

Published in final edited form as:

*Psychol Med.* 2012 October ; 42(10): 2095–2107. doi:10.1017/S0033291712000207.

## Why Do Anxious Children Become Depressed Teenagers?: The Role of Social Evaluative Threat and Reward Processing

Jennifer S. Silk<sup>1</sup>, Stephanie Davis<sup>2</sup>, Dana L. McMakin<sup>1</sup>, Ronald E. Dahl<sup>3</sup>, and Erika E. Forbes<sup>1</sup>

<sup>1</sup>University of Pittsburgh, Department of Psychiatry, Western Psychiatric Institute and Clinic

<sup>2</sup>University of Pittsburgh, Department of Psychology

<sup>3</sup>University of California, Berkeley, School of Public Health

### Abstract

**Background**—Depression is a leading cause of worldwide disability. Adolescence represents a key developmental window in which rates of this disorder increase markedly. Children with an anxiety disorder show a particular risk of developing depression during adolescence.

**Method**—We present and review evidence for a developmental model that considers the intersection of two vulnerabilities relevant to the trajectory from anxiety to depression: difficulties in response to potential social evaluation and changes in reward processing at puberty.

**Results**—Evidence suggests that these vulnerabilities (a) have been associated with depression, (b) are likely to be problematic in many but not all anxious youth, and (c) may be exacerbated by maturational processes that occur around pubertal development in ways that can create a negative spiral into a depressive disorder.

**Conclusions**—We discuss the possibility that early intervention strategies targeting key aspects of these vulnerabilities could alter the trajectory away from depression for many anxious youth.

Depression is a leading cause of worldwide disability, morbidity, and diminished quality of life. About one in seven adolescents will experience an episode of MDD prior to adulthood (Kessler, 1994). Given the high prevalence of this disorder and its pervasive impact on youth, there is a critical need to identify developmental precursors of depressive disorders as well as key windows of time in development that create opportunities to prevent depression. Rates of depression increase markedly during adolescence, especially for girls, and evidence suggests that this increase occurs during mid-puberty (Angold *et al.*, 1998). The time surrounding pubertal maturation is a promising developmental window to investigate mechanisms of vulnerability. Current models hold that environmental experiences prior to and during adolescence and genetic and neurobiological risk factors interact with each other to contribute to the onset of depression (Cicchetti and Toth, 1998, Eley *et al.*, 2004, Kaufman *et al.*, 2006, Kendler *et al.*, 2005, Lau and Eley, 2008). Yet, a greater understanding is needed about how adolescent development specifically triggers risk for depression, which youth are most likely to become depressed during this period, and what targets should be addressed to reduce the onset or recurrence of depression.

Please address correspondence to Jennifer S. Silk, Western Psychiatric Institute and Clinic, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213. Phone: 412-383-8136. Fax: 412-383-5426. silkj@upmc.edu.

Declaration of interest: No conflicts of interest are reported by any of the authors.

## Child Anxiety and Adolescent Depression

One important lead in identifying early intervention targets comes from the finding that anxiety disorders commonly precede the onset of depression in adolescence (Brady and Kendall, 1992, Kovacs *et al.*, 1989, Pine *et al.*, 1998). Epidemiological studies reveal that up to ¾ of depressed youth have a history of at least one anxiety disorder (Kessler *et al.*, 2001). Conversely, in a large community study of adolescents, Ovrachel *et al.* (1995) found that 42% of youth with a first diagnosis of an anxiety disorder developed a second diagnosis of MDD by the one year follow-up. One of the best predictors of the presence of both depression and anxiety in youth is a family history of depression (Weissman *et al.*, 1992, Weissman *et al.*, 2005). A recent meta-analysis of behavioral genetics studies of child anxiety and depression revealed that there is consistent evidence of a partly genetic basis for the comorbidity between anxiety and depression, with the influence of genetic factors increasing in adolescence (Franic *et al.*, 2010). For example, Silberg *et al.* (2001) showed that depression in adolescent girls is genetically correlated with earlier symptoms of anxiety. This literature points to the strong possibility that inherited neurobehavioral vulnerabilities may represent endophenotypes of risk for experiencing a trajectory from anxiety to depression. This paper highlights two neurobehavioral vulnerability factors that may be involved in the pathway from anxiety to depression in youth. Specifically, the model focuses on altered processing of social evaluative threat and reward as two vulnerabilities that: (a) are likely to be present in many, but not all, anxious youth, and (b) if present, are likely to be exacerbated by peri-pubertal developmental processes in ways that create a potential spiral toward depressive disorder (see Figure 1).

## Social-Evaluative Threat and Anxiety

We propose that sensitivity to perceived social threat is a core vulnerability that predisposes youth to early anxiety and later depression. A fundamental human characteristic is the need to preserve the social self, which includes vigilance to threats that may jeopardize social esteem, social-status, and relative self-worth (Baumeister and Leary, 1995, Bowlby, 1969, Maslow, 1987). Social-evaluative threat occurs when a valued aspect of self-identity is, or is feared to be, negatively judged by others (Dickerson and Kemeny, 2004). Social evaluative threats have been shown to be among the most salient stressors to the human neuroendocrine system (Dickerson and Kemeny, 2004) and have also been shown to elicit stronger neural reactions among anxious adults than physical threat stimuli (Goldin *et al.*, 2009).

## Behavioral evidence for the link between social-evaluative threat and anxiety

Biased attention towards threatening information, including social threat, is strongly associated with anxiety during adulthood (Williams *et al.*, 1996) and several behavioral studies have now demonstrated that anxious children show an attentional bias toward threatening social information, including social threat words and faces (see Bar-Haim *et al.*, 2007, Ladouceur *et al.*, 2006, Taghavi *et al.*, 1999, Telzer *et al.*, 2008, Vasey *et al.*, 1996). Anxious children also have a tendency to report more threatening interpretations of ambiguous social scenarios (Barrett *et al.*, 1996, Chorpita *et al.*, 1996, Creswell *et al.*, 2005).

## Neuroimaging evidence for the link between social-evaluative threat and anxiety

Existing neuroimaging research using social stimuli in youth is consistent with this model. Anxious youth show increased amygdala activity to fearful and angry faces relative to healthy controls (McClure *et al.*, 2007a, Monk *et al.*, 2008b, Thomas *et al.*, 2001), especially when attention is constrained toward evaluation of one's own emotion. Furthermore, amygdala activity to fearful and angry faces is associated with anxious symptomatology in

youth with GAD and in non-clinical samples of adolescents (Killgore and Yurgelun-Todd, 2005, Monk *et al.*, 2008b).

One emerging research approach that more directly taps into the evaluative component of social threat processing is the use of virtual interaction and feedback paradigms (Guyer *et al.*, 2008a, Masten *et al.*, 2009, Silk *et al.*, 2012). Guyer *et al.* utilized a virtual chatroom task (Guyer *et al.*, 2008a, Guyer *et al.*, 2009) to investigate youths' neural response to anticipated and rigged feedback from virtual peers they believed had evaluated them as potential interaction partners for an upcoming online chat session. They found that anxious adolescents expected peers to rate them as less desirable and had greater activation in the amygdala than healthy controls when judging how interested the virtual peers would be in chatting with them, especially for peers they did not want to interact with (Guyer *et al.*, 2008a).

Other relevant research has focused on cooperation and conflict in economic exchange tasks, such as the Prisoner's Dilemma (PD) game. McClure *et al.* (2007b) found that adolescents diagnosed with anxiety and/or depressive disorders were more cooperative in response to cooperative overtures from virtual peers compared to healthy adolescents. In a follow-up neuroimaging study, McClure-Tone *et al.* (2011) found that anxious youth differed from healthy youth in neural activation during cooperation and conflict in multiple areas involved in self/other reflection and emotional information processing and were more likely than controls to cooperate after being betrayed by the virtual peer. These findings suggest that maintaining non-threatening interpersonal interactions is a salient goal for anxious youth.

Social-threat biases have been most consistently observed in youth with GAD (Monk *et al.*, 2008a, Taghavi *et al.*, 1999) and social anxiety (Alfano *et al.*, 2006, Guyer *et al.*, 2008a), with some evidence for PTSD (Dalgleish *et al.*, 2001). However, given the high comorbidity among anxiety disorders, it is difficult to ascertain whether these findings were due to youth having comorbid anxiety diagnoses, and little research has been conducted with other types of anxiety-disordered youth. Additional research is needed on the extent to which sensitivity to social evaluative threat characterizes anxious youth who do not have GAD and/or social phobia.

