Depression in Children and Adolescents

25

Judy Garber and Uma Rao

Depression is one of the most common forms of psychopathology and a leading cause of disability in the world (World Health Organization, 2008). Depressive disorders tend to be recurrent, can be chronic, and are associated with significant impairment (Kessler et al., 2012). Mood disorders are relatively rare during childhood, but the rates increase significantly during adolescence, and many depressed adults recall that their first depression occurred when they were an adolescent. Moreover, some factors associated with risk for depression during adolescence and adulthood have their origin earlier in development. The current chapter describes the diagnostic criteria, continuity and phenomenology, epidemiology, and etiology of depression in children and adolescents from a developmental psychopathology perspective.

The term "depression" has been defined as a symptom (sadness), a syndrome (a constellation of associated symptoms), or a diagnosed disorder (a specific set of symptoms with the same course, prognosis, etiology, and response to treatment). Occasional feelings of sadness in the face of disappointment or loss are natural and expected. When such dysphoria lingers for weeks or months, occurs at the same time as other symptoms (e.g., changes in sleep, appetite, concentration), and affects a person's ability to function, then the individual may be experiencing major depressive disorder (MDD).

Diagnostic Criteria

The criteria for depressive disorders outlined in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders-Text Revision* (DSM-IV-TR; American Psychiatric Association, 2000) are essentially the same across development. Two minor variations in DSM-IV are that for children and adolescents (a) irritability is considered a manifestation of dysphoric mood and (b) the duration of dysthymia is one rather than two years. Functional impairment is particularly important for distinguishing depressive disorders from normal mood variability. Thus, according to DSM-IV-TR there are few real developmental differences in the symptoms that comprise the syndromes of major depression or dysthymia.

J. Garber, Ph.D. (✉)
Department of Psychology and Human Development, Vanderbilt University, 0552 Peabody, 230 Appleton Pl., Nashville, TN 37203-5721, USA
e-mail: judy.garber@vanderbilt.edu; jgarber.vanderbilt@gmail.com

U. Rao, M.D.
Kennedy Center, Vanderbilt University, Nashville, TN 37203-5721, USA

Center for Molecular and Behavioral Neuroscience, Meharry Medical College, Nashville, TN, USA

Department of Psychiatry and Behavioral Sciences, Meharry Medical College, Nashville, TN, USA

M. Lewis and K.D. Rudolph (eds.), *Handbook of Developmental Psychopathology*,
DOI 10.1007/978-1-4614-9608-3_25,

The recently revised DSM-V (American Psychiatric Association, 2013) includes the following changes to mood disorders (Moran, 2013): (a) disruptive mood dysregulation disorder (DMDD) is a new diagnosis intended to identify children who experience extreme irritability without changes in mood that are characteristic of bipolar disorder and to reduce the overdiagnosing of children with bipolar disorder. (b) Premenstrual dysphoric disorder (PMDD) is a new diagnostic entity in *DSM-V* and is no longer in the appendix. Although not unique to adolescents, PMDD can begin after puberty and thus can be diagnosed in adolescent girls. (c) The term "dysthymia" now falls under the diagnosis of "persistent depressive disorder," which includes both chronic MDD and what was previously dysthymic disorder (DD) in DSM-IV-TR. (d) The "grief exclusion" has been eliminated, which now means that patients experiencing severe and persistent major depression related to bereavement can be diagnosed and treated.

Continuity and Phenomenology of Depression

Continuity is central to the study of developmental psychopathology (Rutter & Sroufe, 2000). Three types of continuity are particularly relevant to depression: (a) continuity across symptoms, syndrome, and disorder; (b) continuity in the occurrence of depression from childhood through adulthood; and (c) continuity in symptom manifestation across development.

Continuity Across Depressive Symptoms, Syndrome, and Disorder

How is depressed mood or a combination of depressive symptoms (i.e., syndrome) related to more severe and sustained depressive disorders? Subthreshold levels of depressive symptoms in youth significantly predict the onset of a full MDD in adulthood (Klein, Shankman, Lewinsohn, & Seeley, 2009; Kovacs & Lopez-Duran, 2010), and subthreshold depressive symptoms often are associated with significant functional impairment (Lewinsohn, Solomon, Seeley, & Zeiss, 2000), which then can exacerbate the symptoms further. These patterns indicate evidence of some continuity across levels of severity.

A related issue is whether depression is a continuous dimension versus a categorical entity. Studies using taxometric procedures (Waller & Meehl, 1998) to examine the latent structure of depression in children and adolescents have found evidence for a depression taxon (Richey et al., 2009; Solomon, Ruscio, Seeley, & Lewinsohn, 2006), although others have reported a dimensional solution (Hankin, Fraley, Lahey, & Waldman, 2005). These contrary results are partially due to differences in the measures of depression, informants, sample sizes, and data analytic procedures used. Given the increasing emphasis on dimensional approaches to psychopathology (Insel, 2013), further studies are needed to determine to what extent depression is dimensional, categorical, or some combination of the two. The answer likely will depend upon multiple factors including individuals' ages, personal and family history of depression, methods used to assess depression, data analytic strategies applied, and the underlying processes that explain the dimension versus category of depression.

Continuity of Depression from Childhood to Adulthood

A second type of continuity concerns how stable depression is across development (Avenevoli & Steinberg, 2001). Is there continuity between depressions during childhood and those that occur later in adolescence and adulthood? Are the processes that underlie childhood-onset depression the same as those that produce adolescent- or adult-onset depression?

Depression at the symptom level has been found to be relatively stable in children (e.g., Cole, Martin, Powers, & Truglio, 1996; Hofstra, van der Ende, & Verhulst, 2000). Cole et al. (1996) reported high stability of symptoms assessed by multiple informants over 6 months

for children in both grades 3 and 6. In contrast, a prospective study of 3- to 12-year-old children showed a lack of stability in depressive symptoms based on self- and parent report (Pihlakoski et al., 2006). Thus, continuity of depression over time likely depends upon the informant about the symptoms, the amount of time between assessments, and the child's age.

Recurrence, defined as the onset of a new depressive episode, is high in children and adolescents (Kennard, Emslie, Mayes, & Hughes, 2006). Younger age of onset significantly predicts relapse (e.g., Birmaher et al., 1996). MDD has a cumulative probability of recurrence of 40 % by 2 years and 70 % by 5 years (Emslie et al., 1997). A 9-year follow-up study found that 80 % of children with prior dysthymia and 50 % of children with prior MDD had subsequent episodes of depression (Kovacs, 1996a).

Results of investigations of the long-term course of early-onset mood disorders have been inconsistent, however. Some studies have found that prepubertal-onset depression did not show continuity into adulthood, but was sometimes followed by behavioral problems and impaired functioning (e.g., Harrington, Fudge, Rutter, Pickles, & Hill, 1990; Weissman et al., 1999). Other studies (e.g., Dunn & Goodyer, 2006; Fergusson & Woodward, 2002; Kovacs, 1996b) have reported that pediatric-onset depressions recur into adulthood. Copeland, Shanahan, Costello, and Angold (2009), however, showed that depression in adolescence was no longer related to depression in adulthood when they controlled for anxiety and externalizing disorders during adolescence. Finally, other studies (e.g., Geller, Zimerman, Williams, Bolhofner, & Craney, 2001; Weissman et al., 1999) have suggested that some early-onset depressions have a bipolar course that emerges over time.

Differences in the onset, duration, and recurrence of early-onset depression have been linked to demographic (e.g., age, gender), individual (e.g., preexisting diagnosis, negative cognitive style), family (e.g., parental psychopathology), biological (e.g., neurobiological dysregulation), and psychosocial factors (e.g., poor support, stressful life events) (Birmaher et al., 2004; Garber, 2007; Timbremont & Braet, 2004). Prior MDEs might increase vulnerability to subsequent episodes by creating biological and/or psychological *scars* that sensitize individuals to later exposure to even low levels of the etiological agent(s). That is, recurrence of depression may result from *kindling*, sensitization, or *scarring* (Lewinsohn, Steinmetz, Larson, & Franklin, 1981; Monroe & Harkness, 2005). The kindling hypothesis asserts that prior episodes of depression "leave behind neurobiological residues that make patients more vulnerable to subsequent episodes" (Post, 1992; p. 1006). Earlier depressions may change individuals in some ways, which then lead to their generating the kinds of stressful situations that are likely to precipitate future episodes (Hammen, 1991). Finally, Teasdale (1983, 1988) proposed a differential activation hypothesis such that vulnerability to subsequent, more severe depressive episodes is influenced by patterns of information processing that occur during earlier, milder depressions. Depressed mood presumably activates negatively biased interpretations of experiences, which then maintain and exacerbate the dysphoria into further clinical depression.

Phenomenology

A third type of continuity concerns whether the manifestation of the symptoms that comprise the syndrome and disorder (i.e., phenomenology) of depression is similar or different across development. That is, do the symptoms that define depressive disorder reflect homotypic versus heterotypic continuity from childhood through adulthood?

Infants have been observed to experience depression-like symptoms such as sadness, irritability, sleep and eating problems, fatigue, withdrawal, apathy, fussiness, and tantrums (Guedeney et al., 2003). Failure to thrive in infants has several similarities to depression such as psychomotor delay, behavioral difficulties, and feeding problems (Raynor & Rudolf, 1996) and may be a manifestation of a mood disorder in babies. In preschool-age children, a specific constellation

of depressive symptoms has been identified (Luby et al., 2002). Anhedonia was found to be a specific indicator, and mood symptoms (i.e., sadness and irritability) were found to be sensitive indicators. The most severely impaired preschoolers could be diagnosed using unmodified DSM criteria. The modified criteria, however, identified a larger number of seriously impaired children who would have been missed had only the existing DSM-IV criteria been used (Luby et al., 2003).

The symptoms of depressive disorder might not be isomorphic across the life span (Cicchetti & Toth, 1998; Weiss & Garber, 2003). Therefore, the criteria that define depression in adults may "need to be translated into age-appropriate guidelines for children, sensitive to developmental changes in the children's experience and expression of depression" (Cicchetti & Schneider-Rosen, 1984, p. 7). Although there may be a core set of common depressive symptoms across all ages, other symptoms might be uniquely associated with the syndrome at different developmental levels (Avenevoli & Steinberg, 2001; Kovacs, Obrosky, & Sherrill, 2003).

A meta-analysis of 16 empirical studies comparing the rates of depressive symptoms in different age groups revealed developmental effects for 18 of the 29 (62 %) core and associated depressive symptoms (Weiss & Garber, 2003). Older youth had higher levels of anhedonia, hopelessness, hypersomnia, weight gain, and social withdrawal and lower levels of energy. Adolescents had more vegetative symptoms (i.e., low energy, hypersomnia, weight loss), hopelessness/helplessness, and suicidality than preadolescents (Yorbik, Birmaher, Axelson, Williamson, & Ryan, 2004). Thus, developmental differences exist in the rates of some symptoms in children versus adolescents. Evidence is more mixed regarding age differences in the factor structure of depression (Weiss & Garber, 2003). Overall, although some researchers have argued that there are not developmental differences in depressive symptoms (e.g., Kashani, Rosenberg, & Reid, 1989; Ryan et al., 1987), the evidence does *not* support this conclusion.

Epidemiology: Prevalence of Depression in Childhood and Adolescence

MDD is rarely assessed in infants, uncommon in preschool-age children, relatively infrequent during middle childhood, and increases significantly during adolescence. The overall prevalence estimate of depression in school-age children is 2.8 %, although the rate varies by age, informant, and type of depression (Costello, Foley, & Angold, 2006). Among very young children (i.e., ages 2–5), prevalence rates are 1.4 % for MDD, 0.6 % for DD, and 0.7 % for depression not otherwise specified (NOS)/minor depression (Bufferd, Dougherty, Carlson, & Klein, 2011; Egger & Angold, 2006). In children ages 9, 11, and 13, 3-month prevalence rates are 0.03 % for MDD, .13 % for DD, and 0.45 % for depression NOS (Costello et al., 1996). Overall, the rates of diagnosed depressive disorders in preadolescents are relatively low (Rubio-Stipec, Fitzmaurice, Murphy, & Walker, 2003). When impairment criteria are included, lower rates (3.4 %) are found than when they are not (4.1 %; Canino et al., 2004).

Rates rise significantly through adolescence (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). In a nationally representative sample of over 3,000 youth, the 12-month prevalence of a mood disorder was 2.5 % in 8- to 11-year-olds and 4.8 % in 12- to 15-year-olds (Merikangas et al., 2010). With impairment criteria, the prevalence was 1.8 % for 8- to 11-year-olds and 3.9 % for 12- to 15-year-olds. Lifetime prevalence rates of MDD in adolescents range from 9 to 24 % (Merikangas & Knight, 2009). The National Comorbidity Survey—Adolescent Supplement, which interviewed over 10,000 adolescents ages 13–18, reported the lifetime prevalence of mood disorders was 14.3 %; when severe impairment or distress was included, prevalence was 11.2 % (Merikangas et al., 2010). Subclinical depression also is quite high, with about 10–20 % of youth experiencing subsyndromal or minor depression (Kessler & Walters, 1998). An even greater percent of youth

(20–50 %) endorse significant levels of depressive symptoms on self-report measures (Kessler, Avenevoli, & Merikangas, 2001).

Sex Differences

Across cultures, epidemiological studies repeatedly find about twice the rate of depression in females compared to males (Weissman & Olfson, 1995). Whereas some researchers have found the rates of MDD to be about equal in preadolescent girls and boys (e.g., Angold & Rutter, 1992; Fleming, Offord, & Boyle, 1989), others have reported higher rates among preadolescent boys than girls (e.g., Angold, Costello, & Worthman, 1998; Steinhausen & Winkler, 2003). Findings of sex differences in minor depression or depressive symptoms have been more mixed (e.g., Gonzalez-Tejera et al., 2005). A meta-analysis of 310 studies using the Children's Depression Inventory found no significant sex differences in self-reported depressive symptoms in children ages 8–12 (Twenge & Nolen-Hoeksema, 2002). By early adolescence, girls begin to show higher levels of depressive symptoms and disorders than boys (Angold, Erkanli, Silberg, Eaves, & Costello, 2002; Costello et al., 2003). Sex differences in the manifestation of depression also have been noted. Young depressed females are more likely than males to experience appetite and weight problems, worthlessness or guilt (Lewinsohn, Rohde, & Seeley, 1998), and suicidality (Yorbik et al., 2004). MDD tends to be more recurrent and insidious in adolescent females than males (Lewinsohn & Essau, 2002).

