

Review

THE ROLE OF PEER REJECTION IN ADOLESCENT DEPRESSION

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Adolescence is a period of major risk for depression, which is associated with negative personal, social, and educational outcomes. Yet, in comparison to adult models of depression, very little is known about the specific psychosocial stressors that contribute to adolescent depression, and whether these can be targeted by interventions. In this review, we consider the role of peer rejection. First, we present a comprehensive review of studies using innovative experimental paradigms to understand the role of peer rejection in adolescent depression. We show how reciprocal relationships between peer rejection and depressive symptoms across adolescence powerfully shape and maintain maladaptive trajectories. Second, we consider how cognitive biases and their neurobiological substrates may explain why some adolescents are more vulnerable to the effects of, and perhaps exposure to, peer rejection compared to others. Finally, we draw attention to emerging cognitive and functional magnetic resonance imaging-based neurofeedback training, which by modifying aspects of information processing may promote more adaptive responses to peer rejection. A better understanding of the mechanisms underlying adolescent depression may not only alleviate symptoms during a period of substantial developmental challenges, but may also reduce the burden of the disorder across the lifespan. Depression and Anxiety 30:809–821, 2013. © 2013 Wiley Periodicals, Inc.

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THE VULNERABILITY OF ADOLESCENCE

Adolescence is a time of increased vulnerability for depression. One-year point prevalence rates of major depressive disorder (MDD) rise dramatically from around

2% in early adolescence (ages 13–15), to 15% in middle adolescence (ages 15–18).^[1] Adolescent depression predicts poorer educational and psychosocial outcomes,^[2,3] and long-term psychiatric problems, such as substance abuse^[4] and suicidal behavior.^[5] Indeed depression may account for the fact that suicide is the leading cause of death in female adolescents.^[3,6] Given these costs to the individual and to society, identifying effective prevention and treatment is needed to reduce this disease burden. To achieve this, more needs to be understood about the etiology of depression at this developmentally-sensitive juncture.

Psychosocial stress is a powerful predictor of adolescent depression.^[7] As adolescence involves unique upheaval, with young people spending more time with their peers than with their families^[8–11] and exerting a great deal of energy forming peer networks,^[12] peer rejection may be a particularly potent source of psychosocial stress. Furthermore, as social networking sites proliferate, so too does the potential for peer rejection, and understanding how peer interactions come to shape

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typical and atypical adolescent emotional development is critical. Adolescence is also a period of substantial biological change—which likely contributes to the effects of peer rejection during adolescence.^[13] For example, the limbic regions associated with the affective processing of social stimuli are influenced by gonadal hormones, which surge during middle-to-late adolescence.^[14,15] Protracted maturation of brain regions involved in the cognitive control of emotional responding may also explain heightened emotional reactivity.^[14,16–18] Here, we provide a comprehensive review of studies (including those using novel experimental paradigms) to investigate the role of peer rejection in adolescent depression.

Another critical question is why some adolescents react more negatively to peer rejection than others. Diathesis-stress models assume that psychosocial stressors exert their effect on depression by triggering underlying vulnerabilities, and have been widely implicated in adolescent depression.^[19,20] Broad vulnerability factors, such as gender^[21] and genetics,^[22–25] have been shown to influence adolescents' depressogenic responses to psychosocial stress. A review of 48 prospective studies also demonstrated the important role of higher-level cognitive factors, such as hopelessness, negative schemas, and rumination, in modifying the effects of life stress on adolescent depression.^[26] The review did not discuss how cognitive factors might modify responses to peer rejection specifically. Neither did it discuss the moderating role of more automatic information-processing biases on the relationship between peer rejection and adolescent depression. Therefore, a second goal of this review is to consider how differences in more automatic information-processing factors may also bias reactivity to peer rejection among adolescents with depression. As these processing biases may be rooted in differences in neural circuitry functioning, we also sought to review depression-linked differences in the neural substrates of adolescent peer rejection. These findings draw on a growing body of knowledge on the neural correlates of peer rejection in typically developing adolescents.^[15]

Given the potential peer rejection has in precipitating and maintaining adolescent depression, our final section considers the effectiveness of new training techniques which target these maladaptive cognitive and neural responses to emotional situations and considers how these may be applied to social situations more specifically. The framework we propose for understanding how peer rejection influences adolescent depression; cognitive and neural risk factors that enhance its' negative effects; and strategies for targeting these is illustrated in Fig. 1.

HOW ARE PEER REJECTION AND ADOLESCENT DEPRESSION RELATED?

