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Neural Correlates of Emotion Regulation and Adolescent Suicidal Ideation

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ABSTRACT

BACKGROUND: Research on the neural correlates associated with risk for suicidal ideation (SI) has been limited, particularly in one increasingly at-risk group—adolescents. Previous research with adolescents indicates that poor emotion regulation skills are linked with SI, but these studies have not previously examined neural activation in service of emotion regulation between those with and without SI histories.

METHODS: Here we examine whether SI is associated with neural responses during an emotion regulation functional magnetic resonance imaging task in a group of adolescents (N = 49) 13 to 20 years of age (mean = 16.95).

RESULTS: While there were no differences between youths with and without SI in self-reported emotional responses to negative pictures, youths with SI activated the dorsolateral prefrontal cortex more than youths without SI on trials in which they attempted to regulate their emotional responses compared with trials in which they passively viewed negative pictures. In contrast, during passive viewing of negative stimuli, youths with SI activated the dorsolateral prefrontal cortex, temporoparietal junction, and cerebellum less than same-age control subjects.

CONCLUSIONS: These findings were robust to control subjects for depression and adversity exposure and are consistent with the idea that youths with SI have disrupted emotion regulation, potentially related to differences in recruitment of top-down control regions. In contrast, youths without SI activated regions implicated in emotion regulation even when not directed to effortfully control their emotional response. This is the first study to examine neural function during emotion regulation as a potential neural correlate of risk for SI in adolescents.

Keywords: Adolescent suicide, Cognitive reappraisal, DLPFC, Emotion regulation, Suicidal ideation, Top-down control

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Suicide is currently the second leading cause of death worldwide for American youths between 10 and 24 years of age (1,2). Rates of suicidal ideation (SI) (defined as thoughts about death, dying, plans for suicide, or desire for death) are remarkably high in this age range (3). This is because SI increases dramatically during the transition to adolescence (4), with between 12.1% and 18% of high school students seriously considering suicide (4,5). SI is frequently associated with suicidal behavior and suicide death (6,7) and places adolescents at serious risk for premature death. To prevent adolescent suicide, we require greater understanding of factors that identify which adolescents with SI are most at risk for future suicidal behavior. Unfortunately, despite years of research on risk factors for suicide, few reliable within-person predictors or successful interventions have been identified (8). At least one possibility for the stagnation in the adolescent suicide literature is a lack of studies examining neural processes underlying commonly purported risk factors for SI, such as emotion regulation (9,10). Examining neural correlates of processes underlying SI may help identify targets for prevention and intervention. However, few studies to date have linked neural structure or function with SI, leaving this potentially informative avenue virtually unexplored in adolescents.

Some research has examined neural correlates of SI in adults. Although an extensive review of these studies is beyond the scope of this article given our focus on adolescent SI, results generally suggest that dysfunction of frontal control regions is commonly associated with histories of SI across samples of adults with recent-onset schizophrenia (11–13), recent-onset major depressive disorder with psychotic features (14,15), and major depressive disorder (16–20). Surprisingly little research has examined neural correlates of SI or behavior in youths. Johnston *et al.* (21) found that youths with a history of suicide attempts have decreased gray matter volume in the orbitofrontal cortex, hippocampus, and cerebellum as well as decreased functional connectivity between the amygdala and left ventral and right rostral prefrontal cortex (PFC) when viewing emotional faces. Another study found that youths with suicide attempts relative to peers with a history of depression but no suicide attempts exhibited increased activation in the right anterior cingulate gyrus, left dorsolateral PFC (dlPFC), and the right middle temporal gyrus while viewing

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negative relative to positive facial expressions during an emotion perception task (22). In this same sample, activation of the right thalamus during high-risk trials and the left caudate during low-risk trials of the Iowa Gambling Task differentiated adolescents with a suicide attempt history from healthy and depressed peers (23). Together the available research suggests that activation of the PFC, temporal lobe, and limbic regions such as the amygdala, caudate, and thalamus during emotionally evocative tasks may distinguish adolescents with versus without suicidal behavior. However, the available data are limited to only suicidal behavior, and results vary across studies.

One reason that previous findings may vary is that past studies of neural function associated with suicidality in youths have relied on tasks that are only loosely related to risk for SI (e.g., passive viewing of emotional faces). Unmanageable emotional distress is a common antecedent to SI in youths (24–26) and individuals who report more emotion regulation difficulties are at increased risk for SI even after accounting for depression symptoms (27). Yet to date, the neural correlates of emotion regulation have not been measured in association with SI; this is surprising, given that the neural correlates of emotion regulation have been well studied across a wide age range (28–30).

