximum of 4 “it would be hard for me to imagine feeling this emotion more strongly.” Further, as can be seen in Figure 1, we included verbal descriptors on the rating screen to help the participant

¹One person, contrary to our request and after reporting no medication use, took medication for ADHD on the morning of the scan. We re-ran analysis with and without this person included and results were unchanged. To preserve power, we retained this person in all analyses.

remember how to use the ratings, Low (0,1), Medium (2), Strong (3,4). For analyses, we added a constant “1” to all responses, such that the range was 1–5. Negative and neutral pictures were randomized within each run.

In total, participants saw 6 runs lasting 6 minutes and 37 seconds each. The task proceeded as follows: An instructional cue appeared for 2 seconds, the emotional stimulus appeared for 4, 6, or 8 seconds, the rating screen appeared for 4 seconds, and the inter-trial interval (ITI) lasted from .5 to 7.5 seconds (Figure 1). Following accepted guidelines (Ollinger, Corbetta, & Shulman, 2001), we used a pseudo-exponential distribution to select both ITI and stimulus lengths. Specifically, for both the emotional stimulus and ITI, we used approximately 50% of the fastest possible duration, 25% of the middle duration, and 25% of the longest duration. Stimuli were presented in 2 series (Series A/Series B, counterbalanced across participants) each consisting of 3 runs. Participants saw 3 runs of the emotion regulation task (e.g., Series A) then participants completed the Social Evaluation Task described below followed by another three runs of the emotion regulation task (e.g., Series B; See Figure 1). Average valence ($M = 5.09$, Range = 1.76 – 8.50) and arousal ($M = 5.46$, Range = 1.76 – 7.09) (obtained from normed stimuli databases) were equivalent for look negative and decrease trials. The task included 48 trials of each type distributed evenly across runs such that a given run contained eight neutral stimuli with the “look” instruction, eight negative stimuli with the “look” instruction, and eight negative stimuli with the “decrease” instruction.

Social Evaluation Task—The social evaluation task was adapted from several existing social interaction paradigms (Guyer et al., 2008; Silk et al., 2012; Somerville, 2013). Following slightly modified procedures used by Somerville et al. (2013) who informed participants they were going to be watched by an unfamiliar peer, participants were told that they would be watched while in the scanner by a similar age and sex matched unfamiliar peer whom they had indicated they would like to meet and talk to. We first told the participant that they would be interacting with this unfamiliar peer who was completing this study at the exact same time at nearby universities ($N = 4$ major, nationally recognized research universities within driving distance). Participants ranked in order of who they would like to chat with the most four standardized images of girls drawn from the NIMH Child Emotional Faces Picture Set, Happy Direct (Egger et al., 2011). We used two sets of images for younger (ages 9–12) and older (13–16) girls so that the age of the potential peer approximately matched the target. Participants filled out a brief biography (name, favorite color and food, how many siblings they have, what they like to do after school). A research assistant took the participant’s picture and informed the participant that s/he would return after sending this information to the other team so that the other girls could submit their chat partner preferences. After informing participants that they matched to their first choice, they were provided with the chat partners biography (standardized across participants) with answers provided to the same questions.

After participants matched to their top choice, researchers explained that we are interested in learning what girls’ brains look like while they are interacting with a peer for the first time and that while we do not have all the necessary technology to allow both adolescents to chat at the same time at different sites, we recently acquired a camera that would help us do this.

We told the participant that they would help test the camera by having the chosen peer watch our participant in the scanner first and then switch places so that the participant will watch the new peer via live video. We explained that as a part of testing the camera, we were interested in how they felt when the camera was on, and thus, ask that they rate their specific emotions using a similar scale as for the emotion reactivity and regulation task. For example, they were instructed to rate their feelings of rejection on a scale of 0 “I feel almost no rejection” to 4 “I feel an extreme amount of rejection.” As above, we added a constant of 1 for analyses. Prior to scanning, we practiced this with how the participant was currently feeling for each emotion during the training session. Finally, we informed participants that they would later have an opportunity to chat via Skype and earn an extra \$10 dollars for talking with the new peer. In the scanner, they were told that the new peer is ready at the other site to help us test our new camera technology. We explained that because we are still testing the technology, the camera may switch on and off. We asked the participant to keep their eyes open while being watched by the new peer.