Studies of unselected adolescents^[27–30] and adolescents with depression^[19,31–33] demonstrate longstanding and unambiguous support for a correlation be-

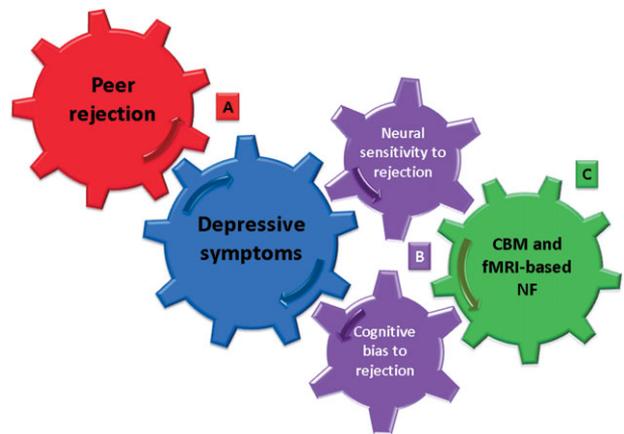


Figure 1. The interdependence of peer rejection, cognitive and neural sensitivity, and depressive symptoms in adolescence. (A) Bidirectional relationship between peer rejection and depressive symptoms; (B) cognitive and neural sensitivity maintain the maladaptive relationship between peer rejection and depressive symptoms; (C) cognitive bias modification (CBM) and fMRI-based neurofeedback paradigms may reduce depressive symptoms and future peer rejection by “reversing” maladaptive neural and cognitive factors.

tween peer rejection and depressive symptoms. What is less clear is the direction of these effects; does peer rejection precede depression, or does depression elicit more rejecting experiences? In this section of the review, highlighted by Fig. 1A, we discuss evidence for a bidirectional relationship between peer rejection and depressive symptoms.

Many though not all^[34] longitudinal studies suggest that peer rejection temporally predicts adolescent depressive symptoms.^[35–41] Longitudinal research enables the temporal associations of real-life peer rejection and depressive symptoms to be studied. However, the experience of naturally occurring peer rejection is likely to vary as a function of the severity of the rejection (e.g., exclusion vs. bullying) and certain contextual factors (e.g., presence vs. absence of other sources of social support). These potential moderators may result in an under- or over-estimate of the role of peer rejection in adolescent depression. In contrast, experimental studies enable standardized delivery of peer rejection. However, in experimental designs, negative emotional responses rather than depressive symptoms are measured, since ethical restrictions prevent the manipulation of peer rejection to the extent that it produces more persistent depressive symptoms. This raises questions over how generalizable data from experimental paradigms of peer rejection are to the understanding of clinical depression. Nevertheless, longitudinal and experimental studies offer complementary means for understanding causal relationships between peer rejection and depression. Longitudinal studies of peer rejection and adolescent depression were the focus of a special issue of *Development and Psychopathology*^[42] and more recent findings are summarized by Nolan et al.^[35] The focus of the

remainder of this review is on experimental studies of peer rejection.

A number of tasks have been developed to simulate peer rejection in order to assess its consequences on affective outcomes (see Table 1 for a summary of studies using these paradigms in adolescent samples). Despite significant variation across tasks, numerous data show that the receipt of peer rejection elicits negative emotional responses in typically developing adolescents,^[13, 43, 44, 49, 51, 53–58] sometimes to a greater degree than in adults or children.^[13, 43, 44, 58] Williams et al. developed the earliest experimental manipulation of peer rejection: “Cyberball”.^[59] A virtual ball-throwing game, participants “play” online with two unknown peers. After several trials, the peers appear to exclude the participant from play. In fact, the participant is playing against a pre-set computer program and fictitious peers. Compared to the inclusion phase, exclusion increases adolescents’ negative mood, anxiety, and threatens feelings of belonging central to self-esteem.^[13, 43, 44]

Whereas Cyberball elicits peer rejection in a gaming context, “Chatroom”^[48] and the Social Judgment task^[63] have been developed to measure the effects of peer rejection during online social communication. As the vast majority of adolescents and young adults have at least one social networking profile^[64] and the Internet is now a common platform for adolescent social communication,^[65] such experimental paradigms go some way to understanding how peer rejection in social networking sites influences adolescent emotions. In the Chatroom task, participants are told that they are taking part in a study of online social interaction, and based on a photo, indicate their preference about which unknown peers they would like to chat to. Then, these peers make a decision as to whether to reject or accept the participant’s request, based on a photo taken of the participant. In the Social Judgment task, participants simply predict, and get feedback about, which peers like them. In both the tasks, feedback is generated randomly by the computer and the peers are child actors.

One advantage of the Chatroom and Social Judgment tasks is that they also enable expectations of social evaluation to be examined, although so far the impact of these effects on depressive symptoms has not been identified.^[48, 52] For adolescents, rejection in the feedback phase of the Chatroom task elicits more negative mood than acceptance, and the response is amplified for peers in whom the participant was particularly interested in.^[49, 50] An adaptation of the paradigm, “Chatroom Interact,” adds ecological validity to the traditional Chatroom paradigm by including age- and gender-specific peer profiles and manipulating peer feedback in relation to specific topics of interest to adolescents.^[51] Using this paradigm, Silk et al. observed increased feelings of anger, sadness, and exclusion as a result of adolescent peer rejection versus peer acceptance.^[51]