Explanations of the increasing rates of depression in females during adolescence emphasize the contribution of biological, psychological, interpersonal, and contextual factors and their interactions during the transition to adolescence (Cyranowski, Frank, Young, & Shear, 2000; Hankin & Abramson, 2001; Hyde, Mezulis, & Abramson, 2008; Nolen-Hoeksema & Hilt, 2009; Strauman, Costanzo, & Garber, 2011). Hormonal changes (e.g., levels of androgen and estradiol) during puberty may be one explanation for the emerging sex difference in depression during adolescence (e.g., Angold, Costello, Erkanli, & Worthman, 1999b). Early maturing girls have been found to be at higher risk for depression than their average-maturing peers (Conley & Rudolph, 2009; Copeland et al., 2010), possibly due to psychosocial factors such as increased social expectations and pressures, less peer support, and greater body dissatisfaction (e.g., Stice, Hayward, Cameron, Killen, & Taylor, 2000; Teunissen et al., 2011).

Girls also report higher levels of stress during the transition to adolescence, particularly interpersonal problems, and are more likely than boys to experience depression at the same level of stress (Hankin, Mermelstein, & Roesch, 2007; Shih, Eberhart, Hammen, & Brennan, 2006). Finally, individual differences in temperament, stress responses, rumination, and attention biases to emotional stimuli may produce depression in girls more than boys, particularly under conditions of stress (Else-Quest, Hyed, Goldsmith, & van Hulle, 2006; Kujawa et al., 2011; Nolen-Hoeksema & Hilt, 2009). Thus, sex differences in the rates of depression become increasing evident postpuberty due to biological, psychological, and social factors.

Comorbidity

Comorbidity with depression is very common in children and adolescents, with rates ranging from about 42 % in community samples (e.g., Rohde, Lewinsohn, & Seeley, 1991) to as high as 75 % in clinical samples (e.g., Kovacs, 1996b; Sorensen, Nissen, Mors, & Thomsen, 2005). DD is the most common comorbid disorder with MDD (Kovacs, 1994). Such *double depression* is associated with more severe and longer depressive episodes, a higher rate of other comorbid disorders (e.g., generalized anxiety disorder), more suicidality, and less social competence (Goodman, Schwab-Stone, Lahey, Shaffer, & Jensen, 2000).

The pattern of comorbidity with depression varies across age and sex (Angold, Costello, & Erkanli, 1999a; Wagner, 2003). In younger

children, anxiety and depression form a unified, indistinguishable construct, whereas in older children a dual-factor or tripartite model is more common (Cole, Truglio, & Peeke, 1997). In pre-adolescents, depression often co-occurs with separation anxiety, ADHD (Yorbik et al., 2004), and conduct problems (Harrington et al., 2000), whereas in adolescents common comorbid conditions include ODD and substance use disorders, particularly in males, and eating disorders, particularly in females (Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993). In general, depressions that are comorbid with other disorders have a higher risk of recurrence, longer duration, more suicide attempts, greater functional impairment, less favorable response to treatment, and greater mental health service utilization (Ezpeleta, Domenech, & Angold, 2006; Rudolph & Clark, 2001).

Etiology of Depression in Children and Adolescents

Depression is a heterogeneous condition with a complicated etiology. No single factor is either necessary or sufficient; rather, multiple risk factors and processes interact to produce depression (Cicchetti & Dawson, 2002). We focus here on factors for which there is the most empirical support including genes, neurobiology, temperament, negative cognitions, self-regulation, stressful life events, and interpersonal relationships as well as interactions among these variables. Although some of these variables (e.g., stress) also are associated with other psychiatric conditions (e.g., anxiety), the particular amalgamation of these vulnerability factors with each other is what uniquely results in one condition rather than another (Garber & Hollon, 1991).

Genetic Factors

Behavioral Genetic Studies

Behavioral genetic studies utilizing family, twin, and adoption designs document effects of both genetic and environmental factors for unipolar depression (Lau & Eley, 2008; Rice, 2010; Sullivan, Neale, & Kendler, 2000). Twin studies with children and adolescents reported marked variability in the heritability estimates for depressive symptoms (ranging from 0 to 55 %) as a function of age, sex, and informant (e.g., Bartels et al., 2004; Happonen et al., 2002; Rice, Harold, & Thapar, 2002; Scourfield et al., 2003). The emerging theme from these studies is that the influence of genetic factors on depression is very modest during childhood and increases during adolescence (Rice, 2010). These age-related differences may be partly due to gene–environment correlations, which increase during adolescence as a function of greater independence in selecting and shaping the environment with increasing age (Rice, Harold, & Thapar, 2003). New genetic influences also might emerge during adolescence due to developmental changes (Scourfield et al., 2003) or functional modifications in the genome induced by the changing environment (Bagot & Meaney, 2010).

Heritability estimates for depressive symptoms have indicated negligible differences between males and females (Bartels et al., 2004; Happonen et al., 2002; Scourfield et al., 2003). Some evidence exists of significant interactions between age and sex on heritability estimates in children and adolescents (Eley & Stevenson, 1999; Silberg et al., 1999). In addition, a study of anxiety and depression in 3- to12-year-old children showed that the same genes were expressed in boys and girls (Boomsma, van Beijsterveldt, & Hudziak, 2005). Heritability estimates also have been found to vary by informant (i.e., child, parent, or teacher). For instance, in the Virginia Twin Study, heritability estimates based on children's self-report were lower than those based on parents' reports of children's depression (Eaves et al., 1997).

One twin study that focused on depressive disorders in 12- to 23-year-old (mean = 15 years) females (Glowinski, Madden, Bucholz, Lynskey, & Heath, 2003) found a heritability estimate of 40 % (95 % confidence interval = 24–55), which is consistent with the findings in adults (Sullivan et al., 2000). A comparison of heritability estimates for a broad phenotype comprised of sadness

and/or anhedonia lasting 2 weeks versus the diagnosis of MDD indicated that the broad phenotype involved largely shared environmental factors, whereas a diagnosis of MDD was related to both genetic and environmental factors (Glowinski et al., 2003). These findings highlight the importance of precision in diagnostic classification for behavioral and molecular genetic studies (Rice, 2010). The relative contribution of genes and environment across development needs further study with large samples and careful characterization of the phenotypes and epigenetic phenomena (i.e., the shaping of gene expression by the rearing environment without altering the nucleotide sequence) (Bagot & Meaney, 2010).

Molecular Genetics

Molecular genetic studies of child and adolescent depression largely have used a candidate gene approach and have focused particularly on functional polymorphisms in genes involved in emotional regulation and the stress response (Rice, 2010). A few genetic association and pharmacogenetic studies with modest sample sizes have been conducted (Rice, 2010).

Among the candidate genes associated with depressive disorder, the serotonin transporter (5-HTT) gene has been studied in both pediatric and adult samples. Humans exhibit polymorphisms in the 5-HTT gene (SLC6A4), based on the number of variable repeat sequences appearing in the promoter region of the gene, and differ in their transcriptional efficiency. The short (S) variant has reduced serotonin transporter expression compared with the long (L) variant (Lesch et al., 1996). More recently, the long allele was discovered to consist of two variants: L_G, which behaves physiologically like the S allele, and the high-functioning (L_A) variant (Hu et al., 2006).

A small-scale study of children and adolescents using a case–control and family-based association design reported a significant relation between SLC6A4 short variant and depression (Nobile et al., 2004). In a community sample of 200 youth, chronic family stress (but not episodic stress) predicted prospective increases in depressive symptoms over 6 months among individuals with the SLC6A4 short allele (Jenness, Hankin, Abela, Young, & Smolen, 2011). In a study of 346 adolescents at low and high risk for depression, chronic family stress at age 15 predicted higher depression scores at age 20 among individuals with the short allele, but the genetic moderation effects were significant only for females (Hammen, Brennan, Keenan-Miller, Hazel, & Najman, 2010). Kaufman et al. (2004) found that positive social support reduced the effects of SLC6A4 short allele on depressive symptoms in children exposed to maltreatment. In contrast, the Christchurch Health and Development Study that followed a birth cohort of 893 children for up to 30 years did not find that the interaction of SLC6A4 genotypes with life stress predicted depressive symptoms in adult life (Fergusson, Horwood, Miller, & Kennedy, 2011).

Gene-by-gene-by-environment interactions also have been found in association with depression vulnerability. For example, the SLC6A4 short variant interacted with Val66Met polymorphism in the gene encoding brain-derived neurotrophic factor (BDNF) to increase the risk for depressive symptoms in maltreated children, but not in healthy controls (Kaufman et al., 2006). Social support further modified the risk for depression by reducing the severity of depression scores in the high-risk group. Similarly, Hammen and colleagues (Conway, Hammen, Brennan, Lind, & Najman, 2010; Hammen et al., 2010) found that the val158met polymorphism in the catechol-O-methyltransferase (COMT) gene moderated SLC6A4 short variant-by-environment interactions on both depressive symptoms and diagnosis. For val158 homozygotes, the SLC6A4 long allele appeared to be protective at higher stress levels.

Other investigations have demonstrated in high-risk youth who exhibited the SLC6A4 short allele compared to those with the long-allele higher morning cortisol levels (Chen, Joormann, Hallmayer, & Gotlib, 2009; Goodyer, Bacon, Ban, Croudace, & Herbert, 2009) and increased cortisol responses to a laboratory-administered stressor (Gotlib, Joormann, Minor, & Hallmayer, 2008). Moreover, the combination of the short variant and higher morning cortisol levels predicted

the onset of depressive disorder over a 12-month follow-up period, controlling for baseline depressive symptoms (Goodyer et al., 2009). In the same study, the combination of Val66Val genotype of the BDNF gene and higher morning cortisol levels increased the risk for a subsequent depressive episode after accounting for the SLC6A4 short variant-by-morning cortisol interactions (Goodyer, Croudace, Dudbridge, Ban, & Herbert, 2010).

With respect to gene-association studies, a genome scan was performed in 146 nuclear families from Hungary consisting of children with either MDD or bipolar disorder and affected siblings (Wigg et al., 2009). No evidence of linkage was found on a genome-wide scan that included 405 microsatellite markers. However, markers on two chromosomes (13q and Xq) showed linkage in regions (D13S779 on 13q and TTTA062 on Xq) previously identified in association with bipolar disorder in adults.

Neurobiology

Sleep Architecture and Electrophysiological Studies

The regulation of sleep is essential to the pathophysiology and treatment of depression. First, there is a significant overlap in the control of sleep and mood regulation (Adrien, 2002; Clarke & Harvey, 2012). Sleep complaints are common in depression and form an essential criterion of the diagnosis (American Psychiatric Association, 2000). Developmental influences on the rates of depression and maturational changes in sleep regulation also imply a close connection between depressive disorders and sleep regulation. Mood disorders are relatively rare prior to puberty but increase dramatically during adolescence (Hankin et al., 1998; Kessler et al., 2001). Sleep regulation at younger ages is relatively "protected" against disruptions. By puberty, however, there is a large drop in slow-wave sleep (Dahl et al., 1990), a decrease in the threshold of arousal to disrupt sleep (Busby, Mercier, & Pivik, 1994), a dramatic increase in daytime sleepiness, and a shift in the circadian pattern, with a preference for late-night schedules (Carskadon, Orav, & Dement, 1983). Objective sleep changes found in adult MDD are rarely seen in prepubertal depression, gradually emerge after puberty, and are consistent biological findings in later adolescence (Kaufman, Martin, King, & Charney, 2001; Rao, 2011).

In contrast to the consistent findings in adults, sleep architecture measures have shown considerable variability in depressed youth despite significant subjective sleep complaints (e.g., Ivanenko & Johnson, 2008; Rao, 2011). The results vary as a function of age, sex, ethnicity, familial risk, severity of illness, and clinical course (Rao, 2011; Rao, Hammen, & Poland, 2009a, 2009b; Robert et al., 2006). Depressed adolescents have relatively more frequent disturbances in circadian rest-activity rhythms, sleep architecture, and EEG rhythms during sleep than depressed children (e.g., Armitage et al., 2000; Rao, 2011). Robert and colleagues (Armitage, Hoffmann, Emslie, Rintelmann, & Robert, 2006; Robert et al., 2006) found an interaction among age, sex, and depression diagnosis such that depressed adolescent males exhibited most severe sleep problems including the highest proportion of stage 1 sleep, shortest REM latency, and lowest percentage of slow-wave sleep. In contrast, adolescent females had the lowest temporal coherence on sleep microarchitecture analysis.

Changes in sleep architecture and sleep-related EEG rhythms also have been documented in healthy adolescents at high familial risk for depression, and these changes were associated with depression during a prospective follow-up (Morehouse, Kusumakar, Kutcher, LeBlanc, & Armitage, 2002; Rao et al., 2009b). Baseline sleep measures also predicted early recurrence (Armitage et al., 2002; Emslie et al., 2001) and differed between depressed adolescents who had a recurrent unipolar course versus those who developed bipolar disorder (Rao et al., 2002). The observed variability in sleep architecture changes in depressed youth may partly reflect heterogeneity in the longitudinal course of these disorders (Rao, 2011).

Electrophysiological studies have documented reduced left frontal electrical activity in infant

and adolescent offspring of depressed mothers (Dawson, Klinger, Panagiotides, Hill, & Spieker, 1992; Tomarken, Dichter, Garber, & Simien, 2004). Evidence of right parietotemporal hypoactivation, but not left frontal hypoactivation, in depressed female adolescents also has been reported (Kentgen et al., 2000). Decreased left frontal EEG activity probably reflects an underactivation of the approach system and reduced positive emotional expression, which also might be a marker of vulnerability to depression (Davidson, Pizzagalli, Nitschke, & Putnam, 2002). Finally, in a sample of adolescent boys, baseline frontal EEG measures predicted the onset of depressive symptoms during a prospective follow-up (Mitchell & Possel, 2012).

Neuroendocrine Studies

Among the neuroendocrine markers of pediatric depression, the hypothalamic–pituitary–adrenal (HPA) system has been a focus of interest, although the findings have been inconsistent (Kaufman et al., 2001; Rao & Chen, 2009). For example, depressed children did not display changes in 24-h cortisol patterns compared to healthy youth. Few differences in basal cortisol secretion have been observed between depressed adolescents and controls; group differences tended to be subtle alterations in normal diurnal patterns. Nonetheless, these subtle differences were relatively robust in predicting the longitudinal clinical course. Higher cortisol secretion in the evening or during sleep, when the HPA axis is relatively quiet, was associated with a longer time to episode recovery (Goodyer, Park, & Herbert, 2001), a propensity for recurrence (Rao et al., 1996; Rao, Hammen, & Poland, 2010), and more suicide attempts (Mathew et al., 2003). Higher cortisol secretion also was detected in at-risk youth who subsequently developed depression (Goodyer, Herbert, Tamplin, & Altham, 2000; Rao et al., 2009b). HPA activity also has been found to vary as a function of exposure to stressful experiences, such that greater HPA activity was observed in youth experiencing particularly high levels of adversity (Kaufman et al., 1997; Rao, Hammen, Ortiz, Chen, & Poland, 2008).