After they completed the first three runs of the emotion reactivity and regulation task, we told them that we were going to take a break from that task to have the new peer watch them in the scanner. We reminded them that they were going to be making periodic ratings throughout the evaluation period. To increase believability and consistent with Somerville et al. (2013), we pseudo-randomly alternated between two screens, “Video On,” which included a red light and “System Off” (see Figure 1). The evaluation period lasted for 5 minutes and 45 seconds, and participants made three sets of mood ratings. Ratings were made at exactly 65 seconds, 177.5 seconds, and 287.5 seconds during the evaluation task. At the end of the task, when the evaluation period was complete, a research assistant came on the intercom and informed the participants that after the new peer watched them and read their biography, they no longer want to interact with the participant. Following this targeted rejection, the participant completed a final set of emotion ratings, and then the final 3 runs of the emotion regulation task. We did not acquire images during the delivery of the targeted rejection.

Following completion of all scanning procedures, participants completed a funneled debrief (Bargh & Chartrand, 2000) moving from open ended to close ended questions to assess believability of the manipulation before being fully debriefed. After asking general questions about whether anything seemed unusual or related, we ended by asking whether participants believed the camera was watching them and whether the confederate was real. Of the girls included in imaging analyses, 97% of girls (30 out of 31) believed that the selected peer was real, and 90% of participants (28 out of 31) believed that there was a camera watching them. To ensure that the inclusion of these three subjects did not substantively change results, analyses were run with and without these participants. Behavioral and whole-brain results were substantively unchanged when the three individuals who reported not being fully deceived were excluded from analyses. We retained these individuals in reported analyses.

Image Acquisition and Processing

Scanning was performed on a 3.0-T Siemens Prisma Scanner, using a 32-channel head coil. We followed standard pediatric scanning acquisition parameters. T1-weighted multi-echo

MPRAGE volumes (anatomical scans) were acquired for coregistration with fMRI images (TR = 2,530 ms, TE = 1670–7,250 ms, flip angle = 7°, FOV = 192×192 mm, 176 slices, in plane voxel size = 1 mm.). A navigator echo prior to scan acquisition was used to reduce artifacts caused by motion. This compares slices to the echo online and permits up to 20% of slices to be reacquired. Blood oxygen level dependent (BOLD) signal during functional runs was acquired using a gradient-echo T2*-weighted EPI sequence. During functional scans, an online prospective motion correction algorithm (PACE) was used to reduce motion artifacts. Forty-four 2.4mm-thick slices were acquired parallel to the anterior commissure-posterior commissure line (TR = 2,500 ms, TE = 28 ms, flip angle = 90°, bandwidth 2,312 Hz/Px, echo spacing = 0.52 ms, FOV = 230 × 230 mm). Prior to each scan, three images were acquired and discarded to allow for longitudinal magnetization to reach equilibrium.

Preprocessing and statistical analysis of fMRI data was performed in FSL (FSL 5.0.9). Preprocessing included motion correction using the MCFLIRT algorithm (Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012), non-brain removal using FSL's Brain Extraction Tool (Smith, 2002), spatial smoothing (5-mm full width at half maximum), and highpass temporal filtering (Gaussian-weighted least-squares). Data were inspected for artifacts using `fsl_motion_outliers`. Single point outlier regressors were included in person-level models to account for any motion exceeding 2mm. Additionally, 6 rigid-body motion regressors were included in person-level models. Individual runs were excluded if participant motion exceed 2mm for greater than 20% of that run. For the emotion regulation and reactivity task, individuals with valid data for 3 out of 6 runs were included in analyses. Due to excessive motion, two participants were excluded from the emotion reactivity and regulation task analyses. Across the available 181 runs of the emotion reactivity and regulation task (31 subjects × 6 runs), 9 runs (5%) were excluded. The number of runs excluded ($N = 9$) due to motion (>20% motion outliers) were as follows: Run 1 – 1 run excluded; Run 2 – 1 run excluded; Run 3 – 2 runs excluded; Run 4 – 0 runs excluded; Run 5 – 1 run excluded; Run 6 – 4 runs excluded. Following person-level model estimation, T2* weighted images were anatomically co-registered to high resolution structural images using the FLIRT algorithm (Boundary-Based Registration, 12 DOF) then registered to standard space with FNIRT nonlinear registration in FSL.

