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Vulnerability to Depression in Youth: Advances from Affective Neuroscience

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Abstract

Vulnerability models of depression posit that individual differences in trait-like vulnerabilities emerge early in life and increase risk for the later development of depression. In this review, we summarize advances from affective neuroscience using neural measures to assess vulnerabilities in youth at high risk for depression due to parental history of depression or temperament style, as well as prospective designs evaluating the predictive validity of these vulnerabilities for symptoms and diagnoses of depression across development. Evidence from multiple levels of analysis indicates that healthy youth at high risk for depression exhibit abnormalities in components of the Research Domain Criteria (RDoC) positive valence systems, including blunted activation in the striatum during reward anticipation and feedback, and that some of these measures can be used to predict later symptoms. In addition, alterations in components of RDoC's negative valence systems, including neural processing of sadness, loss, and threat, have been observed in risk for depression, though effects appear to be more task and method dependent. Within the social processes domain, preliminary evidence indicates that neural processing of social feedback, including heightened reactivity to exclusion and blunted response to social reward, may be related to depression vulnerability. These studies indicate that affective neuroscience can inform understanding of developmental pathways to depression and identify altered emotional processing among youth at high risk. We provide an integrated summary of consistent findings from this literature, along with recommendations for future directions and implications for early intervention.

Keywords

depression; risk; developmental psychopathology; affective neuroscience; EEG/ERP; fMRI

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Depression is a common psychiatric disorder and the second leading cause of disability worldwide (1; 2), highlighting the importance of early intervention for youth at high risk (HR). Although rates of depression increase dramatically in adolescence and young adulthood (3–5), at least some trait-like vulnerabilities emerge earlier in life and increase risk for later depression (6; 7). For example, at the behavioral and self-report level, maladaptive cognitive and affective styles, including hopelessness, rumination, negative attributions, and attentional biases for sad faces have been observed among HR youth and/or shown to prospectively predict the development of depressive symptoms or diagnoses (6; 5; 8; 9). More recent work has begun to apply affective neuroscience methods to identify early vulnerabilities for depression.

The Potential of Affective Neuroscience for Informing Vulnerability Research

Neural and psychophysiological measures can provide relatively objective measures of emotional processing, offer insight into the brain circuitry underlying vulnerability, and add to levels of analysis of constructs of the Research Domain Criteria (RDoC; 10). There is also evidence that along with clinical and behavioral measures, neural measures account for additional variance in predicting future behavior, including clinical status and response to treatment (11), raising the possibility that these measures may aid in identifying youth at greatest risk. The goal of the current review is to synthesize initial efforts to apply affective neuroscience in understanding vulnerability to depression in children and adolescents. We highlight the potential of this work for informing early intervention work, as well as challenges in the field and needs for further research.

To rule out the possibility that altered emotional processing is a correlate of symptoms or consequence of a past depressive episode, we focus on studies of youth prior to the onset of the disorder, including both cross-sectional analyses of HR youth compared to those at lower risk (LR), and prospective studies examining predictors of future depressive symptoms or diagnoses, which are the most direct approach to examining precursors. With regard to HR designs, a common approach is studying offspring of parents with a history of depression, who are at an increased risk of developing the disorder themselves (12; 13). These designs are complemented by studies of child temperament. Specifically, high negative emotionality (NE), characterized by sadness, irritability, and anxiety, and low positive emotionality (PE), characterized by positive affect, appetitive behavior and sociability (14), have been linked to depression and prospectively predict later symptoms (15; 16). Although NE may be a stronger predictor (hazard ratio = 1.31) than PE (hazard ratio = 0.96) of depression onset in adults (17), low PE in early childhood has been shown to prospectively predict increases in depressive symptoms (Cohen's d = .58 to .85) (18), and the combination of low PE and high NE may be particularly predictive of depressive symptoms (18; 19). When possible, we describe studies that tested specificity of effects for parental depression as opposed to other psychopathology or for temperament styles that may be relatively unique to depression, such as PE (20). Such designs provide insight into whether these vulnerabilities are specific to risk for depression or psychopathology more broadly.