Another neuroendocrine marker possibly related to depression is growth hormone. Although the precise role of growth hormone secretion in depression is not known, it appears to be a marker of central noradrenergic and 5-HT systems (Dinan, 1998). Findings in children and adolescents have been variable (Kaufman et al., 2001; Rao & Chen, 2009). One study reported that depressed children with stressful life events had increased growth hormone secretion compared to youth who had not experienced recent stress, suggesting that environmental factors may have a moderating effect (Williamson, Birmaher, Dahl, al-Shabbout, & Ryan, 1996). In contrast, depressed adolescents who subsequently exhibited suicidal behavior were found to have increased growth hormone secretion during sleep when measured at baseline and manifested blunted growth hormone secretion compared with controls (Coplan et al., 2000). Pharmacological challenge studies have documented blunted growth hormone response to a variety of pharmacological agents in depressed children, as in depressed adults (Dinan, 1998), but less so in depressed adolescents. Pubertal changes and sex might account for some of the variability across children, adolescents, and adults (Kaufman et al., 2001; Zalsman et al., 2006).

Neuroimaging Studies

Structural Neuroimaging Studies

In pediatric samples, structural magnetic resonance imaging (sMRI) studies have revealed reductions in left frontal volume (e.g., in the anterior cingulate and orbitofrontal cortex, and subgenual region of the PFC), particularly in youth with familial depression (Botteron, Raichle, Drevets, Heath, & Todd, 2002; Nolan et al., 2002; Steingard et al., 2002). Additionally, reduced caudate nucleus volume recently was observed in a study of adolescents with depression (Shad, Muddasani, & Rao, 2012).

The hippocampus has been a focal area of research in both animal and human studies because depression is considered to be a stress-sensitive illness and the hippocampus is highly sensitive to stress, particularly early in development (MacQueen & Frodl, 2011; McEwen, 1999; Sapolsky, 2003). The hippocampus also is

involved in mood regulation and cognitive function (Campbell & Macqueen, 2004). Studies utilizing both pediatric and adult samples have reported reductions in hippocampal volume in association with depression (MacQueen & Frodl, 2011; McKinnon, Yucel, Nazarov, & MacQueen, 2009). Reduced hippocampal volume has been observed in healthy adolescents at high familial risk for depression, particularly in those who experienced high levels of adversity in childhood, and this reduced hippocampal volume partly accounted for the increased vulnerability to depression during longitudinal follow-up (Rao et al., 2010). Although morphological changes in the hippocampus have been associated with depression, not all studies have replicated these findings due to variability in methods and samples (Campbell, Marriott, Nahmias, & MacQueen, 2004; McKinnon et al., 2009).

The amygdala also is involved in the stress response as well as in emotional and mood regulation. In a pediatric sample of medication-naïve patients with depression, an increased ratio of the amygdala to hippocampal volume was observed compared to age- and gender-matched controls, but this difference was accounted for by the severity of associated anxiety symptoms (MacMillan et al., 2003). Depressed youth also have been found to have significant reductions of left and right amygdala volumes compared with healthy controls (Rosso et al., 2005), but no significant correlations were found between amygdala volumes and depressive symptom severity, age of onset, or episode duration.

Studies utilizing the diffusion tensor imaging (DTI) technique have detected microstructural white matter abnormalities in depressed adolescents (Cullen et al., 2010) and in healthy adolescents at high familial risk for depression (Huang, Fan, Williamson, & Rao, 2011), suggesting these alterations might be vulnerability markers for depression (Huang, Gundapuneedi, & Rao, 2012). Alterations in glial cells in these networks have been noted in postmortem studies; glial cells protect neurons through the production of myelin and participate in brain metabolism and communication between neurons (Rajkowska & Miguel-Hidalgo, 2007).

Functional Neuroimaging Studies

Functional MRI (fMRI) studies have implicated impaired corticostriatal and corticolimbic circuits (Cusi, Nazarov, Holshausen, Macqueen, & McKinnon, 2012; Mayberg, 2003; Price & Drevets, 2012). Patients with depression show increased neural activity in response to negative cues and diminished neural activity in response to positive stimuli in emotion-related brain circuits (e.g., amygdala and ventral striatum) (Hasler & Northoff, 2011; Leppanen, 2006). Some abnormalities in processing of emotional information were found to persist after symptom remission and also were observed in healthy individuals at high risk for the development of mood disorders. In pediatric samples, similar deficits in these neural networks have been found, although the direction of change (i.e., increased versus decreased response) has not been consistent across studies (e.g., Forbes et al., 2006, Forbes et al., 2009; Gotlib et al., 2010; Hulvershorn, Cullen, & Anand, 2011; Roberson-Nay et al., 2006; Shad, Bidesi, Chen, Ernst, & Rao, 2011; Weir, Zakama, & Rao, 2012).

Studies using magnetic resonance spectroscopy have reported altered biochemical concentrations in specific regions of the corticostriatal and corticolimbic networks in depressed adults (Ende, Demirakca, & Tost, 2006; Luykx et al., 2012), and changes in the biochemical concentration in response to treatment (Caverzasi et al., 2012). Research in children is consistent with the adult findings, suggesting some developmental continuity (e.g., Hulvershorn et al., 2011; Kondo et al., 2010; Olvera et al., 2010; Yildiz-Yesiloglu & Ankerst, 2006).

Summary of Neurobiological Research

Pediatric depressive disorders may not necessarily result from the same etiological processes as in adults, and specific subtypes with familial loading or depression with a recurrent unipolar course may or may not be associated with neurobiological changes typically observed in adult unipolar depression (Rao & Chen, 2009). Studies of normal volunteers indicate that neurobiological factors change during the course of development and developmentally influenced neurobiological

processes may become disrupted during depressive episodes (Rao, 2011; Weir et al., 2012). Prospective studies of high-risk samples indicate that several neurobiological measures are premorbid and may be vulnerability markers for depression (e.g., Goodyer et al., 2009; Huang et al., 2012; Rao et al., 2009b; Rao, Chen et al., 2010). Experiential factors also may influence neurobiological findings (e.g., Kaufman & Charney, 2001; Rao et al., 2008). Longitudinal studies with large samples are needed to examine genetic, developmental, and sociocultural influences on neurobiological factors associated with the onset and course of depression in children and adolescents.

Many important developmental questions regarding the neurobiology of pediatric depression remain. For instance, how do the maturational changes across development relate to the vulnerability and maintenance of depression? Which neurobiological changes are specific to depression and how do family history, severity, symptom patterns, and comorbidity affect the findings? Are the neurobiological changes preexisting vulnerabilities to or consequence of the illness? Are observed neurobiological changes temporary conditions that resolve without any sequelae, but place individuals on a delayed trajectory toward normal development, or are they a permanent disruption to the normal maturational process affecting neurobiological systems? The effect of disease course on the neurobiological substrate also needs to be studied (Frodl et al., 2008). The utility of these neurobiological markers in the diagnosis and prognosis of the disorder should be established as well as neurobiological changes in response to intervention (Caverzasi et al., 2012; Clarke & Harvey, 2012; Gerber & Peterson, 2008).

Temperament

Temperament is a stable and consistent behavioral, emotional, and/or cognitive style (Rothbart & Bates, 2006; Shiner & Masten, 2012) thought to have a genetic or biological basis (e.g., Gray, 1991). Indeed, temperament may serve as an intermediate endophenotype between biology and behavior. Traits that have been particularly linked with depression are negative and positive emotionality and constraint and attentional control (Compas, Connor-Smith, & Jaser, 2004; Klein, Kotov, & Bufferd, 2011; Tackett, 2006).

Negative emotionality (NE) is characterized by sensitivity to negative stimuli, increased wariness, vigilance, physiological arousal, and emotional distress (e.g., anxiety, fear, sadness, anger). *Positive emotionality* (PE) is characterized by sensitivity to reward cues, approach, energy, involvement, sociability, and adventurousness. NE and PE, respectively, are conceptually related to negative (NA) and positive affectivity (PA; Clark & Watson, 1991), neuroticism and extraversion (Eysenck & Eysenck, 1985), the behavioral inhibition and activation systems (Gray, 1991), and difficult temperament and activity/approach (Thomas & Chess, 1977). Although different terms are used, these constructs share much conceptual and empirical overlap (Klein et al., 2011).

According to the tripartite model (Clark & Watson, 1991), high levels of NA are associated with both depression and anxiety, whereas low levels of PA are uniquely related to depression, particularly anhedonia. Evidence consistent with this model has been found in children (e.g., Lonigan, Phillips, & Hooe, 2003; Phillips, Lonigan, Driscoll, & Hooe, 2002). Low PA is a significant risk factor for depression, and low extraversion and low emotional stability predict internalizing problems in both clinical and nonclinical child samples (van Leeuwen, Mervielde, De Clercq, & De Fruyt, 2007). Offspring of depressed parents have lower PA and higher NA than children of nondepressed parents (Olino, Klein, Dyson, Rose, & Durbin, 2010).

Temperament may be a risk for depression (e.g., Caspi, Moffitt, Newman, & Silva, 1996; Goodwin, Fergusson, & Horwood, 2004; Nigg, 2006). For example, children who were inhibited, socially reticent, and easily upset at age 3 had elevated rates of depressive disorders at age 21 (Caspi et al., 1996). Wetter and Hankin (2009) reported that levels of NE and PE significantly predicted changes in anhedonia 5 months later.

Sex differences also have been found in the relation between temperament and mood disorders. Gjerde (1995) reported that shy and withdrawn behavior in girls and higher levels of undercontrolled behaviors in boys at ages 3 and 4 predicted chronic depression in adulthood.

The relation between temperament and depression in children has been found to be moderated by parenting behaviors, such as rejection or inconsistent discipline. For example, the link between fearful temperament and depressive symptoms was stronger for girls whose parents were rejecting, whereas parental warmth buffered the relation of child frustration to internalizing problems (Oldehinkel, Veenstra, Ormel, de Winter, & Verhulst, 2006). In families undergoing divorce, low PE predicted higher levels of depression in children experiencing high levels of parental rejection, and impulsivity and depression were significantly associated in children receiving inconsistent parental discipline (Lengua, Wolchik, Sandler, & West, 2000).

Temperament itself can be a *diathesis* that moderates the effect of other risk factors (e.g., stress; rejection) on depression. Under conditions of stress, negative affect leads to emotional arousal, difficulty modulating emotional reactivity, and a greater use of avoidance (Compas et al., 2004). In girls with more reactive temperaments, peer rejection significantly predicted increases in depressed mood (Brendgen, Wanner, Morin, & Vitaro, 2005). Sugimura and Rudolph (2012) reported that in girls with high but not low NE, peer victimization predicted subsequent depressive symptoms. In contrast, boys with high NE had more depressive symptoms regardless of level of victimization, whereas boys with low NE showed more depression only at high levels of victimization. Thus, temperament (e.g., emotionality) may explain individual variation and sex differences in children's depressive reactions to stressors such as parent rejection or peer victimization.

Temperament also may contribute to the development of the cognitive vulnerability to depression (e.g., Garber, 2007; Hankin & Abramson, 2001). Higher levels of withdrawal at ages 1 and 4 interacted with recent life events to predict more negative cognitions at age 11 (Mezulis, Hyde, & Abramson, 2006). Similarly, low PE in early childhood predicted depressive cognitions in middle childhood (Hayden, Klein, & Durbin, 2005). Thus, temperament may be both a direct vulnerability and a diathesis that interacts with other variables (e.g., stress), to predict depression in youth. The link between various temperaments (e.g., frustration, fear, shyness) and depression has tended to vary by age, sex, and family characteristics (Ormel et al., 2005).

Negative Cognitions

Cognitive-stress models of depression (Abramson, Metalsky, & Alloy, 1989; Beck, 1967) assert that negative beliefs and maladaptive information processing are vulnerabilities (i.e., diatheses) that become active in the context of stress. Beck (1967) suggested that negative cognitive schemas (i.e., beliefs about loss, failure, worthlessness) and dysfunctional attitudes bias interpretations of stress; contribute to negative views of the self, world, and future; and thereby result in depression. Hopelessness theory (Abramson et al., 1989) asserts that maladaptive beliefs interact with stressful events to produce negative inferences about the causes, consequences, and self-implications of the events, which then results in hopelessness and depression. Thus, cognitive models of depression posit that various negative cognitions are diatheses that interact with stress to produce depression. Recently, cognitive models have been expanding to incorporate genes and neurobiological processes as more distal diatheses in the causal chain (e.g., Beck, 2008; Hankin, 2012).

Depressed children and adolescents report more hopelessness, cognitive distortions, cognitive errors, negative views of self and future, negative attributional styles, and biases in attention, memory, and information processing as compared to nondepressed children (Abela & Hankin, 2008; Jacobs, Reinecke, Gollan, & Kane, 2008). Prospective studies have shown that these various cognitive vulnerabilities predict increases in depressive symptoms (e.g., Lewinsohn, Joiner, & Rohde, 2001; Rudolph,

Kurlakowsky, & Conley, 2001) and the onset of diagnosed depressive episodes (Bohon, Stice, Burton, Fudell, & Nolen-Hoeksema, 2008; Carter & Garber, 2011; Hankin, Abramson, Miller, & Haeffel, 2004) under conditions of stress. Reviews of over 30 prospective studies (Abela & Hankin, 2008; Lakdawalla, Hankin, & Mermelstein, 2007) indicate that the cognition by stress interaction is a stronger predictor of depression in adolescents than children. This is consistent with the developmental hypothesis that depressive cognitions do not emerge and consolidate until late childhood/early adolescence and that the association of the cognitive vulnerability with depression becomes stronger with increasing age (e.g., Abela, 2001; Cole et al., 2008; Weisz, Southam-Gerow, & McCarty, 2001).