## Social-Evaluative Threat and Depression

While heightened sensitivity to threat in anxiety disorder includes vigilance for both social and physical threat, depression is more specifically linked to interpersonal concerns. Depression is typically characterized by sensitivity to interpersonal threats such as rejection, defeat, and humiliation (Allen and Badcock, 2003, Coyne, 1976). Major theories of depression highlight the role of interpersonal stress and sensitivity, including the interpersonal theory of depression (Coyne, 1976), attachment theory (Gilbert, 1992), social competition theory (Price *et al.*, 1994), social risk theory (Allen and Badcock, 2003), and life stress models (Brown and Harris, 1978).

### Behavioral evidence for the link between social-evaluative threat and depression

A large body of research on depressed adults indicates that they seek excessive reassurance about relationships and rely strongly on social approval for a sense of self-worth (Barnett and Gotlib, 1988, Joiner and Metalsky, 1995, Sheppard and Teasdale, 1996). Interpersonal stressors are prevalent in the peer and family relationships of depressed youth (Abela *et al.*, 2005, Hammen and Brennan, 2001, Messer and Gross, 1995, Olsson *et al.*, 1999, Sheeber and Sorensen, 1998), and these youth are perceived and perceive themselves to be less socially competent than other youth (Connolly *et al.*, 1992, Hammen *et al.*, 2004, Seeds *et al.*, 2010). Life stress research has further shown that interpersonal stressors that threaten

social relationships, such as romantic breakups, often trigger the first episode of depression (Brown and Harris, 1989, Lewinsohn *et al.*, 1999). Research examining depressive symptoms in youth has linked peer rejection (Nolan *et al.*, 2003, Prinstein and Aikins, 2004), perceived lack of support from peers (Galambos *et al.*, 2004), and specific social-evaluative concerns (Rudolph and Conley, 2005) to depressive symptoms in adolescence.

Although interpersonal problems could be a risk factor or a concomitant feature of depression, several longitudinal studies have shown that interpersonal concerns are associated with increases in levels of depressive symptoms over time in community and high-risk samples (Allen *et al.*, 2006, Hammen *et al.*, 2004, Harter and Whitesell, 1996, Lee *et al.*, 2010, Prinstein and Aikins, 2004, Rudolph and Conley, 2005). Although these studies support the importance of investigating social evaluative threat in child and adolescent depression, more research is needed examining specific social evaluative concerns in clinical samples of depressed youth.

### Neuroimaging evidence for the link between social-evaluative threat and depression

Emerging evidence from affective neuroscience research provides further support for altered sensitivity to social threat in depression. For example, Beesdo *et al.* (2009) found that youth with MDD showed amygdala hyperactivation to threatening faces when rating their own fear. Further, Killgore and Yurgelun-Todd (2006) and Forbes *et al.* (2011) have shown that increased activity in the medial prefrontal cortex (mPFC) when viewing threatening faces is associated with increased depressive symptoms in adolescents. Masten *et al.* (2011) have shown using a virtual ball-tossing task that greater activity in the subgenual ACC and the dorsomedial prefrontal cortex during exclusion was associated with increases in depressive symptoms over a year in adolescents. Collectively, these findings suggest that depression in youth is associated with increased reactivity in amygdalar and prefrontal circuits in response to social stimuli; however, additional research is needed in clinical samples using explicit social evaluative stimuli, such as peer feedback tasks.

### Gender differences in social-evaluative threat and depression

Increased sensitivity to interpersonal threat among girls compared to boys may be one mechanism through which the gender difference in rates of depression emerges during adolescence. Females appear to have greater investment in interpersonal relationships and are more concerned about peer evaluation (La Greca and Lopez, 1998, Rose and Rudolph, 2006), potentially making them more sensitive to the effects of interpersonal stress and evaluation than males (Rudolph, 2002). Several models have been put forth linking sensitivity to interpersonal stress in girls to the emergence of gender differences in depression (Cyranowski *et al.*, 2000, Hammen *et al.*, 2008, Leadbeater *et al.*, 1995, Nolen Hoeksema, 1994). Future research is needed to determine whether gender differences in interpersonal sensitivity are also present in anxious youth, and can help to explain the gender differences in the trajectory toward depression in this population.

### Reward Processing and Depression

Our model proposes that a second key neurobehavioral risk factor linking anxiety and depression is alterations in reward processing. Key symptoms of depression, such as anhedonia and social withdrawal, are believed to be related to alterations in seeking rewards and experiencing positive affect in anticipation of, and during receipt of rewards (Forbes, 2009, Forbes and Dahl, 2005). Affective neuroscience models highlight the importance of reward processing in the phenomenology and underlying neurobiology of positive affect (Rolls, 1999). Important aspects of reward processing include the motivation to obtain

rewards, the execution of reward-seeking behaviors, and the hedonic aspects of experiencing a reward (Forbes and Dahl, 2005).

### **Behavioral evidence for the link between reward processing and depression**

Numerous self-report studies have shown that adolescents with depression and/or heightened depressive symptomatology report decreased positive affect relative to healthy adolescents (Chorpita, 2002b, Forbes *et al.*, 2004, Lonigan *et al.*, 2003). Recent laboratory studies focusing specifically on reward processing have also revealed decreased reward responding behavior in depressed adolescents (Forbes *et al.*, 2007, Jazbec *et al.*, 2005). For example, Jazbek *et al.* (2005) found that while healthy adolescents modulated performance on an anti-saccade task as a function of monetary incentives, depressed adolescents' performance was not influenced by manipulations of reward incentives.

### **Neuroimaging evidence for the link between reward processing and depression**

—In neuroimaging studies, adult depression has been associated with reduced activation in striatal areas (Epstein *et al.*, 2006, Lawrence *et al.*, 2004, Surguladze *et al.*, 2005) and enhanced activation in ventromedial PFC areas related to social cognition and contingency evaluation (Keedwell *et al.*, 2005) in response to positive (versus neutral) stimuli. Recent neuroimaging studies of reward processing in youth also show decreased striatal activity and increased medial PFC activity in depressed youth relative to healthy controls (Forbes *et al.*, 2009, Forbes *et al.*, 2006). Forbes *et al.* (2009) found that decreased striatal activity was associated with decreased positive affect in the natural environment reported via ecological momentary assessment. Studies have also reported decreased striatal activity in healthy youth at high risk for depression (Monk *et al.*, 2008a).

## **Reward Processing and Anxiety**

**Behavioral evidence for the link between reward processing and anxiety**—Less is known about the role of reward processing in anxiety, and most studies have focused on the broader construct of positive affect. Although the tripartite model posits that reduced positive affect is specific to depression rather than anxiety in adults (Clark and Watson, 1991), several recent investigations have shown reduced positive affect in anxious youth, especially those with social anxiety (Anderson *et al.*, 2010, Chorpita *et al.*, 2000, Jacques and Mash, 2004, Joiner *et al.*, 1999). Other studies, however, have failed to find evidence for reduced positive affect in child anxiety (Chorpita, 2002a, Lonigan *et al.*, 1999). We argue that disruptions in positive affect and reward processing may be found in a **subset** of anxious youth, and it is this subset of anxious youth that will be most vulnerable to the development of depression.

In support of this model, several studies have shown evidence of positive affect disruptions in anxiety. A recent meta-analysis revealed that anxious individuals have a reduced attentional bias toward positive stimuli compared to low-anxiety individuals (Frewen *et al.*, 2008). Other studies have shown that young adults with anxiety disorders or heightened anxious symptoms tend to focus on anxious feelings during activities that could generate positive emotion, have lower expression of positive emotions, and report elevated fear of positive emotions (Eisner *et al.*, 2009, Kashdan and Steger, 2006, Roemer *et al.*, 2005, Turk *et al.*, 2005). These alterations in self-reported positive emotion in anxious individuals are found even when controlling for depressive symptoms (Eisner *et al.*, 2009, Kashdan and Steger, 2006). In one of the only behavioral studies to focus specifically on reward processing in anxious youth, Jazbec *et al.* (2005) found that incentives improved efficiency of performance on an anti-saccade task for healthy youth but not youth with GAD. This suggests that enhancement of performance by reward may be attenuated in anxious youth who are overly cautious about making errors.



### **Neuroimaging evidence for the link between reward processing and anxiety—**

Consistent with these findings, Forbes *et al.* (2006) have shown similarities between anxious and depressed youth during reward processing on a monetary reward task. Both showed blunted response in the left caudate, but increased amygdala activity to high-reward outcomes relative to healthy controls. Forbes *et al.* (2006) also found that, unlike depressed youth, anxious youth showed heightened orbitofrontal cortex (OFC) activity during anticipation of high magnitude rewards, potentially suggesting enhanced sensitivity to contingencies (Forbes *et al.*, 2006). Two studies have also shown that adolescents who were characterized as behaviorally inhibited as young children show increased striatal response to contingent monetary rewards relative to healthy controls (Bar-Haim *et al.*, 2009, Guyer *et al.*, 2006). These studies point to alterations in reward processing in anxious youth, but additional research is needed to clarify conditions under which anxious youth may be hyper and hypo-responsive to reward and whether there are differences based on anxiety subtype. Furthermore, little research has been conducted using socially relevant stimuli.