fMRI Analysis

Higher-level analysis was carried out using FLAME (FMRIB's Local Analysis of Mixed Effects) stage 1 (Woolrich, Behrens, Beckmann, Jenkinson, & Smith, 2004). For the emotion regulation task, regressors were created for each phase of the task: instructional cue, stimulus, and rating periods separately. For the stimulus period, regressors were created for look and decrease trials and for neutral and negative stimuli. Following standard procedures (Buhle et al., 2014b), we measured emotional reactivity (referred to hereafter as reactivity trials) across all runs as the contrast of look negative > look neutral trials. We measured emotion regulation (referred to hereafter as regulation trials) across all runs as the contrast of decrease > look trials for negative stimuli (i.e., isolating neural response during emotion regulation independent of viewing negative images). Additionally, to test our hypothesized effect of the targeted rejection on recruitment during reactivity and regulation trials immediately before (Run 3) compared to immediately after (Run 4) the rejection, we

examined the contrast of look negative trials Run 4 > Run 3 and the contrast of decrease negative trials Run 4 > Run 3 (See Figure 1). We focused on Run 4>Run 3 because we expected that for this typically developing sample, the effects of the targeted interpersonal rejection would be short lived (i.e., a few minutes compared to 20 minutes) and not affect performance across all three trials following the rejection. A general linear model (GLM) was used to estimate the association between BOLD signal and task demands across time for each subject, prior to normalization. We examined differences in BOLD response during contrasts of interest in whole-brain analyses with cluster-level correction in FSL ($z > 2.3$, $p < .05$), a cluster level correction which, in combination with FLAME, effectively decreases the rate of false positive findings (Eklund, Nichols, & Knutsson, 2016).

ROI Analysis

We examined activity in the right and left amygdala using a structurally defined region of interest (ROI) from the Harvard-Oxford Atlas (25% probability threshold). We examined correlations between amygdala activation and self-report ratings during reactivity trials across all runs. We conducted a repeated measures ANOVA to examine whether amygdala activation significantly varied across all runs. We focused on the post-hoc comparison (Bonferroni corrected) between Run 3 and Run 4 to examine the acute effect of the targeted interpersonal rejection (See Figure 5).

To identify ROIs related to emotion regulation, we chose task-active clusters for regulation trials in the prefrontal cortex which had previously been implicated in emotion regulation tasks (Braunstein et al., 2017; Buhle et al., 2014b). We defined the PFC ROIs functionally because structural definitions of these regions have too little spatial specificity. To ensure our results were not influenced by our selection of ROIs, we choose task-active clusters across all runs before and after targeted interpersonal rejection (Runs 1 – 6) and regardless of self-report ratings. Three clusters in the right and left vIPFC and MFG met these criteria in the current study. ROIs were defined by identifying the peak activation in each of these three clusters and then creating a 6-mm sphere around this activation. Using these three ROIs we examined correlations with self-report ratings of emotions during decrease trials (McRae et al., 2012; Ochsner et al., 2004). For ROIs that significantly predicted self-report ratings (as hypothesized, only the right vIPFC), we conducted a follow-up repeated measures ANOVA to examine whether the vIPFC significantly differed across runs. As above, we focused on the post-hoc comparison (Bonferroni corrected) between Run 3 and Run 4 to examine the acute effects of the targeted rejection. Activation of the vIPFC during decrease trials for each run was modeled as the repeated measure.