The relation of cognitive vulnerability to depression also depends on which cognitions are being studied. Abela (2001) suggested that inferential styles about consequences and the self may develop earlier than causal attributions, which require more abstract, higher order thinking. Abela and colleagues (Abela & Payne, 2003; Abela & Sarin, 2002) proposed the *weakest link hypothesis* that individuals are as vulnerable to depression as their most negative inferential style. Indeed, children's most negative inferential style about causes, consequences, or self has been found to interact with stressful events to predict increases in depressive symptoms (Abela & Payne, 2003; Morris, Ciesla, & Garber, 2008). The weakest link approach explains some of the inconsistent findings on cognitive-stress models of depression in children.

Offspring of depressed parents are at increased risk for depression and also have been found to have significantly lower self-worth, a more negative attributional style, and recall fewer positive and more negative self-descriptive words than children of nondepressed parents (e.g., Garber & Robinson, 1997; Taylor & Ingram, 1999). Following a negative mood induction procedure, never-depressed adolescent daughters of depressed mothers showed a clear information-processing bias (Gotlib, Joormann, Minor, & Cooney, 2006). Thus, children who have not yet experienced depression, but who are at risk, show negative cognitions and processing biases that may serve as vulnerabilities to future depression.

Negative cognitions likely develop through modeling parents' negative beliefs, dysfunctional parent–child relationships, exposure to stressful life events, family adversity, negative feedback from others, and emotional abuse (e.g., Garber & Martin, 2002; Gibb, 2002; Hankin, 2005; Rudolph et al., 2001). Early stress exposure and high levels of negative interpersonal events have been found to predict depressive cognitions in children (Garber & Flynn, 2001; Harkness & Lumley, 2008; Mezulis et al., 2006).

The experience of depression itself also predicts negative cognitions (e.g., McCarty, Vander Stoep, & McCauley, 2007; Pomerantz & Rudolph, 2003). Bidirectional relations between depressive symptoms and perceived competence (Cole, Martin, Peeke, Seroczynski, & Hoffman, 1998; Hoffman, Cole, Martin, Tram, & Serocynski, 2000), negative mood and self-criticism (e.g., Park, Goodyer, & Teasdale, 2005; Rudolph, Hammen, & Burge, 1997), and negative cognitions and depressive symptoms (e.g., Hoffman et al., 2000; Lau & Eley, 2008) have been observed in children and adolescents. Hoffman and colleagues reported that children's underestimation of their competence predicted depressive symptoms over time and prior depression predicted a low evaluation of their competence. In a community sample of 515 children in grades 2 through 9, LaGrange et al. (2011) showed that depressive symptoms predicted negative cognitions but not the reverse. Thus, the association between negative cognitions and depression may be reciprocal and may not be directly causal.

Self-Regulation and Coping

Self-regulation is the way individuals stimulate, modify, or manage their thoughts, affect, and behaviors through biological, cognitive, social, and/or behavioral means (Posner & Rothbart, 2007; Thomson, 1994). *Coping* is a subcategory of self-regulation activated in times of stress (Compas, Connor-Smith, Saltzman, Thomsen, & Wadsworth, 2001; Eisenberg, Spinrad, &

Eggum, 2010). Eisenberg et al. (2010) suggested three coping categories: *emotion regulation* refers to direct attempts to manage affect; *problem-focused coping* involves attempts to regulate the situation; and *behavioral regulation* is the management of behaviors resulting from emotional arousal.

Compas et al. (2001) proposed a broader definition of coping that involves intentional regulation of emotions, cognitions, behaviors, physiology, and the environment. That is, coping is the volitional response to stress, whereas involuntary or automatic reactions reflect individual differences in *temperament.* Compas et al. also distinguished between *engagement coping* (i.e., problem solving, cognitive restructuring, positive reappraisal, distraction) and *disengagement coping* (i.e., avoidance, self-blame, emotional discharge, rumination). Whereas engagement coping is associated with lower internalizing symptoms, disengagement coping is associated with higher symptom levels (Compas et al., 2001). In children ages 9 to 12, active coping predicted fewer depressive symptoms, whereas avoidant coping predicted higher levels of depressive symptoms (Lengua, Sandler, West, Wolchik, & Curran, 1999). Flynn and Rudolph (2007) showed that maladaptive responses to stress (i.e., fewer effortful responses and more involuntary, dysregulated responses) accounted for the association between reduced posterior right hemisphere bias (PRHB) and depressive symptoms in adolescents reporting high levels of stress. Flynn and Rudolph suggested that a reduced PRHB heightens stress reactivity by interfering with effective coping and emotion regulation.

Children with good self-regulation skills are better at delaying maladaptive responses and using active coping strategies in response to stressful situations. Poor self-regulation often involves greater use of automatic and reflexive rather than effortful and reflective cognitive, emotional, and behavioral reactions to the environment, and also may trigger disinhibited cognitions, rumination, negative emotions, and depression (e.g., Carver, Johnson, & Joormann, 2008; Compas et al., 2004; Rothbart & Bates, 2006). In a recent study of self-regulation and social motivation, Rudolph, Troop-Gordon, and Llewellyn (2013) found that poor inhibitory control predicted depressive symptoms in girls with high but not low avoidance motivation. Rudolph and colleagues suggested that the combination of poor self-regulation and high avoidance motivation may contribute to difficulties in shifting attention away from concerns about peer disapproval and toward avoidance, social withdrawal, and depressive symptoms. Thus, the inability to purposefully regulate cognitions, emotions, and behaviors can lead to more maladaptive responses to stress (e.g., rumination, emotional arousal, inaction), which then can contribute to and sustain depressive symptoms (Carver et al., 2008; Compas et al., 2001).

Children at risk for depression show greater difficulty inhibiting negative affect, selectively attend to sad facial expressions, use active distraction less, and are less able to generate positive affect in the face of distraction compared to low-risk youth (e.g., Forbes, Fox, Cohn, Galles, & Kovacs, 2006; Joormann, Talbot, & Gotlib, 2007; Silk, Shaw, Forbes, Lane, & Kovacs, 2006). In a sample of 4- to 7-year-old children, Silk et al. (2006) showed that positive reward anticipation in the context of a negative-emotion-inducing task was associated with lower internalizing problems, and this link was stronger for children of depressed as compared to nondepressed mothers. Thus, in children at risk for depression, positive self-regulatory behavior may protect against the negative effects of stress, whereas self-regulation problems may be a marker of vulnerability.

Stressful Life Events and Trauma

Stress has a prominent role in most theories of depression. Depressive symptoms and disorders in children and adolescents are significantly associated with both major and minor undesirable life events, particularly cumulative or chronic stressors (Grant et al., 2006). Depressed youth experience significantly more negative life events compared to nondepressed children (e.g., Goodyer et al., 2000).

The link between stress and depression emerges even before birth. In animals, both antenatal and prepartum stress impact the developing fetus and later physiological and behavioral outcomes in offspring of stressed animals (e.g., Markham & Koenig, 2011; Schneider, Moore, & Kraemer, 2003). In humans, stress in the fetal environment can affect birth weight and the development of the LHPA axis, both of which may be vulnerabilities for depression (Austin, Leader, & Reilly, 2005; Gale & Martyn, 2004). Stress-induced hormonal changes in mothers (e.g., elevated levels of CRH and cortisol) may lead to increased LHPA fetal activity, difficulty habituating to stimuli, temperamental difficulties, reduced birth weight, and slow growth (Kapoor, Dunn, Kostaki, Andrews, & Matthews, 2006; Weinstock, 2005), resulting in increased sensitivity to stress and greater vulnerability to depression as they mature. Infants exposed to high levels of maternal stress (e.g., maternal depression) show elevated cortisol levels when they encounter maternal stress as preschoolers (Essex, Klein, & Kalin, 2002). Moreover, the relation between a family history of mood disorders and depression in preschoolers was found to be mediated by stress (Luby, Belden, & Spitznagel, 2006).

Childhood-onset depression has been linked with more perinatal insults, parental criminal convictions, parental psychopathology, and peer problems (Jaffee et al., 2002). Stressful events increase from childhood through adolescence (Rudolph & Hammen, 1999), with girls reporting greater increases than boys (Garber, 2007), paralleling increases in rates of depression during adolescence (Hankin et al., 1998). This increasing trajectory of stressful events, particularly interpersonal stressors (Hankin et al., 2007; Shih et al., 2006), predicts growth in depressive symptoms for girls but not for boys (Ge, Lorenz, Conger, Elder, & Simons, 1994). Stress also predicts the onset of clinically significant depressive episodes, controlling for prior symptom levels in children and adolescents (Carter & Garber, 2011; Goodyer et al., 2000).

Although no specific stressful event invariably leads to depression, events occurring during childhood and adolescence such as loss, disappointment, separation, interpersonal conflict, relationship breakups, and rejection (Goodyer et al., 2000; Monroe, Rohde, Seeley, & Lewinsohn, 1999; Rueter, Scaramella, Wallace, & Conger, 1999), as well as parents' marital conflict and divorce, family violence, maltreatment, and economic disadvantage, are particularly likely to predict depression in youth (e.g., Gilman, Kawachi, Fitzmaurice, & Buka, 2003; Hankin, 2005; Uhrlass & Gibb, 2007). Physical and sexual abuse are among the most damaging stressors linked with the onset and recurrence of depression (Harkness & Lumley, 2008). The relation between depression and maltreatment is particularly strong in the presence of high familial loading of depression and polymorphisms in SLCGA4 and BNDF genes (Caspi et al., 2003; Kaufman et al., 2004, Kaufman et al., 2006). Moreover, experience of such early adversity may make children more vulnerable or sensitized to depression when exposed to new stressors later in development (Hammen, Henry, & Daley, 2000; Harkness, Bruce, & Lumley, 2006), although this may vary by age and sex (Rudolph & Flynn, 2007).

Social support also may affect the relation between stress and depression. For example, among children with low as compared to high social support, the interaction between genes and childhood maltreatment significantly predicted higher levels of depressive symptoms (Kaufman et al., 2004; Kaufman et al., 2006). Among youth living in highly disordered neighborhoods (i.e., exposure to gangs, harassment, drug dealing), supportive parenting (i.e., use of inductive reasoning) served as a buffer against depressive symptoms (Natsuaki et al., 2007).

The relation between stress and depression likely is bidirectional. In the stress exposure model, stress precedes the onset of depression (Brown, 1993), whereas the stress generation model asserts that depressed individuals' own behaviors create many of the stressors they encounter, which then further exacerbates their depressive symptoms (Hammen, 1991, 2006). Depressed youth (Hankin et al., 2007; Rudolph et al., 2000; Shih et al., 2006) as well as those with maladaptive interpersonal problem-solving

styles (Davila, Hammen, Burge, Paley, & Daley, 1995) tend to generate more stress. Several studies (Carter, Garber, Ciesla, & Cole, 2006; Cole, Nolen-Hoeksema, Girgus, & Paul, 2006; Gibb & Alloy, 2006) have found a reciprocal relation between stress and depression, thus highlighting the "vicious cycle" between them.

Interpersonal Relationships

Interpersonal perspectives on depression emphasize the transactions between individuals and their social environment (Hammen, 2006; Joiner & Coyne, 1999). The social context can be both a source of support and a source of stress. Depressed individuals are often the recipient as well as the elicitor of interpersonal difficulties. Depression in children and adolescents is associated with considerable family adversity, peer problems, victimization, and interpersonal rejection (Nolan, Flynn, & Garber, 2003; Rudolph, Flynn, & Abaied, 2008). At the same time, depressed youth may have distorted perceptions of their social world, engage in behaviors that elicit negative responses and conflict with others, and generate additional stressors in their relationships (e.g., Hankin et al., 2007; Rudolph et al., 2008).

Family

Attachment theory (Bowlby, 1980) asserts that children with consistently accessible and supportive caregivers develop cognitive representations, or *working models*, of the self and others as positive and trustworthy. Conversely, children with unresponsive or inconsistent caregivers tend to have insecure attachments and working models of self-criticism, abandonment, and dependency. Insecure attachments increase children's vulnerability to depression when exposed to new interpersonal strains (Brumariu & Kerns, 2010). Securely attached toddlers tend to be more cooperative, persistent, enthusiastic, and higher functioning and show lower levels of depressive symptoms when exposed to stress (Abela et al., 2005; Matas, Arend, & Sroufe, 1978). Insecurely attached children have deficits in social-behavioral and emotion regulation that can increase their vulnerability to depression (Rudolph et al., 2008).

Maladaptive parenting also is associated with depression. Currently depressed children describe their parents as controlling, rejecting, and unavailable (e.g., Stein et al., 2000). Ratings of parents' psychologically controlling behaviors predict children's depressive symptoms over and above prior depression levels (Barber & Xia, 2013). Hostile child-rearing attitudes predict increases in children's depression (Katainen, Raikkonen, Keskivaara, & Keltikangas-Jarvinen, 1999), whereas positive parent–child relationships (e.g., clear and consistent expectations, good communication, parent supervision, and shared positive activities) are linked with less depression in children (e.g., Borowsky, Ireland, & Resnick, 2001; Resnick et al., 1997).

Observational studies indicate that low warmth, high hostility, harsh discipline, and family conflict predict internalizing symptoms in youth (e.g., Ge, Best, Conger, & Simons, 1996; Sheeber, Hops, Alpert, Davis, & Andrews, 1997), and escalating parent–child conflict predicts increases in adolescents' internalizing symptoms (Rueter et al., 1999). Mothers of depressed children also are less rewarding and more dominant and controlling than mothers of nondepressed children (e.g., Sheeber, Hops, & Davis, 2001). Levels of maternal criticism of children are higher in mothers of depressed children compared to mothers of children with ADHD or healthy controls (Asarnow, Tompson, Woo, & Cantwell, 2001). Thus, convergence across children's, parents', and observers' ratings indicates that depression in children and adolescents is characterized by considerable family dysfunction (Park, Garber, Ciesla, & Ellis, 2008).

Parental depression also is characterized by dysfunctional parenting (e.g., Garber, 2005; Lovejoy, Graczyk, O'Hare, & Neuman, 2000). Such difficulties likely are one important and possibly malleable mechanism of the intergenerational transmission of depression (Goodman, 2007). Hammen and colleagues (Hammen & Brennan, 2001; Hammen, Shih, & Brennan, 2004) showed that depressed mothers had high levels of interpersonal stress that contributed to

poor parenting as well as interpersonal deficits, stress, and depression in their children. Bifulco et al. (2002) reported that the relation between maternal and child depression was mediated by child-reported neglect and abuse (see also Hammen et al., 2004; Leinonen, Solantaus, & Punamaki, 2003). Other studies (Jones, Forehand, & Neary, 2001; Kim, Capaldi, & Stoolmiller, 2003), however, have not found that parenting attitudes or behaviors significantly explain the relation between parent and child depression.