**Potential for threat processing to interfere with reward processing—**Based on the findings reviewed above, we propose that anxious youth have an intact or even increased capacity to experience reward in non-threatening contexts. However, reward seeking and processing for some anxious youth may be inhibited or interrupted in social contexts by self-referential and threat processing systems which bring fear of failure, negative evaluation, and avoidance to the cognitive forefront. This is consistent with evidence that social comparison plays a key role in reward processing (Fliessbach *et al.*, 2007). Furthermore, it is known that threat and reward processing are performed by distinct and sometimes competing attentional systems, and that threat processing “trumps” or interrupts reward processing, even in healthy individuals (Frewen *et al.*, 2008, Kahneman and Beatty, 1966). For example, in behavioral economics research, fundamental human risk aversion leads healthy adults to predictably choose a safe option over a high reward option that carries potential loss or punishment (Kahneman and Tversky, 2005). Similarly, in a task that includes cues for reward, punishment, and an ambiguous cue that could signal reward or punishment, we have found that healthy youth rarely respond to the ambiguous cue (Schlund *et al.*, 2010).

These findings suggest that when threat and reward are in conflict, threat typically wins. In the short-run, it is adaptive to notice and respond to threats. However, too many small threats that pull for fast attention may begin to override the reward system in the long-run. This process is present in healthy individuals, but is likely more problematic for anxious individuals, for whom threat cues are prevalent even in ambiguous and sometimes innocuous social scenarios (Creswell *et al.*, 2005). Adolescence, in particular, is filled with ambiguous social cues that may easily be misinterpreted by vigilant youth. As a result of differences in fear learning and fear conditioning (see Britton *et al.*, 2011), anxious youth may also have difficulties perceiving ‘safety’ cues present in social situations which might otherwise allow them to enjoy the situation without fear. This conceptualization is consistent with clinical reports of anxious youth who are often too fearful to engage in mildly risky but rewarding activities such as going to a party, sleeping away from home, or going on amusement park rides.

### **Developmental Changes in Processing of Social-Evaluative Information in Adolescence**

From a developmental psychopathology framework, an examination of normative developmental processes can provide important information about processes that may go awry in atypical development, potentially resulting in psychopathology (Cicchetti, 1993). Alterations in both social evaluative threat and reward processing could be amplified in anxious youth by normative developmental processes in ways that may further increase the

likelihood of developing depression during adolescence. Changes in the social context contribute to increased salience of the social sphere and perceived social evaluation in daily life. Parent-child conflict increases around the onset of pubertal maturation (Steinberg, 1988). Social affiliation with peers and romantic interests becomes increasingly important and emotionally charged (Larson and Asmussen, 1991). Adolescent peer and romantic relationships are unstable and volatile and involve increasingly complex and salient social hierarchies (Brown, 2004, Connolly *et al.*, 2000). Social comparison and even mocking of lower status individuals becomes entrenched in daily life, making adolescents particularly sensitive to cues of social acceptance, rejection, and reputation (Adler and Adler, 1998, Brown, 2004).

The adolescent brain also undergoes significant remodeling during adolescence (Spear, 2000). Some of these changes appear to be associated with pubertal development through the activational influences of steroid hormones (see Nelson *et al.*, 2005, Patton and Viner, 2007, Sisk and Foster, 2004). There is some evidence that change in regions of the brain involved in emotional reactions such as responding to social stimuli may be particularly linked to pubertal maturation (see Forbes *et al.*, 2011, Nelson *et al.*, 2005, Steinberg, 2007). The brain systems that respond to social information and emotions appear to become more sensitive and/or active during puberty (see Dahl, 2001, Nelson *et al.*, 2005, Silk *et al.*, 2009, Spear, 2000, Steinberg, 2007). For example, Silk *et al.* (2012) found evidence for increased sensitivity to social evaluation across adolescence in a virtual peer interaction chatroom task. Specifically, papillary reactivity to peer rejection and visual biases toward acceptance stimuli increased linearly with age among 9–17 year olds.

Several neuroimaging studies show increased neural activity on emotional face processing tasks in adolescents compared to adults. Adolescents have been found to have greater amygdala reactivity relative to adults to sad and fearful faces (Guye *et al.*, 2008b, Killgore and Yurgelun-Todd, 2007) and greater activation in the amygdala, medial PFC, and anterior cingulate cortex (ACC) compared to adults during passive viewing of emotional faces (Monk *et al.*, 2003). Monk *et al.* (2003) observed that adolescents were more sensitive to the emotional content than to the attentional demands of a face processing task (Monk *et al.*, 2003), while adults showed the opposite pattern. Furthermore, amygdala activity in adolescence appears to be strongly related to social dimensions of anxiety (Killgore and Yurgelun-Todd, 2005). Research is lacking, however, on neurodevelopmental changes in sensitivity to social and emotional stimuli during the transition from childhood to adolescence. One study has shown increased amygdala activity to interfering emotional faces in adolescents compared to younger children and adults (Hare *et al.*, 2008), but most existing neuroimaging research compares adolescents to adults but not children.

## Developmental Changes in Reward Processing in Adolescence

**Normative development and reward processing**—Adolescence is also associated with a sharp increase in reward seeking and risk taking behavior across species (see Spear, 2000, 2011). Adolescents seek out experiences that create high-intensity feelings and are more prone to risk taking (e.g. Martin *et al.*, 2002). Increased sensation seeking is linked to pubertal maturation and shown to increase between the ages of 10 and 15 (Steinberg *et al.*, 2008). This behavioral change is believed to be related to changes in dopaminergic systems in adolescence, including changes in the firing rates, density, and concentration of dopamine fibers and receptors and a shift in the balance of dopamine receptors across brain regions (see reviews by Ernst *et al.*, 2009, Galvan, 2010, Wahlstrom *et al.*, 2010).

Forbes *et al.* (2010) examined puberty-specific changes in reward responding based on a large sample of early adolescents matched for age but differing in pubertal status. They found that adolescents more advanced in pubertal maturation exhibited less striatal reactivity

to reward receipt than adolescents in pre or early pubertal stages. Additionally, more pubertally mature adolescents exhibited more medial PFC activity during reward outcome than pre/early-pubertal age-matched adolescents (Forbes *et al.*, 2010). Increased reward seeking among typical adolescents could be a compensatory behavior for decreased dopaminergic striatal reactivity (Spear, 2000). However, although several studies have observed hypo-reactivity to reward in adolescents (Bjork *et al.*, 2004, Bjork *et al.*, 2010, Forbes *et al.*, 2010), other studies have reported evidence of hyper-reactivity (Ernst *et al.*, 2005, Galvan *et al.*, 2006). Spear (2011) and Galvan (2010) suggest that these discrepant findings may be related to differences in responding to reward anticipation versus receipt of reward and other contextual features such as the type and magnitude of the reward.

Although the precise neural mechanisms are in need of further clarification, it remains clear that increased reward seeking behaviors are normative in adolescence. Anxious youth may find it particularly difficult or aversive to engage in adolescent-normative sensation-seeking behaviors because of excessive worrying, vigilance, and avoidance behaviors. Avoidance of age-normative risky and sensation seeking behaviors that are high in reward value may result in lower levels of positive affect relative to healthy peers as well as increased social isolation and withdrawal. These differences in motivation, mood, and social interaction could emerge as precipitators or early symptoms of depression.

**Adolescent development and reward processing: Links to depression—**Davey *et al.* (2008) present a complementary model describing how the maturation of the prefrontal cortex during adolescence may also influence reward processing and depression. Cognitive changes in early adolescence, such as advanced hypothetical thinking, allow for representation of increasingly complex social and future-oriented rewards. These cognitive changes converge with the biological and social changes reviewed above to place a premium on abstract social rewards (i.e. becoming “popular”, falling in love, being successful), which are also tenuous and easily frustrated. Davey *et al.* (2008) point out that repeated failure or frustration of social rewards could lead to suppression of the reward system, eventually resulting in anhedonia (Bogdan and Pizzagalli, 2006, Frewen *et al.*, 2008). Animal studies demonstrate that the reward system is suppressed when an expected reward is omitted (Hollerman and Schultz, 1998, Schultz, 1998). Additionally, stress has been shown to increase anhedonic behavior (Berenbaum and Connelly, 1993, Bogdan and Pizzagalli, 2006, Malkesman *et al.*, 2005, Willner, 2005, Wise, 2004, Zacharko *et al.*, 1983). For example, Bogdan and Pizzagalli (2006) found decreased reward responding in adult humans during a laboratory stressor involving social evaluation. Relatedly, first episodes of depression often result from the frustration or omission of highly anticipated social rewards (Davey *et al.*, 2008).