Effortful emotion regulation, an intentional attempt to decrease one's negative response to specific stimuli, is typically accomplished by employing cognitive strategies such as reappraisal (28). A recent meta-analysis of studies employing a cognitive reappraisal emotion regulation task (31) concluded that effortful regulation via cognitive reappraisal consistently activates prefrontal control regions including the dorsomedial PFC, dlPFC, and ventrolateral PFC (28). Thus, available research suggests that emotion regulation is easily studied using existing, well-understood paradigms and that emotional reactivity is likely modulated by activation of the lateral and dorsomedial PFC in healthy samples of adolescents. In addition, current evidence points to the possibility that emotion regulation deficits underlie risk for SI, yet no study to date has examined neural activation in response to an emotion regulation task in youths with and without SI. We address this gap in the current study.

Current Study

Our goal was to examine whether neural regions recruited in support of emotion reactivity and regulation distinguish adolescents with and without SI. Given evidence that adolescents with SI exhibit greater self-reported emotional reactivity (9), we hypothesized that adolescents with versus without SI histories would show greater activity in limbic regions when viewing negative stimuli relative to neutral stimuli. Additionally, adolescents with versus without SI histories self-report greater emotion dysregulation (10). Thus, we hypothesized that adolescents with versus without SI histories would differentially recruit frontal control regions (dorsomedial PFC, dlPFC, and ventrolateral PFC) frequently implicated in cognitive reappraisal (28) during attempts to effortfully regulate emotional responses to negative stimuli relative to passive viewing of negative stimuli. Together, this study will allow us to examine both reactivity and regulation among youths with and without SI histories as an initial step to better understanding the mechanisms that put youths at risk for suicide.

METHODS AND MATERIALS

Participants

Participants included 49 adolescents (13 to 20 years of age[1]; mean = 16.95 years, SD = 1.54; 59% girls) recruited in the context of a larger study examining the effects of childhood maltreatment on development (32,33). The original sample included 51 youths who participated in the scanning procedures described below. Of these 51, 49 individuals provided valid data for the main outcome variable, SI. The current sample included individuals with and without exposure to childhood maltreatment, which we control for in all analyses. Exclusion criteria included psychiatric medications that could not be discontinued for 24 hours before scan (all but stimulant medications), braces, claustrophobia, left handedness, active substance dependence or use on the day of the scan, pervasive developmental disorders, lack of ability to speak/read English, and presence of active safety concerns (acute suicidal crisis). All procedures were approved by the hospital affiliated institutional review board.

Measures

Suicidal Ideation. SI was assessed using data from well-validated self-report and structured clinical interviews. We created a composite present (= 1) or absent (= 0) score for lifetime SI in the current study. SI was considered present (= 1) for any of the following: a score greater than zero on the Scale for Suicidal Ideation (self-report for past 2 weeks) (34), a response of "yes" to the SI question on the Diagnostic Interview Schedule for Children Version IV (DISC-IV) (past year questions) (35), or a response of "yes" to the SI question on the Self-Injurious Thoughts and Behaviors Interview (clinical interview covering SI age of onset and age of most recent SI) (36). All three measures have strong psychometric properties and have been used in numerous previous studies with adolescent SI (7,37). Prior research has noted that multiple methods of assessment of SI (i.e., clinical interview and self-report instruments) are preferable to either method alone [e.g., (38)]. Thus, combining information across these three instruments represents a strength for the current study. Further, we elected to use a dichotomous indicator of SI history because the presence or absence (and not severity) of SI is one of the most consistent and strongest predictors of future SI and suicidal behavior (7).

In the current sample, 9 individuals were included in the SI group for endorsing "yes" to the Self-Injurious Thoughts and Behaviors Interview question, "Have you ever had thoughts of killing yourself?" Four individuals were included in the SI group for endorsing "sometimes" or "often" on the Scale for Suicidal Ideation items "My reasons for living or dying are about equal" or "I have made some preparations for committing suicide." One individual was included in the SI group for endorsing "yes" to the DISC-IV question, "In the past year, did you think about killing yourself?" A total of 14 individuals (28% of total sample)

[1] Only 1 individual was 20 years of age.

were included in the SI group. Of those with SI, 4 individuals endorsed a previous suicide attempt. These rates are similar to other work that has included youths with elevated clinical symptoms (e.g., depression) and exposure to child adversity (39,40).