One possible mediator of the relation between dysfunctional parenting and offspring depression is children's negative cognitions (Abela, Skitch, Adams, & Hankin, 2006; Garber, Robinson, & Valentiner, 1997; Gibb et al., 2001). For example, negative cognitive style partially mediated the relation between parent abuse and neglect and subsequent depressive symptoms (McGinn, Cukor, & Sanderson, 2005), and between emotional maltreatment in childhood and depressive episodes during young adulthood (Gibb et al., 2001).

Peers

Depressed children and adolescents have both real and perceived peer problems. Depressed youth have actual social skills deficits, poorer quality friendships, and higher teacher-rated peer rejection (e.g., Prinstein, Borelli, Cheah, Simon, & Aikins, 2005; Rudolph et al., 2008; Rudolph & Clark, 2001), and they view themselves to be less socially competent and less accepted, and to have lower quality friendships than their nondepressed peers (Brendgen, Vitaro, Turgeon, & Poulin, 2002; Rudolph et al., 1997). Interestingly, *perceived* rejection, even more than actual peer rejection, predicts increases in depressive symptoms in some children (e.g., Kistner, Balthazor, Risi, & Burton, 1999). Regardless of how much a child is actually liked by peers, those with high levels of rejection sensitivity (Rizzo, Daley, & Gunderson, 2006; Sandstrom, Cillessen, & Eisenhower, 2003) or social-evaluative concerns (Rudolph & Conley, 2005) are especially prone to experiencing depression. Perceiving rejection from others may lead to withdrawal from or hostility toward others, which then may elicit actual negative reactions from peers, thereby reinforcing the depressed child's negative perceptions. Thus, a self-perpetuating and transactional cycle of cognitive distortions, negative social interactions, peer rejection, and depression may develop (e.g., Rudolph, 2009).

Longitudinal studies have found that persistent interpersonal difficulties such as excessive reassurance seeking (Prinstein et al., 2005), negative feedback seeking (Borelli & Prinstein, 2006), interpersonal rejection (Nolan et al., 2003), and romantic conflicts and breakups (Hankin et al., 2007; Monroe et al., 1999) significantly predict increases in depressive symptoms. Moreover, social-behavioral deficits were found to interact with some of these relationship disturbances to predict depression in youth (Gazelle & Rudolph, 2004; Rizzo et al., 2006). Additionally, low sociometric status and observer ratings of social disengagement in first grade were associated with increases in depressive symptoms in grades 3 and 4 (Schrepferman, Eby, Snyder, & Stropes, 2006).

Interestingly, both bullies and the bullied have high rates of depression (Ivarsson, Broberg, Arvidsson, & Gillberg, 2005; Kaltiala-Heino, Rimpela, Rantanen, & Rimpela, 2000). Children who were friends with highly aggressive peers had high levels of depressive symptoms across two years, controlling for initial depression levels (Mrug, Hoza, & Bukowski, 2004). Spending time with delinquent peers predicted high levels of self-reported depressive symptoms assessed monthly (Connell & Dishion, 2006). Depressed children might select delinquent peers as a way to "fit in" and obtain a sense of belonging not provided by their broader social networks. Deviant peers, however, typically do not give much positive feedback, which then may further exacerbate the youth's depression (Brendgen, Vitaro, & Bukowski, 2000).

Conclusions and Future Directions

Various vulnerability factors have been associated with depression in children and adolescents. Simply examining the independent contribution

of these individual risk factors, however, is not sufficient for fully understanding the processes that account for the onset, maintenance, recurrence, and offset of depressive disorders throughout development. Rather, we need multivariate models that explain how the various within-individual, biological, and psychological vulnerabilities synergistically combine with external contextual factors to produce depression across time.

Several integrated models of depression have been formulated that include additive and interactive effects of multiple risk factors (e.g., Beck, 2008; Kendler, Gardner, & Prescott, 2002). The classic paper by Akiskal and McKinney (1975) asserted that most distal causal processes (e.g., stress, low rates of positive reinforcement) go through a common final neuroanatomical pathway to depression. Diathesis-stress models highlight that within-person characteristics, such as genetic or cognitive vulnerability, interact with environmental stressors to produce depression (Abramson et al., 1989; Beck, 2008; Caspi et al., 2003; Kendler et al., 1995; Monroe & Simons, 1991). Interpersonal approaches (e.g., Hammen, 2006; Rudolph et al., 2008) suggest that cognitions about important social relationships may be a risk for depression when stressful interpersonal events occur. Negative cognitive schemas about the self and others may be the result of earlier insecure attachment and interpersonal difficulties. In contrast, Ingram, Miranda and Segal (1998) posited that cognitive processes are the common final pathway through which all social and nonsocial information is processed and linked to depression.

A broad, reciprocal, and dynamic model that describes the transactional relations among biological, psychological, social, and contextual risk processes underlying depression is required to capture the complexity of the disorder. The combination of individual vulnerabilities and contextual factors directly, indirectly (i.e., mediation), and interactively (i.e., moderation) produces depression. Some diatheses are more distal and relatively stable (e.g., temperament), whereas others are potentially malleable (e.g., parenting, coping) and may influence how individuals respond to specific proximal stressors (Compas et al., 2009). According to this perspective, children who are born with certain biological propensities, such as stress reactivity, an overactive amygdala, or an irritable temperament, will be more vulnerable to the effects of negative life events and less able to effectively self-regulate in the face of stress.

Children learn, in part through interactions with others, about their own ability to cope with stressors and whether others can be counted on for support. Children also learn through social encounters whether they are worthy of others' love and care. Exposure to stressful life events can activate negative affective structures that connect with developing schemas about the self and others (Ingram et al., 1998). A cycle begins in which children develop some symptoms of depression (e.g., irritability, low self-esteem, anhedonia), which then may generate further stressors, such as interpersonal rejection and academic failure. Experience with chronic or severe stressors can produce neurobiological changes (e.g., in the HPA system), which then further maintains or exacerbates the depressive symptoms. Thus, in this *mediated moderation model*, individual diatheses modify the relation between stress and depression and contribute to how the child responds to adverse events. Such responses to stress mediate the effect of individual diatheses on subsequent depression. Individuals with certain biological and/or psychological vulnerabilities who encounter stressful events and respond ineffectively (e.g., involuntary disengagement), so that the stressor is not adequately managed, then likely will develop depression. These escalating stressful circumstances can alter their biochemistry, self-schema, and information processing and lead to further maladaptive behaviors, thereby generating more negative events, particularly within the social domain (Coyne, 1976; Hammen, 2002), and so the cycle continues. This *scarring* (Lewinsohn, Allen, Seeley, & Gotlib, 1999) or *kindling* (Post, 1992) results in dynamic changes in these biopsychosocial systems over time.

The precise genes and neural pathways that produce the endophenotypes (e.g., temperament, negative cognitions) that then interact with specific contextual factors (e.g., exposure to in

utero and early, severe, and/or chronic stress) to elicit symptoms of depression remain to be discovered. Future research needs to identify specific genetic risk markers, elucidate the pathophysiology from the genetic polymorphisms to neuroendocrine and neurochemical dysregulation, describe how these biological processes affect persons' appraisals and behaviors in response to environmental events, and determine how the combination of these factors results in the specific symptoms of depression. Are all of these risk factors part of a single causal model, or do different combinations of these mechanisms produce subtypes or explain different manifestations of depression across development?

Theories of depression need to account for differences in the phenomenology of depression in children, adolescents, and adults and increases in the rates of depression from childhood to adolescence, particularly in girls. Are the processes that underlie childhood-onset depression different from those that explain the first onset of depression during adolescence or adulthood? Are causal mechanisms different for first versus recurrent episodes of depression? What accounts for the recurrences of depression across the life span? When and how do depressive vulnerabilities develop, unfold, and change over time? What aspects of growth (e.g., age, pubertal status, cognitive, social, or emotional level) are most related to observed developmental differences in prevalence, phenomenology, and etiology? Finally, are the various risks for depression permanent characteristics of individuals, and through what mechanisms are they turned on and off? What biological and psychosocial processes set off latent vulnerabilities, and, conversely, how does spontaneous remission of depression occur? Do vulnerable individuals no longer have the risk factor(s) or do they develop new skills to compensate for them? If so, can we learn from these naturalistic processes to develop more effective interventions?

Acknowledgements This work was supported, in part, by grants to Judy Garber from the National Institute of Mental Health R01MH64735, and RC1MH088329 and by the Vanderbilt CTSA grant UL1RR024975-01 from NCRR/NIH, and to Uma Rao from the National Institutes of Health (RO1 MH068391, G12 RR003032, UL1 RR024975/ TR000445 and U54 RR026140/ MD007593), and by the Endowed Chair in Brain and Behavior Research at Meharry Medical College.

References

Abela, J. R. Z. (2001). The hopelessness theory of depression: A test of the diathesis-stress and causal mediation components in third and seventh grade children. *Journal of Abnormal Child Psychology, 29*, 241–254.

Abela, J. R. Z., & Hankin, B. L. (2008). Cognitive vulnerability to depression in children and adolescents: A developmental perspective. In J. R. Z. Abela & B. L. Hankin (Eds.), *Handbook of depression in children and adolescents* (pp. 35–78). New York: Guilford.

Abela, J. R. Z., Hankin, B. L., Haigh, E. A. P., Adams, P., Vinokuroff, T., & Trayhern, L. (2005). Interpersonal vulnerability to depression in high-risk children: The role of insecure attachment and reassurance seeking. *Journal of Clinical Child and Adolescent Psychology, 34*, 182–192.

Abela, J. R. Z., & Payne, A. V. L. (2003). A test of the integration of the hopelessness and self-esteem theories of depression in school children. *Cognitive Therapy and Research, 27*, 519–535.

Abela, J. R. Z., & Sarin, S. (2002). Cognitive vulnerability to hopelessness depression: A chain is only as strong as its weakest link. *Cognitive Therapy and Research, 26*, 811–829.

Abela, J. R. Z., Skitch, S. A., Adams, P., & Hankin, B. L. (2006). The timing of parent and child depression: A hopelessness theory perspective. *Journal of Clinical Child and Adolescent Psychology, 35*, 253–263.

Abramson, L. Y., Metalsky, G. I., & Alloy, L. B. (1989). Hopelessness depression: A theory-based subtype of depression. *Psychological Review, 96*, 358–372.

Adrien, J. (2002). Neurobiological bases for the relation between sleep and depression. *Sleep Medicine Reviews, 6*(5), 341–351.

Akiskal, H. S., & McKinney, W. T. (1975). Overview of recent research in depression: Integration of ten conceptual models into a comprehensive clinical framework. *Archives of General Psychiatry, 32*, 285–305.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders: DSM-IV-TR*. Washington, DC: American Psychiatric Association.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author.

Angold, A., Costello, E. J., & Erkanli, A. (1999a). Comorbidity. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 40*, 57–87.

Angold, A., Costello, E. J., Erkanli, A., & Worthman, C. M. (1999b). Pubertal changes in hormone levels and depression in girls. *Psychological Medicine, 29*, 1043–1053.

Angold, A., Costello, E. J., & Worthman, C. M. (1998). Puberty and depression: The roles of age, pubertal

status, and pubertal timing. *Psychological Medicine, 28*, 51–61.

Angold, A., Erkanli, A., Silberg, J., Eaves, L., & Costello, E. J. (2002). Depression scale scores in 8–17-year-olds: Effects of age and gender. *Journal of Child Psychology and Psychiatry, 43*, 1052–1063.

Angold, A., & Rutter, M. (1992). Effects of age and pubertal status on depression in a large clinical sample. *Development and Psychopathology, 4*, 5–28.

Armitage, R., Emslie, G. J., Hoffmann, R. F., Weinberg, W. A., Kowatch, R. A., Rintelmann, J., et al. (2000). Ultradian rhythms and temporal coherence in sleep EEG in depressed children and adolescents. *Biological Psychiatry, 47*(4), 338–350.

Armitage, R., Hoffmann, R., Emslie, G., Rintelmann, J., & Robert, J. (2006). Sleep microarchitecture in childhood and adolescent depression: Temporal coherence. *Clinical EEG and Neuroscience, 37*(1), 1–9.

Armitage, R., Hoffmann, R. F., Emslie, G. J., Weinberg, W. A., Mayes, T. L., & Rush, A. J. (2002). Sleep microarchitecture as a predictor of recurrence in children and adolescents with depression. *International Journal of Neuropsychopharmacology, 5*(3), 217–228.

Asarnow, J. R., Tompson, M., Woo, S., & Cantwell, D. P. (2001). Is expressed emotion a specific risk factor for depression or a nonspecific correlate of psychopathology? *Journal of Abnormal Child Psychology, 29*(6), 573–583.

Austin, M. P., Leader, L. R., & Reilly, N. (2005). Prenatal stress, the hypothalamic-pituitary-adrenal axis, and fetal and infant neurobehaviour. *Early Human Development, 81*, 917–926.

Avenevoli, S., & Steinberg, L. (2001). The continuity of depression across the adolescent transition. *Advances in Child Development and Behavior, 28*, 139–173.

Bagot, R. C., & Meaney, M. J. (2010). Epigenetics and the biological basis of gene x environment interactions. *Journal of the American Academy of Child and Adolescent Psychiatry, 49*(8), 752–771.

Barber, B. K., & Xia, M. (2013). The centrality of control to parenting and its effects. In A. S. Morris, R. E. Larzelere, & A. W. Harrist (Eds.), *New directions for authoritative parenting* (pp. 61–87). Washington, DC: American Psychological Association.

Bartels, M., van den Oord, E. J., Hudziak, J. J., Rietveld, M. J., van Beijsterveldt, C. E., & Boomsma, D. I. (2004). Genetic and environmental mechanisms underlying stability and change in problem behaviors at ages 3, 7, 10, and 12. *Developmental Psychology, 40*(5), 852–867.

Beck, A. T. (1967). *Depression: Clinical, experiential, and theoretical aspects*. New York: Harper & Row.

Beck, A. (2008). The evolution of the cognitive model of depression and its neurobiological correlates. *American Journal of Psychiatry, 165*(8), 969–977.

Bifulco, A. T., Moran, P. M., Ball, C., Jacobs, C., Baines, R., Bunn, A., et al. (2002). Child adversity, parental vulnerability and disorder: Examination of intergenerational transmission of risk. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 43*, 1075–1086.