In terms of methods, we focus on neural measures (i.e., physiological and circuit levels of analysis) of responses to emotional stimuli, within the RDoC domains (10) of positive valence systems (PVS), negative valence systems (NVS), and social processes. Recent functional magnetic resonance imaging (fMRI) studies have provided insight into neural circuits involved in emotional processing in HR youth. This work is complemented by studies of event-related potentials (ERP) derived from electroencephalogram (EEG) responses to affective stimuli. ERP measures are economically measured across development, allowing for assessment of large samples of youth, and offer improved temporal resolution, which provides insight into multiple stages of stimulus processing (see Table 1 for a summary of measures). We first present a comprehensive review of this literature (Table 2), followed by summaries of consistent findings emerging across two or more studies (Table 3). Finally, we discuss potential for identifying youth at greatest risk and informing early intervention, as well as directions for future research.

Positive Valence Systems

Reward Processing

Within PVS, a relatively large literature has examined ERP and fMRI measures of reward processing as vulnerability for depression. The reward positivity (RewP) ERP component, also referred to as the feedback negativity, appears as a relative positivity approximately 250–300 ms following reward feedback compared to loss (21; 22). RewP can be reliably assessed across development (23) and correlates with self-report and behavioral measures of reward sensitivity (24), as well as activation in ventral striatum and medial prefrontal cortex (PFC; 25). There is growing evidence that reduced reward reactivity, as measured by RewP, may be a vulnerability for depression. That is, 9-year-old children with a maternal history of depression but not maternal anxiety exhibited a blunted RewP compared to LR children, even when controlling for subthreshold child symptoms (26). A similar pattern was observed in a smaller sample of HR adolescents who reported increases in sad mood following a mood induction (27). RewP may also be linked to temperamental risk, as low observed and self-reported PE predicted a more blunted RewP in a large sample of children (28). Finally, in two studies of adolescent girls, a reduced RewP prospectively predicted the first onset of depression when accounting for baseline symptoms (29; 30), and appeared to be a relatively specific vulnerability for depression rather than anxiety (29).

In addition, evidence from fMRI indicates that healthy youth with a parental history of depression or who are low in PE exhibit reduced activation in subcortical regions involved in reward processing, including ventral and dorsal striatum in anticipation of (31–33) and following receipt of reward (34; 31–33; 35) compared to LR youth. Furthermore, one study indicated that reduced activation in ventral striatum during reward anticipation prospectively predicted increases in depressive symptoms in middle to late puberty (36). Risk for depression has also been characterized by alterations in regions of the insula and PFC, which integrate information and regulate responses to feedback. Specifically, there is some evidence that HR youth exhibit reduced insula activation during reward anticipation or outcome compared to LR youth (34; 31), and one study found that increased ventromedial

PFC activation to rewards prospectively predicted greater increases in depressive symptoms in adolescent boys (36).

Processing of Positive Images

There is also evidence of blunted neural responses to positive images, including happy faces and pleasant scenes, among HR youth. Several studies with large samples have measured the late positive potential (LPP), a positivity in the ERP wave beginning around 300 ms after stimulus onset that indexes sustained attention towards salient information and activation of motivational systems in the brain (37; Table 1). Youth at HR due to parental depression exhibited a blunted LPP in response to happy faces and pleasant images compared to LR youth (38; 39). A blunted LPP to pleasant images has also been observed in children and adolescents who are lower in PE (40; 41). Finally, in one small fMRI study of offspring of depressed parents, HR youth showed reduced activation of ventral striatum to happy faces compared to LR youth (42). Despite these effects of risk status on neural measures, HR youth did not appear to exhibit abnormalities in behavioral performance when responding to targets presented following emotional images (38; 40; 41).

Summary

Paralleling behavioral evidence that lower reward-seeking may be a vulnerability for later depression (43), consistent evidence from affective neuroscience indicates that altered processing of reward and positive images is observable among HR youth before the onset of the disorder. Similar to findings in depressed adolescents and adults (44–46), youth at HR exhibit blunted ERPs to reward feedback and positive images, as well as reduced activation in the striatum during reward anticipation and feedback (e.g., 29; 31; 40).

