Resilience among children and adolescents at risk for depression: Mediation and moderation across social and neurobiological contexts

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Abstract

This article offers a multilevel perspective on resilience to depression, with a focus on interactions among social and neurobehavioral systems involved in emotional reactivity and regulation. We discuss models of cross-contextual mediation and moderation by which the social context influences or modifies the effects of resilience processes at the biological level, or the biological context influences or modifies the effects of resilience processes at the social level. We highlight the socialization of emotion regulation as a candidate process contributing to resilience against depression at the social context level. We discuss several factors and their interactions across levels—including genetic factors, stress reactivity, positive affect, neural systems of reward, and sleep—as candidate processes contributing to resilience against depression at the neurobehavioral level. We then present some preliminary supportive findings from two studies of children and adolescents at high risk for depression. Study 1 shows that elevated neighborhood level adversity has the potential to constrain or limit the benefits of protective factors at other levels. Study 2 indicates that ease and quickness in falling asleep and a greater amount of time in deep Stage 4 sleep may be protective against the development of depressive disorders for children. The paper concludes with a discussion of clinical implications of this approach.

Depressive disorders during childhood and adolescence are associated with marked emotional and social impairments that can interfere with children's relationships and academic and occupational functioning into adulthood (Birmaher, Ryan, Williamson, & Brent, 1996; Rao et al., 1995; Weissman et al., 1999). Estimates of the point prevalence of major depressive disorder (MDD) range from 0.4 to 8% in childhood and from 0.4 to 8.3% in adolescence, with a lifetime prevalence between 15 and 20% during adolescence (Birmaher, Ryan, et al., 1996). Most children and adolescents with depression will go on to have recurrent episodes, increased rates of attempted and completed suicides, and persistent social impairment between episodes (Kovacs, 1996; Kovacs, Feinberg, Crouse-Novak, Paulauskas, & Finkelstein, 1984; Weissman et al., 1999).

Given the serious consequences of early-onset depressive disorders, a better understanding of

factors that can lead to the prevention of the first onset of depressive episodes is crucial. A number of risk factors for child and adolescent depression have been delineated, including familial genetic risk (Weissman, Warner, Wickramaratne, Moreau, & Olfson, 1997), hostile and rejecting family relationships (Asarnow, Tompson, Hamilton, Goldstein, & Guthrie, 1994; Sheeber & Sorensen, 1998), stressful life events (Williamson, Birmaher, Anderson, Al-Shabbout, & Ryan, 1995), depressogenic cognitive style (Garber, Weiss, & Shanley, 1993), and neurobiological abnormalities (Ryan & Dahl, 1993). However; many children exposed to multiple risk factors for depression follow normative developmental trajectories and become healthy adults. For example, although approximately 45% of children with an affectively ill parent will develop an episode of major depression by late adolescence (Beardslee, Versage, & Gladstone, 1998), the remaining 55% of these children will *not* experience depression. Presently, we know very little about what distinguishes resilient and nonresilient trajectories among children and adolescents at high risk for depression. Understanding this phenomenon of *resilience* to depression is of critical importance because it may provide a window into processes that can be enhanced and targeted in prevention approaches among high-risk populations.

This article offers a multilevel perspective on resilience to depression, with a focus on interactions among social and neurobehavioral systems involved in emotional reactivity and regulation. This perspective is informed by a developmental psychopathology framework, which seeks to understand individual differences in adaptation across the life course by integrating multidisciplinary perspectives on typical and atypical development (Cicchetti, 1993). In this article, we (a) define resilience as it applies to child and adolescent depression, (b) discuss the value of a multilevel perspective on resilience that focuses on mediational and moderational effects across social and biological contexts, (c) discuss candidate social and biological processes involved in resilience against depression that show evidence of cross-contextual mediation and moderation, and (d) provide examples of research benefiting from

this multilevel perspective from two studies of children and adolescents at high risk for depression. We conclude with a discussion of potential clinical implications of this approach.

Defining Resilience in the Context of Risk for Depression

We define resilience as a dynamic process through which positive adaptation is achieved in the context of adversity (Luthar, Cicchetti, & Becker, 2000). We view resilience as a *process* rather than a static state or fixed characteristic of an individual (Egeland, Carlson, & Sroufe, 1993). As suggested by this definition, to infer that resilience processes have occurred, a measurable positive outcome must be observed. With regard to child and adolescent depression, most investigators have defined resilience as the absence of a clinical diagnosis of a depressive disorder or low levels of depressive or internalizing symptomatology. Few studies have also included positive indices of social or academic functioning in operationalizing resilience against depression, although we believe there may be value in this approach (Masten, 2001). Other issues in inferring resilience among children at risk for depression include the decision to operationalize depression using categorical or dimensional approaches, and decisions about whether high-risk children who fail to develop depression but develop other psychiatric or behavioral problems should be considered resilient. In addition, the cyclical and recurrent nature of depression complicates decisions about whether or not resilience processes have occurred, as a child may appear resilient at one point in time and nonresilient at another.

Our conceptualization of resilience as a process also highlights the role of ontogenic development, as emerging strengths and vulnerabilities dynamically influence resilience processes at each new stage of development (Egeland et al., 1993). Changes in the manifestations of resilience are particularly likely during developmental transitions in which new risk factors emerge and established protective factors are challenged. Masten (2004) describes these "prevention windows" as periods that occur before and during key developmental transitions when adaptive

social and biological systems are organizing and reorganizing. The transition into adolescence is probably a crucial window for understanding resilience to depression, given significant development of neural and neuroendocrine systems and reorganization of social relationships during this period, as well as the dramatic increase in risk for depression during adolescence compared to earlier in childhood (Birmaher, Ryan, et al., 1996; Masten, 2004). Attention is therefore needed on the ways in which resilience processes may change during this and other developmental phases.

Cross-Contextual Mediation and Moderation of Resilience Processes

We offer a multilevel perspective on resilience against depression that focuses on transactional interactions across contexts, especially social and neurobiological contexts. This perspective builds upon an ecological transactional model that views the development and maintenance of depressive disorders in childhood and adolescence as emerging from the interplay among biological characteristics and the individual's social environment (Cicchetti & Toth, 1998; Sameroff & Chandler, 1975). Emerging insights from the growing fields of social and affective neuroscience suggest that there are bidirectional relationships between social contextual and neurobiological influences on development (Cacioppo, Berntson, Sheridan, & McClintock, 2000). For example, there is now clear evidence that experiences within the social context can alter the organization of neural systems, particularly when they occur during sensitive periods of heightened brain plasticity (Cacioppo et al., 2000; Greenough, Black, & Wallace, 1987). Developing neural systems involved in stress reactivity and emotional processing are sensitive to negative and positive influences in the social environment, particularly the parent–child relationship (Essex, Klein, Cho, & Kalin, 2002; Meaney, 2001). Brain–behavior interactions have typically been studied early in development. However, given new evidence that frontal regions of the brain thought to be implicated in emotion regulation (ER) continue to mature throughout adolescence (Casey, Giedd,

& Thomas, 2000; Giedd, 2004), these regions have the potential for continued plasticity and probably remain sensitive to socialization influences through adolescence.

We argue that a focus on *cross-contextual mediation and moderation* of resilience processes is likely to yield advances in our understanding of resilience against depression. As depicted in Figure 1, *cross-contextual mediation* refers to the potential for social factors to influence children's resilience through their effects on biological factors, or for biological factors to influence children's resilience through their effects on social processes. In the first example, the social context may contribute to adaptive development of the neurobiological systems involved in emotional reactivity and regulation. For example, emotion-related socialization experiences, such as parental responses to children's emotions or the emotional climate of the family or neighborhood, could contribute to neural alterations in systems underlying regulation of sadness or enhancement of pleasant mood. As such, neurobiological processes would mediate the relationship between socialization experiences and children's resilience. Little research has directly investigated this possibility; however, several important studies have demonstrated that experiences within the social environment influence how the brain responds to emotional stimuli (Hooley, Gruber, Scott, Hiller, & Yurgelun-Todd, 2005; Pollak, Cicchetti, Klorman, & Brumaghim, 1997).

Although less widely studied, the effects of biological characteristics on children's resilience may also be mediated by the social context. For example, some evidence suggests that children lower in traitlike emotional reactivity may elicit more positive responses to emotions among caregivers, which in turn are associated with better adjustment (Eisenberg, 1994). In this example, the relationship between neurobiological processes (e.g., emotional reactivity) and children's resilience could be partially accounted for by the social responses (e.g., positive parenting) elicited by these biological characteristics.