Associations between self-report ratings and activation in a priori defined ROIs were analyzed using SPSS 24. Using self-report data, we examined whether self-reported emotional intensity to negative pictures during either reactivity or regulation trials differed following the targeted rejection using paired-samples t-tests. All analyses hereafter that reference change used residualized change scores. For these scores, the post-measure was regressed onto the pre-measure, and the standardized residual was used in analyses. We examined whether changes in feeling of rejection after the targeted rejection correlated with

changes in neural activation or self-reported emotion from Run 3 to Run 4 of the emotion task using Pearson correlations.

Functional Connectivity

To further examine the effects of the targeted rejection on the ability to engage prefrontal cortex regions to modulate subcortical activation, we conducted a whole brain psychophysiological interaction (PPI) analysis with the vIPFC. Following accepted guidelines (O'Reilly, Woolrich, Behrens, Smith, & Johansen-Berg, 2012), we (1) extracted the deconvolved time series for the right vIPFC for each participant across runs of the emotion reactivity and regulation task to create the physiological variables; (2) convolved each trial type with the canonical HRF, creating the psychological regressors; and (3) multiplied the time series for the psychological regressor for regulation trials with the physiological variable resulting in the PPI interaction. We then compared relative whole-brain connectivity during regulation trials before and after the targeted rejection (Run 4 > Run 3).

Demographic Controls

While the age range is tightly constrained to the early adolescent period, we sought to ensure that age did not interact in meaningful ways with emotion regulation, interpersonal rejection, or the interaction of these two tasks with each other. We approached this analysis in a hypothesis driven manner to reduce multiple comparisons. Given evidence that cognitive reappraisal improves with age (McRae et al., 2012), we examined whether age correlated with activation in frontal control regions during regulation relative to reactivity trials. We examined whether age was related with self-reported emotional intensity ratings on reactivity and regulation trials. Given evidence that social sensitivity increases during the adolescent years (Somerville, 2013), we examined whether age was associated with changes in feelings of rejection and changes in frontal ROI activation during regulation trials as a result of the targeted rejection. Finally, we examined whether age correlated with the believability of our paradigm.

Because some research indicates that responses to interpersonal rejections may vary by race (Masten, Telzer, & Eisenberger, 2010), we examined if response to interpersonal rejection was related to minority status (white/non-white). We did not observe a significant association between change in rejection rating after the targeted rejection and minority status ($r = -.16$, $p = .39$), and thus, we do not include this control in subsequent analyses.

Results

Emotion Regulation Main Effects Across All Runs

Self-report of Emotion Intensity—For neutral stimuli, the mean rating across trials was 1.88 (range = 1.11 – 3.35, $SD = 0.67$). For negative stimuli across all reactivity trials, the mean rating was 3.01 (range = 2.03 – 4.55, $SD = 0.69$). For negative stimuli across all decrease trials, the mean rating was 2.31 (range = 1.27 – 3.95, $SD = 0.64$). Compared to neutral stimuli, participants reported significantly higher emotion intensity to negative pictures during reactivity trials $t(32) = 7.78$, $p < .001$, $d = 1.78$, and regulation trials $t(32) =$

2.66, $p = .01$, $d = 0.65$. When reactivity and regulation trials were directly compared, participants rated higher emotional intensity during reactivity trials, $t(32) = 8.58$, $p < .001$, $d = 0.66$.

Neural Responses During Reactivity Trials—In reactivity relative to neutral trials, adolescents exhibited greater activation in six clusters with peaks in the right lateral occipital cortex, right vIPFC, cerebellum, left precentral gyrus, right orbitofrontal cortex, and right superior frontal gyrus (see Figure 2 and Table 1).