Moreover, findings of blunted neural processing of reward and positive images are consistent with a large body of EEG asymmetry research indicating that HR youth show reduced relative left frontal activation at rest compared to LR youth, which is thought to reflect reductions in tendencies towards approach motivation (for reviews, 47; 48). Taken together, these studies suggest that HR youth exhibit broad deficits in approach-related motivation and reward processing. Interestingly, altered EEG asymmetry in depression risk is apparent even in infancy (47). As ERP and fMRI studies have typically focused on later childhood and adolescence, it remains unclear when these potential vulnerabilities emerge, but at least some of these measures appear to predict later development of depression (29).

Negative Valence Systems

Processing of Loss and Sadness

Compared to PVS, studies of NVS in depression risk are more mixed and task dependent. Although processing of sadness and loss may be particularly relevant (49), only a few small fMRI studies have examined these responses in HR youth. A recent study found that children of depressed mothers exhibited deactivation of striatum, anterior insula, and parahippocampus when losing a reward, possibly reflecting enhanced sensitivity to loss (34). An earlier small study of adolescent girls found a similar pattern, with HR youth exhibiting less activation in caudate and putamen in response to loss compared to LR youth, along with

increased activation in dorsal anterior cingulate cortex (ACC; 31). With regard to sad mood, HR adolescent girls in one study exhibited greater activation in amygdala and ventrolateral PFC while viewing sad film clips and less activation in regions involved in emotion regulation (e.g., dorsolateral PFC) during mood repair compared to LR girls (50).

Processing of Threatening or Negative Stimuli

A larger literature has examined ERP and fMRI measures of reactivity to threatening or negative images in depression risk. ERP studies tend to indicate that depression risk is characterized by disengagement from both positive and negative emotional stimuli, consistent with evidence of emotion context insensitivity in adult depression (51). Specifically, several large studies have indicated that HR youth exhibit an attenuated LPP to negative faces and unpleasant images, possibly reflecting less activation of motivational systems in response to salient stimuli. Two studies indicated that offspring of depressed parents exhibited a decreased LPP to negative or threatening faces and scenes compared to LR youth, findings that were not accounted for by parental anxiety (38; 39), and in a third study, lower PE in adolescent girls predicted a blunted LPP to unpleasant images (40). Despite effects observed on the LPP, depression risk was unrelated to behavioral measures, including accuracy and reaction time when responding to targets presented following emotional images (38; 40). Recent evidence indicates that a blunted LPP response may be specific to emotional images, with distinct patterns emerging for self-referential processing. That is, when evaluating adjectives as self-referential, HR girls showed an enhanced LPP response to negative words compared to LR girls (52).

A few fMRI studies have examined threat reactivity in HR youth, with a focus on activation in amygdala and PFC regions involved in emotion regulation. A small study indicated that HR youth exhibited increased amygdala activation to threatening faces compared to LR youth, though groups did not differ in subjective ratings of fear (42). In a relatively large sample, a similar effect of depression risk on amygdala activation was shown to emerge across development. That is, HR youth exhibited an increase in amygdala activation to fearful faces over 2 years, while LR youth exhibited a decrease in amygdala activation over time (53). Finally, one study found that adolescents of depressed parents exhibited decreased dorsolateral PFC activation when processing fearful faces, compared to LR youth, indicating less engagement of regions involved in emotion regulation (54).

Error Monitoring

In addition to responses to threatening images, the error-related negativity (ERN) is an ERP component appearing around the time of commission of an error that is thought to reflect sensitivity to internal sources of threat and activation of cognitive control systems (55; 56). Although an enhanced ERN has been shown to predict the development of anxiety (57; 58), there is some evidence that the ERN may be blunted in risk for depression. A recent study found that despite comparable behavioral performance, 9- to 17-year-old offspring of mothers with recurrent depression exhibited a reduced ERN compared to LR youth, and this effect remained significant when accounting for maternal anxiety (59). A blunted ERN was also observed among 6-year-old children high in temperamental NE (60), though this study found a similar pattern among offspring of mothers with anxiety disorders and failed to find

an effect of parental depression on the ERN in offspring. ERN effects among offspring of depressed parents may be specific to youth with greater exposure to maternal depression or emerge later in development. Additional research is needed to evaluate these possibilities and further explore effects among youth at risk for anxiety compared to depression.