Another computerized manipulation of peer rejection combines both social communication and gaming, and has been used to measure young adolescents’ appraisals

of peer rejection and consequential coping strategies (“Survivor”).^[53] Based on the TV show of the same name, participants are led to believe that they will be competing in a number of challenges against unknown peers, to become the “Survivor Champion.” Having had their photo taken and answered personal questions about their interests, academic performance, and romantic relationships, all players vote on who should be eliminated from the next round. In actual fact the peers are confederates and the participant is randomized to receive negative (eliminated at first round) or positive (survived first round) feedback. For young adolescents who took part in Survivor, peer rejection lowered mood,^[53–56] led to dwelling on negative feedback^[55] and maladaptive coping strategies.^[55] Their computerized format enables these novel tasks to deliver standardized peer rejection experiences that are not only relatively easy to recreate and more ethically appropriate, but also simulate a common format of adolescent social communication.

A noncomputerized task, the child and adolescent version of the Yale Interpersonal Stressor task (YIPS-C),^[66] measures the effects of face-to-face peer rejection. Participants chat with same-aged peers on a wide range of salient adolescent topics. In reality the peers are trained confederates, and given specific topics to discuss. Toward the end of the conversation, the confederates use verbal and nonverbal means to exclude the participant. Compared to previous tasks described, YIPS-C has increased ecological validity, while standardizing delivery across all participants. Although peer rejection in the YIPS-C task has been shown to negatively impact on mood in adolescents, data are yet to show that this is more so than a nonrejection-based performance stressor.^[57, 58] As for the computerized tasks described previously, the effects of the YIPS-C task are perhaps also limited by interactions with unknown peers, and a reliance on participants not only believing that these peers are real, but also being sensitive to their feedback. Together, the experimental paradigms described suggest that peer rejection plays a causal role in eliciting negative emotional responses. These complement findings from longitudinal studies of the temporally predictive role of peer rejection in adolescent depression.^[35–41] Although somewhat limited in their generalizability, nevertheless these peer rejection paradigms lend themselves well to comparing patterns of responding between adolescents with and without depression (Table 1).

In the Social Judgment task, Davey et al. found that depressed youths (aged 15–24) showed less enjoyment from peer acceptance than healthy controls, although a peer rejection condition was not included in this study.^[46] Although no other studies have investigated responses to peer rejection in clinically depressed adolescents, studies of variation in symptoms of depression in unselected adolescents offer valuable insights into differential peer rejection responses relevant to adolescent depression. For example, adolescents with more depressive symptoms were more likely to use ruminative coping strategies^[53] and negative

TABLE 1. Experimental studies of the behavioral effects of peer rejection in adolescents

Paradigm	Study	Sample	Outcome measure(s)	Summary of results
Cyberball	Abrams et al. (2011) ^[43]	79 adolescents aged 13–14, ~50% female 41 children aged 8–9, ~50% female 46 students (mean age = 20), 74% female	(1) Distress (NTQ) (2) Mood (enjoyment; single item)	Rejection worsened mood and increased distress. Rejection affected adolescents' feelings of belonging more than children's or adults'
	Sebastian et al. (2010) ^[44]	26 female adolescents aged 11.9–13.9 (mean = 12.8, SD = 0.59), 25 female adolescents aged 14.0–15.8 (mean = 15.0, SD = 0.53), 26 female adults aged 22.2–47.1 (mean = 27.4, SD = 6.2),	(1) Distress (NTQ) (2) Mood (NTQ) (3) Anxiety (STAI)	Participants felt more excluded following rejection (compared to inclusion). Rejection worsened mood, anxiety, and distress for both groups of adolescents compared to adults
	Sebastian et al. (2011) ^[13]	19 female adolescents aged 14–16 (mean = 15.44, SD = 0.81), 16 female adults (mean age = 28.70, SD = 3.91)	(1) Distress (NTQ) (2) Mood (NTQ)	Peer rejection increased feelings of exclusion, reduced mood, and increased distress. The effect of rejection on exclusion was stronger for adolescents than adults
	White et al. (2012) ^[45]	10 insecurely attached adolescents aged 11–15, 10% female 13 securely attached adolescents aged 11–15, 54% female	Distress (NTQ)	No difference between groups in the amount of distress reported during rejection
	Chatroom	Davey et al. (2011) ^[46]	17 youths with depression aged 15–24 (mean = 18.7, SD = 2.2), 65% female 19 healthy youths aged 15–24 (mean = 19.3, SD = 2.9), 63% female	Retrospective rating of response to positive feedback (single item)
Guyer et al. (2008) ^[47]		14 children and adolescents with anxiety disorder (mean age = 12.30, SD = 2.76), 71% female 14 healthy children and adolescents (mean age = 12.58, SD = 2.54), 71% female	Predicted interest of peers (single item for each of 40 peers)	Patients anticipated more negative feedback from peers than controls. The effects were restricted to salient (vs. nonsalient) peers
Guyer et al. (2009) ^[48]		34 healthy children and adolescents aged 8.9–17.5 (mean = 13.6, SD = 2.4), 47% female	Predicted interest of peers (single item for each of 40 peers)	Participants expected salient peers to provide more positive feedback than nonsalient peers. There was no effect of gender or age on anticipated peer feedback
Guyer et al. (2012) ^[49]		36 healthy children and adolescents aged 8.6–17.5 (mean = 13.54, SD = 2.5), 44% female	Affective response (single item for each of 40 peers)	Peer rejection reduced affect, compared to peer acceptance. There were more negative response to rejection from salient (vs. nonsalient) peers
Lau et al. (2012) ^[50]		12 children and adolescents with anxiety disorder (mean age = 11.88, SD = 2.48), 67% female 12 healthy children and adolescents (mean age = 12.23, SD = 2.44), 67% female	Affective response (single item for each of 40 peers)	No main effect of peer rejection was reported. There were more negative response to rejection from salient (vs. nonsalient) peers
Silk et al. (2012) ^[51]		60 children and adolescents aged 9–17 (mean = 13.2, SD = 2.5), 53% female	Retrospective rating of mood and exclusion/inclusion (six items)	Participants felt angrier, sadder, more excluded, less happy, and less included following rejection (vs. acceptance)