Neural Responses During Regulation Trials—In regulation relative to reactivity trials, adolescents exhibited greater activation in eight clusters with peaks in the left and right inferior parietal lobes, right and left vIPFC, left MFG, right lateral occipital cortex, left lingual gyrus, and precuneus. (see Figure 3 and Table 1).

ROI Analysis—Greater bilateral amygdala activation was observed in reactivity compared to neutral trials (right: $t(30) = 4.70$, $p < .001$ and left: $t(30) = 4.44$, $p < .001$). However, activation of the amygdala did not significantly differ between reactivity and regulation trials (p 's $> .2$). Activation in the left amygdala, $r = -.45$, $p = .01$, but not the right amygdala, $r = -.29$, $p = .12$, was negatively correlated with emotional intensity ratings during reactivity trials.

Of the three PFC clusters which were more active during regulation trials, only activation in the right vIPFC was negatively correlated with self-reported emotional intensity during regulation trials, $r = -.49$, $p = .006$ ($n = 3$, $p < .05$, Bonferroni corrected). Activation in the left vIPFC and left MFG did not correlate significantly with self-reported emotional intensity during regulation trials (p 's $= .44 - .98$). All subsequent ROI analyses examining the impact of targeted rejection on neural activity during reactivity and regulation trials focus on the bilateral amygdala and right vIPFC.

Social Evaluation and Rejection

Self-report of Emotion—Across the three mood ratings prior to the targeted rejection, adolescents reported a mean rejection intensity of 1.29 (range = 1 – 2.67, $SD = .49$).

Following the targeted rejection, adolescents reported a mean rejection intensity rating of 2.41 (range = 1 – 5, $SD = 1.32$). Adolescents reported significantly more intense feelings of rejection after, compared to before the targeted rejection, $t(31) = 5.11$, $p < .001$, $d = 1.24$.

Emotion Regulation Before and After Social Rejection

Impact of Rejection on Self-report of Emotion—Immediately after compared to immediately before (Run 4 > Run 3) the targeted rejection, adolescents reported significantly greater emotional intensity in reactivity trials, $t(32) = 2.32$, $p = .03$, $d = 0.29$, and neutral trials, $t(33) = 2.62$, $p = .01$, $d = 0.33$, but not regulation trials ($p = .73$, $d = 0.03$).

Impact of Rejection on Neural Correlates of Emotion Reactivity—Immediately after compared to immediately before (Run 4 > Run 3) the targeted rejection, adolescents exhibited significantly greater activation during reactivity trials in one cluster (see Figure 4

and Table 1). Peak activation was located posteriorly in right occipital cortex but spanned several regions, including the amygdala, bilateral putamen, bilateral anterior cingulate, and right precentral gyrus.

Impact of Rejection on Neural Correlates of Emotion Regulation—Immediately after compared to immediately before (Run 4 > Run 3) the targeted rejection, adolescents exhibited significantly greater activation during regulation trials in seven clusters with peaks in bilateral occipital cortex, right supramarginal gyrus, right insular cortex, left frontal pole, and left anterior cingulate gyrus (See Figure 3 and Table 1). In addition, results from the PPI analysis revealed relatively greater functional connectivity between the vLPFC and amygdala during regulation trials following the targeted rejection (Run 4 > Run 3; see Figure 4).

ROI Analysis—Results from the repeated measures ANOVA revealed that left amygdala activation during reactivity trials, but not neutral or regulation trials (p 's = .10 - .55), significantly differed across runs, $F(5, 120) = 2.80, p = .02$. Post hoc comparisons revealed that activation in the amygdala during reactivity trials directly after the targeted rejection, $M = .31, SD = .05$, was significantly higher than directly before the targeted rejection, $M = .09, SD = .07, p = .03$, Bonferroni corrected (See Figure 5). Changes in activation in the amygdala between Runs 3 and 4 did not correlate with change in self-report feelings of rejection (*all* p 's > .05).