Summary

HR youth exhibit alterations in components of NVS, though effects vary depending on the stimulus and measure. Few studies have examined fMRI or ERP responses specifically to loss and sadness, which may be particularly relevant to depression risk. Though there is some evidence that HR youth exhibit deactivation in regions of the striatum in response to losing rewards (31; 34), these findings rely on two studies with small samples. Additional work in this area may clarify the role of NVS in the development of depression. For example, there is evidence from pupillometry, a peripheral measure of neural reactivity indexing attentional capacity and emotional reactivity (61), that HR youth exhibit greater pupil dilation to sad, but not angry or happy, faces compared to LR (62). Moreover, when followed across two years, only responses to sad faces predicted trajectories of depression (63). Relatedly, in behavioral tasks, youth at HR have been shown to exhibit attentional biases when processing sad faces (64–66); however, ERP and fMRI measures of responses to sad faces among HR youth have yet to be examined.

A larger literature has examined neural responses to threat and more generally negative stimuli. Consistent with observations of adults with depression (67–69), HR youth exhibit a blunted LPP to negative images compared to LR youth, with some evidence that depression risk may also be characterized by a reduced ERN (38–40; 59; 60). Although it has been suggested that the ERN may be a specific marker of anxiety rather than depression (70) and two studies of the ERN in offspring of depressed parents have yielded conflicting results, a blunted ERN in HR youth parallels some observations in depressed adolescents and adults (69; 71). Taken together, the existing ERP literature indicates that HR youth exhibit broad emotional disengagement, which may play a role in the later development of symptoms.

On the other hand, two fMRI studies provided evidence of hyperactivation of amygdala to threatening faces among HR youth (42; 53). There are several possible explanations for these seemingly distinct patterns. Given differences in temporal resolutions of fMRI and ERP, one possibility is that HR youth show blunted responses initially, but later difficulty disengaging from negative content. In addition, there is likely variability among HR youth, and distinct patterns of emotional processing may predict specific subtypes of depression (e.g., melancholic depression) or comorbidities (e.g, anxious-depression). In particular, heightened amygdala response to threat is a feature of anxiety disorders (72). Although there is evidence that effects of parental depression on ERP measures in offspring remain significant when accounting for parental anxiety disorders, the unique effects of parental depression and anxiety on amygdala activation in offspring have yet to be examined.

Social Processes

The importance of social factors in the development and treatment of depression has long been recognized (73), but this work has only recently been extended to affective

neuroscience to explore how individual differences in neural processing of social interactions relates to risk. Only a few small studies to date have examined fMRI and ERP measures of social processes in depression risk. In one study, youth who exhibited greater subgenual ACC activation during peer exclusion, thought to reflect greater sensitivity to exclusion, exhibited greater increases in depressive symptoms one year later (74). In addition, one study indicated that HR children showed an enhanced P300, an ERP component appearing around 300 ms after a stimulus and reflecting enhanced attention, when completing a cognitive task under threat of social evaluation (i.e., instructed that poor performance would require them to give an embarrassing speech) (75). Finally, though only one study has examined social reward processing in the context of depression risk, preliminary results indicated that HR youth exhibited reduced responses to social acceptance in reward processing regions, including caudate, insula, and ACC (76).

Summary

Though this work is still in early stages, initial evidence indicates that depression risk may be characterized by increased reactivity to negative social feedback (74) and blunted responses to social reward (76). Novel ERP and fMRI paradigms for measuring neural responses during social interactions are in development (77; 78), and may further inform our understanding of trajectories to depression. Despite the majority of this work being focused on peer feedback, there is also growing interest in measuring physiological and neural responses during parent-child interactions (79), which may be particularly relevant for informing mechanisms involved in intergenerational transmission of depression.

