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Neural Markers of Emotion Reactivity and Regulation Before and After a Targeted Social Rejection: Differences Among Girls With and Without Suicidal Ideation and Behavior Histories

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ABSTRACT

BACKGROUND: Suicidal thoughts and behaviors (STBs) are common among adolescent girls and increase risk for suicide death. Emotion regulation difficulties are linked with STBs, particularly in response to targeted social rejection. However, neural correlates of this link have not been investigated and may identify novel targets for interventions. Here, we examined neural correlates of emotion regulation before and after an experimentally delivered targeted social rejection in adolescent girls with STBs and girls without STBs (i.e., control participants).

METHODS: Girls (*N* = 138; age range, 9–15 years; mean [SD] age = 11.6 [1.79] years) completed a functional neuroimaging emotion regulation task. In the middle of the task, participants were socially rejected by an unfamiliar confederate whom the participants had elected to meet. Participants also completed a multimethod STB assessment.

RESULTS: Before rejection, girls with a history of STBs, compared with control participants, showed greater activation in the right superior frontal gyrus when passively viewing negative stimuli, and girls with suicidal behavior (SB) versus those without SB showed less activation in the right frontal pole during emotion regulation attempts. Following the rejection, girls with STBs, compared with control participants, showed greater activation in the right inferior frontal gyrus during emotion regulation.

CONCLUSIONS: Before social rejection, girls with SB versus without SB may not activate brain regions implicated in emotion regulation, suggesting a vulnerability to poor regulation at their baseline emotional state. After social rejection, girls with any history of STBs showed altered activation in a brain region strongly associated with inhibition and emotion regulation success, possibly reflecting increased effort at inhibiting emotional responses during regulation following stress exposure.

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Suicide is a leading cause of death worldwide (1,2). Rates of suicidal thoughts and behavior (STBs) are alarmingly high in adolescent girls (3). Indeed, 30% of U.S. high school girls experienced suicidal ideation (SI), and 13% reported making a suicide attempt (3). Emotion dysregulation is a potent risk factor for STBs (4,5). Prior studies in youths and adults have examined disruptions in emotion regulation using self-report (6,7) and physiological markers (8,9). Neural markers of emotion regulation among youths with STBs are less studied and have the potential to identify novel targets of suicide prevention and intervention. In this study, we aimed to examine neural correlates of emotion reactivity and regulation before and after an experimentally delivered, targeted social rejection among girls with histories of STBs.

Adolescence is marked by increased sensitivity to interpersonal stressors (10–14), particularly among girls (15,16). While normative, interpersonal stressors, especially targeted social rejections (i.e., exclusive, active, and intentional rejection of an individual by others) (17), trigger STBs for some youths (5,18–20). Studying factors linking interpersonal stressors with STBs, such as differences in neural processing of emotion following an interpersonal stressor, may identify malleable pathways to risk of STBs.

Developmental theories regarding STBs suggest that the inability to regulate emotions following interpersonal stressors may precipitate a suicidal crisis (5,8,21). However, research has not captured the acute effects of a targeted social rejection on emotion processing in girls with histories of STBs. Functional magnetic resonance imaging (fMRI) studies offer the possibility to examine this process. Some studies have examined neural correlates of social exclusion (22–28) and social evaluation (29) in adolescents, primarily using peer

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selection/chatroom tasks (30,31) or Cyberball (22,24–26,28,32) to elicit temporary negative emotions during a targeted social rejection. In adolescents, targeted social rejection is associated with increased activation in the ventrolateral prefrontal cortex (PFC) (26,30), medial PFC (33), and amygdala (30,31). However, these tasks capture the effects of the targeted social rejection itself and not how that rejection directly affects emotion reactivity and regulation.

Emotion reactivity reflects an automatic response to emotional information, whereas emotion regulation encompasses effortful attempts to decrease emotional reactivity. Passive viewing of negative stimuli activates brain regions implicated in salience processing, including the occipital cortex, ventrolateral PFC, and amygdala in youths and adults (34–36). In adults, fMRI studies examining emotional reactivity have shown that adults with suicidal behavior (SB) versus those without SB demonstrate increased activation in the inferior frontal gyrus (IFG) and lateral and medial orbitofrontal cortex when viewing angry faces (relative to happy, sad, or neutral faces) (37,38) and increased activation in the lateral orbitofrontal cortex when recalling negative autobiographical memories (39). An early study found that youths with versus without SB histories showed increased dorsolateral PFC and dorsal anterior cingulate cortex activation when viewing angry faces (40). Recently, we demonstrated that youths with versus without SI histories demonstrated greater activation in the left temporal pole during passive viewing of negative relative to neutral stimuli (41).