TABLE 1. Continued

Paradigm	Study	Sample	Outcome measure(s)	Summary of results
Social Judgment	Gunther-Moor et al. (2010) ^[52]	12 children aged 8–10 (mean age = 9.7, SD = 0.9), 58% female 14 adolescents aged 12–14 (mean age = 13.3, SD = 0.8), 57% female 15 adolescents aged 16–17 (mean age = 17.1, SD = 0.6), 47% female 16 young adults aged 19–25 (mean age = 21.7, SD = 1.9), 50% female	Predicted interest of peers (Yes/No response for each of 120 peers)	Young adults predicted peers would be more interested in them than did children and 12–14-year-old adolescents. There was no difference in reaction time to predict rejection versus acceptance and no effect of age on reaction time to predict rejection (vs. acceptance)
Survivor	Reijntjes et al. (2006) ^{[53]a}	186 children and adolescents aged 10–13 (mean = 11.5, SD = 0.73), 51% female	(1) Mood (SAM) (2) Observed passivity, distraction, and approach behavior	Peer rejection worsened mood compared to peer acceptance. Rejected participants spent less time on distraction activities and more time looking at folders of previous participants than those accepted. The latter effects were stronger for those with more symptoms of depression
	Reijntjes et al. (2006) ^{[54]a}	186 children and adolescents aged 10–13 (mean = 11.5, SD = 0.73), 51% female	(1) Mood (PANAS) (2) Observed emotion regulation behavioral strategies (3) Self-reported cognitive reactions (five items)	Peer rejection worsened mood compared to peer acceptance. Participants who showed a reliable change in mood showed improvements when they engaged in distraction activities and deterioration when they showed passive behaviors. Participants showed worsening mood if they engaged in “cognitive analysis”
	Reijntjes et al. (2007) ^{[55]b}	142 children and adolescents aged 10–13 (mean = 11.2, SD = 0.66), 49% female	(1) Mood (single item) (2) Feedback preference (single item)	Peer rejection worsened mood compared to peer acceptance and was associated with a preference for negative feedback. More symptoms of depression predicted a preference for negative feedback following peer rejection but not acceptance
	Reijntjes et al. (2009) ^{[56]b}	142 children and adolescents aged 10–13 (mean = 11.2, SD = 0.66), 49% female	(1) Mood (PANAS) (2) Cognitive appraisal of feedback (seven items)	Peer rejection worsened mood compared to peer acceptance. Participants who showed a reliable change in mood following rejection (vs. those who showed no change) did not differ in the number of depressive symptoms but took longer to return to baseline mood. Children with more depressive symptoms had more negative appraisals of rejection than those with fewer symptoms
Yale interpersonal stressor task (YIPS-C)	Allwood et al. (2011) ^[57]	56 healthy children and adolescents aged 7–16 (mean = 12.0, SD = 2.4), 52% female	(1) Positive affect (four items) (2) Negative affect (two items)	Reduced positive affect and increased negative affect after stressor tasks. No comparison of the two stressor tasks
	Stroud et al. (2009) ^[58]	43 healthy adolescents aged 13–17, 47% female 39 healthy children aged 7–12, 56% female	(1) Positive affect (four items) (2) Negative affect (two items)	Peer rejection reduced positive affect and increased negative effect. Stressors had a greater effect on physiological response in adolescents than children

SD, standard deviation; NTQ, need threat questionnaire^[59]; STAI, state trait anxiety inventory^[60]; SAM, self-assessment manikin^[61]; PANAS, positive and negative affect schedule^[62].

^aSame sample.