Conclusions

The current review indicates that children and adolescents at risk for depression exhibit altered neural responses to both positive and negative emotional stimuli. Importantly, these vulnerabilities are apparent before the onset of the disorder, with evidence that some measures prospectively predict the development of depression into adolescence. Given the range of methods and samples included in these studies, we focus our conclusions on findings emerging across two or more studies (Table 3).

Across levels of analysis, consistent evidence indicates that depression risk in youth is characterized by deficits in approach motivation and PVS, including reduced ERP and striatal responses to reward (e.g., 26; 31; 52). Consistent with theories that reductions in positive reinforcement in the environment increase risk for the development of depression (80), reduced approach motivation and blunted reward responses may serve as vulnerabilities for depression that, in combination with life stress, increase tendencies to withdraw from the environment and failure to adjust behavior to increase positive reinforcement.

Depression risk is also characterized by alterations in NVS, though findings appear to be more dependent on the type of stimulus and measure. Although there is emerging evidence that HR youth exhibit deactivation of regions in the striatum when processing loss of rewards (31; 34), only a few small studies have evaluated responses to loss or sadness in HR youth. With regard to threat reactivity, several ERP studies have indicated that depression

risk is characterized by blunted reactivity to negative images and faces, as measured by the LPP (38–41), and consistent with patterns of emotional disengagement observed in depression (51; 81). On the other hand, when viewing threatening emotional faces, there is evidence that HR youth exhibit increased amygdala activation compared to LR youth (42; 53). Heterogeneity in outcomes among youth at risk may contribute to discrepant findings, raising the importance of accounting for risk for other forms of psychopathology when examining depression vulnerability. Understanding of the role of NVS in risk for depression could be clarified by comparing types of negative stimuli (e.g., dysphoric vs. threatening) and by multi-method approaches, such as combined EEG-fMRI or integration of neural measures with assessments of gaze patterns and pupil dilation, which could provide insight into the direction and time course of attentional allocation (82).

Lastly, recent work has begun to examine neural and physiological measures during social processes, including peer rejection/acceptance. Though this work is still in the very early stages and results have yet to be replicated or extended to larger samples and additional levels of analysis, this area of research has the potential to further inform understanding of pathways to depression.

Implications for Prevention and Intervention

The current review highlights several processes that may serve as promising targets for prevention and early intervention. Brain-based measures have the potential to inform prediction of outcomes (11), and identifying youth most likely to develop depression may lead to more targeted depression prevention strategies (83). Combining established risk factors (e.g., parental depression) and affective measures (e.g., blunted reward responses) may further improve efforts to identify youth at greatest risk, while providing a specific target and objective marker of outcome (e.g., increasing reward reactivity). We recently demonstrated that a more blunted RewP among adult patients with depression and anxiety predicted greater treatment gains with cognitive behavior therapy (84), supporting the possibility that affective neuroscience methods can be used to identify those most likely to benefit from intervention.

Future Directions

Despite the promise of this work, future research is needed to further clarify vulnerability to depression and to translate neuroscience into clinical practice. First, although some of the measures appear to assess alterations in emotional processing that may not be reflected in overt behavior, additional work is needed to evaluate the extent to which vulnerabilities identified through affective neuroscience correspond with behavioral and self-report observations of maladaptive cognitive and affective styles in depression risk (5; 6; 8; 9). It should also be noted that although effect sizes for neural measures assessed in smaller samples were large in magnitude, these may be overestimates of true effects (85; 86). Indeed, evidence from meta-analyses of FA (47; 48) and studies in large samples indicate that effect sizes for depression risk and neural measures in youth are likely more modest (Table 2), which may be partly attributed to lack of shared method variance between clinical and physiological measures (87). Moreover, many HR youth will not go on to develop the disorder, which may also contribute to modest effect sizes. An essential future direction is

examining factors that moderate whether youth at HR develop vulnerabilities. For example, among children of depressed parents, low positive parenting in early childhood predicted a more blunted RewP later in childhood (88), suggesting that the early family environment may be particularly important in shaping the reward system among HR youth. In addition to environmental variables, future studies should consider the role of genetic factors (89), as well as sex differences in vulnerabilities to elucidate factors that make girls more vulnerable to depression (90; 91).