We argue that the Davey *et al.* (2008) model is particularly relevant to anxious youth at risk for depression. Anxious youth desire complex social rewards just like other adolescents, but fearful avoidance inhibits many anxious youth from seeking and ultimately attaining such rewards. Thus, anxious adolescents who are less likely to seek and obtain social and high-risk rewards and are also more sensitive to social evaluation regarding reward status, are at especially high risk for distress related to failure to obtain reward. Repeated and chronic suppression of the dopaminergic reward system due to fear, avoidance, and related stress may therefore lead to anhedonia over time, providing a link between anxiety and depression. Again, this process may be heightened for girls, since affiliative rewards are known to have greater salience for females than males (Davey *et al.*, 2008).



## Conclusions and Implications

We have reviewed evidence that the processing of social evaluative threat and reward may play a role in the trajectory from anxiety to depression in adolescence, but additional research is needed to validate this model. First, although existing research suggests that anxious and depressed youth are both reactive to threatening or negative socio-emotional stimuli, research is needed using ecologically valid paradigms that can more specifically assess reactions to social evaluation. Second, although there is strong evidence of alterations in reward processing in adolescent depression, the role of reward processing in child anxiety is not as well understood. Additional research is needed to understand whether there are subtypes of anxious youth who show altered reward processing, or specific conditions in which anxious youth show altered reward processing. Third, prospective longitudinal research is needed to determine whether anxious youth with greater behavioral and neural alterations in responses to social evaluative and reward-related stimuli are more likely than other anxious and healthy youth to develop depression during the transition to adolescence.

Another important direction is to consider how reactivity to social evaluative threat and reward may interact with each other. For example, Gardner and Steinberg (2005) have shown that the presence of peers makes adolescents more likely to engage in high-risk/high-reward behaviors. Spear (2011) proposes that cross-reactivity between circuitry involved in the processing of reward-relevant and threatening stimuli may be particularly high in adolescence. Heightened interactivity between these systems during adolescence could further help to explain the spiral toward depression among vulnerable youth.

One critical question for future research is whether providing early intervention for anxious youth that addresses alterations in social evaluative threat and reward processing could prevent the onset of later depressive disorders in these youth. Existing research on depression prevention reveals that programs targeted at individuals at specific risk are more effective than universal prevention (Horowitz and Garber, 2006). Bolstering or directing treatment efforts towards anxious youth, particularly those with deficits in these areas, could be a cost-effective and efficacious approach for depression prevention.

This model also suggests that existing treatments for child anxiety might benefit from increased attention to social evaluative concerns and reward processing. CBT for child anxiety typically involves completion of exposures to a hierarchy of feared situations. Although social evaluative fears are common in anxious youth, it is difficult to create exposures in the clinic that capture the types of peer-related social concerns that adolescents encounter in daily life. Creative use of new social media technologies may provide one means for integrating peer interaction into clinic-based exposures. Approaches that address positive affect and reward processing (e.g. pleasant event planning) have been incorporated into treatments for adolescent depression, but positive affect is rarely addressed explicitly in treatments for child anxiety. Interventions that help anxious youth not just to plan and engage in pleasant events, but also to sustain positive affective states through strategies such as savoring may be useful to consider (Bryant and Veroff, 2006, McMakin *et al.*, 2011). For example, anticipating the positive aspects of an upcoming event (e.g. anticipatory savoring), such as a sleepover, may increase appetitive drives and help to overcome perceived threats (e.g. negative evaluation) related to the event. It may also be helpful to teach youth who have a tendency to get thwarted by perceived threat or anxious feelings in otherwise positive situations to use strategies to flexibly switch back toward positive affective states. Using strategies such as these to sustain positive affective states may help to stimulate mesolimbic areas involved in activating positive emotions and appetitive drives, and also potentially improve or strengthen connections between mesolimbic reward-related areas and prefrontal regulatory control areas. Importantly, these are the same areas that undergo remodeling

during the adolescent period, suggesting there may be an enhanced opportunity for such strategies to alter developmental trajectories of reward related circuitry.

Future research on components of this model may also provide information about the optimal timing of interventions. Successful interventions that occur prior to the destabilizing effects of pubertal development may be more effective at preventing future depressive symptoms by resolving problems in threat and reward processing before they have a chance to interact with the exacerbating developmental features of adolescence.

## Acknowledgments

This research was supported by National Institute of Mental Health (NIMH) Grant R01 MH091327 (P.I. Silk).

## References

- Abela JR, Hankin BL, Haigh EA, Adams P, Vinokuroff T, Trayhern L. Interpersonal vulnerability to depression in high-risk children: the Role of insecure attachment and reassurance seeking. *Journal of Clinical Child and Adolescent Psychology*. 2005; 34:182–192. [PubMed: 15677292]
- Adler, PA.; Adler, P. *Peer Power*. New Brunswick, NJ: Rutgers University Press; 1998.
- Alfano CA, Beidel DC, Turner SM. Cognitive correlates of social phobia among children and adolescents. *J Abnorm Child Psychol*. 2006; 34:189–201. [PubMed: 16514553]
- Allen JP, Insabella G, Porter MR, Smith FD, Land D, Phillips N. A social-interactional model of the development of depressive symptoms in adolescence. *J Consult Clin Psychol*. 2006; 74:55–65. [PubMed: 16551143]
- Allen NB, Badcock PB. The social risk hypothesis of depressed mood: evolutionary, psychosocial, and neurobiological perspectives. *Psychol Bull*. 2003; 129:887–913. [PubMed: 14599287]
- Anderson ER, Veed GJ, Inderbitzen-Nolan HM, Hansen DJ. An evaluation of the applicability of the tripartite constructs to social anxiety in adolescents. *J Clin Child Adolesc Psychol*. 2010; 39:195–207. [PubMed: 20390811]
- Angold A, Costello EJ, Worthman CM. Puberty and depression: The roles of age, pubertal status and pubertal timing. *Psychological Medicine*. 1998; 28:51–61. [PubMed: 9483683]
- Bar-Haim Y, Fox NA, Benson B, Guyer AE, Williams A, Nelson EE, Perez-Edgar K, Pine DS, Ernst M. Neural correlates of reward processing in adolescents with a history of inhibited temperament. *Psychological Science*. 2009; 20:1009–1018. [PubMed: 19594857]
- Bar-Haim Y, Lamy D, Pergamin L, Bakermans-Kranenburg MJ, van Ijzendoorn MH. Threat-related attentional bias in anxious and nonanxious individuals: A metaanalytic study. *Psychological Bulletin*. 2007; 133:1–24. [PubMed: 17201568]
- Barnett PA, Gotlib IH. Psychosocial functioning and depression: Distinguishing among antecedents, concomitants, and consequences. *Psychological Bulletin*. 1988; 104:97–126. [PubMed: 3043529]
- Barrett PM, Rapee RM, Dadds MM, Ryan SM. Family enhancement of cognitive style in anxious and aggressive children. *Journal of Abnormal Child Psychology*. 1996; 24:187–203. [PubMed: 8743244]
- Baumeister RF, Leary MR. The need to belong: Desire for interpersonal attachments as a fundamental human motivation. *Psychological Bulletin*. 1995; 117:497–529. [PubMed: 7777651]
- Beesdo K, Lau JY, Guyer AE, McClure-Tone EB, Monk CS, Nelson EE, Fromm SJ, Goldwin MA, Wittchen H-U, Leibenluft E, Ernst M, Pine DS. Common and distinct amygdala-function perturbations in depressed vs anxious adolescents. *Archives of General Psychiatry*. 2009; 66:275–285. [PubMed: 19255377]
- Berenbaum H, Connelly J. The effect of stress on hedonic capacity. *J Abnorm Psychol*. 1993; 102:474–481. [PubMed: 8408960]
- Bjork JM, Knutson B, Fong GW, Caggiano DM, Bennett SM, Hommer DW. Incentive-elicited brain activation in adolescents: similarities and differences from young adults. *Journal of Neuroscience*. 2004; 24:1793–1802. [PubMed: 14985419]