^bSame sample.

appraisals^[56] in response to rejection, although there was no evidence of worsened mood following rejection compared to adolescents with less depressive symptoms.^[53]

Because symptoms of depression are themselves relatively rare in the general population, low self-esteem (a cognitive symptom of depression) may better capture normally-occurring variation in mood symptoms in unselected samples. Young adults (aged 18–24) with low self-esteem estimated the amount of negative feedback to be greater than did those with high self-esteem in the Social Judgment task.^[16] A final study found no evidence that insecurely attached adolescents reported greater distress in response to rejection than securely attached adolescents.^[45] Findings from studies of peer rejection in adolescents with anxiety disorders are also worth noting. For example, adolescents with social anxiety disorder predicted peers to be less interested in chatting to them than did healthy controls,^[47] although no differences emerged in the immediate response to peer rejection between anxious and healthy adolescents,^[50] consistent with adult studies.^[67] To date no study has directly tested the specificity of rejection sensitivity to depression, as opposed to comorbid social anxiety, fears, and worries.

Interpersonal theories propose that in addition to peer rejection eliciting symptoms of depression, depressive symptoms may also predict later peer rejection.^[68] One possibility is that depressed individuals experience more rejection because of increased reassurance seeking (i.e., the need to have their self-worth confirmed by others).^[69] Another possibility is that depressed adolescents are more attracted to people who confirm their negative self-beliefs.^[70] Observations of interpersonal interaction have found that depressed adolescents are more often rejected than healthy controls.^[71,72] Compared to healthy adolescents, depressed adolescents' behaviors decreased positive behavior from a partner.^[73] Similarly, adolescents rated depressed peers less positively than non-depressed peers in videos of their interactions.^[74] Longitudinal studies suggest that adolescent depressive symptoms predict peer rejection 6 months later.^[68] Correlational studies suggest that interest in negative feedback correlates with depressive symptoms and predicts peer rejection.^[32,33]

In summary, peer rejection and adolescent depressive symptoms are closely associated. Longitudinal and experimental studies suggest that peer rejection predicts depressive symptoms and negative affect, respectively. In particular, a few experimental studies have shown that when faced with the same peer rejection experience, symptomatic or at-risk adolescents show more negative expectations and appraisals of rejection compared to others. Other experimental studies have found no evidence that rejection elicits more negative mood in adolescents at-risk of depression compared to those not at risk. Symptomatic adolescents may also be more likely to attract rejection experiences. The interdependence of peer rejection and negative emotional responses which may maintain the depressive state is illustrated in Fig. 1A.

These findings raise the question of what underlying cognitive and neurobiological factors may explain these destructive cycles.

ARE COGNITIVE BIASES IMPLICATED IN MALADAPTIVE RESPONSES TO PEER REJECTION?

Latent cognitive biases may explain why psychosocial stressors affect some adolescents more negatively than others.^[20,26] A review of 48 prospective studies demonstrated the important role of cognitive factors, such as hopelessness, negative schemas, and rumination, in modifying the effects of life stress on adolescent depression.^[26] As illustrated in Fig. 1B, we argue that these cognitive vulnerabilities may also explain heightened emotional responses to peer rejection specifically. For example, adolescents with depression exhibit negative attributional styles—meaning that they attribute negative events, such as peer rejection to internal (“I am not a likeable person”), stable (“I have never been well-liked”), and global (“I am no good at anything”) causes, and positive events, such as being invited to a party to external (“they are just being nice”), unstable (“this is just a one-off invitation”), and specific (“at least one person likes me”) causes.^[75] Negative attributional style has been shown to moderate the relationship between peer rejection and depressive symptoms in unselected adolescents.^[36] Negative cognitive schemas about the self also moderate the effect of peer rejection on depressive symptoms in adolescent psychiatric patients.^[19] As far as we are aware, no studies have measured attributions to experimentally manipulated peer rejection in clinically depressed adolescents.

In contrast to these “higher-level” cognitive biases, relatively little research has considered the role of interpretive or attention biases in modifying depressogenic responses to psychosocial stress in adolescence in general or to peer rejection in particular. Analogous to adult findings of depression, the tendency to select negative interpretations of ambiguous social situations may also characterize adolescent depression. Following a negative mood induction, female adolescents at risk of developing depression interpreted ambiguous words and sentences more negatively, than low-risk female adolescents.^[76] However, these between-group effects were restricted to nonsocial words and sentences. Furthermore, no studies have investigated whether this bias influences responses to peer rejection specifically. Therefore, future research might investigate the extent to which depressed and non-depressed adolescents draw rejection-related interpretations of ambiguous social scenarios.

There is also mixed evidence as to whether attention biases to socially threatening information underlie adolescent depression. There is no evidence of a bias toward socially threatening faces in adolescents with a clinical diagnosis of depression,^[77] although the

small sample in this study (19 depressed patients and 26 healthy controls) may account for these findings. Both young adults with low self-esteem^[78] and adolescents at risk of depression^[79] demonstrate an attention bias toward socially threatening (vs. neutral) facial stimuli. This suggests that negative attention biases are not the by-product of depression. Further studies of adolescents with a clinical diagnosis of depression may provide more conclusive evidence about the role of attention biases in adolescent depression, and the extent to which these biases relate to peer rejection specifically.