Developmental changes in neural systems involved in emotional processing may further inform understanding of vulnerability (53; 92), raising the need for additional longitudinal research. Further prospective work is also needed to evaluate whether potential vulnerabilities predict changes in symptoms into adolescence and adulthood, whether they mediate associations between early risk factors (e.g., parental depression) and later outcomes, and to identify factors moderate outcomes (e.g., peer relationships, life stress, puberty). Determining whether these processes are risk factors, which increase the probability of depression but do not explain how they influence the likelihood of the condition, or risk mechanisms, which explain the intervening paths that link the risk factor to the outcome, will be essential for identifying processes to target (93). Relatedly, while there is some evidence that blunted RewP and LPP may be relatively specific vulnerabilities for depression rather than anxiety (26; 29; 38; 39), the extent to which other measures reflect affective styles that predict risk for psychopathology more broadly or depression specifically must be further examined in future prospective work.

Finally, it will be imperative to examine psychometric properties of these measures in order to inform intervention. Large studies of diverse samples are needed to examine reliability and validity across development, and ultimately develop norms, including cut points, sensitivity/specificity, and positive and negative predictive power. Moreover, future work is needed to develop guidelines for scoring and interpreting these measures, including development of software packages that are accessible to practitioners. Similarly, it will be important to capitalize on tools that are economical and easily assessed in clinical or community settings, such as EEG/ERP, pupillometry, and autonomic measures.

The current review indicates that advances from affective neuroscience are contributing to our understanding of factors that shape vulnerability to depression across development. Though additional research is needed, several prospective studies support the possibility that these measures can be used to predict which children and adolescents will develop depression, with the potential for informing early intervention efforts and improving long-term outcomes for youth at risk for depression.

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Table 1

Overview of neural measures used to examine positive and negative valence systems and social processes in depression vulnerability research.

Measure	Affective Process	Possible Neural Circuit
Functional Magnetic Resonance Imaging (fMRI)		
Blood-oxygen-level dependent (BOLD) Signal in Reward Systems	Wanting and liking rewards, decision-making, reward learning (94; 95)	Striatum, anterior insula, amygdala, thalamus, posterior cingulate cortex (PCC), prefrontal cortex (PFC), anterior cingulate cortex (ACC), orbitofrontal cortex (OFC; 94; 95)
BOLD Signal in Threat/Negative Emotion Systems[1]	Identifying, appraising and regulating responses to threat and negative emotions (96; 97)	Amygdala/hippocampus, insula, striatum, thalamus, PCC, ACC, supplementary motor area, PFC, occipitotemporal cortex (97; 98)
Event-Related Potentials (ERP)		
Reward Positivity (RewP)	Processing reward outcomes, reinforcement learning (99)	Striatum, medial PFC (25; 100)
Late Positive Potential (LPP)	Sustained attention towards salient stimuli, activation of motivational systems (37; 101)	Occipitotemporal cortex, amygdala/hippocampus, insula, temporal pole, OFC, PFC (102; 103)
Error-Related Negativity (ERN)	Performance monitoring, cognitive control, sensitivity to errors/ endogenous threat (55; 56; 104)	ACC (104)
P300	Stimulus evaluation and attentional allocation (105)	Frontal and temporal/parietal regions; correlated with activation in insula and medial frontal gyrus (105–107)

[1] Note: We have separated reward and negative emotion systems to parallel the order of the review and distinct literatures on reward processing and negative mood/face processing in depression vulnerability; however, these systems overlap, with common neural circuitry involved in emotional processing regardless of valence (98)