As shown in Figure 2, *cross-contextual moderation* refers to the potential for processes within the social context to modify the influence
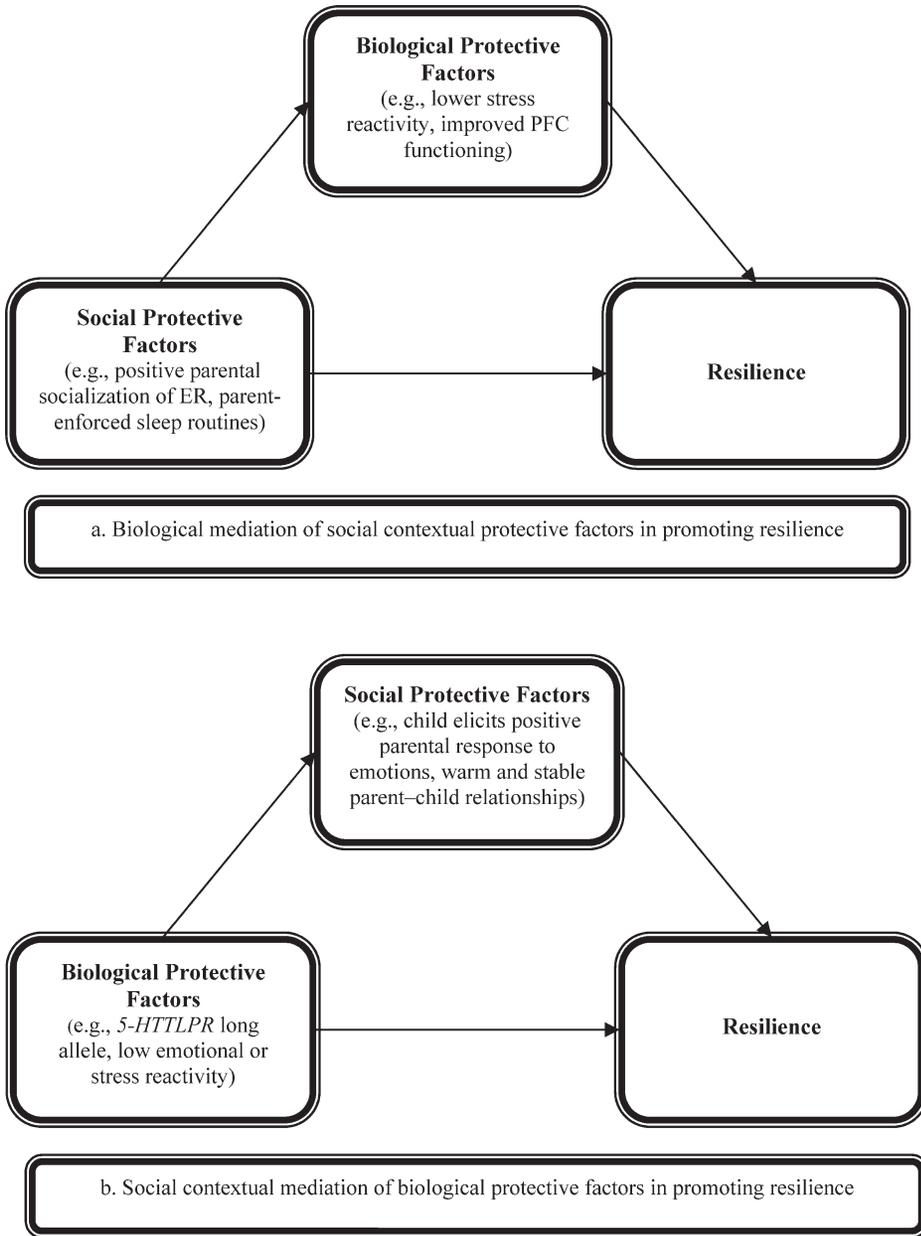
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              ┌─────────────────────────┐
              │  Biological Protective   │
              │         Factors          │
              │   (e.g., lower stress    │
              │ reactivity, improved PFC │
              │       functioning)       │
              └─────────────────────────┘
           ↗                              ↘
┌────────────────────┐            ┌────────────────────┐
│ Social Protective  │            │                    │
│      Factors       │            │     Resilience     │
│ (e.g., positive    │ ─────────→ │                    │
│ parental           │            │                    │
│ socialization of   │            │                    │
│ ER, parent-        │            │                    │
│ enforced sleep     │            │                    │
│ routines)          │            │                    │
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│   a. Biological mediation of social contextual protective factors │
│   in promoting resilience   │
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              ┌─────────────────────────┐
              │ Social Protective Factors│
              │   (e.g., child elicits   │
              │   positive parental      │
              │   response to emotions,  │
              │   warm and stable        │
              │   parent–child           │
              │   relationships)         │
              └─────────────────────────┘
           ↗                              ↘
┌────────────────────┐            ┌────────────────────┐
│ Biological         │            │                    │
│ Protective Factors │            │     Resilience     │
│ (e.g., 5-HTTLPR    │ ─────────→ │                    │
│ long allele, low   │            │                    │
│ emotional or       │            │                    │
│ stress reactivity) │            │                    │
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│ b. Social contextual mediation of biological protective factors   │
│   in promoting resilience   │
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Figure 1. Examples of cross-contextual mediation of pathways to resilience in risk for depression.

of protective and risk factors within the neurobiological context, and for processes within the neurobiological context to modify the influence of protective and risk factors within the social context. Protective processes at either the social or neurobiological level may compensate for or buffer children against risk factors at the other level. For example, the effects of a genetic or neurobehavioral vulnerability to depression may be buffered by growing up in a low-stress caregiving environment (e.g., Eley et al., 2004). The negative effects of severe social stress, such as maltreatment, also appear to be attenuated among children with genetic protective factors (e.g., Kaufman et al., 2006). Extreme levels of adversity at one level may also constrain or limit
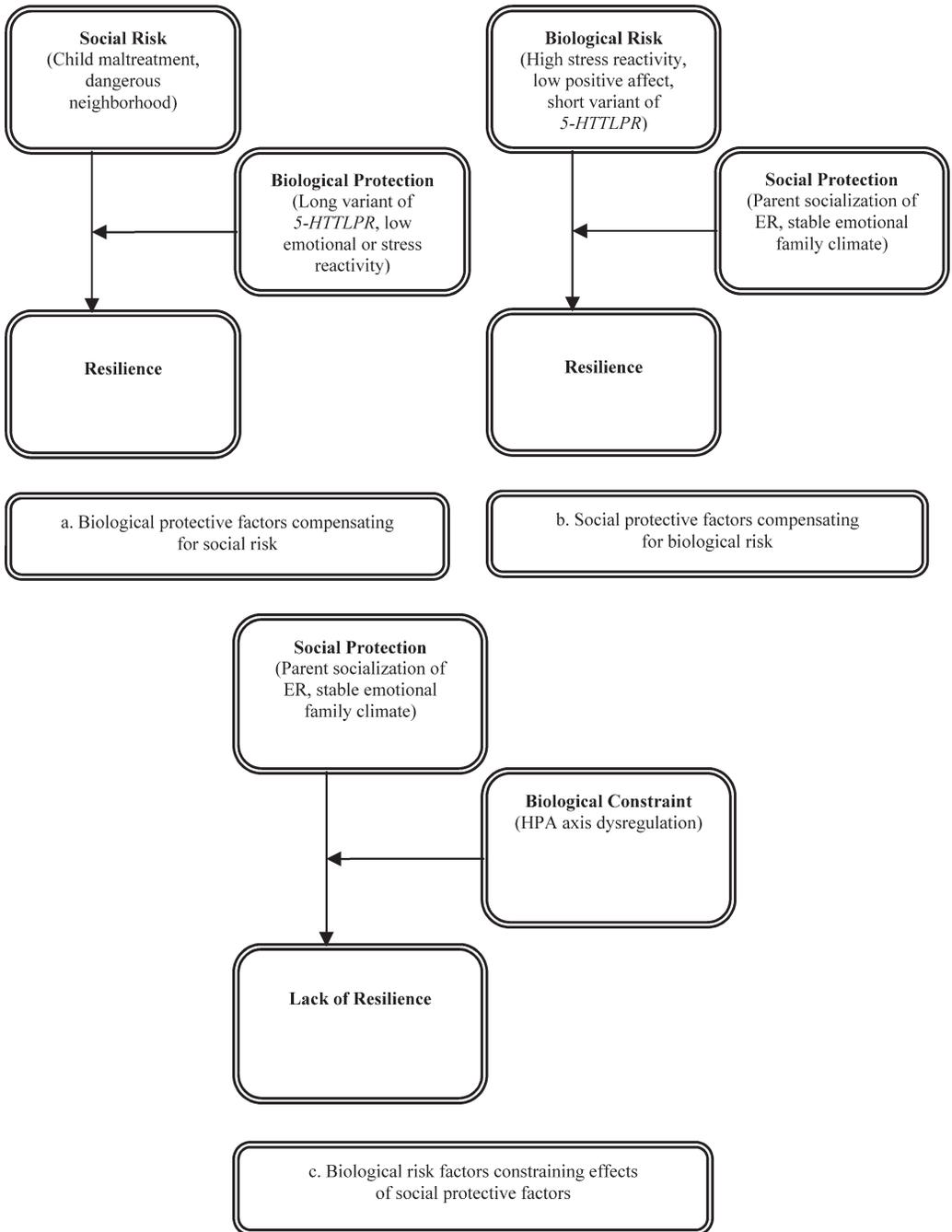
Figure 2. Examples of cross-contextual moderation of pathways to resilience in risk for depression.

the positive influences of protective processes at the other level (e.g., Rutter, O'Connor, & Team, 2004).