Cognitive reappraisal is an emotion regulation strategy that downregulates emotional reactivity to negative stimuli (34,42) and reliably activates ventral and medial PFC regions (34,35). Less fMRI work has examined the association between STBs and neural correlates of emotion regulation in adolescents. In our research, youths with SI versus without SI activated the dorsolateral PFC more when using cognitive reappraisal to regulate emotion to negative images relative to passively viewing negative images (41). Together, these studies suggest that the PFC may be a key region linked to differences in emotional reactivity and regulation in individuals experiencing suicidality.

While modern developmental theories of suicide suggest that targeted social rejections play a key role in disrupting emotion regulation and potentially precipitating a suicidal crisis, no studies have examined the acute effects of a targeted social rejection on neural correlates of emotion reactivity and regulation among girls with STBs. The present study aimed to address these major gaps by examining neural activation in the context of a well-established emotion regulation task before and after exposure to a targeted social rejection in a sample of girls with and without STBs.

Based on our prior work, we hypothesized that girls with versus without STBs would exhibit greater activation in the temporal pole during emotional reactivity before a targeted social rejection. We hypothesized that girls with versus without STBs would exhibit greater neural activation in regions associated with emotional reactivity (e.g., amygdala, visual processing regions, anterior cingulate) following a targeted social rejection compared with before rejection.

We hypothesized that girls with versus without STBs would demonstrate greater activation in the dorsolateral PFC during effortful emotion regulation before the rejection, potentially reflecting increased effort to engage explicit cognitive reappraisal skills (41). We hypothesized that girls with versus without STBs would demonstrate less activation in regions associated with reappraisal (e.g., IFG) following the targeted rejection, potentially reflecting difficulties in engaging reappraisal strategies. STBs increase with age (43), and depression symptoms and medication are positively associated with experiencing STBs (44,45). Prior research also suggests that age (46), depression symptoms (47,48), and medication use (49,50) are related to differences in neural markers of emotion regulation. Thus, these variables were included as covariates in all brain activation analyses involving STBs to minimize confounding. We also explored age as a moderator in fMRI models.

METHODS AND MATERIALS

Participants

Participants (N = 138; age range, 9–15 years at baseline; mean [SD] age = 11.6 [1.79] years) were drawn from a larger study (N = 229) investigating altered biological and behavioral responses to stress as risk factors for depression and STBs. Of these 229 participants, 138 (63%) underwent an fMRI scan. Of the 138 participants, 120 youths provided valid data for the prerejection analyses, and 110 provided valid data for the targeted rejection analyses (see Supplement).

As part of the parent study, youths completed a baseline clinical assessment and 3 follow-up visits at 4, 8, and 12 months. A baseline fMRI scan was completed a mean [SD] of 4.6 [6.86] months after the baseline clinical assessment. The scanning sample self-identified as American Indian or Alaska Native (n = 2, 1.4%), Asian (n = 3, 2.2%), Black (n = 45, 32.6%), Hispanic/Latina (n = 8, 5.8%), White (n = 59, 42.8%), or more than one race/other (n = 21, 15.2%). Participants self-identified their gender as female (n = 127, 92%), male (n = 4, 2.9%), or another gender (n = 7, 5.1%).[1] Three participants did not indicate a gender. Participants provided informed assent, and caregivers provided informed consent. Procedures were approved by the local institutional review board.

Measures

Suicidal Ideation and Suicidal Behavior. Consistent with recent research on multi-informants of adolescent SI (51), SI was coded from responses to 4 instruments: 1) Suicidal Ideation Questionnaire Junior version (52) (participant report), 2) Moods and Feelings Questionnaire (MFQ) (53) (participant and caregiver report), 3) Mini International Neuropsychiatric Interview for Children and Adolescents (54) (participant and caregiver report), and 4) Self-injurious Thoughts and Behaviors Interview (55) (participant report). Participants were considered to have a lifetime history of active SI if either the parent or the

[1]As we were interested in the effects of a targeted social rejection among girls, the 4 participants who identified as male were excluded from the targeted rejection analyses. Of the 7 participants who identified as another gender, 3 identified as nonbinary, 3 identified as she or girl, and one participant did not report an identity. Throughout, we use the term girl to refer to participants who identified as girl or other.

youth endorsed SI on any of the 4 SI measures at any time point regardless of the timing of their baseline fMRI scan. Consistent with our past research (56,57), participants were considered to have a lifetime history of SB (1 = yes, 0 = no) if they reported yes to an aborted or actual suicide attempt.[2] See the Supplement.