Depressive Symptoms. Past-year depressive symptoms were assessed using the DISC-IV (35). Trained graduate students administered the DISC-IV, which is a structured clinical interview that assesses the presence of DSM-IV symptoms and disorders. Total symptom count for the prior 12 months was derived from all questions in the major depressive disorder module.

Childhood Maltreatment. Participants completed the Childhood Trauma Questionnaire (41) and were considered to have experienced lifetime maltreatment (= 1) or not (= 0) based on their total score using a validated threshold (42).

Functional Magnetic Resonance Imaging Task

During the functional magnetic resonance imaging scan, participants completed an event-related task assessing neural markers of emotion regulation (31), which has been used with children (30,32). Design and contrasts of this task were based on previous literature (30,31). Participants viewed neutral, negative, and positive images from the International Affective Picture System (43). Before each negative picture, participants saw a cue to "look" or "decrease"; before each positive picture participants saw a cue to "look" or "increase." Neutral pictures were preceded by a "look" cue. Positive and negative images were presented in a quasi-blocked design; in each run participants viewed mixed negative and neutral images in a randomized order for half the run and mixed positive and neutral images in a randomized order for half the run (32). As our interest was in the regulation of negative emotion as a potential marker of risk for SI, we did not analyze positive trials. During look trials, participants were instructed to simply look at the image and allow their emotions to unfold naturally without altering their emotional reaction. During decrease trials, participants were instructed to use specific cognitive reappraisal strategies to reduce their emotional reaction to the negative stimuli. After each stimulus, participants rated the strength of their emotional reaction on a 5-point Likert-type scale.

Before 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 from those used in the scanner. Participants were instructed to think about the image as more psychologically distant by imagining the scene as farther away, not involving them, or simply involving actors. These strategies have been used in previous studies (30,31,44).

Stimuli were presented in four runs each lasting 9 minutes each. Average valence (mean = 2.64, range = 1.76 to 4.69), arousal (mean = 5.82, range = 4.47 to 7.09), and number of faces within each image were equivalent for look negative and decrease trials (all $ps > .45$). The task included 26 trials of each type, and the emotional stimulus and intertrial interval were jittered [see (32)].

Image Acquisition

Scanning was performed on a Siemens 3T Trio Scanner (Siemens Corp., Erlangen, Germany) at the Harvard Center for Brain Science, using a 32-channel head coil (see the Supplement for full acquisition parameters and image processing information). Blood oxygen level–dependent signal during functional runs was acquired using a gradient-echo T2*-weighted echo-planar imaging sequence. Thirty-nine 3-mm-thick slices were acquired parallel to the anterior commissure-posterior commissure line (repetition time = 2500 ms, echo time = 30 ms, flip angle = 90°, bandwidth 2240 Hz/Px, echo spacing = 0.51 ms, field of view = 216 × 216 mm, matrix size = 72 × 72 mm). Before each scan, four images were acquired and discarded to allow for longitudinal magnetization to reach equilibrium. An online prospective motion correction algorithm was used to reduce motion artifacts.

Preprocessing and statistical analysis of functional magnetic resonance imaging data was performed in Nipype (45). Preprocessing included spatial realignment, slice-time correction, and spatial smoothing (6-mm full width at half maximum), implemented in FSL. Data were inspected for artifacts, and single-point outlier regressors were modeled to account for any motion exceeding 1.5 mm. Additionally, six rigid-body motion regressors were included in person-level models.

Functional Magnetic Resonance Imaging Analysis. Regressors were created for each phase of the task: instructional cue, stimulus, and rating periods separately for look and decrease trials for neutral and negative stimuli. A general linear model was used to estimate the association between blood oxygen level–dependent signal and task demands across time for each subject, before normalization (see Supplement for more information). As has been done in previous studies (28), we measured emotional reactivity as the contrast of look negative > look neutral trials and emotion regulation as the contrast of decrease > look trials for negative stimuli (i.e., isolating neural response during emotion regulation independent of viewing negative images). We examined differences in blood oxygen level–dependent response during contrasts of interest as a function of SI in whole-brain analyses. We applied cluster-level correction in FSL ($Z > 2.3$, $p < .05$). To aid in interpretation of our results, we also include within-group comparisons during look versus baseline (fixation cross) and decrease versus baseline in the Supplement (see Supplemental Figure S2).