Birmaher, B., Ryan, N. D., Williamson, D. E., Brent, D. A., Kaufman, J., & Nelson, B. (1996). Childhood and adolescent depression: A review of the past ten years. Part I. *Journal of the American Academy of Child and Adolescent Psychiatry, 35*, 1427–1439.

Birmaher, B., Williamson, D. E., Dahl, R. E., Axelson, D. A., Kaufman, J., Dorn, L., et al. (2004). Clinical presentation and course of depression in youth: Does onset in childhood differ from onset in adolescence? *Journal of the American Academy of Child and Adolescent Psychiatry, 43*, 63–70.

Bohon, C., Stice, E., Burton, E., Fudell, M., & Nolen-Hoeksema, S. (2008). A prospective test of cognitive vulnerability models of depression with adolescent girls. *Behavior Therapy, 39*(1), 79–90.

Boomsma, D. I., van Beijsterveldt, C. E., & Hudziak, J. J. (2005). Genetic and environmental influences on Anxious/Depression during childhood: A study from the Netherlands Twin Register. *Genes, Brain, and Behavior, 4*(8), 466–481.

Borelli, J. L., & Prinstein, M. J. (2006). Reciprocal, longitudinal associations between adolescents' negative feedback-seeking, depressive symptoms, and friendship perceptions. *Journal of Abnormal Child Psychology, 34*, 159–169.

Borowsky, I. W., Ireland, M., & Resnick, M. D. (2001). Adolescent suicide attempts: Risks and protectors. *Pediatrics, 107*, 485–493.

Botteron, K. N., Raichle, M. E., Drevets, W. C., Heath, A. C., & Todd, R. D. (2002). Volumetric reduction in left subgenual prefrontal cortex in early onset depression. *Biological Psychiatry, 51*(4), 342–344.

Bowlby, J. (1980). *Attachment and loss: Vol 3. Loss, sadness, and depression*. New York: Basic Books.

Brendgen, M., Vitaro, F., & Bukowski, W. (2000). Deviant friends and early adolescents' emotional and behavioral adjustment. *Journal of Research on Adolescence, 10*, 173–189.

Brendgen, M., Vitaro, F., Turgeon, L., & Poulin, F. (2002). Assessing aggressive and depressed children's social relations with classmates and friends: A matter of perspective. *Journal of Abnormal Child Psychology, 30*, 609–624.

Brendgen, M., Wanner, B., Morin, A. J. S., & Vitaro, F. (2005). Relations with parents and with peers, temperament, and trajectories of depressed mood during early adolescence. *Journal of Abnormal Child Psychology, 33*, 579–594.

Brown, G. W. (1993). Life events and affective disorder: Replications and limitations. *Psychosomatic Medicine, 55*, 248–259.

Brumariu, L. E., & Kerns, K. A. (2010). Parent–child attachment and internalizing symptoms in childhood and adolescence: A review of empirical findings and future directions. *Development and Psychopathology, 22*(1), 177–203.

Bufferd, S. J., Dougherty, L. R., Carlson, G. A., & Klein, D. N. (2011). Parent-reported DSM-IV disorders in a

community sample of preschoolers. *Comprehensive Psychiatry, 52*, 359–369.

Busby, K. A., Mercier, L., & Pivik, R. T. (1994). Ontogenetic variations in auditory arousal threshold during sleep. *Psychophysiology, 31*(2), 182–188.

Campbell, S., & Macqueen, G. (2004). The role of the hippocampus in the pathophysiology of major depression. *Journal of Psychiatry and Neuroscience, 29*(6), 417–426.

Campbell, S., Marriott, M., Nahmias, C., & MacQueen, G. M. (2004). Lower hippocampal volume in patients suffering from depression: A meta-analysis. *American Journal of Psychiatry, 161*(4), 598–607.

Canino, G., Shrout, P. E., Rubio-Stipec, M., Bird, H. R., Bravo, M., & Martinez-Taboas, A. (2004). DSM-IV rates of child and adolescent disorders in Puerto Rico: Prevalence, correlates, service use, and the effects of impairment. *Archives of General Psychiatry, 61*, 85–93.

Carskadon, M. A., Orav, E. J., & Dement, W. C. (1983). Evolution of sleep and daytime sleepiness in adolescents. In C. G. Lugaresi (Ed.), *Sleep/wake disorders: Natural history, epidemiology, and long-term evolution* (pp. 201–216). New York: Raven.

Carter, J., & Garber, J. (2011). Predictors of the first onset of a major depressive episode and changes in depressive symptoms across adolescence: Stress and negative cognitions. *Journal of Abnormal Psychology, 120*, 779–796.

Carter, J. S., Garber, J., Ciesla, J. A., & Cole, D. A. (2006). Modeling relations between hassles and internalizing and externalizing symptoms in adolescents: A four-year prospective study. *Journal of Abnormal Psychology, 115*, 428–442.

Carver, C. S., Johnson, S. L., & Joormann, J. (2008). Serotonergic function, two-mode models of self-regulation, and vulnerability to depression: What depression has in common with impulsive aggression. *Psychological Bulletin, 134*, 912–943.

Caspi, A., Moffitt, T. E., Newman, D. L., & Silva, P. A. (1996). Behavioral observations at age 3 years predict adult psychiatric disorders: Longitudinal evidence from a birth cohort. *Archives of General Psychiatry, 53*, 1033–1039.

Caspi, A., Sugden, K., Moffitt, T. E., Taylor, A., Craig, I. W., Harrington, H., et al. (2003). Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene. *Science, 301*(5631), 386–389.

Caverzasi, E., Pichiecchio, A., Poloni, G. U., Calligaro, A., Pasin, M., Palesi, F., et al. (2012). Magnetic resonance spectroscopy in the evaluation of treatment efficacy in unipolar major depressive disorder: A review of the literature. *Functional Neurology, 27*(1), 13–22.

Chen, M. C., Joormann, J., Hallmayer, J., & Gotlib, I. H. (2009). Serotonin transporter polymorphism predicts waking cortisol in young girls. *Psychoneuroendocrinology, 34*(5), 681–686.

Cicchetti, D., & Dawson, G. (2002). Multiple levels of analysis. *Development and Psychopathology, 14*, 581–611.

Cicchetti, D., & Schneider-Rosen, K. (Eds.). (1984). *Childhood depression. New directions in child development* (pp. 5–27). San Francisco: Jossey-Bass.

Cicchetti, D., & Toth, S. L. (1998). The development of depression in children and adolescents. *American Psychologist, 53*, 221–241.

Clark, L. A., & Watson, D. (1991). Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. *Journal of Abnormal Psychology, 100*, 316–336.

Clarke, G., & Harvey, A. G. (2012). The complex role of sleep in adolescent depression. *Child and Adolescent Psychiatric Clinics of North America, 21*(2), 385–400.

Cole, D. A., Ciesla, J., Dallaire, D. H., Jacquez, F. M., Pineda, A., LaGrange, B., et al. (2008). Emergence of attributional style and its relation to depressive symptoms. *Journal of Abnormal Psychology, 117*, 16–31.

Cole, D. A., Martin, J. M., Peeke, L. G., Seroczynski, A. D., & Hoffman, K. (1998). Are cognitive errors of underestimation predictive or reflective of depressive symptoms in children?: A longitudinal study. *Journal of Abnormal Psychology, 107*, 481–496.

Cole, D. A., Martin, J. M., Powers, B., & Truglio, R. (1996). Modeling causal relations between academic and social competence and depression: A multi-trait-multimethod longitudinal study of children. *Journal of Abnormal Psychology, 105*, 258–270.

Cole, D. A., Nolen-Hoeksema, S., Girgus, J., & Paul, G. (2006). Stress exposure and stress generation in child and adolescent depression: A latent trait-state-error approach to longitudinal analyses. *Journal of Abnormal Psychology, 115*, 40–51.

Cole, D. A., Truglio, R., & Peeke, L. (1997). Relation between symptoms of anxiety and depression in children: A multitrait-multimethod-multigroup assessment. *Journal of Consulting and Clinical Psychology, 65*, 110–119.

Compas, B. E., Connor-Smith, J., & Jaser, S. S. (2004). Temperament, stress reactivity, and coping: Implications for depression in childhood and adolescence. *Journal of Clinical Child and Adolescent Psychology, 33*, 21–31.

Compas, B. E., Connor-Smith, J. K., Saltzman, H., Thomsen, A. H., & Wadsworth, M. E. (2001). Coping with stress during childhood and adolescence: Problems, progress, and potential in theory and research. *Psychological Bulletin, 127*, 87–127.

Compas, B. E., Forehand, R., Keller, G., Champion, J., Rakow, A., & Cole, D. A. (2009). Randomized controlled trial of a family cognitive-behavioral preventive intervention for children of depressed parents. *Journal of Consulting and Clinical Psychology, 77*(6), 1007–1020.

Conley, C., & Rudolph, K. (2009). The emerging sex difference in adolescent depression: Interacting contributions of puberty and peer stress. *Development and Psychopathology, 21*(2), 593–620.

Connell, A. M., & Dishion, T. J. (2006). The contribution of peers to monthly variation in adolescent depressed

mood: A short-term longitudinal study with time-varying predictors. *Development and Psychopathology, 18*, 139–154.

Conway, C. C., Hammen, C., Brennan, P. A., Lind, P. A., & Najman, J. M. (2010). Interaction of chronic stress with serotonin transporter and catechol-O-methyltransferase polymorphisms in predicting youth depression. *Depression and Anxiety, 27*(8), 737–745.

Copeland, W. E., Shanahan, L., Costello, J., & Angold, A. (2009). Child and adolescent psychiatric disorders as predictors of young adult disorders. *Archives of General Psychiatry, 66*, 764–772.

Copeland, W., Shanahan, L., Miller, S., Costello, E. J., Angold, A., & Maughan, B. (2010). Outcomes of early pubertal timing in young women: A prospective population-based study. *American Journal of Psychiatry, 167*, 1218–1225.

Coplan, J. D., Wolk, S. I., Goetz, R. R., Ryan, N. D., Dahl, R. E., Mann, J. J., et al. (2000). Nocturnal growth hormone secretion studies in adolescents with or without major depression re-examined: Integration of adult clinical follow-up data. *Biological Psychiatry, 47*(7), 594–604.

Costello, E. J., Angold, A., Burns, B. J., Stangl, D. K., Tweed, D. L., Erkanli, A., et al. (1996). The Great Smoky Mountains study of youth: Goals, design, methods, and prevalence of DSM-III-R disorders. *Archives of General Psychiatry, 53*, 1129–1136.

Costello, E. J., Foley, D. L., & Angold, A. (2006). 10-year research update review: The epidemiology of child and adolescent psychiatric disorders: II. Developmental epidemiology. *Journal of the American Academy of Child and Adolescent Psychiatry, 45*, 8–25.

Costello, E. J., Mustillo, S., Erkanli, A., Keeler, G., & Angold, A. (2003). Prevalence and development of psychiatric disorders in childhood and adolescence. *Archives of General Psychiatry, 60*, 837–844.

Coyne, J. C. (1976). Toward an interactional description of depression. *Psychiatry, 39*, 28–40.

Cullen, K. R., Klimes-Dougan, B., Muetzel, R., Mueller, B. A., Camchong, J., Houri, A., et al. (2010). Altered white matter microstructure in adolescents with major depression: A preliminary study. *Journal of the American Academy Child and Adolescent Psychiatry, 49*(2), 173–183 e171.

Cusi, A. M., Nazarov, A., Holshausen, K., Macqueen, G. M., & McKinnon, M. C. (2012). Systematic review of the neural basis of social cognition in patients with mood disorders. *Journal of Psychiatry and Neuroscience, 37*(3), 154–169.

Cyranowski, J. M., Frank, E., Young, E., & Shear, M. K. (2000). Adolescent onset of the gender difference in lifetime rates of major depression. *Archives of General Psychiatry, 57*, 21–27.

Dahl, R. E., Puig-Antich, J., Ryan, N. D., Nelson, B., Dachille, S., Cunningham, S. L., et al. (1990). EEG sleep in adolescents with major depression: The role of suicidality and inpatient status. *Journal of Affective Disorders, 19*(1), 63–75.

Davidson, R. J., Pizzagalli, D., Nitschke, J. B., & Putnam, K. (2002). Depression: Perspectives from affective neuroscience. *Annual Review of Psychology, 53*, 545–574.

Davila, J., Hammen, C., Burge, D., Paley, B., & Daley, S. E. (1995). Poor interpersonal problem solving as a mechanism of stress generation in depression among adolescent women. *Journal of Abnormal Psychology, 104*, 592–600.

Dawson, G., Klinger, L. G., Panagiotides, H., Hill, D., & Spieker, S. (1992). Frontal lobe activity and affective behavior of infants of mothers with depressive symptoms. *Child Development, 63*(3), 725–737.

Dinan, T. G. (1998). Psychoneuroendocrinology of depression. Growth hormone. *Psychiatric Clinics of North America, 21*(2), 325–339.

Dunn, V., & Goodyer, I. M. (2006). Longitudinal investigation into childhood- and adolescence-onset depression: Psychiatric outcome in early adulthood. *British Journal of Psychiatry, 188*, 216–222.

Eaves, L. J., Silberg, J. L., Meyer, J. M., Maes, H. H., Simonoff, E., Pickles, A., et al. (1997). Genetics and developmental psychopathology: 2. The main effects of genes and environment on behavioral problems in the Virginia Twin Study of Adolescent Behavioral Development. *Journal of Child Psychology and Psychiatry, 38*(8), 965–980.

Egger, H. L., & Angold, A. (2006). Common emotional and behavioral disorders in preschool children: Presentation, nosology, and epidemiology. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 47*, 313–337.

Eisenberg, N., Spinrad, T. L., & Eggum, N. D. (2010). Emotion-related self-regulation and its relation to children's maladjustment. *Annual Review of Clinical Psychology, 6*, 495–525.

Eley, T. C., & Stevenson, J. (1999). Exploring the covariation between anxiety and depression symptoms: A genetic analysis of the effects of age and sex. *Journal of Child Psychology and Psychiatry, 40*(8), 1273–1282.

Else-Quest, N., Hyed, J., Goldsmith, H., & van Hulle, C. (2006). Gender differences in temperament: A meta-analysis. *Psychological Bulletin, 132*, 33–72.

Emslie, G. J., Armitage, R., Weinberg, W. A., Rush, A. J., Mayes, T. L., & Hoffmann, R. F. (2001). Sleep polysomnography as a predictor of recurrence in children and adolescents with major depressive disorder. *The International Journal of Neuropsychopharmacology, 4*(2), 159–168.