Depression Symptoms. The 33-item MFQ (53) assessed baseline depression symptoms. Participants indicated how true statements were to them in the past 2 weeks (0 = not true, 1 = sometimes true, 2 = mostly true). Consistent with our prior research (56), we removed the 4 SI items to eliminate overlap with the STB variables. A total sum score was computed across the remaining 29 items, with greater scores indicating higher depressive symptoms. The MFQ has good psychometric properties (58), and internal reliability was excellent (Cronbach's α in full sample = 0.92).

fMRI Acquisition and Tasks

We used identical fMRI acquisition parameters, tasks, contrasts, and design as our previously published study (36) (Supplement).

Emotion Regulation Task. Participants completed a well-established emotion reactivity and regulation (42) task. Participants viewed neutral and negative images from the International Affective Picture System (59) and from a set of similar images normed for youths (https://osf.io/43hfq/) (60). Youths either passively viewed negative or neutral pictures (look negative or neutral trials) or used cognitive reappraisal strategies taught before the scan to decrease emotional reactions to negative images (decrease negative trials). After each stimulus, participants rated the strength of their emotional reaction on a 5-point scale from 0 (minimal/no emotion) to 4 (maximal/strong). Participants saw 6 runs lasting 6 minutes 37 seconds each. Participants completed the social evaluation task (below), between the third and fourth run of the emotion regulation task. There were series A/series B stimulus presentation orders (consisting of 3 runs each with the same order of stimuli) to counterbalance which pictures were viewed before and after the social rejection.

Social Evaluation Task. This task was adapted from existing social evaluation paradigms (29,30,61) and is described in detail elsewhere [see (55,56) and Supplement]. Participants were told they would be watched via a camera in the scanner by an age- and gender-matched unfamiliar peer whom they indicated interest in meeting. While being observed, they made periodic ratings about how rejected they felt from 0 ("I feel almost no rejection") to 4 ("I feel an extreme amount of rejection"). After the evaluation period, we told the participant that after the peer watched them and read their biography, they no longer wanted to interact with the participant. Following the targeted social rejection, participants immediately completed a final set of emotion ratings and then participated in the final 3 runs of the emotion regulation tasks. Consistent with our previous study (36), 90% of girls (n = 100) reported believing that the peer was real.[3]

fMRI Image Acquisition and Preprocessing. Scans were acquired on a 3T MAGNETOM Prisma (Siemens Healthineers) scanner using a 32-channel head coil.[4] T1-weighted multiecho magnetization-prepared rapid acquisition gradient-echo volumes were acquired for coregistration with fMRI images (repetition time = 2530 ms, echo time = 1670–7250 ms, flip angle = 7°, field of view = 192 × 192 mm, 176 slices, in-plane voxel size = 1 mm). Blood oxygen level–dependent signal during functional runs was acquired with a gradient echo T2*-weighted echo-planar imaging sequence. A total of 44 2.4-mm-thick slices were acquired parallel to the anterior commissure–posterior commissure line (repetition time = 2500 ms, echo time = 28 ms, flip angle = 90°, bandwidth = 2312 Hz/pixel, echo spacing = 0.52 ms, field of view = 230 × 230 mm). Preprocessing was conducted through an in-house pipeline with standard analysis preparation, including motion outlier detection (>0.9 mm framewise), motion and slice-time correction, skull stripping, coregistration, normalization, and spatial smoothing (Gaussian kernel of 5 mm full width at half maximum). See the Supplement.

Analysis Plan

fMRI Analysis. fMRI data analysis was carried out in FEAT version 6.00. For each individual and run, a general linear model was created with 6 regressors of interest for each phase of the emotion task: 1) look or 2) decrease instructional cue, 3) look neutral trial, 4) look negative trial, 5) decrease negative trial, and 6) ratings. Nuisance regressors were included for 6 rigid motion parameters, their first derivatives, and single point motion outliers (framewise displacement >0.9 mm). Each run was high-pass filtered (Gaussian-weighted least squares) to remove low-frequency drift.

Higher-level analysis was conducted with FLAME 1 in FSL (62). Because we experimentally delivered a targeted social rejection in between the third and fourth run of the emotion regulation task, our prerejection models included the first 3 runs only. For these, 2 standard contrasts were created (34) comparing 1) look negative versus look neutral to isolate emotion reactivity and 2) decrease negative versus look negative to isolate emotion regulation. Consistent with our past approaches (60) and current recommendations (63), whole-brain analyses were cluster corrected using AFNI 3dClustSim (https://afni.nimh.nih.gov/pub/dist/doc/program_help/3dClustSim.html) with threshold of $p < .005$ and $\alpha = 0.05$. To examine the targeted social rejection effects (36), we compared activation immediately after versus before (run 4 > 3) the targeted social rejection for look negative (vs. baseline) and decrease negative (vs. baseline) trials separately using 3dMVM (64) in AFNI version 20.3.00 (http://afni.nimh.nih.gov/afni/).