- Bjork JM, Smith AR, Chen G, Hommer DW. Adolescents, adults and rewards: comparing motivational neurocircuitry recruitment using fMRI. *PLoS ONE* [Electronic Resource]. 2010; 5:e11440.
- Bogdan R, Pizzagalli DA. Acute stress reduces reward responsiveness: implications for depression. *Biol Psychiatry*. 2006; 60:1147–1154. [PubMed: 16806107]
- Bowlby, J. Attachment and loss, Vol. 1: Attachment. New York: Basic Books; 1969.
- Brady EU, Kendall PC. Comorbidity of anxiety and depression in children and adolescents. *Psychological Bulletin*. 1992; 111:244–255. [PubMed: 1557475]
- Britton JC, Lissek S, Grillon C, Norcross MA, Pine DS. Development of anxiety: The role of threat appraisal and fear learning. *Depression and Anxiety*. 2011; 28:5–17. [PubMed: 20734364]
- Brown, BB. Adolescents' relationships with peers. In: Lerner, RM.; Steinberg, LD., editors. *Handbook of Adolescent Psychology*. 2nd Ed. Hoboken, NJ: Wiley; 2004. p. 363–394.
- Brown, GW.; Harris, TO. *Social Origins of Depression: A Study of Psychiatric Disorder in Women*. London, England: Tavistock; 1978.
- Brown, GW.; Harris, TO. *Stressful life events and illness*. New York: Guilford Press; 1989.
- Bryant, FB.; Veroff, J. *Savoring: A new model of positive experience*. Mahwah, NJ: Lawrence Erlbaum Associates Publishers; 2006.
- Chorpita BF. The tripartite model and dimensions of anxiety and depression: An examination of structure in a large school sample. *Journal of Abnormal Child Psychology*. 2002a; 30:177–190. [PubMed: 12002397]
- Chorpita BF. The tripartite model and dimensions of anxiety and depression: An examination of structure in a large school sample. *Journal of Abnormal Child Psychology*. 2002b; 30:177–190. [PubMed: 12002397]
- Chorpita BF, Albano AM, Barlow DH. Cognitive processing in children: Relation to anxiety and family influences. *Journal of Clinical Child Psychology*. 1996; 25:170–176.
- Chorpita BF, Plummer C, Moffitt CE. Relations of tripartite dimensions of emotion to childhood anxiety and mood disorders. *Journal of Abnormal Child Psychology*. 2000; 28:299–310. [PubMed: 10885687]
- Cicchetti D. Developmental psychopathology: Reactions, reflections, projections. *Developmental Review*. 1993; 13:471–502.
- Cicchetti D, Toth SL. The development of depression in children and adolescents. *American Psychologist*. 1998; 53:221–241. [PubMed: 9491749]
- Clark LA, Watson D. Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. *Journal of Abnormal Psychology*. 1991; 100:316–336. [PubMed: 1918611]
- Connolly J, Furman W, Konarski R. The role of peers in the emergence of heterosexual romantic relationships in adolescence. *Child Development*. 2000; 71:1395–1408. [PubMed: 11108103]
- Connolly J, Geller S, Marton P, Kutcher S. Peer responses to social interaction with depressed adolescents. *Journal of Clinical Child Psychology*. 1992; 21:365–370.
- Coyne JC. Depression and the response of others. *Journal of Abnormal Psychology*. 1976 Apr; Vol 85(2):186–193. 1976. [PubMed: 1254779]
- Creswell C, Schniering CA, Rapee RM. Threat interpretation in anxious children and their mothers: Comparison with nonclinical children and the effects of treatment. *Behaviour Research and Therapy*. 2005; 43:1375–1381. [PubMed: 16086987]
- Cyranowski JM, Frank E, Young E, Shear MK. Adolescent onset of the gender difference in lifetime rates of major depression: a theoretical model. *Arch Gen Psychiatry*. 2000; 57:21–27. [PubMed: 10632229]
- Dahl RE. Affect regulation, brain development, and behavioral/emotional health in adolescence. *CNS Spectrums*. 2001; 6:1–12.
- Dagleish T, Moradi A, Taghavi M, Neshat-Doost H, Yule W. An experimental investigation of hypervigilance for threat in children and adolescents with post-traumatic stress disorder. *Psychological Medicine*. 2001; 31:541–547. [PubMed: 11305862]

- Davey CG, Yucel M, Allen NB. The emergence of depression in adolescence: Development of the prefrontal cortex and the representation of reward. *Neuroscience & Biobehavioral Reviews*. 2008; 32:1–19. [PubMed: 17570526]
- Dickerson SS, Kemeny ME. Acute stressors and cortisol responses: a Theoretical integration and synthesis of laboratory research. *Psychological Bulletin*. 2004; 130:355–391. [PubMed: 15122924]
- Eisner LR, Johnson SL, Carver CS. Positive affect regulation in anxiety disorders. *J Anxiety Disord*. 2009; 23:645–649. [PubMed: 19278820]
- Eley T, Sugden K, Corsico A, Gregory A, Sham P, McGuffin P, Plomin R, Craig I. Gene-environment interaction analysis of serotonin system markers with adolescent depression. *Molecular Psychiatry*. 2004; 9:908–915. [PubMed: 15241435]
- Epstein J, Pan H, Kocsis JH, Yang Y, Butler T, Chusid J, Hochberg H, Murrough J, Strohmayer E, Stern E, Silbersweig DA. Lack of ventral striatal response to positive stimuli in depressed versus normal subjects. *Am J Psychiatry*. 2006; 163:1784–1790. [PubMed: 17012690]
- Ernst M, Nelson EE, Jazbec S, McClure EB, Monk CS, Leibenluft E, Blair J, Pine DS. Amygdala and nucleus accumbens in responses to receipt and omission of gains in adults and adolescents. *Neuroimage*. 2005; 25:1279–1291. [PubMed: 15850746]
- Ernst M, Romeo RD, Andersen SL. Neurobiology of the development of motivated behaviors in adolescence: A window into a neural systems model. *Pharmacology, Biochemistry and Behavior*. 2009; 93:199–211.
- Fliessbach K, Weber B, Trautner P, Dohmen T, Sunde U, Elger C, Falk A. Social comparison affects reward-related brain activity in the human ventral striatum. *Science*. 2007; 318:1305–1308. [PubMed: 18033886]
- Forbes EE. Where's the fun in that? Broadening the focus on reward function in depression. *Biol Psychiatry*. 2009; 66:199–200. [PubMed: 19577042]
- Forbes EE, Dahl RE. Neural systems of positive affect: Relevance to understanding child and adolescent depression? *Development and Psychopathology*. 2005; 17:827–850. [PubMed: 16262994]
- Forbes EE, Hariri AR, Martin SL, Silk JS, Moyles DL, Fisher PM, Brown SM, Ryan ND, Birmaher B, Axelson DA, Dahl RE. Altered striatal activation predicting real-world positive affect in adolescent major depressive disorder. *American Journal of Psychiatry*. 2009; 166:64–73. [PubMed: 19047324]
- Forbes EE, May CJ, Siegle GJ, Ladouceur CD, Ryan ND, Carter CS, Birmaher B, Axelson DA, Dahl RE. Reward-related decision-making in pediatric major depressive disorder: an fMRI study. *Journal of Child Psychology and Psychiatry*. 2006; 47:1031–1040. [PubMed: 17073982]
- Forbes EE, Phillips ML, Silk JS, Ryan ND, Dahl RE. Neural systems of threat processing in adolescents: Role of pubertal maturation and relation to measures of negative affect. *Dev Neuropsychol*. 2011; 36:429–452. [PubMed: 21516542]
- Forbes EE, Ryan ND, Phillips ML, Manuck SB, Worthman CM, Moyles DL, Tarr JA, Sciarillo SR, Dahl RE. Healthy adolescents' neural response to reward: associations with puberty, positive affect, and depressive symptoms. *J Am Acad Child Adolesc Psychiatry*. 2010; 49:162–172. e1-5. [PubMed: 20215938]
- Forbes EE, Shaw DS, Dahl RE. Alterations in reward-related decision making in boys with recent and future depression. *Biological Psychiatry*. 2007; 61:633–639. [PubMed: 16920074]
- Forbes EE, Williamson DE, Ryan ND, Dahl RE. Positive and negative affect in depression: Influence of sex and puberty. *Annals of the New York Academy of Sciences*. 2004; 1021:341–347. [PubMed: 15251907]
- Franic S, Middeldorp CM, Dolan CV, Ligthart L, Boomsma DI. Childhood and adolescent anxiety and depression: Beyond heritability. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2010; 49:820–829. [PubMed: 20643315]
- Frewen PA, Dozois DJ, Joanisse MF, Neufeld RW. Selective attention to threat versus reward: meta-analysis and neural-network modeling of the dot-probe task. *Clin Psychol Rev*. 2008; 28:307–337. [PubMed: 17618023]