Emslie, G. J., Rush, A. J., Weinberg, W. A., Kowatch, R. A., Hughes, C. W., Carnody, T., et al. (1997). A double-blind, randomized, placebo-controlled trial of Fluoxetine in children and adolescents with depression. *Archives of General Psychiatry, 54*, 1031–1037.

Ende, G., Demirakca, T., & Tost, H. (2006). The biochemistry of dysfunctional emotions: Proton MR spectroscopic findings in major depressive disorder. *Progress in Brain Research, 156*, 481–501.

Essex, M. J., Klein, M. H., & Kalin, N. H. (2002). Maternal stress beginning in infancy may sensitize children to later stress exposure: Effects on cortisol and behavior. *Biological Psychiatry, 52*, 776–784.

Eysenck, H. J., & Eysenck, M. W. (1985). *Personality and individual differences: A natural science approach*. New York: Plenum.

Ezpeleta, L., Domenech, J. M., & Angold, A. (2006). A comparison of pure and comorbid CD/ODD and depression. *Journal of Child Psychology and Psychiatry, 47*, 704–712.

Fergusson, D. M., Horwood, L. J., Miller, A. L., & Kennedy, M. A. (2011). Life stress, 5-HTTLPR and mental disorder: Findings from a 30-year longitudinal study. *British Journal of Psychiatry, 198*(2), 129–135.

Fergusson, D. M., & Woodward, L. J. (2002). Mental health, educational, and social role outcomes of adolescents with depression. *Archives of General Psychiatry, 59*, 225–331.

Fleming, J., Offord, D., & Boyle, M. (1989). Prevalence of childhood and adolescent depression in the community. Ontario child health study. *British Journal of Psychiatry, 155*(5), 647–654.

Flynn, M., & Rudolph, K. D. (2007). Perceptual asymmetry and youths' responses to stress: Understanding vulnerability to depression. *Cognition and Emotion, 21*, 773–788.

Forbes, E. E., Christopher May, J., Siegle, G. J., Ladouceur, C. D., Ryan, N. D., Carter, C. S., et al. (2006). Reward-related decision-making in pediatric major depressive disorder: An fMRI study. *Journal of Child Psychology and Psychiatry, 47*(10), 1031–1040.

Forbes, E. E., Fox, N. A., Cohn, J., Galles, S., & Kovacs, M. (2006). Children's affect regulation during a disappointment: Psychophysiological responses and relation to parent history to parent history of depression. *Biological Psychiatry, 71*, 264–277.

Forbes, E. E., Hariri, A. R., Martin, S. L., Silk, J. S., Moyles, D. L., Fisher, P. M., et al. (2009). Altered striatal activation predicting real-world positive affect in adolescent major depressive disorder. *American Journal of Psychiatry, 166*(1), 64–73.

Frodl, T. S., Koutsouleris, N., Bottlender, R., Born, C., Jager, M., Scupin, I., et al. (2008). Depression-related variation in brain morphology over 3 years: Effects of stress? *Archives of General Psychiatry, 65*(10), 1156–1165.

Gale, C. R., & Martyn, C. N. (2004). Birthweight and later risk of depression in a national birth cohort. *British Journal of Psychiatry, 184*, 28–33.

Garber, J. (2005). Depression and the family. In J. L. Hudson & R. M. Rapee (Eds.), *Psychopathology and the family* (pp. 227–283). Oxford, UK: Elsevier.

Garber, J. (2007). Depression in youth: A developmental psychopathology perspective. In A. Masten & A. Sroufe (Eds.), *Multilevel dynamics in developmental psychopathology: Pathways to the future* (Vol. 34, pp. 181–242). New York: Erlbaum.

Garber, J., & Flynn, C. (2001). Predictors of depressive cognitions in young adolescents. *Cognitive Therapy and Research, 25*, 353–376.

Garber, J., & Hollon, S. D. (1991). What can specificity designs say about causality in psychopathology research? *Psychological Bulletin, 110*, 129–136.

Garber, J., & Martin, N. C. (2002). Negative cognitions in offspring of depressed parents: Mechanisms of risk. In S. H. Goodman & I. H. Gotlib (Eds.), *Children of depressed parents: Mechanisms of risk and implications for treatment* (pp. 121–153). Washington, DC: APA.

Garber, J., & Robinson, N. S. (1997). Cognitive vulnerability in children at risk for depression. *Cognitions and Emotions, 11*, 619–635.

Garber, J., Robinson, N. S., & Valentiner, D. (1997). The relation between parenting and adolescent depression: Self-worth as a mediator. *Journal of Adolescent Research, 12*, 12–33.

Gazelle, H., & Rudolph, K. D. (2004). Moving toward and away from the world: Social approach and avoidance trajectories in anxious solitary youth. *Child Development, 75*, 829–849.

Ge, X., Best, K. M., Conger, R. D., & Simons, R. L. (1996). Parenting behaviors and the occurrence and co-occurrence of adolescent depressive symptoms and conduct problems. *Developmental Psychology, 32*, 717–731.

Ge, X., Lorenz, F. O., Conger, R. D., Elder, G. H., & Simons, R. L. (1994). Trajectories of stressful life events and depressive symptoms in young adults: Gender differences in developmental trajectories. *Developmental Psychology, 30*, 467–483.

Geller, B., Zimerman, B., Williams, M., Bolhofner, K., & Craney, J. L. (2001). Bipolar disorder at prospective follow-up of adults who had prepubertal major depressive disorder. *American Journal of Psychiatry, 158*, 125–127.

Gerber, A. J., & Peterson, B. S. (2008). Applied brain imaging. *Journal of the American Academy of Child and Adolescent Psychiatry, 47*(3), 239.

Gibb, B. E. (2002). Childhood maltreatment and negative cognitive styles: A quantitative and qualitative review. *Clinical Psychology Review, 22*, 223–246.

Gibb, B. E., & Alloy, L. B. (2006). A prospective test of the hopelessness theory of depression in children. *Journal of Clinical Child and Adolescent Psychology, 35*, 264–274.

Gibb, B. E., Alloy, L. B., Abramson, L. Y., Rose, D. T., Whitehouse, W. G., & Tierney, S. (2001). History of childhood maltreatment, negative cognitive styles, and episodes of depression in adulthood. *Cognitive Therapy and Research, 25*, 425–446.

Gilman, S. E., Kawachi, I., Fitzmaurice, G. M., & Buka, S. L. (2003). Family disruption in childhood and risk of adult depression. *American Journal of Psychiatry, 160*, 939–946.

Gjerde, P. F. (1995). Alternative pathways to chronic depressive symptoms in young adults: Gender differences in developmental trajectories. *Child Development, 66*, 1277–1300.

Glowinski, A. L., Madden, P. A., Bucholz, K. K., Lynskey, M. T., & Heath, A. C. (2003). Genetic epidemiology of self-reported lifetime DSM-IV major depressive disorder in a population-based twin sample of female adolescents. *Journal of Child Psychology and Psychiatry, 44*(7), 988–996.

Gonzalez-Tejera, G., Canino, G., Ramirez, R., Chavez, L., Shrout, P., Bird, H., et al. (2005). Examining minor and major depression in adolescents. *Journal of Child Psychology and Psychiatry, 46*, 888–899.

Goodman, S. (2007). Depression in mothers. *Annual Review of Clinical Psychology, 3*, 107–135.

Goodman, S. H., Schwab-Stone, M., Lahey, B. B., Shaffer, D., & Jensen, P. S. (2000). Major depression and dysthymia in children and adolescents: Discriminant validity and differential consequences in a community sample. *Journal of the American Academy of Child and Adolescent Psychiatry, 36*, 761–770.

Goodwin, R. D., Fergusson, D. M., & Horwood, L. J. (2004). Early anxious/withdrawn behaviours predict later internalizing disorders. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 45*, 874–883.

Goodyer, I. M., Bacon, A., Ban, M., Croudace, T., & Herbert, J. (2009). Serotonin transporter genotype, morning cortisol and subsequent depression in adolescents. *British Journal of Psychiatry, 195*(1), 39–45.

Goodyer, I. M., Croudace, T., Dudbridge, F., Ban, M., & Herbert, J. (2010). Polymorphisms in BDNF (Val66Met) and 5-HTTLPR, morning cortisol and subsequent depression in at-risk adolescents. *British Journal of Psychiatry, 197*(5), 365–371.

Goodyer, I. M., Herbert, J., Tamplin, A., & Altham, P. M. (2000). Recent life events, cortisol, dehydroepiandrosterone and the onset of major depression in high-risk adolescents. *British Journal of Psychiatry, 177*, 499–504.

Goodyer, I. M., Park, R. J., & Herbert, J. (2001). Psychosocial and endocrine features of chronic first-episode major depression in 8–16 year olds. *Biological Psychiatry, 50*(5), 351–357.

Gotlib, I. H., Hamilton, J. P., Cooney, R. E., Singh, M. K., Henry, M. L., & Joormann, J. (2010). Neural processing of reward and loss in girls at risk for major depression. *Archives of General Psychiatry, 67*(4), 380–387.

Gotlib, I. H., Joormann, J., Minor, K. L., & Cooney, R. E. (2006). Cognitive and biological functioning in children at risk for depression. In T. Canli (Ed.), *Biology of personality and individual differences* (pp. 353–382). New York, NY: Guilford.

Gotlib, I. H., Joormann, J., Minor, K. L., & Hallmayer, J. (2008). HPA axis reactivity: A mechanism underlying the associations among 5-HTTLPR, stress, and depression. *Biological Psychiatry, 63*(9), 847–851.

Grant, K. E., Compas, B. E., Thurm, A. E., McMahon, S. D., Gipson, P. Y., & Westerholm, R. I. (2006). Stressors and child and adolescent psychopathology: Evidence of moderating and mediating effects. *Clinical Psychology Review, 26*, 257–283.

Gray, J. A. (1991). The neuropsychology of temperament. In J. Strelau & A. Angleitner (Eds.), *Explorations in temperament: International perspectives on theory and measurement* (pp. 105–128). New York: Plenum.

Guedeney, N., Guedeney, A., Rabouam, C., Mintz, A. S., Danon, G., Huet, M. M., et al. (2003). The Zero-to-Three diagnostic classification: A contribution to the validation of this classification from a sample of 85 under-threes. *Infant Mental Health Journal, 24*, 313–336.

Hammen, C. (1991). The generation of stress in the course of unipolar depression. *Journal of Abnormal Psychology, 100*, 555–561.

Hammen, C. (2002). The context of stress in families of children with depressed parents. In S. Goodman & I. Gotlib (Eds.), *Children of depressed parents: Mechanisms of risk and implications for treatment* (pp. 175–199). Washington, D.C.: American Psychological Association.

Hammen, C. (2006). Stress generation in depression: Reflections on origins, research, and future directions. *Journal of Clinical Psychology, 62*, 69–82.

Hammen, C., & Brennan, P. A. (2001). Depressed adolescents of depressed and nondepressed mothers: Tests of an interpersonal impairment hypothesis. *Journal of Consulting and Clinical Psychology, 69*, 284–294.

Hammen, C., Brennan, P. A., Keenan-Miller, D., Hazel, N. A., & Najman, J. M. (2010). Chronic and acute stress, gender, and serotonin transporter gene-environment interactions predicting depression symptoms in youth. *Journal of Child Psychology and Psychiatry, 51*(2), 180–187.

Hammen, C., Henry, R., & Daley, S. E. (2000). Depression and sensitization to stressors among young women as a function of childhood adversity. *Journal of Consulting and Clinical Psychology, 68*, 782–787.

Hammen, C., Shih, J. H., & Brennan, P. A. (2004). Intergenerational transmission of depression: Test of an interpersonal stress model in a community sample. *Journal of Consulting and Clinical Psychology, 72*, 511–522.

Hankin, B. L. (2005). Childhood maltreatment and psychopathology: Prospective tests of attachment, cognitive vulnerability, and stress as mediating processes. *Cognitive Therapy and Research, 29*, 645–671.

Hankin, B. L. (2012). Future directions in vulnerability to depression among youth: Integrating risk factors and processes across multiple levels of analysis. *Journal of Clinical Child and Adolescent Psychology, 41*(5), 695–718.

Hankin, B. L., & Abramson, L. (2001). Development of gender differences in depression: An elaborated cognitive vulnerability-transactional stress theory. *Psychological Bulletin, 127*, 773–796.

Hankin, B. L., Abramson, L., Miller, N., & Haeffel, G. (2004). Cognitive vulnerability-stress theories of depression: Examining affective specificity in the prediction of depression versus anxiety in three prospective studies. *Cognitive Therapy & Research, 28*, 309–345.

Hankin, B. L., Abramson, L. Y., Moffitt, T. E., Silva, P. A., McGee, R., & Angell, K. E. (1998). Development of depression from preadolescence to young adulthood: Emerging gender differences in a 10-year longitudinal study. *Journal of Abnormal Psychology, 107*, 128–140.

Hankin, B. L., Fraley, R. C., Lahey, B. B., & Waldman, I. D. (2005). Is depression best viewed as a continuum or

discrete category? A taxometric analysis of childhood and adolescent depression in a population-based sample. *Journal of Abnormal Psychology, 114*, 96–110.

Hankin, B. L., Mermelstein, R., & Roesch, L. (2007). Sex differences in adolescent depression: Stress exposure and reactivity models in interpersonal and achievement contextual domains. *Child Development, 78*, 279–295.

Happonen, M., Pulkkinen, L., Kaprio, J., Van der Meere, J., Viken, R. J., & Rose, R. J. (2002). The heritability of depressive symptoms: Multiple informants and multiple measures. *Journal of Child Psychology and Psychiatry, 43*(4), 471–479.

Harkness, K. L., Bruce, A. E., & Lumley, M. N. (2006). The role of childhood abuse and neglect in the sensitization to stressful life events in adolescent depression. *Journal of Abnormal Psychology, 115*, 730–741.

Harkness, K. L., & Lumley, M. N. (2008). Child abuse and neglect and the development of depression in children and adolescents. In J. R. Z. Abela & B. L. Hankin (Eds.), *Handbook of depression in children and adolescents* (pp. 466–488). New York: Guilford.

Harrington, R., Fudge, H., Rutter, M., Pickles, A., & Hill, J. (1990). Adult outcomes of childhood and adolescent depression. *Archives of General Psychiatry, 47*, 465–473.

Harrington, R., Peters, S., Green, J., Byford, S., Woods, J., & McGowan, R. (2000). Randomised comparison of the effectiveness and costs of community and hospital based mental health services for children with behavioral disorders. *British Journal of Medicine, 321*, 1–5.