Given the prominence of emotional dysregulation in depression, we focus on processes involved in emotional reactivity and regulation in understanding resilience in the face of risk for depression. We define ER as the internal and external processes involved in the initiation, maintenance, or modification of the quality, intensity, or chronometry of emotional responses (Forbes & Dahl, 2005). Emotional reactivity,

in contrast, refers to individual differences in the intensity of an individual's response to an emotional stimulus (Derryberry & Rothbart, 1997). A growing number of studies suggest that failure to regulate negative emotions adaptively is associated with internalizing symptoms among young children and with depressive symptoms and disorders among older children and adolescents (Eisenberg et al., 2001; Garber, Braafladt, & Weiss, 1995; Rubin, Coplan, Fox, & Calkins, 1995; Sheeber, Allen, Davis, & Sorensen, 2000; Silk, Steinberg, & Morris, 2003). Although most research in the area of depression has considered problems in emotional reactivity and regulation as risk factors, low levels of negative emotionality, high levels of positive emotionality, and/or the ability to effectively regulate emotions may contribute to resilience among children at risk for depression (Masten, 2004).

Social Contextual Mechanisms of Resilience in Children at Risk for Depression: Socialization of ER

Over decades, research has led to the identification of many processes within the social environment that are associated with children's resilience. These include positive characteristics of the family and community such as warm and responsive parents, harmonious interparental relationships, a supportive and close relationship with one parent or an adult outside of the family, prosocial friends, effective schools, and safe neighborhoods (see Masten, 2004; Masten, Best, & Garmezy, 1990; Rutter, 1990). The social context is likely to be of particular relevance to depression based on evidence of increased interpersonal sensitivity among depressed children (Rudolph, Hammen, & Burge, 1997).

Although a review of social mechanisms in resilience is beyond the scope of this paper, we highlight social contextual processes implicated in the socialization of emotion and ER. We believe that parents have the potential to contribute to children's resilience against risk for depression by socializing adaptive and flexible skills for managing emotion. Broader contextual influences are also likely implicated in the socialization of ER, including interactions with peers, other family members, and other supportive adults such as teachers, neighbors, or coaches, particularly with children's increasing developmental status and contact with adults outside of the family. However, very little research to date has examined the role of the broader social context in children's development of skills for regulating emotion.

Parents are key social resources in supporting the acquisition and refinement of skills and strategies for regulating emotions (Eisenberg, Cumberland, & Spinrad, 1998; Gottman, Katz, & Hooven, 1996). Parental socialization of ER occurs through at least three mechanisms (Morris, Silk, Steinberg, Myers, & Robinson, 2007): observational learning, modeling, and social referencing (e.g., Parke, 1994), practices specifically related to emotion and ER (e.g., Eisenberg et al., 1998), and the emotional climate of the family (e.g., Cummings & Davies, 1994). First, children receive implicit messages about how to express and manage emotions by observing the emotional responses and ER strategies used by their parents (Denham et al., 1997). Children of depressed mothers have been found to show a limited repertoire of ER strategies, and to utilize strategies that are considered to be less effective compared to children of never depressed mothers (Garber Braafladt, & Zeman, 1991; Silk, Shaw, Skuban, Oland, & Kovacs, 2006). These problems in ER are presumed to result from modeling of depressed mothers' maladaptive ER responses, although research has not directly tested this assumption.

Second, parents engage in specific emotion-related parenting practices that are believed to influence children's ability to regulate emotion. For example, parental responses to children's emotions and parents' meta-emotion philosophies convey implicit and explicit messages about how to manage emotions (Eisenberg, Fabes, & Murphy, 1996; Gottman et al., 1996). Positive responses to emotions can support ER by encouraging or providing models of potentially adaptive ER strategies. Parents may initiate a strategy or, as is often the case for older children and adolescents, may help the child to discuss or enact a strategy he or she has initiated. These supportive responses help children and adolescents refine and rehearse strategies for managing emotion that can be relied upon

during interactions with peers in the neighborhood and at school.

In contrast, parents who view negative emotions as aversive, or who lack a sense of efficacy in their own ability to manage emotions, may minimize or criticize their children's emotional displays (Gottman, Katz, & Hooven, 1997). These negative responses, that have the effect of upregulating versus downregulating negative emotions, are hypothesized to interfere with the development of ER over time by encouraging the suppression of emotion and the use of avoidant or aggressive ER strategies (Eisenberg et al., 1996). Growing evidence demonstrates that parents' meta-emotion philosophies and responses to children's emotions are related to the development of ER and subsequent psychosocial adjustment (Eisenberg et al., 1996; Gottman et al., 1996).

Third, children's ER is thought to be influenced by the emotional climate of the family, as reflected in the quality of the attachment relationship, styles of parenting, family expressiveness, and the quality of the marital relationship (Cummings & Davies, 1994). Important components of the emotional environment include the overall predictability and stability of the environment, the degree of positive emotionality expressed in the family, and the degree of negative emotionality expressed in the family (Morris et al., 2007). Evidence suggests that disruptions in the emotional climate of the family are an important mechanism in the intergenerational transmission of depression (Cummings & Davies, 1994). Parents can therefore contribute to resilience in children at risk for depression by engendering an emotional climate within the family that is conducive to a sense of emotional security.

Cross-contextual mediation and moderation of the socialization of ER

Although little research has directly tested this proposition, we argue that the influences of parental socialization of ER on children's resilience are probably mediated by the biological context. In other words, social relationships probably contribute to the development of neural systems that are involved in promoting resilience. Hofer (1987) provided evidence,

initially from animal models, demonstrating that social relationships can serve to regulate physiological systems. From this perspective, adaptive socialization of ER might contribute to optimal development of neural systems underlying emotional reactivity and regulation. This possibility is consistent with evidence that socioemotional experiences can alter the organization of neurobiological systems (Greenough et al., 1987).

Consistent with this proposition, Gottman et al. (1996) found that parents who reported more adaptive coaching of children's emotions had children who were higher in vagal tone, which is thought to indicate flexible emotional response and effective regulation. Although this work was based on cross-sectional data, it suggests the possibility that emotion coaching could contribute to more optimal functioning of physiological regulatory systems. Evidence consistent with a mediational model also comes from studies of altered neural functioning among populations exposed to atypical emotion socialization experiences. For example, Pollak and colleagues have examined event-related potentials to affective stimuli among maltreated children, who provide an example of exposure to extreme aberrations in the emotional climate of the family (Pollak et al., 1997). Compared to normal controls, maltreated children showed a greater P300 to angry faces relative to happy faces, suggesting greater reactivity of brain structures involved in processing negative emotion among children exposed to maltreatment (Pollak et al., 1997).

In a relevant functional magnetic resonance imaging study, Hooley et al. (2005) found differences in activation of the dorsolateral prefrontal cortex (DLPFC) to parental critical statements among adults with a history of depression versus controls. Relative to control subjects, participants with a history of depression failed to activate the DLPFC when their parents made critical remarks. The DLPFC is an area of the PFC that has been implicated in effortful regulation of attention and emotion (Phillips, Drevets, Rauch, & Lane, 2003). This suggests that adults with a history of depression may not engage in expected ER processes in response to parental criticism. This finding raises the possibility that socialization experiences may influence the neural substrates of emotion

processing in depressed individuals, especially for interpersonally relevant emotional material. Although little work has been carried out integrating emotion-related socialization experiences with neurobiological measures of emotion processing, these initial studies highlight the potential value of this approach. These studies, however, have not directly tested whether changes in neural structures actually mediate the relation between socialization experiences and children's adjustment. Prospective, longitudinal research measuring both neurobiological and social processes at multiple time points will be required to formally test such mediational models.

Theory and research also suggest that emotion related socialization experiences interact with neurobiological mechanisms in predicting children's resilience. Researchers have proposed that the influence of parental socialization of ER on children's socioemotional functioning depends on the child's emotional reactivity, presumed to vary as a function of neurobiological regulatory mechanisms (Calkins, 1994; Morris et al., 2007). Children who are emotionally reactive tend to experience more frequent and intense levels of emotional arousal, and as a result, will require successful emotion regulatory skills to manage such arousal. We argue that highly reactive children stand to benefit the most from parenting practices related to refining and rehearsing skills for regulating emotions, but also stand to be harmed the most by critical and minimizing responses to emotions.

There is a paucity of research that has directly examined interactions among emotion socialization and negative reactivity. A growing literature on Parenting × Temperament interactions, however, suggests that negative reactivity moderates the influence of the parent–child relationship on children's internalizing symptoms. These studies show that the effects of negative parent–child relationships on children's internalizing symptoms are amplified among children who are high in negative reactivity (Belsky, Hsieh, & Crnic, 1998; Gilliom & Shaw, 2004; Morris et al., 2002). From a resilience perspective, these findings raise the possibility that positive parent–child relationships might serve as a buffer against internalizing symptoms for children who are high

in negative reactivity. Findings also suggest that low levels of reactivity to negative emotional stimuli may promote resilience in the context of environmental stress.