Because we felt it was important to determine whether our results held when controlling for well-known correlates of SI, including depression symptoms (46), age (4), and child maltreatment (47), we controlled for these variables. Results below are presented with all covariates included; however, when including depression changed the findings, we additionally report that finding. Results for the main effects of task and child maltreatment status were reported in McLaughlin *et al.* (32). Associations between the emotion regulation task and psychopathology are available in McLaughlin *et al.* (48).

Behavioral Analysis. We compared self-reported emotional intensity for any trial between those with and without SI using independent-samples *t* tests.

Table 1. Demographic Information and Comparisons Between Those With and Without Suicidal Ideation Histories

	Individuals With Suicidal Ideation Histories (n = 14)		Individuals Without Suicidal Ideation Histories (n = 32)			
	%	n	%	n	χ^2 Value (df)	p Value
Female	71.4	10	54.3	19	1.22 (1)	.34
Race					5.33 (4)	.26
White	21.4	3	31.4	11		
Black	28.6	4	34.3	12		
Hispanic/Latino	35.7	5	11.4	4		
Asian	0.0	0	11.4	4		
Other/biracial	14.3	2	11.4	4		
Parent Education					5.12 (3)	.16
High school or less	14.3	2	19.4	6		
Some college	35.7	5	12.9	4		
College degree	14.3	2	41.9	13		
Graduate school	35.7	5	25.8	8		
	Mean	SD	Mean	SD	t Value (df)	p Value (d)
Age, Years	16.70	1.73	17.06	1.47	0.73 (47)	.47 (0.22)
CTQ Abuse Subscale	17.57	7.84	11.28	2.02	−4.45 (47)	<.001 (1.3)
Major Depression Symptoms	9.93	3.60	5.09	3.73	−4.448 (47)	<.001 (1.3)

CTQ, Childhood Trauma Questionnaire.

RESULTS

Descriptive Statistics

Table 1 presents comparisons between those with and without SI histories including gender, race, parental education, age, scores on the Childhood Trauma Questionnaire, and major depression symptoms.

Self-Report of Emotion Intensity

There were no differences in self-reported emotional intensity for any trial for those with (vs. without) SI (t_{47} = −1.38 to −0.27, ps = .17 to .79, ds = 0.10 to 0.37), and the change in self-reported emotional intensity from look negative to decrease trials did not vary by SI (t_{47} = 0.46, p = .65, d = 0.14).

Neural Response to Passive Viewing of Negative Emotional Stimuli

In the look negative > look neutral contrast, youths with SI, relative to youths without SI, exhibited significantly less activation in four separate clusters with peaks in the thalamus, dlPFC, temporoparietal junction (TPJ), and the cerebellum, respectively (see Figure 1 and Table 1). Youths with versus without SI histories exhibited greater activation in the temporal pole for this same contrast (see Table 1). In analyses that did not control for depression, the TPJ activation was not significantly different between groups (see Supplemental Figure S1). All other results remained the same.

Neural Response to Effortful Emotion Regulation Toward Negative Stimuli

In the decrease > look negative trials, youths with SI exhibited significantly greater activation in the dlPFC relative to youths without SI histories (see Table 2). Results were unchanged in analyses with and without covariates included (see Supplemental Figure S1). There were no areas with significantly greater activation for youths without SI compared with youths with SI for this contrast.

DISCUSSION

The purpose of the present study was to examine neural processes underlying emotion regulation that may differ between adolescents with versus without SI histories. This is the first study to examine patterns of neural activation during an emotion regulation task between those with and without SI histories, representing an important first step in better understanding the mechanisms driving this significant public health concern. Our results partially supported our hypotheses, demonstrating that adolescents with SI histories show differential patterns of activation compared with adolescents without SI when passively viewing negative stimuli and when attempting to effortfully regulate their responses to negative stimuli. For both kinds of trials, we observed significant differences between youths with and without SI in frontal control regions, but no differences in limbic system reactivity for either trial type. These findings highlight the importance of future work on the relative importance of emotional control and PFC function in the pathophysiology of SI.