[2]Only 3 girls had a new onset of SI, and 3 girls had a new onset of SB after their baseline assessment. Because of variability in timing of the fMRI scan, we did not aim to longitudinally predict STBs from neural markers in the present study. Additionally, of the 34 girls who reported a history of SB, only 5 reported a history of an aborted suicide attempt alone. The remaining girls reported a history of an actual suicide attempt.

[3]This did not significantly differ by STB status, $\chi^2_2 = 3.57$, $p = .17$.

[4]In 2 individuals, a 20-channel head coil was used, but they were included because leaving them out of analyses did not change the overall main task results as described below.

To test study hypotheses across imaging analyses, we first compared girls with STBs and control participants (i.e., girls without STBs; STB > control). Second, we compared girls with versus without SB (SB > SI only + control). Third, we compared girls with SB and girls with SI only (SB > SI only).[5]

fMRI Quality Checks. Individual runs were excluded for 1) >40% of time points, >0.9-mm framewise displacement, and single motion spike >5 mm within run and 2) <50% of the 24 emotion ratings. Two runs were required for the prerejection analyses, and valid runs 3 and 4 were required for the rejection analyses. Therefore, 120 youths were included in the prerejection analyses, and 110 were included in the postrejection analyses.[6] See the Supplement.

Behavioral Analysis, Covariates, and Sensitivity/Exploratory Models. Behavioral analyses compared ratings during the emotion reactivity and regulation trials and self-reported feelings of rejection before and after rejection. Across all behavioral analyses, there were no differences between girls with and without STBs; therefore, the Supplement presents all behavioral analyses. For neural activation models, we included exact age at scan, presence of medications (i.e., yes/no), and mean depression symptoms (MFQ). Parents reported that 55 youths (45.8%) were taking a medication, including psychiatric medication (35.8%) or allergy medication (20%). A stimulant medication was being taken by 16 youths, but 12 of the youths committed to a 24-hour washout before the day of the scan. Two sensitivity models for these primary analyses were run separately: 1) age only and 2) age and time between the baseline study visit and the neuroimaging scan. Overall results were largely unchanged (see Supplement). Finally, we explored age by group interactions by adding centered age separately between groups of interest to prerejection and postrejection whole-brain models. See the Supplement for details on how we explored significant interactions.

Missing Data

See the Supplement for details regarding missing data. Of the 120 participants included in analyses, 117 (97.5%) completed at least one follow-up STB assessment; 25 participants (20.8%) missed one or more follow-up assessments. If participants did not complete a follow-up assessment, we conservatively estimated no STBs for that period.

RESULTS

Descriptive Statistics

Of participants, 55 girls (45.83%) had no STB history (i.e., control participants), 65 girls (54.2%) reported SI, and 34 girls (28.6%) reported SB (Table 1). All girls with SB reported SI. Mean (SD) baseline depressive symptom severity was 13.08 (11.31) (range, 0–52), indicating, on average, elevated depression symptoms.

Emotion Reactivity Before and After Targeted Interpersonal Rejection

Main effects of the emotion reactivity and regulation task for all girls before and after the rejection are available in the Supplement. All girls reported feeling more rejected after rejection (mean [SD] = 1.97 [1.44]) compared with before rejection (mean [SD] = 1.34 [0.77]; mean difference = 0.64; $F_{1,109}$ = 26.02, p < .001). Before rejection, girls with STBs (STBs > control) exhibited greater activation in the right superior frontal gyrus (SFG) in reactivity trials (look negative > look neutral) (Figure 1; Table 2). There were no significant differences between girls with STB histories and control participants in the reactivity trials before versus after rejection (look negative after rejection > look negative before rejection).

Emotion Regulation Before and After Targeted Interpersonal Rejection

Before rejection, girls with SB versus SI only and control girls (SB < SI only + control) showed less activation in the right frontal pole in regulation trials (decrease negative > look negative). Girls with SB (SB < SI only) showed less activation in the right frontal pole in addition to the left superior parietal lobule in regulation trials (Figure 2; Table 2). After rejection, girls with STBs versus control participants showed greater activation in the right IFG (STB > control) in regulation trials after versus before targeted social rejection (decrease negative after rejection > decrease negative before rejection).