Table 2

Summary of studies included in the review

Study	HR definition	Measure	Sample size (*N*)	Age *M*(*SD*)	Primary finding	Estimated Cohen's *d*
Positive Valence Systems						
Bress et al., 2013 (30)	Prospective prediction	RewP to reward and loss feedback	68 (16 MDE at follow up)	17.72 (0.89)	↓ RewP predicted MDE onset and depressive symptoms	.50
Foti et al., 2011 (27)	Parental depression	RewP to reward and loss feedback following negative mood induction	44 LR, 37 HR	16.04 (0.89)	No main effect of risk on RewP; ↓ RewP in HR who reported greater sadness during mood induction	–
Forbes et al., 2010 (33)	Low PE	fMRI during anticipation and receipt of reward/loss	77	11.81 (0.64)	↓ striatum during reward anticipation and feedback among youth lower in PE	.68–.77
Gotlib et al., 2010 (31)	Maternal recurrent depression	fMRI during anticipation and receipt of reward/loss	13 LR, 13 HR	12.45 (1.56)	↓ striatum to reward anticipation/feedback, ↓ left and ↑ right insula during reward anticipation in HR	1.27–1.51
Kessel et al., *under review* (41)	Low PE	LPP to emotional images	340	9.14 (0.35)	Lower PE predicted ↓ LPP to pleasant images	.22
Kujawa et al., 2012 (39)	Maternal depression	LPP to emotional faces	218 LR, 116 HR	6.12 (0.46)	↓ LPP to happy faces in HR	.29
Kujawa et al., 2014 (26)	Maternal depression	RewP to reward and loss feedback	179 LR, 70 HR	9.18 (0.40)	↓ RewP in HR youth with maternal history of depression without comorbid anxiety	.33
Kujawa et al., 2015 (28)	Low PE	RewP to reward and loss feedback	381	9.20 (0.40)	Lower observed and self-reported PE predicted ↓ RewP	.18–.22
Luking et al., 2016 (34)	Maternal depression	fMRI during anticipation and receipt of reward/loss	31 LR, 16 HR	9.17 (0.40)	↓ ventral striatum and insula during reward feedback in HR	.84–1.26
Monk et al., 2008 (42)	Parental depression	fMRI to faces	22 LR, 17 HR	14.10 (2.30)	↓ ventral striatum to happy faces in HR	.58–.60
Morgan et al., 2013 (36)	Prospective prediction	fMRI during anticipation and receipt of reward/loss	72 (40 mid-to-late pubertal, 32 boys)	11.94 (0.60)	↓ striatum to reward anticipation predicted symptoms in mid- to late-pubertal adolescents; ↑ ventromedial PFC to reward feedback predicted depressive symptoms in boys	1.06–1.40
Nelson et al., 2015 (38)	Parental depression	LPP to emotional images	422 LR, 107 HR	14.39 (0.63)	↓ LPP to pleasant images in HR	.20
Nelson et al., 2016 (29)	Prospective prediction	RewP to reward and loss feedback	444 (40 depressive disorder at follow up)	14.39 (0.63)	↓ RewP predicted depressive disorder onset and symptoms	.26
Olino et al., 2014 (32)	Maternal depression	fMRI during anticipation and receipt of reward/loss	12 LR, 14 HR	15.72 (2.82)	↓ striatum during reward anticipation in HR	1.50
Sharp et al., 2014 (35)	Maternal recurrent depression	fMRI during anticipation and receipt of reward/loss	19 LR, 19 HR	13.36 (1.89)	↓ striatum to reward feedback in HR	1.13