Biological Mechanisms of Resilience in Risk for Depression

Although few researchers in the affective neurosciences have framed their findings from within a resilience perspective, there is actually a growing body of evidence suggesting that neurobiological processes play an important role in resilience among children and adolescents at risk for depression. In this section, we identify four candidate neurobiological mechanisms associated with emotional reactivity and regulation that may contribute to resilience processes in depression: genetic factors, function of neural systems of positive affect and reward, stress reactivity, and sleep. For each neurobehavioral processes, we provide evidence suggestive of cross-contextual mediation and/or moderation effects by which the social context influences or modifies the effects of resilience processes at the biological level, or the biological context influences or modifies the effects of resilience processes at the social level.

Genetic factors in resilience in children at risk for depression

Although geneticists have generally thought of genes as risk factors, there is increasing recognition that genetic factors also contribute to resilient adaptation (Curtis & Cicchetti, 2003). These contributions are probably at least partially mediated by the social environment, as it is now widely recognized that environmental factors modulate gene expression (Gottlieb, 1998). Changes in gene expression associated with environmental stress have, in fact, been implicated in the development of affective disorders (Post, Weiss, & Leverich, 1994).

A recent wave of research on gene–environment interactions has also provided evidence that the social context moderates the effects of genetic risk factors on the development of depression (Caspi et al., 2003; Eley et al., 2004; Kaufman et al., 2006; Kendler, Kuhn, Vittum, Prescott, & Riley, 2005). One candidate gene

variant that appears to play a role in resilience among individuals at risk for depression is the serotonin transporter length polymorphism repeat (5-HTTLPR). Studies suggest that individuals homozygous for the 5-HTTLPR short allele are at increased risk for 5-HT mediated psychopathology, such as depressive disorders, but only in the context of environmental risk (Caspi et al., 2003; Eley et al., 2004; Kendler et al., 2005).

In a widely cited example, Caspi et al. (2003) reported that the 5-HTTLPR moderated the influence of stressful life events on the development of depression in adults. Individuals with one or two copies of the short allele of the 5-HTT promoter polymorphism exhibited more depressive symptoms and depressive disorders in relation to stressful life events than individuals homozygous for the long allele. Kendler et al. (2005) also reported a gene–environment interaction, demonstrating that stressful life events had little impact on depression risk for adults possessing the SL and LL genotypes of the 5-HTTLPR. This finding has also been replicated among adolescent girls (Eley et al., 2004).

Animal studies have also established that stressful social environments can have enduring behavioral effects associated with changes in brain serotonergic systems (Suomi, 2000). For example, Bennett et al. (2002) found associations between the short allele and lower cerebrospinal fluid concentration of the serotonin metabolite 5-hydroxyindoleacetic acid (CSF 5-HIAA) concentrations in rhesus monkeys, but only in those raised by peers rather than mothers, indicating an environment dependent effect of the 5-HTTLPR genotype on central nervous system 5-HT functioning.

Evidence suggests that the effects of genetic variations in the serotonergic system on depression risk may be mediated by amygdala reactivity to environmental threat (Hariri et al., 2002, 2005). Hariri et al. (2002) have shown enhanced amygdala reactivity to affective stimuli among individuals carrying the 5-HTTLPR short allele compared to individuals homozygous for the long allele. Short allele carriers have also been shown to have reduced gray matter volume in the perigenual anterior cingulate cortex and amygdala, two brain areas critical for processing negative emotion (Pezawas et al., 2005). Evidence also points to a moderate decoupling of the amygdala–cingulate feedback circuit among short allele carriers, suggesting that this polymorphism may alter the structure and connectivity of neural structures involved in ER (Pezawas et al., 2005).

Overall, these findings suggest that possessing the long allele of 5-HTTLPR is one example of a genetic protective factor that has the potential to compensate for risks within the social environment. Initial evidence suggests that the protective effects of this gene may operate by reducing the reactivity of neurobiological systems to emotional and threatening stimuli in the environment. Conversely, these findings also suggest that genetic risk (e.g., possessing the short allele of the 5-HTTLPR) can also be compensated for by social factors, such as living in a low-stress environment.

The role of positive affect and reward systems in resilience in children at risk for depression

Another set of biologically based systems hypothesized to play a role in children's resilience in the context of risk for depression are motivational systems involved in the generation and regulation of positive affect and reward-related behavior (Forbes & Dahl, 2005). Behavioral scientists are increasingly recognizing the role of positive emotions in contributing to mental health and adjustment (Seligman & Csikszentmihalyi, 2000). Models of depression, including emotion-based, motivational, and behavioral models, all implicate disruptions in positive affect systems in depression (Clark & Watson, 1991; Depue & Iacono, 1989; Lewinsohn, Hoberman, Teri, & Hautzinger, 1985). Prominent symptoms of depression, such as anhedonia, social withdrawal, and reduced activity level can also be conceptualized as reflecting altered positive affect and reward processing. Depression may involve decreased motivation to obtain reward, reduced frequency of reward-seeking behavior, or diminished experience of rewarding outcomes (Forbes & Dahl, 2005). In line with these theoretical models and clinical observations, there is growing evidence for altered positive affect systems in adult depression across several domains, including self-report and physiological and behavioral

responses to positive emotional stimuli (for a review, see Forbes & Dahl, 2005).

Neurobiological measures have the potential to contribute to our understanding of positive affect and reward-related processes implicated in resilience against depression. Neural circuits implicated in reward processing include the striatum, orbitofrontal cortex, amygdala, and the dopamine neurotransmitter system (for a review, see Schultz, 2000). Neuroimaging studies of depression in adults have indicated disruption in the structure and function of several reward-related brain areas (Drevets, 2001; Lawrence et al., 2004). If replicated in studies with children and adolescents, these findings could suggest a role for greater activation of neural circuits associated with positive affect in children's resilience in the context of risk for depression.

Research on frontal electroencephalogram (EEG) asymmetry indicates that greater relative left frontal activation of the cerebral cortex may be one neurobiological marker of approach-related behavior that could contribute to resilience in the context of depression risk. Left frontal EEG asymmetry is postulated to be correlated with approach behavior, including positive affect (Davidson & Fox, 1982). Depressed adults and infants of depressed mothers exhibit decreased left frontal resting EEG activity (Dawson et al., 1999; Henriques & Davidson, 1991). These findings suggest that a tendency toward greater approach-related behavior, as reflected in greater relative left frontal EEG activity, may be a protective factor in depression. More research on clinical samples of older children and adolescents is needed, however, to further test this speculation.

Although several studies have reported that low subjective positive affect is associated with child and adolescent depression (Forbes, Williamson, Ryan, & Dahl, 2004; Lonigan, Phillips, & Hooe, 2003), few studies have utilized neurobiological indices of reward-related behavior in depressed children. Supportive evidence, however, comes from several recent behavioral studies (Forbes, Shaw, & Dahl, 2007; Jazbec, McClure, Hardin, Pine, & Ernst, 2005; Silk, Shaw, Forbes, Lane, & Kovacs, 2006). For example, Jazbek et al. (2005) found that although healthy adolescents modulated performance on an antisaccade task as a function of monetary incentives, depressed adolescents' performance was not influenced by manipulations of reward incentives.

Positive affect as a moderator of social contextual risk. Recent behavioral studies with children at risk for depression also provide preliminary evidence that positive affect systems may buffer the effects of an adverse social context on the development of internalizing problems (Forbes et al., 2007; Silk, Shaw, Forbes et al., 2006). For example, we have reported evidence for moderation effects of positive emotionality in a study of children of mothers with childhood onset of depression (Silk, Shaw, Forbes, et al., 2006). In this study, children's affective displays and ER strategies were coded during a delay of gratification task. We found that the link between parental depression and internalizing symptoms was attenuated among children who displayed high positive affect and excitement about receiving the prize. These findings suggest that the ability to experience and upregulate positive emotion in a negative emotion-inducing context may be a protective factor against internalizing problems for children of depressed mothers (Silk, Shaw, Forbes, et al., 2006). Low motivation and emotional withdrawal among depressed mothers may result in a family environment with less naturally occurring reward experiences and less reciprocity of positive emotions. Thus, children who are more self-sufficient at seeking out and upregulating positive affect may be buffered against the negative effects of this family environment.

Although preliminary, these results suggest that children who are more prone to seek out and enjoy rewarding experiences may find sources of joy and happiness in otherwise adverse social contexts. Future research using neurobiological measures of positive affect systems, such as functional magnetic resonance imaging and EEG methods, as well as direct measures of the social environment, are needed to further test this model.