Exploratory Moderation Analyses

Exploratory analyses revealed one significant interaction in prerejection reactivity trials between age and STB > control (Figure 3; Table 3). Follow-up region-of-interest analyses[7] showed that the correlation between age and activation in the occipital lobe was positive in girls with STBs (r = 0.26, p = .04) and negative in control participants (r = −0.26, p = .05). In prerejection regulation trials, there were significant interactions between age and the following contrasts: STB < control, SB < SI only + control, SB < SI (Figure 4; Table 3). When comparing STB < control, the correlation between age and activation in the occipital lobe and SFG was negative for girls with STBs (r = −0.17, p = .17 and r = −0.17, p = .19, respectively) and positive in control participants (r = 0.34, p = .01 and r = 0.35, p = .01, respectively). When comparing SB < SI only + control, the relationship between age and activation in the SFG was negative in girls with SB (r = −0.33, p = .05) and positive in girls without SB (r = 0.18, p = .10). The same pattern between age and SFG activation was observed when comparing SB < SI only (SB, r = −0.33, p = .05; SI only, r = 0.10, p = .58).

[5]We did not include the SI only > control comparison given that prior research does not typically exclude girls with a history of SB from analyses examining SI. Additionally, we did not have an a priori reason to believe that questions about neural markers of SI would be relevant only among girls without a history of SB.

[6]One individual who was excluded from prerejection analyses was eligible for the targeted rejection analysis. This individual was not included in descriptive and bivariate analyses reported.

[7]See the Supplement for full details regarding region-of-interest analyses. Note that these regions of interest are just for illustrating the significant interaction effects at the whole-brain level. Therefore, individual significance levels should be interpreted with caution and in the context of the larger pattern of whole-brain results.

Table 1. Demographics

	All Participants, N = 120	Control Participants, n = 55	SI Only Participants, n = 31	SB Participants, n = 34	p Value	Statistics
Age at Scan, Years, Mean (SD)	12.83 (1.94)	12.12 (1.87)	12.88 (1.70)	13.94 (1.76)	<.001	ANOVA, $F_{2,117}$ = 10.74
Household Income, $, Mean (SD)	71,301.66 (56,175.48)	69,515.75 (56,339.51)	80,557.26 (63,796.85)	64,806.00 (47,374.69)	.58	ANOVA, $F_{2,98}$ = 0.55
Depressive Symptom Severity, Mean (SD)	13.08 (11.31)	7.84 (6.22)	12.97 (11.03)	21.64 (12.89)	<.001	Welch's ANOVA, $F_{2,53.24}$ = 18.08
Medications, n (%)	55 (45.8%)	15 (27.3%)	15 (48.4%)	25 (73.5%)	<.001	χ^2_2 = 18.22

This table reports the demographics of the 120 girls who were included in the main analyses. Race did not significantly differ across groups (χ^2_{10} = 9.25, p = .51). We did not report race broken down by category to protect participants' privacy.

ANOVA, analysis of variance; SB, suicidal behavior; SI, suicidal ideation.

DISCUSSION

This study examined neural correlates of emotion reactivity and regulation among girls with and without STBs before and after a targeted social rejection. Contrary to hypotheses, girls with STBs exhibited altered neural activation patterns in PFC regions (vs. temporal pole) when passively viewing negative stimuli. Further, no neural differences were found in reactivity based on STBs after rejection. Our hypotheses were partially supported during effortful attempts to regulate emotions. Specifically, girls with SB versus without SB showed less activation in PFC and visual processing regions implicated in successful emotion regulation. After rejection, girls with STBs versus control participants demonstrated greater IFG activation, a key region implicated in emotion regulation success (34). Our results showed that girls with SB do not engage neural regions implicated in emotion regulation to the same degree as girls without STBs when they are at their baseline emotional state. However, when exposed to a stressful targeted social rejection, girls with STBs engage key regions associated with inhibition and emotion regulation more, potentially reflecting a compensatory increase in regulatory neural processes (65).