- Galambos NL, Leadbeater BJ, Barker ET. Gender differences in and risk factors for depression in adolescence: A 4-year longitudinal study. *International Journal of Behavioral Development*. 2004; 28:16–25.
- Galvan A. Adolescent development of the reward system. *Frontiers in Human Neuroscience*. 2010; 4:6. [PubMed: 20179786]
- Galvan A, Hare TA, Parra CE, Penn J, Voss K, Glover G, Casey B. Earlier development of the accumbens relative to orbitofrontal cortex might underlie risk-taking behavior in adolescents. *The Journal of Neuroscience*. 2006; 26:6885–6892. [PubMed: 16793895]
- Gardner M, Steinberg L. Peer Influence on risk taking, risk preference, and risky decision making in adolescence and adulthood: An Experimental study. *Developmental Psychology*. 2005; 41:625–635. [PubMed: 16060809]
- Gilbert, P. *Depression: The evolution of powerlessness*. New York: Guilford; 1992.
- Goldin PR, Manber T, Hakimi S, Canli T, Gross JJ. Neural bases of social anxiety disorder: Emotional reactivity and cognitive regulation during social and physical threat. *Archives of General Psychiatry*. 2009; 66:170–180. [PubMed: 19188539]
- Guyer AE, Lau JY, McClure-Tone EB, Parrish J, Shiffrin ND, Reynolds RC, Chen G, Blair R, Leibenluft E, Fox NA, Ernst M, Pine DS, Nelson EE. Amygdala and ventrolateral prefrontal cortex function during anticipated peer evaluation in pediatric social anxiety. *Archives of General Psychiatry*. 2008a; 65:1303–1312. [PubMed: 18981342]
- Guyer AE, McClure-Tone EB, Shiffrin ND, Pine DS, Nelson EE. Probing the neural correlates of anticipated peer evaluation in adolescence. *Child Development*. 2009; 80:1000–1015. [PubMed: 19630890]
- Guyer AE, Monk CS, McClure-Tone EB, Nelson EE, Roberson-Nay R, Adler AD, Fromm SJ, Leibenluft E, Pine DS, Ernst M. A developmental examination of amygdala response to facial expressions. *Journal of Cognitive Neuroscience*. 2008b; 20 pp.
- Guyer AE, Nelson EE, Perez-Edgar K, Hardin MG, Roberson-Nay R, Monk CS, Bjork JM, Henderson HA, Pine DS, Fox NA, Ernst M. Striatal functional alteration in adolescents characterized by early childhood behavioral inhibition. *J Neurosci*. 2006; 26:6399–6405. [PubMed: 16775126]
- Hammen C, Brennan PA. Depressed adolescents of depressed and nondepressed mothers: Tests of an Interpersonal Impairment Hypothesis. *Journal of Consulting and Clinical Psychology*. 2001; 69:284–294. [PubMed: 11393605]
- Hammen C, Brennan PA, Keenan-Miller D. Patterns of adolescent depression to age 20: The role of maternal depression and youth interpersonal dysfunction. *Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology*. 2008; 36:1189–1198.
- Hammen C, Shih JH, Brennan PA. Intergenerational Transmission of Depression: Test of an Interpersonal Stress Model in a Community Sample. *Journal of Consulting and Clinical Psychology*. 2004; 72:511–522. [PubMed: 15279534]
- Hare TA, Tottenham N, Galvan A, Voss HU, Glover GH, Casey BJ. Biological substrates of emotional reactivity and regulation in adolescence during an emotional go-nogo task. *Biological Psychiatry*. 2008; 63:927–934. [PubMed: 18452757]
- Harter S, Whitesell NR. Multiple pathways to self-reported depression and psychological adjustment among adolescents. *Development and Psychopathology*. 1996; 8:761–777.
- Hollerman JR, Schultz W. Dopamine neurons report an error in the temporal prediction of reward during learning. *Nat Neurosci*. 1998; 1:304–309. [PubMed: 10195164]
- Horowitz JL, Garber J. The prevention of depressive symptoms in children and adolescents: A meta-analytic review.[see comment]. *Journal of Consulting & Clinical Psychology*. 2006; 74:401–415. [PubMed: 16822098]
- Jacques HA, Mash EJ. A test of the tripartite model of anxiety and depression in elementary and high school boys and girls. *Journal of Abnormal Child Psychology*. 2004; 32:13–25. [PubMed: 14998108]
- Jazbec S, McClure E, Hardin M, Pine DS, Ernst M. Cognitive control under contingencies in anxious and depressed adolescents: An Antisaccade task. *Biological Psychiatry*. 2005; 58:632–639. [PubMed: 16018983]