Results of the repeated measures ANOVA revealed that activation in the right vLPFC during regulation trials did not significantly differ across all runs, $F(5, 120) = 0.81, p = .41$. However, change in activation from Run 3 to Run 4 in the right vLPFC was correlated at a trend level with changes in self-reported feelings of rejection during regulation trials following the targeted rejection, $r = .32, p = .10$. Here, increased feelings of social rejection following interpersonal rejection were correlated with greater increases in recruitment from Run 3 to Run 4 of the right vLPFC during regulation trials.

Associations with Age

Age was positively correlated with increased recruitment of the right vLPFC ($r = .37, p = .04$) during regulation trials across runs and was positively correlated with increased feelings of rejection following the targeted rejection, $r = .37, p = .04$. However, age was not associated with changes in bilateral amygdala during reactivity trials or the right vLPFC during regulation trials following the targeted rejection (p 's > .05). Finally, age was not associated with whether or not the participant believed that another person was watching them, $r = .03, p = .88$.

Discussion

This study examined neural correlates of emotion reactivity and regulation before and after a targeted interpersonal rejection in a sample of adolescent girls. Previous research has examined neural activation to peer stress and engaging cognitive reappraisal in the service of emotion regulation in separate studies. Here, we address a gap in research by examining whether girls experienced stronger reactions to negative stimuli and were less able to engage in cognitive reappraisal immediately after a targeted rejection. Our results support two main

conclusions. First, adolescent girls are more reactive to unrelated negative stimuli following a targeted rejection. Second, typically developing girls appear to successfully engage in cognitive reappraisal in the service of emotion regulation immediately following a targeted rejection, although this successful regulation is accompanied by increased activation of prefrontal regulatory regions.

The targeted rejection significantly increased emotion reactivity in self-report data and neural activation in areas associated with emotion reactivity. Girls self-reported greater reactivity to both neutral and negative images and exhibited greater activation when passively viewing negative stimuli in subcortical regions, including the bilateral amygdala, following the targeted rejection. Examination of the plot of mean amygdala activation across trials suggests an expected (Gee et al., 2015; Plichta et al., 2014) habituation to stimuli. Although amygdala activation increased across trial types following the social evaluation and rejection task, this activation was highest to negative stimuli and only significantly higher in reactivity trials. This suggests a selective increase in emotion reactivity to negative stimuli after targeted rejection. Unlike other studies that have examined neural activation within a peer exclusion task (Guyer et al., 2008; Silk et al., 2013), we demonstrate that a targeted rejection delivered in the middle of an unrelated task affects neural and emotional reactivity towards negative stimuli in an age group uniquely vulnerable to interpersonal stress (Rudolph, 2014).

Our second hypothesis that girls would be able to engage in emotion regulation but with increased neural recruitment in frontal control regions following a targeted rejection was supported. Girls self-reported emotional intensity to negative stimuli during regulation trials did not significantly differ before and after the targeted rejection. While nonsignificant findings should be interpreted with caution, it is possible that girls were able to successfully reduce their emotions using cognitive reappraisal strategies regardless of the rejection. Consistent with the idea that regulation was more effortful following interpersonal rejection, results from the whole brain analysis revealed greater activation in several prefrontal regions following the rejection compared to before. Girls showed greater activation in the vIPFC, ACC, and insula. Additionally, results from a connectivity analysis suggest greater connectivity between the vIPFC and amygdala following the targeted rejection. One possibility is that girls are recruiting these regions more to facilitate emotion regulation following a targeted rejection. In support of this idea, across all trials, activation in the right vIPFC was negatively associated with self-reported emotional intensity during regulation trials. In addition, girls who reported feeling more rejected following the experimental manipulation were more likely to exhibit increased vIPFC activation following the rejection, although this was only significant at a trend level. A study by Chester and Dwall (2014) found that greater activation of the right vIPFC during the exclusion portion of the Cyberball task predicted greater perceived social rejection in the week following participation in the task. Further, they found that the greater vIPFC during exclusion predicted greater nucleus accumbens activity in a substance use cue paradigm. The authors concluded that exclusion during Cyberball may be associated with self-regulation difficulty. Together, our results are complimentary to these findings and extend them by demonstrating that social rejection affects real-time emotional reactivity and regulation.