In summary, higher-level cognitive biases, such as attributional style and negative expectations, may increase adolescents' depressive responses to psychosocial stress, with preliminary data suggesting this may relate to responses to peer rejection specifically. Data on interpretive and attentional biases are fewer and more mixed. Some studies suggest adolescents at risk of depression may be more likely to interpret ambiguous situations negatively (compared to healthy controls), although the extent to which these data represent biases for negative interpretations of social scenarios specifically (e.g., peer rejection) is unclear. Emerging data also suggest attention biases toward socially threatening faces may characterize adolescents at risk of depression, although replication of these findings in clinical samples is needed. Speculatively then, interpretive and attentional cognitive biases may serve to generate more negative social experiences among depressed adolescents, as illustrated in Fig. 1B.

WHAT ARE THE NEURAL SUBSTRATES UNDERLYING MALADAPTIVE RESPONSES TO PEER REJECTION?

Neuroscientific methods such as functional magnetic resonance imaging (fMRI) play an important role in improving our understanding of how the brain mediates the differential impact of peer rejection on typical and atypical emotion regulation and behavior.^[48] Moreover, because differences in brain activity may occur in the absence of behavioral differences, these data could implicate more subtle differences in how adolescents respond to rejecting stimuli. Adolescent models commonly posit three overlapping neural systems involved in stages of social-emotional processing: (1) detection of social threat via the fusiform gyrus, superior temporal sulcus, anterior temporal cortex, (2) an initial affective response via the amygdala, ventral striatum, hypothalamus, orbitofrontal cortex, and (3) cognitive regulation of the emotional response via the ventro-lateral prefrontal cortex (VLPFC) and dorsomedial PFC (DMPFC).^[14, 16, 44, 80] These models posit that imbalances between heightened affectivity and immature regulatory regions underlie adolescent depression. Although these models provide a compelling platform upon which individual differences may be explained and

interpreted, they may also be too simplistic in capturing the complex networks of coactivation between these regions—and their roles in other cognitive domains.^[81]

Regions within these overlapping systems continue to develop structurally and functionally throughout adolescence^[80, 82] and this ongoing neural development has been implicated in the susceptibility of adolescents to peer rejection via heightened affectivity and impaired ability to regulate emotional reactivity.^[44] Studies across varying paradigms suggest that peer rejection in typically developing adolescents appears to elicit neural activation in affective regions such as the insula, anterior cingulate cortex (ACC), and precuneus, as well as regulatory regions, such as the VLPFC and DMPFC (see Pfeifer and Blakemore, 2012 for a review on typically developing adolescents^[15]). Importantly, these studies suggest that neural activation during peer rejection modulates behavioral responses of distress. For example, Masten et al. demonstrated that adolescents' self-reported ratings of distress to peer rejection correlated with increased activation in the insula and sub-ACC; regions known to be involved in the processing of social and emotional "pain."^[83] Masten et al. also found that activation of the VLPFC and DMPFC was negatively correlated with distress during peer rejection and to activation in the insula—tentatively implicating these regions in the regulation of behavioral and neural reactivity to peer rejection. Subsequent studies suggest that neural responses to peer rejection correlate with self-esteem,^[52] prosocial behavior,^[84] resistance to peer influence,^[13] time spent with friends,^[85] and symptoms of depression.^[86]

Although these studies of typically developing adolescents are informative on the neural substrates of social processing, fMRI studies of peer rejection in clinical (or analogue) samples are necessary to infer the cognitive and neural mechanisms likely to explain why depressed adolescents respond more negatively than their non-depressed peers. Based on emerging fMRI data, we suggest that neural sensitivity to peer rejection may play an important role in the development of adolescent depression (see Fig. 1B). Davey et al. conducted the only study to date on depressed youths' (aged 15–24) neural responses to positive (but not negative) social feedback.^[46] Both depressed and healthy youths showed heightened amygdala activity to positive versus neutral faces, however, this difference was greater for depressed participants compared to healthy controls. Both groups showed similar patterns of greater PFC and dorsal ACC activity in the same positive versus neutral contrast.

While fMRI has enabled further exploration of the effect of peer rejection on emotion regulation and behavior, interpretations of fMRI data should be treated with caution. Since fMRI measures blood oxygen level dependent (BOLD) changes (rather than direct neural activity), its accuracy and temporal precision in detecting brain mechanisms is somewhat limited. Furthermore, the direction of group differences is not always consistent between studies, raising questions over whether greater or weaker activity is problematic.