The role of stress reactivity in resilience in children at risk for depression

Neuroendocrine research on stress reactivity also provides evidence that neurobiological responses

to adverse experiences in the environment are associated with risk for depression (McEwen, 1998; Meyer, Chrousos, & Gold, 2001). The neural substrate of the stress response includes two distinct systems: the corticotropin-releasing hormone (CRH) system and the locus coeruleus–norepinephrine (LC-NE) system. These systems are functionally linked, and are also linked with regions of the brain involved in emotional processing, including the amygdala, the anterior cingulate, the mesolimbic dopaminergic system, and the medial PFC (McEwen, 1998; Meaney, 2001).

Activation of the CRH and LC-NE systems produces a coordinated set of physiological and behavioral changes that prepares the individual for a "fight or flight" response. Individuals who are high in stress reactivity mount excessively vigorous or persistent responses to stressors that may have been evolutionarily adaptive in the prehistoric human environment, but when chronically activated, are associated with pathogenic processes (McEwen, 1998). For example, chronic elevated glucocorticoid secretion is associated with adverse effects on neural structure and function, particularly in the hippocampus, including decreased dendritic branching, neuronal loss, changes in synaptic terminal structure, and inhibition of the neuron regeneration (Bremner & Vermetten, 2001; Sapolsky, 1996).

These degenerative processes in brain regions associated with the regulation of emotion may be one mechanism through which stress reactivity is associated with depression (Meyer et al., 2001). A large body of research from studies of depressed adults supports the role of dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis in adult MDD (Plotsky, Owens, & Nemeroff, 1998). Evidence suggests that children exposed to maternal depression during infancy show elevated cortisol responses later in childhood (Ashman, Dawson, Panagiotides, Yamada, & Wilkinson, 2002; Essex et al., 2002). Several studies have also linked elevated baseline cortisol and elevated cortisol in response to social stressors to increased levels of internalizing symptomatology (Ashman et al., 2002; Granger, Weisz, McCracken, Ikeda, & Douglas, 1996; Klimes-Dougan, Hastings, Granger, Usher, & Zahn-Waxler, 2001).

Reports of altered functioning of stress response systems in clinically depressed children and adolescents, however, have been inconsistent, with most cross-sectional studies finding no differences in HPA axis activity among depressed children and normal controls (Birmaher, Dahl, et al., 1996; Dahl et al., 1989, 1992; Dorn et al., 1996; Ryan & Dahl, 1993). Some studies have reported elevated cortisol secretion in child and adolescent depression around sleep onset, particularly among adolescents and among maltreated children with depressive symptoms (Dahl et al., 1991; Forbes et al., 2006; Hart, Gunnar, & Cicchetti, 1996; Kaufman et al., 1997). Longitudinal research suggests that elevated levels of plasma cortisol at sleep onset in adolescence are associated with a recurrent course of MDD into adulthood (Rao et al., 1996). Although inconclusive, these findings indicate a potential role for altered stress reactivity in the development of internalizing symptoms and depression among subtypes of children and adolescents.

The social context mediates and moderates the effects of stress reactivity. Research on stress reactivity also highlights the role of protective processes in the social context that can contribute to lower levels of stress reactivity, or can buffer children from the negative effects of high stress reactivity. First, research on children and nonhuman primates provides evidence that adverse early environments and early trauma predispose individuals toward greater stress reactivity (Essex et al., 2002; Meaney, 2001). For example, when infant rodent pups are separated from their mothers for prolonged periods, they show chronically upregulated CRH activity in the HPA axis, amygdala, bed nucleus of the stria terminalis, and the LC (Meaney, 2001; Sanchez, Ladd, & Plotsky, 2001). Some studies in human and nonhuman primates also find evidence of blunting or downregulation of the adrenocortical response associated with chronic exposure to adverse early rearing conditions (Boyce, Champoux, Suomi, & Gunnar, 1995; Gunnar & Vazquez, 2001). Studies in both human and nonhuman primates highlight the centrality of close and nurturing early attachment relationships in the adaptive development

of the stress response system (Hertsgaard, Gunnar, Erickson, & Nachmias, 1995; Hofer, 1987; Meaney, 2001). Relationships within the social context may therefore promote resilience by contributing to the development of less reactive CRH and LC-NE systems.

Second, stress reactivity interacts with social contextual factors such that highly reactive individuals are at the greatest risk for maladjustment if they are also exposed to a negative social environment. As argued by Belsky (2005), children vary in their susceptibility to influences within the social environment. Boyce and Ellis (2005) refer to this phenomenon as "biological sensitivity to context," and argue that highly reactive children are more sensitive to both the positive and negative influences of the social environment. Suomi's (1997) research with rhesus macaques provides a compelling example of this phenomenon. In this study, rhesus macaques were bred for high or average levels of stress reactivity, and were cross-fostered by nurturing or average mothers. Highly reactive infants raised by average mothers had the worst developmental outcomes, and highly reactive infants raised by nurturing mothers had the best developmental outcomes. These findings provide further evidence that positive social relationships can promote resilience even in the context of biological vulnerability. Furthermore, there is evidence from both animal and human studies that a positive caregiving environment can modify the adverse effects of early stress on HPA axis functioning (Barbazanges et al., 1996; Francis, Diorio, Plotsky, & Meaney, 2002; Kaufman et al., 1997).

Neurobehavioral processes, such as stress reactivity, may also place limitations on the influence of protective factors within the social context. In the following example, we present an analysis of data collected from a low socioeconomic status (SES) sample of boys exposed to varying levels of neighborhood adversity. We hypothesized that positive family relationships and ER skills would buffer against depression in this high-risk sample. This example highlights, however, that exposure to high levels of adversity may limit the protective potential of positive social factors that normally contribute to adaptive ER and reduced risk for depression.

Study 1

Participants and procedure

Participants in this study were part of the Pitt Mother and Child Project (PMCP), an on-going longitudinal study of risk and resilience in low-income boys. More details on the methods are available in earlier publications (Shaw, Gilliom, Ingoldsby, & Nagin, 2003). In 1991 and 1992, 6- to 27-month-old boys ($N = 310$) and their mothers were recruited from Allegheny County Women, Infants, and Children Nutrition Supplement Clinics. The sample was primarily European American and African American (53 and 41%, respectively), with a mean per capita income of $241 per month ($2,892 per year) and an average Hollingshead SES score of 24.5, or working class. Consequently, a large proportion of the families in this sample were considered high risk because of low SES status. Of the initial 310 participants, 90–95% completed visits at ages 5 and 6, and some data are available on 89% of participants at ages 10, 11, or 12.

Target boys and their mothers participated in home and/or lab visits at ages 1.5, 2, 3.5, 5, 5.5, 6, 8, 10, 11, and 12. Mothers completed various questionnaires on sociodemographic information, child behavior, and family issues, such as marital quality, parenting, and maternal depression. Mothers and target children were also videotaped during various interaction tasks. At ages 6–12, teachers completed several questionnaires on the child's adjustment.

Child behavioral distraction was assessed observationally during a waiting task at age 3.5 (Marvin, 1977). Family characteristics included parent–child relationship quality (composite of the openness and conflict factors of the Adult–Child Relationship Scale at ages 5 and 6; Pianta, Steinberg, & Rollins, 1995), maternal nurturance (sum of acceptance and verbal/responsivity subscales on the Home Observation for Measurement of the Environment at age 2; Caldwell & Bradley, 1984), maternal depressive symptomatology (composite of total scores on the Beck Depression Inventory at child ages 1.5, 2, 3.5; Beck, Rush, Shaw, & Emery, 1979), and marital quality (composite of scores on the Marital Adjustment Test at

ages 1.5, 2, and 3.5; Locke & Wallace, 1959). Adversity was established at the community level by averaging standardized 1990 and 2000 census variables (e.g., percentage unemployed, percentage families in poverty, percentage on public assistance) to determine neighborhood risk. To create a measure of positive child adjustment at ages 11 and 12 that incorporated the absence of a negative outcome *and* the presence of a positive outcome, mother-rated child internalizing scores (Child Behavior Checklist; Achenbach, 1991) were subtracted from a composite of mother- and teacher-rated social skills (Social Skills Rating System; Gresham & Elliott, 1990). This was done to ensure that "positive adjustment" not only reflect an absence of internalizing but also included a measure of positive functioning.

Although analyses were conducted using the continuous measure of positive adjustment described above, we also explored the data to see how many children in this high-risk sample had better than expected outcomes (i.e., below the sample median for externalizing behavior *and* above the sample median for social skills). Using this strategy, 80 out of 300 children could be classified as "positively adjusted."

Results

Estimated trajectories of neighborhood risk. Following a semiparametric, group-based approach for analyzing trajectories (Nagin, 1999),

children were assigned to trajectories of neighborhood risk based on their individual data from ages 1.5 to 10 (for more details, see Vanderbilt-Adriance & Shaw, 2007). The Bayesian information criteria (BIC), which informs the selection of the optimal number of trajectories, was compared for three-, four-, five-, and six-group models, and the five-group model was ultimately selected as the most appropriate model (BIC = −1889.18; see Figure 3). BIC scores emphasize parsimony and impose a penalty for each additional trajectory group (taking into account sample size). Model selection was corroborated by high posterior probabilities (.89–.98), indicating that the trajectories were reasonably accurate in representing the observed data. Two of the groups were considered to reflect higher neighborhood risk (high chronic and high descending risk) and three groups reflected lower neighborhood risk (lowest stable, low stable, and moderate stable risk).