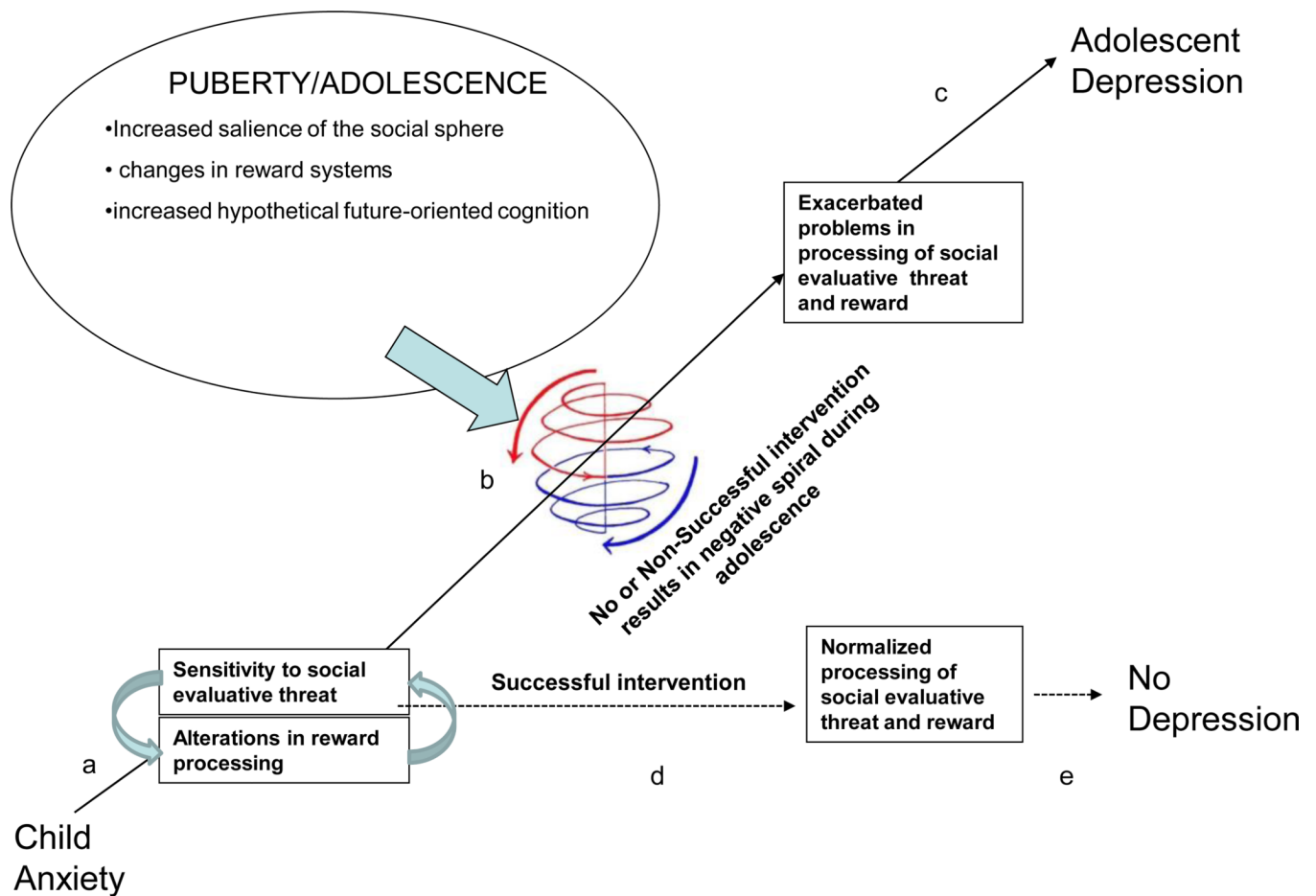


- Joiner TE Jr, Blalock JA, Wagner KD. Preliminary examination of sex differences in depressive symptoms among adolescent psychiatric inpatients: the role of anxious symptoms and generalized negative affect. *J Clin Child Psychol*. 1999; 28:211–219. [PubMed: 10353080]
- Joiner TE, Metalsky GI. A prospective test of an integrative interpersonal theory of depression: A naturalistic study of college roommates. *Journal of Personality and Social Psychology*. 1995; 69:778–788. [PubMed: 7473031]
- Kahneman D, Beatty J. Pupil diameter and load on memory. *Science*. 1966; 154:1583–1585. [PubMed: 5924930]
- Kahneman, D.; Tversky, A. Conflict Resolution: A Cognitive Perspective. In: Max, H., editor. Bazerman. 2005. p. 116-134.
- Kashdan TB, Steger MF. Expanding the topography of social anxiety. An experience-sampling assessment of positive emotions, positive events, and emotion suppression. *Psychol Sci*. 2006; 17:120–128. [PubMed: 16466419]
- Kaufman J, Yang B-Z, Douglas-Palumberi H, Grasso D, Lipschitz D, Houshyar S, Krystal JH, Gelernter J. Brain-derived neurotrophic factor-5-HT<sub>1A</sub> gene interactions and environmental modifiers of depression in children. *Biological Psychiatry*. 2006; 59:673–680. [PubMed: 16458264]
- Keedwell PA, Andrew C, Williams SC, Brammer MJ, Phillips ML. A double dissociation of ventromedial prefrontal cortical responses to sad and happy stimuli in depressed and healthy individuals. *Biol Psychiatry*. 2005; 58:495–503. [PubMed: 15993859]
- Kendler KS, Kuhn JW, Vittum J, Prescott CA, Riley B. The interaction of stressful life events and a serotonin transporter polymorphism in the prediction of episodes of major depression. *Archives of General Psychiatry*. 2005; 62:529–535. [PubMed: 15867106]
- Kessler RC. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: Results from the National Comorbidity Study. *Archives of General Psychiatry*. 1994; 51:8–19. [PubMed: 8279933]
- Kessler RC, Avenevoli S, Merikangas KR. Mood disorders in children and adolescents: An epidemiologic perspective. *Biological Psychiatry*. 2001; 49:1002–1014. [PubMed: 11430842]
- Killgore WD, Yurgelun-Todd DA. Social anxiety predicts amygdala activation in adolescents viewing fearful faces. *Neuroreport: For Rapid Communication of Neuroscience Research*. 2005; 16:1671–1675.
- Killgore WD, Yurgelun-Todd DA. Ventromedial prefrontal activity correlates with depressed mood in adolescent children. *Neuroreport: For Rapid Communication of Neuroscience Research*. 2006; 17:167–171.
- Killgore WD, Yurgelun-Todd DA. Unconscious processing of facial affect in children and adolescents. *Soc Neurosci*. 2007; 2:28–47. [PubMed: 18633805]
- Kovacs M, Gatsonis C, Paulauskas SL, Richards C. Depressive disorders in childhood. IV. A longitudinal study of comorbidity with and risk for anxiety disorders. *Arch Gen Psychiatry*. 1989; 46:776–782. [PubMed: 2774847]
- La Greca AM, Lopez N. Social anxiety among adolescents: Linkage with peer relations and friendships. *Journal of Abnormal Child Psychology*. 1998; 26:83–94. [PubMed: 9634131]
- Ladouceur CD, Dahl RE, Williamson DE, Birmaher B, Axelson DA, Ryan ND, Casey BJ. Processing emotional facial expressions influences performance in a Go/NoGo task in pediatric anxiety and depression. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2006; 47:1107–1115.
- Larson, RW.; Asmussen, L. Anger, worry, and hurt in early adolescence: An enlarging world of negative emotions. In: Colten, ME.; Gore, S., editors. *Adolescent stress: Causes and consequences*. Hawthorne, NY: Aldine de Gruyter; 1991. p. 21-41.
- Lau JYF, Eley TC. Disentangling gene-environment correlations and interactions on adolescent depressive symptoms. *Journal of Child Psychology & Psychiatry & Allied Disciplines*. 2008; 49:142–150.
- Lawrence NS, Williams AM, Surguladze S, Giampietro V, Brammer MJ, Andrew C, Frangou S, Ecker C, Phillips ML. Subcortical and ventral prefrontal cortical neural responses to facial expressions

- distinguish patients with bipolar disorder and major depression. *Biological Psychiatry*. 2004; 55:578–587. [PubMed: 15013826]
- Leadbeater BJ, Blatt SJ, Quinlan DM. Gender-linked vulnerabilities to depressive symptoms, stress, and problem behaviors in adolescents. *Journal of Research on Adolescence*. 1995; 5:1–29.
- Lee A, Hankin BL, Mermelstein RJ. Perceived social competence, negative social interactions, and negative cognitive style predict depressive symptoms during adolescence. *Journal of Clinical Child and Adolescent Psychology*. 2010; 39:603–615. [PubMed: 20706914]
- Lewinsohn PM, Allen NB, Seeley JR, Gotlib IH. First onset versus recurrence of depression: Differential processes of psychosocial risk. *Journal of Abnormal Psychology*. 1999; 108:483–489. [PubMed: 10466272]
- Lonigan CJ, Hooe ES, David CF, Kistner JA. Positive and negative affectivity in children: Confirmatory factor analysis of a two-factor model and its relation to symptoms of anxiety and depression. *Journal of Consulting and Clinical Psychology*. 1999; 67:374–386. [PubMed: 10369058]
- Lonigan CJ, Phillips BM, Hooe ES. Relations of positive and negative affectivity to anxiety and depression in children: Evidence from a latent variable longitudinal study. *Journal of Consulting and Clinical Psychology*. 2003; 71:465–481. [PubMed: 12795571]
- Malkesman O, Braw Y, Zagoory-Sharon O, Golan O, Lavi-Avnon Y, Schroeder M, Overstreet D, Yadid G, Weller A. Reward and anxiety in genetic animal models of childhood depression. *Behavioural Brain Research*. 2005; 164:1–10. [PubMed: 16055204]
- Martin CA, Kelly TH, Rayens MK, Brogli BR, Brenzel A, Smith WJ, Omar HA. Sensation seeking, puberty and nicotine, alcohol and marijuana use in adolescence. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2002; 41:1495–1502. [PubMed: 12447037]
- Maslow, AH. *Motivation and Personality*. New York: Addison-Wesley Educational Publishers, Inc; 1987.
- Masten CL, Eisenberger NI, Borofsky LA, McNealy K, Pfeifer JH, Dapretto M. Subgenual anterior cingulate responses to peer rejection: A marker of adolescents' risk for depression. *Development and Psychopathology*. 2011; 23:283–292. [PubMed: 21262054]
- Masten CL, Eisenberger NI, Borofsky LA, Pfeifer JH, McNealy K, Mazziotta JC, Dapretto M. Neural correlates of social exclusion during adolescence: understanding the distress of peer rejection. *Soc Cogn Affect Neurosci*. 2009; 4:143–157. [PubMed: 19470528]
- McClure-Tone EB, Nawa NE, Nelson EE, Detloff AM, Fromm SJ, Pine DS, Ernst M. Preliminary findings: Neural responses to feedback regarding betrayal and cooperation in adolescent anxiety disorders. *Developmental Neuropsychology*. 2011; 36:453–472. [PubMed: 21516543]
- McClure EB, Monk CS, Nelson EE, Parrish JM, Adler A, Blair R, Fromm S, Charney DS, Leibenluft E, Ernst M, Pine DS. Abnormal attention modulation of fear circuit function in pediatric generalized anxiety disorder. *Archives of General Psychiatry*. 2007a; 64:97–106. [PubMed: 17199059]
- McClure EB, Parrish JM, Nelson EE, Easter J, Thorne JF, Rilling JK, Ernst M, Pine DS. Responses to conflict and cooperation in adolescents with anxiety and mood disorders. *Journal of Abnormal Child Psychology*. 2007b; 35:567–577. [PubMed: 17340177]
- McMakin DL, Siegle GJ, Shirk SR. Positive Affect Stimulation and Sustainment (PASS) module for depressed mood: A preliminary investigation of treatment-related effects. *Cognitive Therapy and Research*. 2011; 35:217–226. [PubMed: 22140287]
- Messer SC, Gross AM. Childhood depression and family interaction: A naturalistic observation study. *Journal of Clinical Child Psychology*. 1995; 24:77–88.
- Monk CS, Klein RG, Telzer EH, Schroth EA, Mannuzza S, Moulton JL III, Guardino M, Masten CL, McClure T, Fromm S, Blair R, Pine DS, Ernst M. Amygdala and nucleus accumbens activation to emotional facial expressions in children and adolescents at risk for major depression. *American Journal of Psychiatry*. 2008a; 165:90–98. [PubMed: 17986682]
- Monk CS, McClure EB, Nelson EE, Zarahn E, Bilder RM, Leibenluft E, Charney DS, Ernst M, Pine DS. Adolescent immaturity in attention-related brain engagement to emotional facial expressions. *Neuroimage*. 2003; 20:420–428. [PubMed: 14527602]