Complementary neurobiological methods, such as Magnetoencephalography, eye-tracking and pupil dilation, and neuroendocrine measures, offer some advantages over fMRI and have begun to be used to study peer rejection in adolescence.^[51,57,58] Neuroendocrine and cardiovascular measures provide information about how pathways in the autonomic nervous system may mediate the effects of peer rejection on neural responses and self-reported distress,^[58] enabling more elaborate, multilevel models of peer rejection to be developed. Since pupillary dilation has temporal resolution of around 16 ms (compared to around 3,000 ms in fMRI), it allows for differential investigation of initial versus sustained responses to peer rejection.^[51] For example, Silk et al. found increased pupil dilation during adolescent peer rejection (vs. acceptance) within the first 2 s following feedback.^[51] Pupil dilation during rejection also correlated with shift in attentional focus within the first 0.5–0.75 s following rejection. Finally, increased pupil reactivity to peer rejection correlated with lower feelings of social connectedness in real life.

In summary, emerging fMRI studies in adolescents with various emotional difficulties are vital for understanding how potential neural sensitivity to peer rejection might influence maladaptive responses to rejection in adolescent depression. Initial studies suggest that neural activity during peer rejection correlates with various markers for depression (e.g., depressive symptoms in typically developing adolescents). Furthermore, a study of depressed adolescents and young adults demonstrated heightened amygdala activity during peer acceptance in patients compared to controls. However, to date no study has investigated the neural correlates of peer rejection in depressed and non-depressed adolescents. The extent to which amygdala hyperactivity during peer rejection is regulated by prefrontal activity is yet to be tested. Figure 1B illustrates how neural sensitivity may potentially influence the relationship between peer rejection and adolescent depression.

CAN WE PROMOTE ADAPTIVE RESPONSES TO PEER REJECTION BY TARGETING COGNITIVE BIASES AND UNDERLYING NEURAL CIRCUITS?

Given mounting evidence that peer rejection is involved in the etiology and maintenance of adolescent depression, perhaps via activation of underlying cognitive and neural vulnerabilities, there is growing interest in the extent to which responses to peer rejection can be specifically targeted to more effectively prevent and treat adolescent depression. Many current treatment options already target maladaptive rejection responses. For example, cognitive behavioral therapy (CBT) targets negative cognitive patterns, including those relating to peer rejection, through behavioral training. Despite being the frontline treatment for adolescent de-

pression in the United Kingdom,^[87] many adolescents fail to respond or experience relapses.^[88,89] Another psychotherapy that shows promise is interpersonal psychotherapy (IPT). Similar to CBT but targeting interpersonal difficulties specifically, IPT seems to be particularly effective for adolescents with high levels of interpersonal conflict.^[90,91] Randomized controlled trials suggest it is better than treatment as usual, but comparison with CBT has produced mixed findings.^[90] Nevertheless, CBT and IPT require self-reflection, mentalizing, self-monitoring, and numerous other higher-level cognitive skills.^[92] Since metacognition and executive function continue to develop throughout adolescence,^[93] and executive dysfunction is thought to be a core feature of depression,^[94–96] the effectiveness of CBT for adolescents with depression may in part be limited due to this ongoing cognitive and neural development.^[97] Treatment tools which rely less heavily on these processes may therefore offer additional benefits.

There has been great excitement about the possibility of using computerized cognitive training tasks to target maladaptive cognitive biases toward peer rejection in adolescent depression.^[98] Figure 1C shows how reversing cognitive biases might lead to downstream effects on the experience of both peer rejection and depressive symptoms. Through repeated training, cognitive bias modification (CBM) tasks aim to make more benign cognitive patterns automatic such that they override negative cognitive biases (causally linked to symptoms) and lead to a reduction in symptoms. CBM paradigms for anxiety disorders have shown great promise in adolescents,^[99,100] but are only recently emerging for use in depressed populations.^[101] Given that they can be relatively easily and cheaply delivered, CBM paradigms may be particularly effective for the treatment, and eventual prevention of adolescent depression. CBM currently encompasses training tasks for both attentional biases (CBM-A) and interpretive biases (CBM-I), which may be implicated in the effect of peer rejection on depressive symptoms.

Several CBM-I tasks have been developed^[102–104] which target the negative interpretive bias that may underlie depressed adolescents' responses to peer rejection.^[76,105] In the most common paradigm, Ambiguous Situations (AS),^[104] participants read or hear a variety of social scenarios that are ambiguous (e.g., "Having finished painting the lounge, you invite friends around to dinner. As they walk into the room, you can see that they are surprised. Their reaction is one of . . ."). Participants are then asked to complete a word fragment that resolves each scenario. The researcher systematically targets the word fragment such that the solution is positive (e.g., "pleasure") or benign (e.g., "confusion") rather than negative (e.g., "horror"). As a result, correct completion of the scenario encourages a benign resolution of ambiguity, which over multiple training trials, becomes reinforced, and presumably, increasingly habitual.

A meta-analysis of CBM-I studies found that benign training increased positive interpretive biases and mood, particularly for participants with an emotional disorder.^[106] Studies of depressed adults confirmed that even in a sample who have difficulties with motivation and concentration, CBM-I appears to be effective.^[107,108] CBM-I also reduces negative biases in healthy children^[109,110] and adolescents,^[99,111–113] although just one study reports a mood improvement.^[99] Disparity could be due to the fact that these adolescents are not symptomatic to begin with, or because multiple training sessions are required for effects on mood to be found. Future CBM-I studies that are tested in clinically depressed adolescents are important.