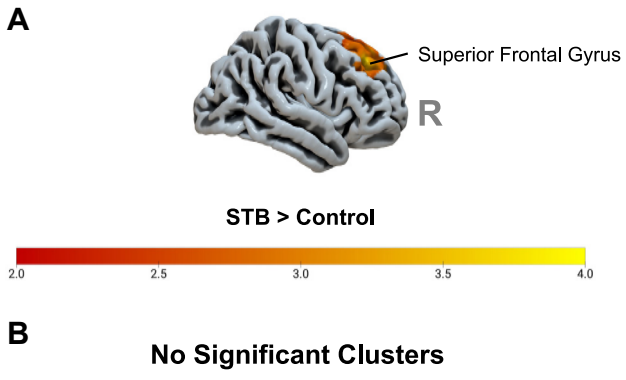

Figure 1. Neural activation during emotion reactivity before and after a targeted social rejection in girls with vs. without suicidal ideation and behavior. **(A)** Before rejection look negative > look neutral. **(B)** Look negative after rejection > before rejection. R, right; STB, suicidal thoughts and behaviors.

Emotion Reactivity Before and After Targeted Social Rejection

Before rejection, girls with STBs compared with control participants demonstrated greater activation in the SFG when passively viewing negative images. The SFG is a core PFC region involved in cognitive control (66). Although the contrast of interest captured emotion reactivity, the SFG is also associated with emotion regulation (34,67). Prior research has found that greater functional activation in the SFG at rest is associated with perceived stress among both adolescents and adults (68,69). It is possible that the increased SFG activation reflects a similar association, such that girls with STBs experienced viewing negative stimuli as more stressful than control participants. However, note that no subjective self-reported emotion ratings differed between the girls with and without STBs raising the possibility that girls with STBs may show differences at the neural, but not behavioral, level. Finally, exploratory age moderation analyses suggested that older girls with STBs exhibited greater visual cortex activation, potentially suggesting that they attend more to negative stimuli. However, we recommend caution in interpreting this finding until replicated in larger samples. Overall, future research is needed to identify robust neural markers underlying responses to negative stimuli in girls with STBs.

Because targeted social rejections are hypothesized to disrupt emotion reactivity and potentially lead to a suicidal crisis (5), we expected that girls with STBs would show increased neural activation in subcortical and emotion processing regions after rejection. Contrary to our hypotheses, we did not observe any differences before versus after rejection between girls with STBs compared with control participants during emotion reactivity. This is surprising given prior research and theory (5,70). However, recent suicide theories emphasize a proximal link between interpersonal stressors and increased STB risk within the next few hours, days, or weeks (5,71), and day-to-day fluctuations of SI occur (72). Therefore, the hypothesized emotional reactivity to interpersonal stress and STB link may be a more dynamic, fluctuating phenomenon rather than static risk conferred by past STBs.

Emotion Regulation Before and After Rejection

Contrary to hypotheses, we found that girls with SB versus without SB showed less activation in lateral PFC regions

Table 2. Peak Activations for Emotion Reactivity and Regulation Before and After Targeted Social Rejection in Girls With and Without Suicidal Ideation and Behaviors

Trial Type	Region of Peak Activation	BA	Cluster Size	x	y	z	*z* Value
Emotion Reactivity							
Before rejection look negative > look neutral							
STB > control	Superior frontal gyrus (R)	8	411	22	34	44	4.40
Look negative after > before rejection							
	No significant clusters						
Emotion Regulation							
Before rejection decrease negative > look negative							
SB < SI only + control	Frontal pole (R)	10	204	42	54	6	3.69
SB < SI only	Frontal pole (R)	10	386	34	56	20	4.17
	Superior parietal lobule (L)	39	207	−40	−58	42	3.59
Decrease negative after > before rejection							
STB > control	Inferior frontal gyrus (R)	44	217	58	14	4	4.42

Exact age, medication, and depression severity were included as covariates.
BA, Brodmann area; L, left; R, right; SB, suicidal behavior; SI, suicidal ideation; STB, suicidal thoughts and behaviors.

hypothesized to support cognitive reappraisal (34,46) before rejection. Additionally, girls with SB versus SI showed less activation only in the superior parietal lobule, which is an area previously associated with emotion reactivity and regulation (34,73,74). Interestingly, research with youths has demonstrated that the superior parietal lobule may be implicated in emotion expression recognition (75). Our prior pilot work found that youths with SI versus without SI demonstrated greater dorsolateral PFC activation during effortful emotion regulation (41). Here, we more thoroughly assessed STBs and saw differences emerge for youths with SB in lateral PFC and superior parietal areas. This may suggest that girls with SB engage these key regions less when attempting to regulate emotions. Results from exploratory age moderation analyses demonstrated that, overall, increasing age was associated with greater activation in key PFC regions implicated in emotion regulation for girls without STBs, especially when compared with girls with SB. Though preliminary, this finding may suggest that girls with STBs may not have age-related effects on neural regions supporting emotion regulation as strong as girls without STBs. Girls with SB may actually show reductions in activation in these regions at older ages; however, as mentioned above, caution is warranted. Overall, future work is required to determine whether these activation differences