- Monk CS, Telzer EH, Mogg K, Bradley BP, Mai X, Louro HM, Chen G, McClure-Tone EB, Ernst M, Pine DS. Amygdala and ventrolateral prefrontal cortex activation to masked angry faces in children and adolescents with generalized anxiety disorder. *Archives of General Psychiatry*. 2008b; 65:568–576. [PubMed: 18458208]
- Nelson EE, Leibenluft E, McClure E, Pine DS. The social re-orientation of adolescence: A neuroscience perspective on the process and its relation to psychopathology. *Psychological Medicine*. 2005; 35:163–174. [PubMed: 15841674]
- Nolan SA, Flynn C, Garber J. Prospective relations between rejection and depression in young adolescents. *Journal of Personality and Social Psychology*. 2003; 85:745–755. [PubMed: 14561127]
- Nolen Hoeksema S. An interactive model for the emergence of gender differences in depression in adolescence. *Journal of Research on Adolescence*. 1994; 4:519–534.
- Olsson GI, Nordstrom M-L, Arinell H, von Knorring A-L. Adolescent depression: Social network and family climate: A case-control study. *Journal of Child Psychology and Psychiatry*. 1999; 40:227–237. [PubMed: 10188705]
- Orvaschel H, Lewinsohn PM, Seeley JR. Continuity of psychopathology in a community sample of adolescents. *J Am Acad Child Adolesc Psychiatry*. 1995; 34:1525–1535. [PubMed: 8543521]
- Patton GC, Viner R. Pubertal transitions in health. *The Lancet*. 2007; 369:1130–1139.
- Pine DS, Cohen P, Gurley D, Brook J, Ma Y. The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. *Archives of General Psychiatry*. 1998; 55:56–64. [PubMed: 9435761]
- Price J, Sloman L, Gardner R Jr, Gilbert P, Rohde P. The social competition hypothesis of depression. *Br J Psychiatry*. 1994; 164:309–315. [PubMed: 8199784]
- Prinstein MJ, Aikins JW. Cognitive moderators of the longitudinal association between peer rejection and adolescent depressive symptoms. *Journal of Abnormal Child Psychology*. 2004; 32:147–158. [PubMed: 15164857]
- Roemer L, Salters K, Raffa SD, Orsillo SM. Fear and avoidance of internal experiences in GAD: Preliminary tests of a conceptual model. *Cognitive Therapy and Research*. 2005; 29:71–88.
- Rolls, ET. *The brain and emotion*. New York: Oxford University Press; 1999.
- Rose AJ, Rudolph KD. A review of sex differences in peer relationship processes: Potential trade-offs for the emotional and behavioral development of girls and boys. *Psychological Bulletin*. 2006; 132:98–131. [PubMed: 16435959]
- Rudolph KD. Gender differences in emotional responses to interpersonal stress during adolescence. *Journal of Adolescent Health*. 2002; 30:3–13. [PubMed: 11943569]
- Rudolph KD, Conley CS. The socioemotional costs and benefits of social-evaluative concerns: do girls care too much? *J Pers*. 2005; 73:115–138. [PubMed: 15660675]
- Schlund MW, Siegle GJ, Ladouceur CD, Silk JS, Cataldo MF, Forbes EE, Dahl RE, Ryan ND. Nothing to fear? Neural systems supporting avoidance behavior in healthy youths. *Neuroimage*. 2010; 52:710–719. [PubMed: 20430103]
- Schultz W. Predictive reward signal of dopamine neurons. *Journal of Neurophysiology*. 1998; 80:1–27. [PubMed: 9658025]
- Seeds PM, Harkness KL, Quilty LC. Parental maltreatment, bullying, and adolescent depression: Evidence for the mediating role of perceived social support. *Journal of Clinical Child and Adolescent Psychology*. 2010; 39:681–692. [PubMed: 20706920]
- Sheeber L, Sorensen E. Family relationships of depressed adolescents: A multimethod assessment. *Journal of Clinical Child Psychology*. 1998; 27:268–277. [PubMed: 9789187]
- Sheppard LC, Teasdale JD. Depressive thinking: Changes in schematic mental models of self and world. *Psychological medicine*. 1996; 26:1043–1055. [PubMed: 8878336]
- Silberg J, Rutter M, Neale M, Eaves L. Genetic moderation of environmental risk for depression and anxiety in adolescent girls. *British Journal of Psychiatry*. 2001 Aug. Vol 179:116–121. 2001. [PubMed: 11483472]
- Silk JS, Siegle GJ, Whalen DJ, Ostapenko L, Ladouceur CD, Dahl RE. Pubertal changes in emotional information processing: pupillary, behavioral, and subjective evidence during emotional word identification. *Development and Psychopathology*. 2009; 21:7–16. [PubMed: 19144220]

- Silk JS, Stroud LR, Siegle GJ, Dahl RE, Lee KH, Nelson EE. Peer acceptance and rejection through the eyes of youth: Pupillary, eyetracking, and ecological data from the Chatroom Interact Task. *Social Cognitive and Affective Neuroscience*. 2012; 7:93–105. [PubMed: 21775386]
- Sisk CL, Foster DL. The neural basis of puberty and adolescence. *Nature Neuroscience*. 2004; 7
- Spear LP. The adolescent brain and age-related behavioral manifestations. *Neuroscience & Biobehavioral Reviews*. 2000; 24:417–463. [PubMed: 10817843]
- Spear LP. Rewards, aversions and affect in adolescence: Emerging convergences across laboratory animal and human data. *Developmental Cognitive Neuroscience*. 2011; 1:390–403.
- Steinberg L. Reciprocal relation between parent-child distance and pubertal maturation. *Developmental Psychology*. 1988; 24:122–128.
- Steinberg L. Risk-taking in adolescence: New perspectives from brain and behavioral science. *Current Directions in Psychological Science*. 2007; 16:55–59.
- Steinberg L, Albert D, Cauffman E, Banich M, Graham S, Woolard J. Age differences in sensation seeking and impulsivity as indexed by behavior and self-report: Evidence for a dual systems model. *Developmental Psychology*. 2008; 44 pp.
- Surguladze S, Brammer MJ, Keedwell P, Giampietro V, Young AW, Travis MJ, Williams SCR, Phillips ML. A differential pattern of neural response toward sad versus happy facial expressions in major depressive disorder. 2005; 57:201.
- Taghavi MR, Neshat-Doost HT, Moradi AR, Yule W, Dalglish T. Biases in visual attention in children and adolescents with clinical anxiety and mixed anxiety-depression. *Journal of Abnormal Child Psychology*. 1999; 27:215–223. [PubMed: 10438187]
- Telzer EH, Mogg K, Bradley BP, Mai X, Ernst M, Pine DS, Monk CS. Relationship between trait anxiety, prefrontal cortex, and attention bias to angry faces in children and adolescents. *Biological Psychology*. 2008; 79:216–222. [PubMed: 18599179]
- Thomas KM, Drevets WC, Dahl RE, Ryan ND, Birmaher B, Eccard CH, Axelson D, Whalen PJ, Casey BJ. Amygdala response to fearful faces in anxious and depressed children. *Archives of General Psychiatry*. 2001; 58:1057–1063. [PubMed: 11695953]
- Turk CL, Heimberg RG, Luterek JA, Mennin DS, Fresco DM. Emotion dysregulation in generalized anxiety disorder: A comparison with social anxiety disorder. *Cognitive Therapy and Research*. 2005; 29:89–106.
- Vasey MW, El-Hag N, Daleiden EL. Anxiety and the processing of emotionally threatening stimuli: Distinctive patterns of selective attention among high- and low-test-anxious children. *Child Development*. 1996; 67:1173–1185. [PubMed: 8706516]
- Wahlstrom D, Collins P, White T, Luciana M. Developmental changes in dopamine neurotransmission in adolescence: Behavioral implications and issues in assessment. *Brain and Cognition*. 2010; 72:146–159. [PubMed: 19944514]
- Weissman MM, Fendrich M, Warner V, Wickramaratne P. Incidence of psychiatric disorder in offspring at high and low risk for depression. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1992; 31:640–648. [PubMed: 1644726]
- Weissman MM, Wickramaratne P, Nomura Y, Warner V, Verdelli H, Pilowsky DJ, Grillon C, Bruder G. Families at high and low risk for depression: a 3- generation study. *Arch Gen Psychiatry*. 2005; 62:29–36. [PubMed: 15630070]
- Williams J, Mathews A, MacLeod C. The emotional Stroop task and psychopathology. *Psychological Bulletin*. 1996; 120:3–24. [PubMed: 8711015]
- Willner P. Chronic mild stress (CMS) revisited: Consistency and behavioural-neurobiological concordance in the effects of CMS. *Neuropsychobiology*. 2005; 52:90–110. [PubMed: 16037678]
- Wise RA. Dopamine, learning and motivation. *Nature Reviews Neuroscience*. 2004; 5:483–494.
- Zacharko RM, Bowers WJ, Kokkinidis L, Anisman H. Region-specific reductions of intracranial self-stimulation after uncontrollable stress: possible effects on reward processes. *Behav Brain Res*. 1983; 9:129–141. [PubMed: 6603854]



**Figure 1.**

Theoretical model of proposed trajectory from anxiety to depression. This model proposes that many anxious youth experience increased sensitivity to social evaluative threat and altered reward processing (path a), which are also vulnerabilities for depression. These vulnerabilities are exacerbated by normative developmental changes of adolescence (path b), potentially leading to the development of depression in adolescence (path c). Although speculative at this point, the model proposes that successful intervention that alters these vulnerabilities could prevent the development of depression in anxious youth (path d/e).