Direct effects of child and family factors. In line with hypotheses, high levels of observed child behavioral distraction ($r = .15, p < .05$), maternal nurturance ($r = .19, p < .01$), parent–child relationship quality ($r = .43, p < .001$), marital quality ($r = .14, p < .05$), and low levels of maternal depressive symptomatology ($r = −.20, p < .01$) were all associated with higher levels of child positive adjustment.
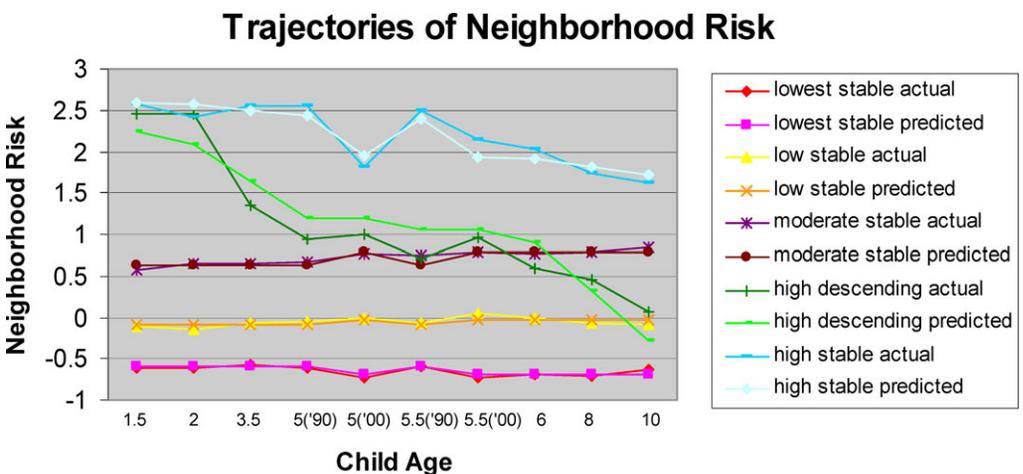

Figure 3. Trajectories of neighborhood risk. [A color version of this figure can be viewed online at www.journals.cambridge.org]

Interactions between protective factors and neighborhood risk. To examine the hypothesis that the relationship between the protective factors and positive outcome would be moderated by the level of neighborhood risk, a series of hierarchical regressions were conducted. Independent variables were centered prior to creating interaction terms, and the neighborhood risk trajectories were dummy coded. With the chronic risk trajectory as the reference group, there was a significant interaction between the low-risk trajectory and parent–child relationship quality ($B = .67, p < .05$; see Figure 4). Post hoc analyses explored the relationship between the protective factor and positive outcome separately within each trajectory group. High levels of parent–child relationship quality were associated with high positive adjustment for children in the three lowest risk trajectory groups (lowest risk: $B = .78, p < .01$; low risk: $B = .94, p < .001$; moderate risk: $B = .52, p < .001$), but not for children experiencing high descending or chronic neighborhood risk (all *ns*).

With the high descending risk trajectory as the reference group, there was a significant interaction between the second lowest risk trajectory and marital quality ($B = .04, p < .05$; see Figure 4) and maternal depressive symptomatology ($B = -.14, p < .05$; see Figure 4). Post hoc analyses revealed that high levels of marital quality were associated with child positive adjustment only for those in the low-risk trajectory group ($B = .03, p < .01$). Finally, low levels of maternal depressive symptomatology were associated with positive child adjustment only in the context of low and moderate neighborhood risk ($B = -.11, p < .01$; $B = -.06, p < .05$, respectively).

Discussion

This example highlights several important points. Children's skill in using behavioral distraction to regulate emotion, as well as social contextual factors associated with the emotional climate of the family (maternal nurturance, parent–child relationship quality, marital quality, and low levels of maternal depressive symptomatology) all predicted positive adjustment, defined by low levels of internalizing and high levels of social skills. It should be

noted, however, that some of these direct effects were small and should be interpreted cautiously. More importantly, the findings point to important interactions across levels of context. Parent–child relationship quality, marital quality, and low levels of maternal depressive symptomatology were all found to be moderated by the level of neighborhood adversity in predicting positive functioning. In all three cases, the protective effects of these social contextual factors were attenuated among children at higher (descending or chronic) levels of neighborhood risk. This suggests that elevated neighborhood level adversity has the potential to constrain or limit the benefits of protective factors at other levels. Specifically, family context factors that normally lead to a sense of emotional security and adaptive ER may not promote well-being in the context of chronic stress and arousal.

Although we do not have biological data on the children in this study, this finding raises the possibility that neurobiological factors, such as stress reactivity, are implicated in the constraining effect of neighborhood adversity. For example, a chronically unsafe environment may lead to increased HPA axis reactivity and subsequent pathogenic effects on neural structures (McEwen, 1998), which in turn, might limit the potential effects of social protective factors. This is consistent with other evidence that exposure to early stress and adversity may cause damage to neural structures or result in persistent negative effects on the neuroendocrine system. For example, research on institutionalized Romanian children indicates persistent effects of early social adversity even among some infants who were later adopted and reared in positive caregiving environments (Rutter et al., 2004). Chronic arousal associated with neighborhood adversity may also interfere with other biological systems implicated in ER, such as systems involved in sleep and arousal.

The role of sleep in resilience in children at risk for depression

Another potential protective factor against depressive disorders in childhood and adolescence is obtaining adequate quantity and quality of sleep. Although the exact function of sleep
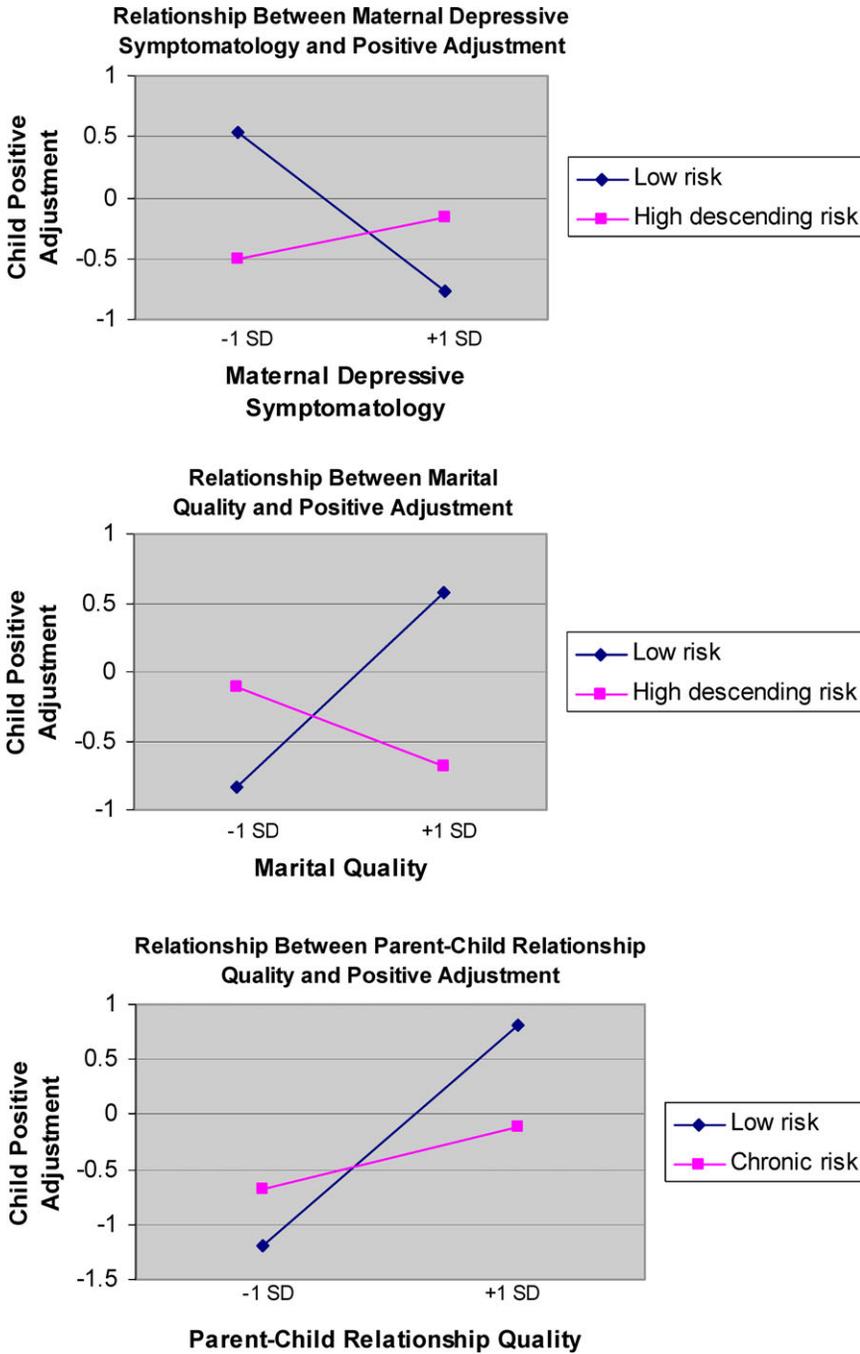
Figure 4. Interactions between social context and neighborhood risk. [A color version of this figure can be viewed online at www.journals.cambridge.org]

remains unknown, there is increasing evidence that sleep promotes more adaptive and integrated control of behavior, emotion, and attention (Dahl, 1996b). Good sleep during childhood and adolescence may therefore contribute to resilience by maintaining or enhancing children's ability to regulate emotion. Support for this mechanism comes primarily from studies of the effects of sleep deprivation. Anyone who has stayed up all night writing a paper or

caring for a newborn is well aware of the effects sleep loss can have on one's subsequent ability to control mood and emotions. In research with children, sleep deprivation has been associated with difficulties of focusing attention, a decreased threshold to express negative affect, and difficulty modulating impulses and emotions (Dahl, 1996a). In particular, lack of sleep appears to have the strongest influence on integration across affective and cognitive systems (Dahl, 1996b).