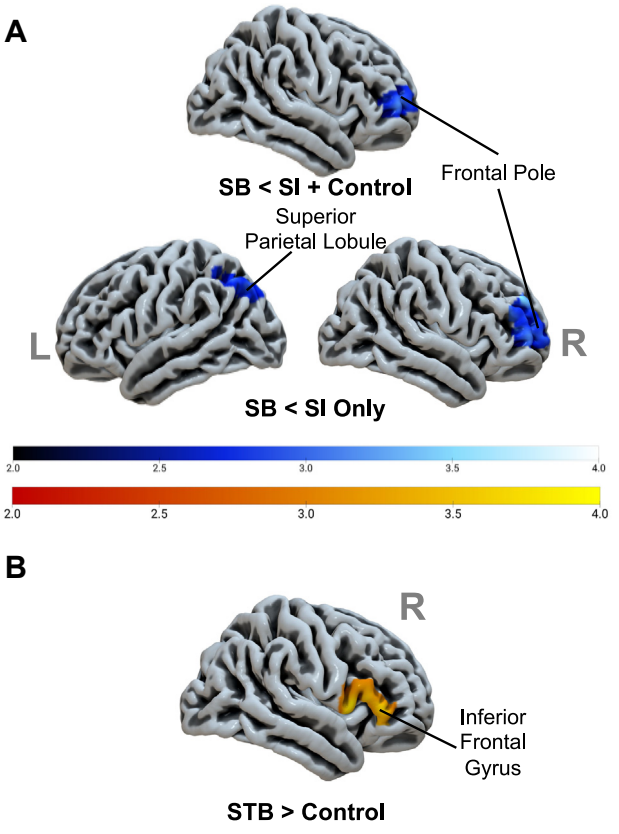

Figure 2. Neural activation during emotion regulation before and after a targeted social rejection in girls with vs. without suicidal ideation (SI) and suicidal behavior (SB). **(A)** Before rejection decrease negative > look negative. **(B)** Decrease negative after rejection > before rejection. L, left; R, right; STB, suicidal thoughts and behaviors.

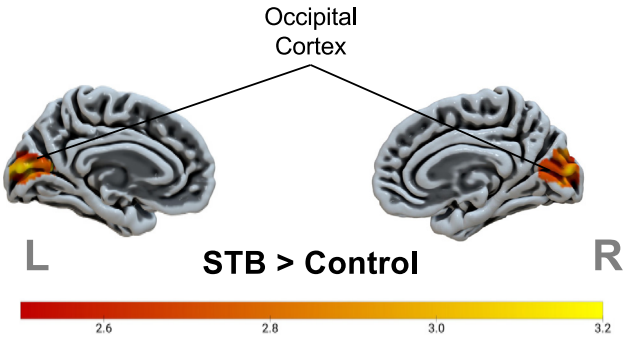

Figure 3. Association between increasing age and neural activation during emotion reactivity before a targeted rejection in girls with vs. without suicidal ideation and behaviors. L, left; R, right; STB, suicidal thoughts and behaviors.

Table 3. Prerejection Peak Activation When Examining Association Between Increasing Age and Activation During Emotional Reactivity and Regulation

Trial Type	Region of Peak Activation	BA	Cluster Size	x	y	z	*z* Value
Emotion Reactivity							
Before rejection look negative > look neutral							
STB > control	Occipital cortex (L)	17	346	−6	−84	10	3.82
Emotion Regulation							
Before rejection decrease negative > look negative							
STB < Control	Occipital cortex (L)	17	1595	−14	−82	6	4.67
	Superior frontal gyrus (L)	8	440	−22	38	46	4.48
	Occipital cortex (L)	19	210	−40	−86	12	4.15
SB < SI only + control	Superior frontal gyrus (R)	6	1010	4	14	60	4.43
SB < SI only	Superior frontal gyrus (L)	8	561	−6	24	58	4.45

Models included depression severity and medication status.
BA, Brodmann area; L, left; R, right; SB, suicidal behavior; SI, suicidal ideation; STB, suicidal thoughts and behaviors.

reflect a true deficit in the ability to engage in emotion regulation in real-world contexts.