The original CBM-A paradigm used a modified version of the dot-probe task to train attention focus away from, or toward, threat cues.^[114] In the dot-probe task, an angry and a neutral face are presented simultaneously for a brief period, before a probe appears in the location of one of the images (e.g., two dots). Trials where the probe appears in the location of the angry face are congruent trials, whereas in incongruent trials the probe appears in the location of the neutral face. Participants are required to perform a recognition task related to the probe (e.g., “Did you see ‘.’ or ‘.’ ?”). In contrast to the original dot-probe task, where congruent and incongruent trials are presented with equal frequency, CBM-A training involves systematically increasing the frequency of incongruent trials. By this means, participants learn to attend to the neutral face and ignore the angry face.

This CBM-A task appears to effectively modify symptoms of anxiety when delivered to children^[100,115,116] and adolescents.^[100,117] The task also appears to reduce depressive symptoms in dysphoric students,^[118,119] although not in highly symptomatic students or clinically depressed adults (Baert et al., 2010 study 2^[118]). Although the task may reduce depressive symptoms in adolescents with anxiety disorder,^[117] to date no studies have tested its efficacy in clinically depressed adolescent populations.

Recently, a CBM-A paradigm based on the faces-in-the-crowd task^[120] has been developed to more directly target rejection biases in young adults with low self-esteem.^[78] In this task, participants are presented with a grid of 15 frowning (rejecting) faces and a single smiling (accepting) face. Participants learn to disengage from rejection and selectively attend to acceptance by identifying the smiling face as fast as they can. Across a series of studies, Baldwin and colleagues showed that compared to a control training task, the paradigm is effective in reducing characteristic vigilance toward rejection in adults with low self-esteem,^[78,121,122] and in increasing levels of self-esteem.^[121,122] It has also been shown to reduce self-reported exam stress, physiological markers of stress (e.g., salivary cortisol reactivity),^[121] and the impact of a rejection manipulation.^[122] To date no studies have investigated the efficacy of the visual search CBM-A task at reducing vigilance to rejection and depressive symptoms in adolescent populations.

In summary, the application of CBM paradigms for the treatment and prevention of adolescent depression shows initial promise, although further investigation of the precise parameters and quantity of training needed to yield significant symptom reduction is required. If adolescents with depression indeed show attention and interpretative biases for rejection-specific information (over and beyond more general social threats), CBM-A and CBM-I tasks that adapt target stimuli to modify these biases (e.g., frowning rather than angry faces) and interpretive biases (e.g., being ignored in the classroom) could be particularly fruitful (Fig. 1C).

In addition to modifying maladaptive cognitive biases that underlie adolescent depression, there is growing interest in the extent to which the neural networks involved in the processing of peer rejection can be modified for therapeutic purposes. fMRI-based neurofeedback (NF) is a newly emerging technique that utilizes the latest developments of real-time data processing and pattern analysis in order to train participants in the self-modulation of neural networks. In a similar manner to CBM techniques, addressing sensitivity to negative emotional responses at the brain level could serve to reduce the negative impacts of peer rejection on affect (Fig. 1C). In fMRI-based NF studies, participants are presented with real-time brain activation in specific regions of interest, such as those brain regions involved in the processing of emotional information, and they can be trained to reliably regulate their online brain response with high spatial precision.^[123–127] fMRI-based NF has proven particularly useful for up- or down-regulating the brain regions supporting emotion processing in healthy adults.^[125,128,129] A recent study of adult patients with depression found that NF was associated with significant improvements in symptoms, whereas cognitive training alone was not^[130] (see also Esmail and Linden, in press^[131] for a review). No studies have extended fMRI-based NF to pediatric populations, despite this being a period of critical brain development and plasticity. Future studies could focus on directly targeting emotional circuitry involved in peer rejection responses. This approach could not only directly influence neural responses in emotion regulation, but also support interventional strategies at the behavioral level (e.g., CBM).^[132]

CONCLUSIONS

Adolescent depression is a major public health problem for which models are relatively underdeveloped. Peer rejection is a salient source of stress during adolescence, and the studies reviewed here suggest a bidirectional relationship between peer rejection and depressive symptoms, which may contribute to the etiology and maintenance of adolescent depression. A number of cognitive vulnerabilities, such as negative interpretive biases and heightened detection of threat, may explain individual differences in responses to peer rejection. fMRI studies have helped identify the neural systems involved in typical processing of peer rejection in adolescence,

and are likely to be useful for further understanding mechanisms in atypical emotional development. CBM paradigms that specifically target rejection-based biases may be valuable tools for the prevention and treatment of adolescent depression. Finally, fMRI-based NF techniques may also offer novel ways for investigating the plasticity of neural networks implicated in adolescent depression.

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