Our first hypothesis, that adolescents with SI histories would exhibit greater activation in limbic regions compared with adolescents without SI histories during passive viewing trials, was not supported. However, results from whole-brain analyses demonstrated that youths with versus without SI showed greater activation in the left temporal pole when passively viewing negative versus neutral stimuli. Accumulating evidence suggests that the temporal pole plays a role in emotional control by modulating emotional reactions to evocative visual stimuli, particularly when perceiving or imaging emotions, as in the present study (49). Whether recruitment

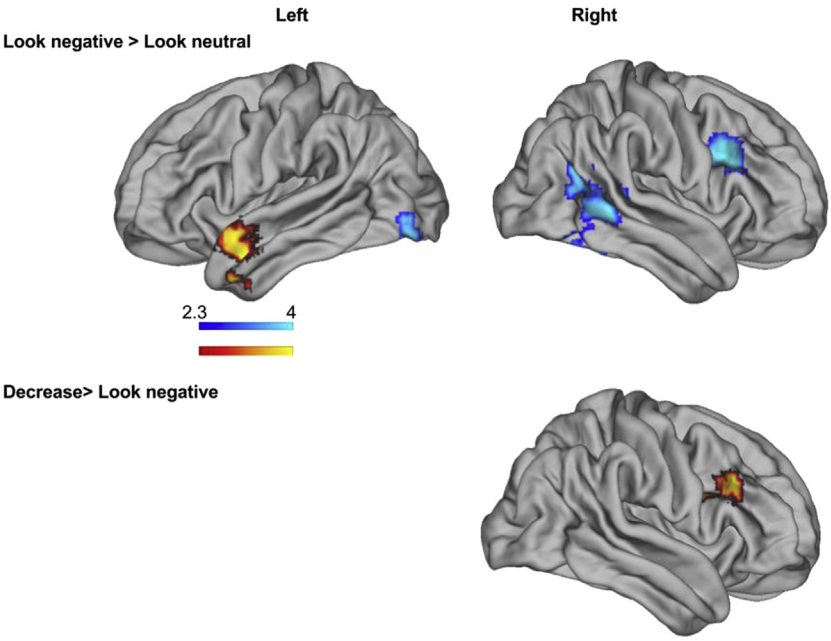

Figure 1. Neural responses to passive viewing and effortful regulation of negative emotional stimuli in individuals with suicidal ideation histories versus those without suicidal ideation histories. Regions with significant blood oxygen level–dependent activation are depicted. Control variables included age, maltreatment status, and depression severity.

of the left temporal pole when viewing negative stimuli is further implicated in adolescent suicide remains an intriguing question for future research.

In contrast to youths with SI, during passive viewing relative to neutral trials, youths without SI activated the dlPFC, and TPJ to a greater extent. Historically, in this task the dlPFC is implicated in active emotion regulation (28), and in other studies activation of the dlPFC is associated with working memory (50). In the context of emotion regulation, it is thought that activation in this region may reflect holding potential reappraisals in mind while examining stimuli (28,29). Thus, it is possible that youths without SI histories were more likely to engage this region during passive viewing compared with neutral trials to downregulate emotional reactions even without prompting. A robust body of literature has linked the TPJ with deciphering others' mental states or "theory of mind" (51). In the context of this emotion reactivity task for which we specifically selected pictures from the International Affective Picture System, which included human figures and often those depicting interpersonal violence, it is possible that control youths were activating this region to imagine others' mental states. Again, it may be that this enhanced representation was in the service of unprompted emotion regulation for control participants. Finally, the cerebellum and thalamus were significantly more active for control youths relative to youths with SI. Increased activation of these regions may indicate enhanced salience or perceptual processing of these stimuli for control youths relative to youths with SI. Interestingly, a recent study found increased resting-state connectivity between cerebellum and lingual gyrus of depressed youths with suicide attempt histories (52). Further exploration of this area with regard to adolescent SI and behavior is warranted.

Because we and many others observe differences in PFC activation for regulate versus look trials and a decrease in self-reported emotion for regulate relative to look trials across all subjects (28,32), it is unlikely that the observation that control youths activated the dlPFC and TPJ during look trials means that youths without SI were not properly engaged with the task most of the time. However, it may be that relative to control youths, youths with SI were less likely to spontaneously bring

Table 2. Regions of Peak Activation

Trial Type	Region of Peak Activation	Brodmann Area	Cluster Size	x	y	z	*Z* Value
Look Negative > Look Neutral							
Youths with SI < youths without SI	dlPFC (R)	44	715	44	18	30	4.03
	Thalamus (R)	—	809	14	−10	10	3.99
	Cerebellum/lateral occipital (L)	—	768	−8	−74	−22	3.67
	Temporoparietal junction (R)	39	1782	40	−58	22	3.94
Youths with SI > youths without SI	Temporal pole (L)	38	647	−50	2	−20	3.48
Decrease > Look Negative							
Youths with SI > youths without SI	dlPFC (R)	9	463	50	22	30	3.71