Sleep and depression. A large body of literature implicates sleep dysregulation in adult depression, with several studies suggesting that sleep difficulties precede the onset of depressive disorders (for a review, see Riemann & Voderholzer, 2003). The most consistent findings from adult samples include difficulty falling asleep and staying asleep, decreased latency to rapid eye-movement (REM) sleep, higher density of REM sleep, and decreased slow-wave sleep (Benca, Obermeyer, Thisted, & Gillin, 1992). Subjective sleep complaints are common in children and adolescents with MDD (Bertocci et al., 2005; Ryan et al., 1987). However, studies comparing depressed children and adolescents with normal controls using objective EEG measures of sleep polysomnography have produced inconsistent findings. Among prepubertal depressed children, there is limited evidence for increased sleep latency (Emslie, Rush, Weinberg, Rintelmann, & Roffwarg, 1990) and decreased REM latency (Dahl et al., 1994; Emslie et al., 1990); however, most studies have failed to find differences between depressed children and controls (Dahl et al., 1996; Puig-Antich et al., 1983).

Several studies of depressed adolescents have found evidence of increased sleep latency, reduced REM latency, and decreased sleep efficiency (Dahl et al., 1990, 1996; Emslie, Rush, Weinberg, Rintelmann, & Roffwarg, 1994; Kutcher, Williamson, Marton, & Szalai, 1992), although these differences are not always reported (Goetz et al., 1987; Khan & Todd, 1990). Increased REM density has also been seen in some studies, and has been linked with recurrence of depressive episodes (Rao et al., 1996). A meta-analysis of sleep studies across the life span suggests that decreased sleep latency is the strongest factor in differen-tiating depressed and control subjects under the age of 20 (Benca et al., 1992). No differences have been reported in Stage 3 or Stage 4 sleep.

Few studies have considered the role of sleep in children as a potential protective process. In the next example we present new evidence from a reanalysis of our data suggesting that sleep may promote resilience to depression among children at high risk for depressive disorders.

Study 2

Participants and procedure

This report focuses on a subsample of participants at high genetic risk for depression who participated in a sleep study using polysomnography during childhood and who were followed up with yearly psychiatric evaluations into young adulthood. Given evidence for puberty-related changes in sleep systems (Carskadon, Acebo, & Jenni, 2004), we focused on a narrow age range of children who were prepubertal (Tanner Stage 1) at their initiation into the study. Participants ($N = 22$, 14 females) ranged in age from 6 to 11 ($M = 8.60$, $SD = 1.69$) at their initial assessment. Participants were reassessed annually until reaching adulthood. The follow-up period ranged from 8 to 17 years ($M = 13.41$, $SD = 2.25$). Participants' ages at the last assessment ranged from 18 to 29 years ($M = 21.93$, $SD = 2.61$).

High familial genetic risk for depression was determined at the initial assessment by requiring participants to have at least one first-degree and at least one second-degree relative with a lifetime history of one of the following four types of depression: childhood onset, recurrent, bipolar, or psychotic depression. In addition, the high-risk children were required to have no lifetime episode of any mood disorder. Children were allowed to have other psychiatric disorders, including anxiety disorders ($N = 5$) and behavior disorders ($N = 3$).

The methods for the initial study have been described in detail elsewhere and are reviewed here briefly (Dahl et al., 1996). Participants were recruited from radio and newspaper advertisements. Structured diagnostic interviews were administered to establish lifetime and present psychiatric diagnoses and familial genetic loading for affective disorder. Subjects' lifetime and present

DSM-III-R (American Psychiatric Association, 1987) psychiatric symptomatology was assessed using the Kiddie Schedule for Affective Disorders and Schizophrenia—Epidemiologic Version (K-SADS-E; Orvaschel, Puig-Antich, Chambers, Tabrizi, & Johnson, 1982) and the K-SADS (6–18 Years)—Present Episode Version (Chambers et al., 1985), respectively, with both the child and parent(s) or guardian(s) serving as informants. To determine familial loading for mood disorders, first-degree and second-degree relatives were directly interviewed using the K-SADS-E for relatives aged 6–18 years and the SADS—Lifetime Version (SADS-L; Endicott & Spitzer, 1978) for adult relatives. Adult first-degree and second-degree relatives unavailable for direct interview were assessed indirectly using a modified version of the Family History Interview (Weissman et al., 1997), with the child's parent(s) and other available relatives serving as informant(s). At each follow-up assessment, subjects less than 18 years of age were interviewed along with the parent/guardian using the K-SADS-E and subjects 18 years of age or older were interviewed using the SADS-L.

Participants were admitted to the Child and Adolescent Sleep and Neurobehavioral Laboratory for a neurobiological assessment that included three consecutive nights of polysomnography. The first night was considered an adaptation night. Sleep-related EEG activity was measured during the second night of the visit. During the second night, participants maintained their usual sleep schedule. Sleep was assessed and scored through standard polysomnographic procedures (see Dahl et al., 1996).

Results

Diagnostic information from all assessments conducted between the initial visit and the final follow-up visit were used to determine whether each participant had experienced an episode of major depression during the duration of the study. Twelve participants (54%) met criteria for MDD during the follow-up period. The remaining 10 participants (46%) were considered resilient with regard to depression, having shown no evidence of depressive disorder in young adulthood despite familial risk. It should be noted, however, that some of these "resili-

ent" participants met criteria for other psychiatric disorders at some point during the follow-up interval, including anxiety disorders ($N = 1$), behavior disorders ($N = 3$), and substance use disorders ($N = 2$). Depression-resilient and nonresilient participants did not differ on age at baseline, age at the most recent follow-up, gender, or SES status.

Independent samples t tests were used to compare resilient and nonresilient participants in young adulthood on childhood sleep EEG variables. As shown in Table 1, resilient young adults differed from nonresilient young adults on childhood sleep latency and, at a trend level, time spent in Stage 4 sleep. Resilient young adults demonstrated a shorter latency to falling asleep during the childhood sleep laboratory assessment compared to nonresilient participants, $t (1, 20) = -2.37$, $p < .05$; Cohen $d = -1.05$. There was a trend for resilient young adults to have spent increased time in Stage 4 sleep during the childhood sleep laboratory assessment compared to nonresilient participants, $t (1, 20) = 1.93$, $p = .07$; Cohen $d = 0.84$. There were no significant group differences on any other sleep variables.

Discussion

These findings indicate that a shorter latency to fall asleep and a greater quantity of Stage 4 sleep may be protective against the development of depressive disorders for children at high familial genetic risk for depression. These findings are striking because, although decreased sleep latency and increased slow-wave sleep are strongly associated with adult depression (Riemann & Voderholzer, 2003), these associations have generally not been found in studies that assessed sleep in prepubertal children. Only one prior study has reported an association between increased sleep latency and depression in children assessed prior to puberty (Emslie et al., 1990). This is the first study, to our knowledge, to report an association between slow-wave sleep in childhood or adolescence and depression, regardless of pubertal status. Although the Stage 4 sleep finding only approached statistical significance, effect sizes for both findings were in the range generally considered large (Cohen, 1977). These findings may be attributable to the use

Table 1. *Sleep EEG variables in childhood by resilience status in young adulthood*

| | Resilient (N = 10) | | Nonresilient (N = 12) | | | | |
	M	SD	M	SD	t	p	Cohen d
Sleep architecture							
Stage 1 sleep	16.10	9.07	19.58	7.84	−0.97	.35	−0.41
Stage 2 sleep	275.44	43.31	308.27	53.72	−1.56	.12	−0.67
Stage 3 sleep	48.95	20.80	37.69	18.35	1.35	.19	−0.57
Stage 4 sleep	104.70	25.53	78.79	35.4	1.93†	.07	−0.84
Sleep continuity							
Sleep latency	11.90	4.12	22.50	13.60	−2.37*	.03	−1.05
Total sleep time	591.90	26.89	588.75	33.46	0.24	.81	0.10
No. awakenings	5.70	2.75	6.08	2.61	−0.34	.74	−0.14
Time awake	23.70	24.52	25.50	33.29	−0.14	.89	−0.06
REM sleep							
REM latency	102.50	38.19	135.50	48.20	−1.75	.10	−0.76
REM density	1.67	0.40	1.60	0.72	0.24	.81	−0.12
REM duration	123.00	19.91	118.42	12.63	0.66	.52	−0.27

Note: REM density is in units/minute. All other variables (except number of awakenings) are in minutes.
†$p < .10$. *$p < .05$.

of a well-defined sample of children at high risk for depression who were assessed in a narrow range of pubertal development, as well as the lengthy follow-up period into young adulthood. Despite these strengths, given the small sample size and the presence of other forms of psychiatric comorbidity in the sample, these findings should be interpreted with caution.