Study	HR definition	Measure	Sample size (*N*)	Age *M*(*SD*)	Primary finding	Estimated Cohen's *d*
Speed et al., 2015 (40)	Low PE	LPP to pleasant images	523	14.39 (0.63)	↓ LPP to pleasant images among youth low in PE	.28
Negative Valence Systems						
Gotlib et al., 2010 (31)	Maternal recurrent depression	fMRI during anticipation and receipt of reward/loss	13 LR, 13 HR	12.45 (1.56)	↓ striatum and ↑ dorsal ACC activation in response to loss of reward in HR	1.14–1.69
Joormann et al., 2012 (50)	Maternal recurrent depression	fMRI during sad mood induction and mood repair	27 LR, 20 HR	11.82 (1.25)	↑ ventrolateral PFC and amygdala during mood induction in HR; ↑ amygdala, parahippocampus, OFC and ↓ dorsal ACC and dorsolateral PFC during mood repair in HR	.69–1.29
Kujawa et al., 2012 (39)	Maternal depression	LPP to emotional faces	218 LR, 116 HR	6.12 (0.46)	↓ LPP to negative faces, including sad, angry, and fearful faces, in HR	.29
Luking et al., 2016 (34)	Maternal depression	fMRI during anticipation and receipt of reward/loss	31 LR, 16 HR	9.17 (0.40)	↓ striatum, insula, and parahippocampus in response to loss of reward in HR	.88–1.59
Mannie et al., 2011 (54)	Parental depression	fMRI to faces	28 LR, 28 HR	19.24 (1.42)	↓ dorsolateral PFC to fearful faces in HR	.59
Meyer et al., 2016 (59)	Maternal recurrent depression	ERN	38 LR, 24 HR	12.93 (1.96)	↓ ERN in HR	.77
Monk et al., 2008 (42)	Parental depression	fMRI to faces	22 LR, 17 HR	14.10 (2.30)	↑ amygdala and ventral striatum to fearful faces in HR	.84–.95
Nelson et al., 2015 (38)	Parental depression	LPP to emotional images	422 LR, 107 HR	14.39 (0.63)	↓ LPP to unpleasant images in HR	.20
Speed et al., 2015 (40)	Low PE	LPP to emotional images	523	14.39 (0.63)	↓ LPP to unpleasant images among youth low in PE	.22
Speed et al., 2016 (52)	Maternal depression	LPP to emotional words during self-referential encoding task	92 LR, 29 HR	12.67 (1.64)	↑ LPP to negative words in HR	.46
Swartz et al., 2015 (53)	Family depression	fMRI to faces	112 LR, 120 HR	13.58 (0.97)	Amygdala activation to fearful faces ↑ across 2 years among HR	.40
Torpey et al., 2013 (60)	High NE; Parental depression	ERN	326	6.14 (0.42)	High NE predicted ↓ ERN; no effect of parental depression	.25
Social Processes						
Masten et al., 2011 (74)	Prospective prediction	fMRI to social exclusions	20	12.94	↑ sgACC during social exclusion predicted depressive symptoms	.84
Olino et al., 2015 (76)	Maternal depression	fMRI to peer acceptance	23 LR, 10 HR	12.98 (2.14)	↑ precuneus and IPL and ↓ ACC, insula, and caudate during social acceptance in HR	.84–1.30
Pérez-Edgar et al., 2006 (75)	Parental depression	P300 during Posner task under threat of social evaluation	17 LR, 16 HR	7.80 (0.80)	↑ P300 during Posner task under threat of social evaluation in HR	

Note: ACC = anterior cingulate cortex; ERN = error related negativity; fMRI = functional magnetic resonance imaging; IPL = inferior parietal lobule; LPP = late positive potential; LR = lower risk; HR = high risk; MDE = major depressive episode; NE = negative emotionality; PE = positive emotionality; PFC = prefrontal cortex; RewP = reward positivity; sgACC = subgenual anterior cingulate cortex.

Table 3

Summary of consistent patterns (observed across two or more studies) of altered emotional processing associated with risk for depression in youth by type of stimulus and measurement.

	BOLD fMRI	ERP
Positive Valence	**Reward anticipation/feedback** ↓ striatum	**Reward feedback:** ↓ RewP **Positive faces/scenes:** ↓ LPP
Negative Valence	**Loss:** ↓ striatum **Threatening faces:** ↑ amygdala	**Negative faces/scenes:** ↓ LPP

BOLD fMRI = blood-oxygen-level-dependent functional magnetic resonance imaging; ERP = event-related potentials; LPP = late positive potential; RewP = reward positivity