Exact age, child maltreatment history, and depression symptom severity were included as nuisance repressors in all analyses.
dlPFC, dorsolateral prefrontal cortex; L, left; R, right; SI, suicidal ideation.

to mind ways of reappraising negative stimuli, and this may be linked with their self-reported and observed emotion regulation deficits elsewhere (10). Importantly, our interpretation of these findings is limited; we did not observe behavioral differences in self-reported emotion between youths with and without SI. In the context of a null behavioral result, it is difficult to interpret these findings as firm evidence of enhanced spontaneous emotion regulation in youths without SI. Future research with larger samples may be able to confirm our findings and extend them by linking self-reported emotion on this task with real world behavior for adolescents with SI.

Our second hypothesis, that youths with SI would differentially recruit frontal control regions during effortful regulation trials compared with passive viewing of negative images, was supported. During trials in which youths were told to effortfully downregulate their emotional responses to negative stimuli compared with passively viewing negative stimuli, youths with SI histories demonstrated greater activation in the dlPFC compared youths without SI histories. This indicates that differences in activation of this dlPFC region between regulation and passive viewing trials were greater for youths with SI versus youths without SI. Thus, it appears that youths with SI can successfully recruit this region in the service of emotion regulation, but unlike youths without SI, they only do so only when explicitly instructed. This observation, coupled with the lack of behavioral difference in self-reported emotion between controls and youths with SI for regulate trials, is consistent with the possibility that youths with SI can respond to explicit instruction to successfully recruit the dlPFC in the service of emotion regulation. In the contrast where regulation trials were compared with reactivity trial, youths with SI evidence increased in activation in the dlPFC compared with youths without SI. An alternative explanation to the one we provide above is that individuals with SI inefficiently recruit the dlPFC during regulation trials. This offers an intriguing alternative comparison to be explored in future, larger studies.

Taken together, results demonstrate that youths without SI histories may activate regions implicated in emotion regulation, including the dlPFC, even when instructed to passively view emotional stimuli. In contrast, youths with SI do not engage these regions during passive viewing trials. However, youths with SI are able to engage the dlPFC in the service of cognitive reappraisal (28,32) but only when explicitly instructed. Generally, these results are consistent with studies with adults, which suggest specific frontal control region dysfunction among individuals with (vs. without) SI histories [e.g., (14)]. Although much more research is necessary to further untangle these relationships, it is possible that the pattern observed during this task relates to experiences of youths with SI in real-world settings. Indeed, research from the behavioral literature suggests that during emotional crises, youths with SI demonstrate limited access to emotion regulation (10) and problem-solving (53,54) strategies, but that explicit instruction in emotion regulation, in the form of dialectical behavioral therapy, can mitigate these deficits (55). Given that the transition from thinking about suicide to acting on suicidal thoughts tends to be quite rapid (56), treatment targeting access to automatic emotion regulation strategies could be beneficial in preventing suicidal behavior.

The current study represents an important first step in examining neural underpinnings of adolescent SI. However, future work should address limitations from this study. The present study was cross-sectional. Future studies with a longitudinal design can determine whether neural processes observed in the current study are prospective risk factors for, or consequences of, SI. While one quarter of the current sample had SI, future studies should make efforts to recruit larger samples with a greater incidence of SI and a wider range of suicidal behavior to replicate the current study's findings and provide more precise testing of neural differences between those youths without any kind of SI or suicidal behaviors, those with SI alone, and those that have made a suicide attempt. Further, a larger sample of youths with SI will allow examination of differences between passive and active SI [see (57)]. The emotion regulation strategies in this study were tested in a controlled setting; however, it is possible that youths with SI may exhibit more difficulty regulating emotions in the context of real-world experiences or even with more naturalistic stimuli. Future research should address this possibility.

The current study is among the first to investigate neural mechanisms underlying emotion regulation—a commonly purported risk factor for SI in adolescence. Results suggest that youths with and without SI differentially recruit regions implicated in emotion regulation when viewing negative stimuli and regulating responses to negative stimuli. These findings build on a growing body of work suggesting a critical role of disruptions in emotion regulation as a process underlying SI in adolescents and extend previous findings by examining neural markers of emotion regulation rather than relying on self-report.

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