Previous research on cognitive reappraisal as an emotion regulation strategy finds the vIPFC robustly and routinely activated on regulation trials. The vIPFC is commonly interpreted as playing a role in selecting goal-oriented interpretations intended to distance oneself from the negative stimuli (Braunstein et al., 2017). In other tasks, the vIPFC is observed to be recruited in the context of inhibiting inappropriate distractors (see Aron, Robbins, & Poldrack, 2014 for review). Thus, an alternate possibility is that it played a similar role here in that girls had to work harder to suppress lingering thoughts about why they were just rejected by a pre-selected peer in order to focus on reappraisal strategies.

Examining self-report ratings and neural activation across all trials, results largely replicate previous research that has used this emotion regulation paradigm. While we hypothesized a temporary increase in reactivity and altered regulation following the targeted rejection, we expected this alteration to be temporary on the order of minutes rather than persisting throughout the full remainder of the task. Girls reported significantly higher emotional intensity during reactivity compared to regulation trials. Further, neural activation patterns across all trials replicated findings from recent metanalytic work on this same emotion task (Buhle *et al.*, 2014). Girls demonstrate greater activation in frontal control regions, including the bilateral vIPFC and left MFG during regulation relative to reactivity trials. Surprisingly, across all trials greater left amygdala activation was associated with lower emotional intensity ratings to negative stimuli. This is the opposite pattern of what we would expect given previous research. While it is possible that this reflects a mismatch between girls' self-reported experience with neural activation, we recommend caution in drawing firm conclusions from this single correlation given that it is inconsistent with previous work with larger samples. Our results contribute to the body of research emphasizing the role of domain-general cognitive control processes in cognitive reappraisal (Braunstein et al., 2017; Ochsner & Gross, 2005) and that adolescent girls are able to successfully engage in this emotion reactivity and regulation task (Miller et al., 2018; Silvers et al., 2015), even when a temporary negative state is introduced via targeted rejection.

As assessed in the present study, age appeared to play a minimal role in the effect of the targeted rejection on emotion reactivity and regulation in the present study. While older girls reported feeling more rejected, age was not associated with change in activation in either the amygdala or vIPFC following the targeted rejection. Given our constrained age range focused on early adolescence, we only tested for linear age-related changes. It is possible that testing for non-linear or more complex age-related effect would have uncovered more pronounced differences. Indeed, other work with youth has shown age specific changes in neural activation patterns in this emotion task (Silvers et al., 2017, 2012). Thus, future work with a larger sample would allow testing age-based interactions with the social rejection and emotion regulation paradigm used in the present study.

The current study represents an important first step towards measuring emotion reactivity and regulation to targeted rejection. While our study benefited from use of a well-replicated emotion regulation task and a within-person design, future work would benefit from addressing some limitations. Future work would benefit from a larger sample size. Additionally, our main study findings compared performance in Run 4 to Run 3. While we expected the effects of the targeted interpersonal rejection to be relatively short lived, we

recommend caution in interpreting our findings until they are replicated with a larger sample size with a greater number of trials immediately before and after the rejection. Given prior work demonstrating differential reactivity in samples of adolescents with psychopathology (Silk et al., 2013; Stephanou, Davey, Kerestes, Whittle, & Harrison, 2017), future work should examine this paradigm in a sample of girls with and without psychopathology. Our sample was comprised of adolescent girls. Although significant prior work suggests that girls are more affected by social rejection compared to boys (Rose & Rudolph, 2006), it is unclear if adolescent boys may exhibit the same pattern seen in this study. The emotion regulation strategies and targeted rejection were tested in a controlled setting; however, it is likely that adolescents experience much stronger reactivity to targeted rejection in more naturalistic environments. Future studies could consider a between- and within-person design where half of subjects are exposed to the targeted rejection and the other half are exposed to no rejection or positive feedback to examine reactivity and regulation differences. Elegant work conducted by Silvers and colleagues (Silvers et al., 2016, 2017) demonstrates age effects within this cognitive reappraisal tasks. Although we examined correlations with age, we were unable to test age interactions, such as whether younger participants experienced the social rejection differently than older participants.