We hypothesized that girls with STBs would demonstrate less activation in regions associated with reappraisal after rejection. Partially supporting our hypotheses, we found that girls with STBs versus without STBs exhibited greater (not less) activation in the right IFG, a key PFC region implicated in inhibition (76,77) and emotion regulation (34). Although in the opposite direction hypothesized, this finding is consistent with the overarching hypothesis that targeted social rejections disrupt typical emotion regulation processes for girls with STBs. It is intriguing that this difference was not observed when comparing girls with SB versus girls with SI only. This suggests a potentially more generalized difference associated with any STBs. Girls with STBs may have engaged the IFG to inhibit conflicting or distracting cognitions related to the social rejection while attempting to employ cognitive control in a compensatory manner (65). If replicated, this would suggest that interpersonal stressors disrupt neural correlates of emotion regulation, which could engender vulnerability to future STBs. While caution is warranted in drawing firm conclusions due to the correlational nature of our analysis, this type of work could ultimately clarify the importance of when and how to engage emotion regulation skills, particularly following a targeted social rejection. If replicated, this work lends additional support for including emotion regulation skills as a core component in psychosocial treatments addressing STBs (78).

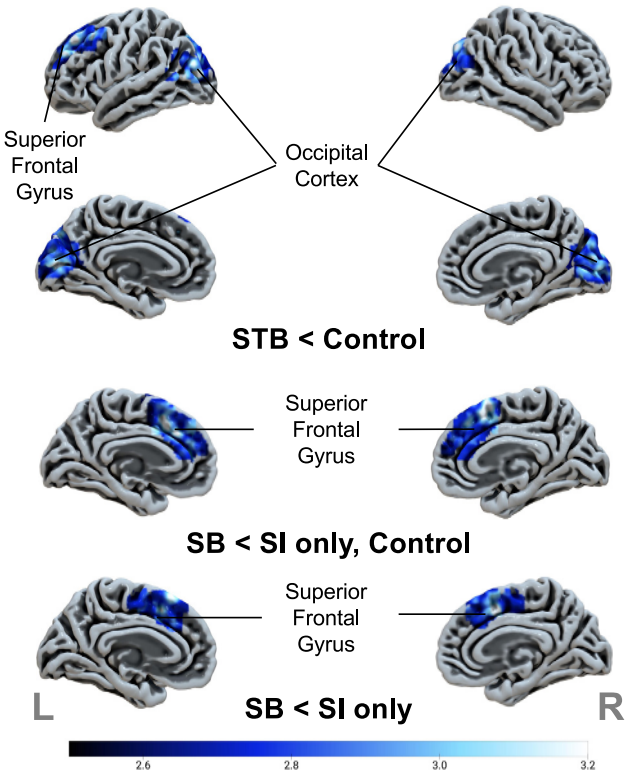

Figure 4. Association between increasing age and neural activation during emotion regulation before a targeted rejection in girls with vs. without suicidal ideation (SI) and suicidal behavior (SB). L, left; R, right; STB, suicidal thoughts and behaviors.

Strengths and Limitations

This study has several strengths. Suicide theories suggest that targeted social rejections may lead to suicidal crises because of disruptions in emotion regulation; yet, prior research has not examined the neural correlates of emotion regulation before and after rejection in girls at risk for STBs. Compared with prior work, we used a novel, more ecologically valid social rejection task that effectively elicited feelings of rejection (36). This study used validated measures of STBs and emotion regulation.

Given variability in the timing of the fMRI scan, we did not prospectively predict STBs. Future studies with larger samples will be critical for identifying robust neural markers of prospective suicide risk. Although adolescent girls report higher STBs compared with boys, additional research is needed to examine whether similar processes are observable in boys.

The laboratory-based rejection task is not a naturalistic life event, and external validity could be an issue. The well-established emotion regulation task includes using cognitive

reappraisal of standardized images, and for the rejection comparison (run 4 > 3) there were a small number of trials within individual runs [see (57)]. There likely are many other types of real-world emotion regulation strategies that differentiate adolescent girls with and without STBs.

Nonsuicidal self-injury is distinct from STBs. However, there is some overlap, and future research with this study's paradigm may build on the growing literature in this area (79,80). Our age range spanned from 9 to 15. In our main models, we covaried for age, which may obscure important developmental differences. While we found some preliminary significant moderation by age in prerejection models, we likely were underpowered to detect significant postrejection findings. Additionally, pubertal status may be an equally important moderator given recent research in the area of pubertal onset and STBs (81).

Conclusions

We demonstrated that before rejection, girls with SB versus without SB may activate lateral PFC regions less when attempting to effortfully control emotional reactions to negative stimuli. After rejection, girls with STBs compared with control participants showed increased activation in a region specifically implicated in inhibition of behavioral and cognitive emotional responses. Future research could build on these findings to explore whether these differences observed in a controlled laboratory-based setting predict disrupted emotion regulation and subsequent STBs following targeted social rejections in real-world settings.

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