Although these findings are preliminary, we offer several potential explanations for the mechanisms through which decreased sleep latency and increased slow-wave sleep may promote resilience among children at high risk for depression. Higher quality sleep may facilitate improved affect regulation through its effects on the PFC. The PFC regulates executive functions involved in the control of attention and emotion and is involved in the functional integration of arousal, affect, and higher order cognitive systems (Davidson, Jackson, & Kalin, 2000; Posner & Petersen, 1990). The PFC also plays a role in sleep regulation, and is particularly vulnerable to the negative effects of sleep deprivation (Horne, 1993). Sleep deprivation weakens PFC control over other brain regions, causing impairment in tasks requiring integration of cognitive processing with social and emotional regulatory demands (Dahl, 1996b; Horne, 1993). By extension, higher quality sleep likely contri-

butes to better affect regulation by supporting PFC functioning, especially the ability to use higher cognitive processes to modulate emotion. This support may be particularly important during childhood and adolescence, as areas of the PFC undergo continued maturation (Casey et al., 2000; Giedd, 2004).

Another possibility is that shorter sleep latency may be a marker for the ability to control cognitive processes and physiological arousal that can interfere with sleep. In other words, children who fall asleep faster are probably better at utilizing affect regulation skills to "turn off" thoughts and emotions that might otherwise keep them awake. For many depressed and anxious children, the transition to sleep can be a time for rumination over events of the day or worrying about the activities of the next day. Evidence suggests that the transition into sleep is a vulnerable period among depressed adolescents, many of whom show spikes in HPA axis activity around bedtime (Forbes et al., 2006).

The evidence reviewed above suggests that better affect regulation facilitates the transition into sleep, and better sleep improves the ability to regulate affect. Thus, affect regulation and sleep appear to influence each other in a bidirectional and mutually reinforcing fashion. There are probably also reciprocal links between

sleep regulation and HPA axis reactivity, both of which involve contributions from overlapping neural structures such as the LC and the suprachiasmatic nucleus (Buijs, Hermes, & Kalsbeek, 1998; Dahl, 1996b). Through these reciprocal links, positive sleep and affect regulation may promote a synergistic protective effect over time among children at risk for depression.

Sleep can also be mediated and moderated by social context. Like each of the biological processes reviewed above, children's sleep is highly sensitive to influences within the social context. There are strong evolutionarily adaptive links between the ability to fall asleep and perceptions of safety versus threat. Sleep involves a fundamental loss of awareness and responsiveness to the external environment. During sleep, most sensory information stops at the level of the thalamus, preventing perception of potential threats in the environment. As a result, most species have evolved mechanisms to ensure that sleep behavior is limited to safe places. For social primates, safety from predators was primarily accomplished through a close-knit protective social group. The human brain evolved under conditions in which this sense of social belonging and social connectedness formed the underpinning for feelings of safety. Natural tendencies in the modern human brain continue to reflect these links, such that social stresses evoke powerful feelings of threat and sleep disruption, but feelings of love, caring, and social connection create a sense of safety and promote sleep (Dahl & Lewin, 2002). In modern society, this sense of safety is anchored within the emotional climate of the family. A sense of emotional security will activate brain circuitry that is conducive to going to sleep, whereas an unsafe, hostile, or threatening environment will activate systems of threat and vigilance, thereby interfering with sleep.

Recently, scientists have turned their attention to other social contextual influences on children's sleep habits, particularly during adolescence (Carskadon et al., 2004). Adolescents are increasingly exposed to an alluring array of stimulating and arousing activities that are often accessible in their own bedrooms. These include video games, television, loud music, surfing the internet, and communicating with friends via instant messaging, text messaging, and cellular phones (and sometimes all of the above at the same time). Many of these activities occur late at night without parental supervision, as adolescents are also increasingly allowed to determine their own bedtimes and to stay up later than their parents. Busy work and social schedules and early school start times in high school also influence sleep schedules, foreshortening the number of hours devoted to sleep.

This scenario represents another example of the ways in which the social context can amplify (or compensate for) the effects of a biological vulnerability. These social contextual influences on adolescent sleep exacerbate naturally occurring biological changes in the circadian rhythm during puberty, including a shift toward a more "owl-like" pattern of staying up late and sleeping in (Carskadon et al., 2004; Dahl & Lewin, 2002). Conversely, there are many things that parents can do to promote adolescents' sleep despite this biological shift, such as facilitating a relaxing bedtime routine, limiting access to highly stimulating activities before bed, enforcing a regular bedtime schedule, maintaining environmental conditions conducive to good sleep, and promoting a general sense of safety and emotional security. This is by no means an easy task, and many parents find bedtime and waking routines to be among the most challenging aspects of parenting. Nevertheless, parents who help their children to obtain adequate sleep, especially during the vulnerable period of early adolescence, may be able to help buffer them against the negative effects of other risk factors contributing to emotion dysregulation and depression risk.

Integrative Discussion

These examples show that both social and biological influences can contribute to resilience among children at risk for depression. Social factors include warm parenting, nonconflictual marital relationships, and safe communities, whereas sleep represents a biological factor contributing to resilience. One thing that these factors have in common is that they each contribute to adaptive functioning of systems involved in affect regulation. Like most research to date on resilience in children, both examples

provide data that is limited to only the biological or social context. Although they provide hints about mechanisms of cross-contextual mediation and moderation, they highlight the need for future research that concurrently assesses and integrates neurobiological and social processes involved in resilience.

Clinical Implications

A focus on biological factors in resilience may at first seem to have limited utility for researchers interested in developing psychosocial prevention and intervention approaches with high-risk and depressed children and adolescents. The idea that presumably fixed biological characteristics can contribute to resilience tells us little about how to help individuals who are not lucky enough to possess these biological characteristics. However, the concept of cross-contextual mediation highlights the fact that biological characteristics can be malleable, and that positive features of the social environment have the potential to contribute to adaptive changes in neurobiological systems. Strong evidence for this point comes from preliminary findings from neuroimaging studies demonstrating that psychosocial interventions for adult depression, such as cognitive behavioral therapy, are associated with changes in neural functioning following treatment (e.g., Goldapple et al., 2004). The concept of cross-contextual moderation also suggests that, even when neurobiological systems cannot be modified, positive experiences within the social environment can compensate for and buffer children against the negative effects of neurobiological vulnerabilities. Thus, both models provide optimistic support for the notion that psychosocial interventions that enhance children's social contextual resources have the potential to contribute to resilience in children at risk for depression.

In particular, the evidence reviewed above points to the potential value of preventive interventions that focus on children's skills for regulating emotion and familial influences on children's ER. Prevention programs that focus on these factors have already shown supportive results in the prevention of anxiety and depression (Barrett & Turner, 2001; Gillham, Reivich, Jaycox, & Seligman, 1995; Kam, Greenberg, & Kusche, 2004). For example, the FRIENDS Program is an empirically supported cognitive–behavioral prevention program that focuses on building "emotional resilience" by teaching children how to manage emotions, and teaching parents how to assist children in this process (Barrett & Turner, 2001). Other studies suggest that parent-training programs that focus on emotion socialization can be effective in improving children's ER abilities (Havighurst, Harley, & Prior, 2004).

Approaches that more specifically address biological systems may also be valuable. For example, anxiety intervention programs often teach children how to identify features of physiological arousal and how to apply relaxation skills to down regulate physiological reactivity (Kendall, 1994). Although not yet widely utilized, sleep intervention approaches that focus on teaching children and their parents how to implement improved sleep hygiene routines may also prove valuable in promoting resilience to depression. In addition, a greater understanding of the precise mechanisms through which psychosocial interventions "get into the brain" is needed. Future research on biological mediators and moderators of children's response to psychosocial interventions will likely lead to advances in treatment approaches, and also in our understanding of the complex etiological factors involved in risk and resilience. We are optimistic that in the coming years, the integration of affective neuroscience methodologies with the ecological and transactional perspective offered by the developmental psychopathology framework will lead to major advances in promoting resilience among children and adolescents at risk for depression.

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