It is no coincidence that social sensitivity and disruptions in emotion regulation coincide with increased risk for psychopathology during the adolescent years, especially for girls. Our study offers an intriguing glimpse into how a long-purported mechanism of risk, emotion reactivity and regulation, is affected in real time by a social stressor. We demonstrated that a targeted interpersonal rejection results in greater self-reported emotional intensity to negative stimuli and increased neural activation in areas implicated in emotion reactivity and regulation.

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Emotion Regulation Task

Order of Tasks

Figure 1.

Depiction of the emotion regulation task, social evaluation task, and order of tasks. The delivery of the targeted rejection occurred at the very end of the social evaluation task. The next run of the emotion regulation task began immediately.

**BOLD activation during Reactivity Trials
(Look Negative > Look Neutral)**

Figure 2.
Whole brain findings across all reactivity trials.

BOLD activation across all regulation trials (left) with correlation between ventrolateral prefrontal cortex and emotional intensity ratings across all regulation trials (right).

Figure 3.

Whole brain findings across all regulation trials and the association between ventral lateral prefrontal cortex (vIPFC) activation and emotion intensity ratings.

BOLD activation following targeted interpersonal rejection (Run 4 > Run 3).

Figure 4.

Whole brain findings depicting the effects of a targeted interpersonal rejection on emotional reactivity and regulation.

Figure 5.
Mean BOLD activation in the left amygdala during reactivity trials plotted for each run.

Table 1.

Peak activations across trial types.

Trial Type	Region of Peak Activation	Cluster Size	x	y	z	z Value
All Reactivity Trials						
	Occipital Cortex (R)	32,612	52	-72	4	8.42
	vlPFC (R)	1,958	4	64	26	5.73
	Cerebellum	1,513	-10	-74	-26	5.6
	Precentral Gyrus (L)	1,336	-38	-4	38	4.13
	mPFC (R)	932	4	44	-16	5.42
	Superior Frontal Gyrus (R)	429	6	12	54	3.38
All Regulation Trials						
	Inferior Parietal (L)	6,374	-52	-52	48	5.44
	Inferior Parietal (R)	3,662	52	-50	46	5.02
	vlPFC (R)	3,356	50	40	-10	4.28
	vlPFC (L)	1,083	-36	62	-2	4.34
	MFG (L)	624	-44	22	46	4.11
	Occipital Cortex (R)	506	50	-74	12	3.79
	Lingual Gyrus (L)	486	-10	-78	0	4.31
	Precuneus (L)	399	-2	-68	42	3.92
Reactivity Trials						
Run 4 > Run 3						
	Occipital Cortex (R)	23,220	38	-88	-2	4.80
Regulation Trials						
Run 4 > Run 3						
	Occipital Cortex, superior (L)	4,298	-22	-60	52	4.57
	Supramarginal Gyrus (R)	1,701	68	-32	30	4.28
	Occipital Cortex, inferior (L)	1,136	-48	-70	-14	4.04
	Insula (R)	589	36	-18	6	3.62
	Occipital Cortex (R)	587	12	-62	54	3.67
	vlPFC (L)	530	-34	42	32	3.61
	ACC (L)	485	-2	16	28	3.93
Connectivity During Regulation Trials						
Run 4 > Run 3						
	Frontal Pole (R)	4,479	38	46	4	3.51
	Amygdala (L)	3,041	-22	4	-14	3.92
	Precuneus (L)	1,793	-24	-60	6	3.53
	Temporal Pole (R)	1,539	46	20	-22	3.97
	Posterior Cingulate	1,272	2	-26	34	3.11