Hasler, G., & Northoff, G. (2011). Discovering imaging endophenotypes for major depression. *Molecular Psychiatry, 16*(6), 604–619.

Hayden, E. P., Klein, D. N., & Durbin, C. E. (2005). Parent reports and laboratory assessments of child temperament: A comparison of their associations with risk for depression and externalizing disorders. *Journal of Psychopathology & Behavioral Assessment, 27*, 89–100.

Hoffman, K. B., Cole, D. A., Martin, J. M., Tram, J., & Serocynski, A. D. (2000). Are the discrepancies between self- and others' appraisals of competence predictive or reflective of depressive symptoms in children and adolescents?: A longitudinal study, Part II. *Journal of Abnormal Psychology, 109*, 651–662.

Hofstra, M. B., van der Ende, J., & Verhulst, F. C. (2000). Continuity and change in psychopathology from childhood into adulthood: A 14-year follow-up study. *Journal of the American Academy of Child and Adolescent Psychiatry, 39*, 850–858.

Hu, X. Z., Lipsky, R. H., Zhu, G., Akhtar, L. A., Taubman, J., Greenberg, B. D., et al. (2006). Serotonin transporter promoter gain-of-function genotypes are linked to obsessive-compulsive disorder. *American Journal of Human Genetics, 78*(5), 815–826.

Huang, H., Fan, X., Williamson, D. E., & Rao, U. (2011). White matter changes in healthy adolescents at familial risk for unipolar depression: A diffusion tensor imaging study. *Neuropsychopharmacology, 36*(3), 684–691.

Huang, H., Gundapuneedi, T., & Rao, U. (2012). White matter disruptions in adolescents exposed to childhood maltreatment and vulnerability to psychopathology. *Neuropsychopharmacology, 37*(12), 2693–2701.

Hulvershorn, L. A., Cullen, K., & Anand, A. (2011). Toward dysfunctional connectivity: A review of neuroimaging findings in pediatric major depressive disorder. *Brain Imaging and Behavior, 5*(4), 307–328.

Hyde, J. S., Mezulis, A. H., & Abramson, L. Y. (2008). The ABCs of depression: Integrating affective, biological, and cognitive models to explain the emergence of the gender difference in depression. *Psychological Review, 115*, 291–313.

Ingram, R. E., Miranda, J., & Segal, Z. V. (1998). *Cognitive vulnerability to depression*. New York: Guilford.

Insel, T. (2013, April 29). *Transforming diagnosis* [Web log post]. Retrieved from http://www.nimh.nih.gov/about/director/index.shtml

Ivanenko, A., & Johnson, K. (2008). Sleep disturbances in children with psychiatric disorders. *Seminars in Pediatric Neurology, 15*(2), 70–78.

Ivarsson, T., Broberg, A. G., Arvidsson, T., & Gillberg, C. (2005). Bullying in adolescence: Psychiatric problems in victims and bullies as measured by the youth self report (YSR) and the depression self-rating scale (DSRS). *Nordic Journal of Psychiatry, 59*, 365–373.

Jacobs, R. H., Reinecke, M. A., Gollan, J. K., & Kane, P. (2008). Empirical evidence of cognitive vulnerability for depression among children and adolescents: A cognitive science and development perspective. *Clinical Psychology Review, 28*, 759–782.

Jaffee, S. R., Moffitt, T. E., Caspi, A., Fombonne, E., Poulton, R., & Martin, J. (2002). Differences in early childhood risk factors for juvenile-onset and adult-onset depression. *Archives of General Psychiatry, 59*, 215–222.

Jenness, J. L., Hankin, B. L., Abela, J. R., Young, J. F., & Smolen, A. (2011). Chronic family stress interacts with 5-HTTLPR to predict prospective depressive symptoms among youth. *Depression and Anxiety, 28*(12), 1074–1080.

Joiner, T. E., & Coyne, J. C. (Eds.). (1999). *The interactional nature of depression*. Washington, DC: American Psychological Association.

Jones, D. J., Forehand, R., & Neary, E. M. (2001). Family transmission of depressive symptoms: Replication across Caucasian and African American mother-child dyads. *Behavior Therapy, 32*, 123–138.

Joormann, J., Talbot, L., & Gotlib, I. H. (2007). Biased processing of emotional information in girls at risk for depression. *Journal of Abnormal Psychology, 116*, 135–143.

Kaltiala-Heino, R., Rimpela, M., Rantanen, P., & Rimpela, A. (2000). Bullying at school: An indicator of adolescents at risk for mental disorders. *Journal of Adolescence, 23*, 661–674.

Kapoor, A., Dunn, E., Kostaki, A., Andrews, M. H., & Matthews, S. G. (2006). Fetal programming of hypothalamo-pituitary-adrenal function: Prenatal

stress and glucocorticoids. *Journal of Physiology, 572*, 31–44.

Kashani, J. H., Rosenberg, T. K., & Reid, J. C. (1989). Developmental perspectives in child and adolescent depressive symptoms in a community sample. *American Journal of Psychiatry, 146*, 871–875.

Katainen, S., Raikkonen, K., Keskivaara, P., & Keltikangas-Jarvinen, L. (1999). Maternal child-rearing attitudes and role satisfaction and children's temperament as antecedents of adolescent depressive tendencies: Follow-up study of 6- to 15-year olds. *Journal of Youth and Adolescence, 28*, 139–163.

Kaufman, J., Birmaher, B., Perel, J., Dahl, R. E., Moreci, P., Nelson, B., et al. (1997). The corticotropin-releasing hormone challenge in depressed abused, depressed nonabused, and normal control children. *Biological Psychiatry, 42*(8), 669–679.

Kaufman, J., & Charney, D. (2001). Effects of early stress on brain structure and function: Implications for understanding the relationship between child maltreatment and depression. *Development and Psychopathology, 13*(3), 451–471.

Kaufman, J., Martin, A., King, R. A., & Charney, D. (2001). Are child-, adolescent-, and adult-onset depression one and the same disorder? *Biological Psychiatry, 49*(12), 980–1001.

Kaufman, J., Yang, B. Z., Douglas-Palumberi, H., Grasso, D., Lipschitz, D., Houshyar, S., et al. (2006). Brain-derived neurotrophic factor-5-HTTLPR gene interactions and environmental modifiers of depression in children. *Biological Psychiatry, 59*(8), 673–680.

Kaufman, J., Yang, B. Z., Douglas-Palumberi, H., Houshyar, S., Lipschitz, D., Krystal, J. H., et al. (2004). Social supports and serotonin transporter gene moderate depression in maltreated children. *Proceedings of the National Academy of Sciences of the United States of America, 101*(49), 17316–17321.

Kendler, K. S., Gardner, C. O., & Prescott, C. A. (2002). Toward a comprehensive developmental model for major depression in women. *American Journal of Psychiatry, 159*, 1133–1145.

Kendler, K. S., Kessler, R. C., Walters, E. E., MacLean, C., Neale, M. C., Heath, A. C., et al. (1995). Stressful life events, genetic liability, and onset of an episode of major depression in women. *American Journal of Psychiatry, 152*, 833–842.

Kennard, B. D., Emslie, G. J., Mayes, T. L., & Hughes, J. L. (2006). Relapse and recurrence in pediatric depression. *Child and Adolescent Psychiatric Clinics of North America, 15*, 1057–1079.

Kentgen, L. M., Tenke, C. E., Pine, D. S., Fong, R., Klein, R. G., & Bruder, G. E. (2000). Electroencephalographic asymmetries in adolescents with major depression: Influence of comorbidity with anxiety disorders. *Journal of Abnormal Psychology, 109*(4), 797–802.

Kessler, R., Avenevoli, S., Costello, E., Georgiades, K., Green, J., Gruber, M., et al. (2012). Prevalence, persistence, and sociodemographic correlates of DSM-IV disorders in the National Comorbidity Survey Replication Adolescent Supplement. *Archives of General Psychiatry, 69*(4), 372–380.

Kessler, R. C., Avenevoli, S., & Merikangas, K. R. (2001). Mood disorders in children and adolescents: An epidemiologic perspective. *Biological Psychiatry, 49*(12), 1002–1014.

Kessler, R. C., & Walters, E. E. (1998). Epidemiology of DSM-III-R major depression and minor depression among adolescents and young adults in the National Comorbidity Survey. *Depression and Anxiety, 7*, 3–14.

Kim, H., Capaldi, D., & Stoolmiller, M. (2003). Depressive symptoms across adolescence and young adulthood in men: Predictions from parental and contextual risk factors. *Development and Psychopathology, 15*(2), 469–495.

Kistner, J., Balthazor, M., Risi, S., & Burton, C. (1999). Predicting dysphoria in adolescence from actual and perceived peer acceptance in childhood. *Journal of Clinical Child Psychology, 28*, 94–104.

Klein, D. N., Kotov, R., & Bufferd, S. J. (2011). Personality and depression: Explanatory models and review of the evidence. *Annual Review of Clinical Psychology, 7*, 269–295.

Klein, D. N., Shankman, S. A., Lewinsohn, P. M., & Seeley, J. K. (2009). Subthreshold depressive disorder in adolescents: Predictors of escalation to full syndrome depressive disorders. *Journal of the American Academy of Child and Adolescent Psychiatry, 48*, 703–710.

Kondo, D. G., Hellem, T. L., Sung, Y. H., Kim, N., Jeong, E. K., Delmastro, K. K., et al. (2010). Review: Magnetic resonance spectroscopy studies of pediatric major depressive disorder. *Depression Research and Treatment, 2011*, 1–13.

Kovacs, M. (1994). Childhood-onset dysthymic disorder: Clinical features and prospective naturalistic outcome. *Archives of General Psychology, 51*, 365–374.

Kovacs, M. (1996a). The course of childhood-onset depressive disorders. *Psychiatric Annals, 26*, 326–330.

Kovacs, M. (1996b). Presentation and course of major depressive disorder during childhood and later years of the life span. *Journal of the American Academy of Child and Adolescent Psychiatry, 35*, 705–715.

Kovacs, M., & Lopez-Duran, N. (2010). Prodromal symptoms and atypical affectivity as predictors of major depression in juveniles: Implications for prevention. *Journal of Child Psychology and Psychiatry, 51*, 472–496.

Kovacs, M., Obrosky, D. S., & Sherrill, J. (2003). Developmental changes in the phenomenology of depression in girls compared to boys from childhood onward. *Journal of Affective Disorders, 74*, 33–48.

Kujawa, A., Torpey, D., Kim, J., Hajcak, G., Rose, S., Gotlib, I., et al. (2011). Attentional biases for emotional faces in young children of mothers with chronic or recurrent depression. *Journal of Abnormal Child Psychology, 39*, 125–135.

LaGrange, B., Cole, D. A., Jacquea, F., Ciesla, J., Dallaire, D., Pineda, A., et al. (2011). Disentangling the prospective relations between maladaptive cognitions and depressive symptoms. *Journal of Abnormal Psychology, 120*, 511–527.

Lakdawalla, Z., Hankin, B. L., & Mermelstein, R. (2007). Cognitive theories of depression in children and adolescents: A conceptual and quantitative review. *Clinical Child and Family Psychology Review, 10*, 1–24.

Lau, J. Y., & Eley, T. C. (2008). Disentangling gene-environment correlations and interactions on adolescent depressive symptoms. *Journal of Child Psychology and Psychiatry, 49*(2), 142–150.

Leinonen, J. A., Solantaus, T. S., & Punamaki, R. L. (2003). Parental mental health and children's adjustment: The quality of marital interaction and parenting as mediating factors. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 44*, 227–241.

Lengua, L. J., Sandler, I. N., West, S. G., Wolchik, S. A., & Curran, P. J. (1999). Emotionality and self-regulation, threat appraisal, and coping in children of divorce. *Development and Psychopathology, 11*, 15–37.

Lengua, L. J., Wolchik, S. A., Sandler, I. N., & West, S. G. (2000). The additive and interactive effects of parenting and temperament in predicting adjustment problems of children of divorce. *Journal of Clinical Child Psychology, 29*, 232–244.

Leppanen, J. M. (2006). Emotional information processing in mood disorders: A review of behavioral and neuroimaging findings. *Current Opinion in Psychiatry, 19*(1), 34–39.

Lesch, K. P., Bengel, D., Heils, A., Sabol, S. Z., Greenberg, B. D., Petri, S., et al. (1996). Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region. *Science, 274*(5292), 1527–1531.

Lewinsohn, P. M., Allen, N. B., Seeley, J. R., & Gotlib, I. H. (1999). First onset versus recurrence of depression: Differential processes of psychosocial risk. *Journal of Abnormal Psychology, 108*, 483–489.

Lewinsohn, P. M., & Essau, C. A. (2002). Depression in adolescents. In I. H. Gotlib & C. L. Hammen (Eds.), *Handbook of depression* (pp. 541–559). New York, NY: Guilford.

Lewinsohn, P. M., Hops, H., Roberts, R. E., Seeley, J. R., & Andrews, J. A. (1993). Adolescent psychopathology: I. Prevalence and incidence of depression and other DSM-III-R disorders in high school students. *Journal of Abnormal Psychology, 102*, 133–144.

Lewinsohn, P. M., Joiner, T. E., & Rohde, P. (2001). Evaluation of cognitive diathesis-stress models in predicting major depressive disorder in adolescents. *Journal of Abnormal Psychology, 110*, 203–215.

Lewinsohn, P. M., Rohde, P. M., & Seeley, J. R. (1998). Major depressive disorder in older adolescents: Prevalence, risk factors, and clinical implications. *Clinical Psychology Review, 18*, 765–794.

Lewinsohn, P. M., Solomon, A., Seeley, J. R., & Zeiss, A. (2000). Clinical implications of "subthreshold" depressive symptoms. *Journal of Abnormal Psychology, 109*, 345–351.

Lewinsohn, P. M., Steinmetz, J. L., Larson, D. W., & Franklin, J. (1981). Depression related cognitions: Antecedent or consequence? *Journal of Abnormal Psychology, 91*, 213–219.

Lonigan, C. J., Phillips, B. M., & Hooe, E. S. (2003). 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, 71*, 465–481.

Lovejoy, M. C., Graczyk, P. A., O'Hare, E., & Neuman, G. (2000). Maternal depression and parenting: A meta-analytic review. *Clinical Psychology Review, 20*, 561–592.

Luby, J. L., Belden, A. C., & Spitznagel, E. (2006). Risk factors for preschool depression: The mediating role of early stressful life events. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 47*, 1292–1298.

Luby, J. L., Heffelfinger, A. K., Mrakotsky, C., Hessler, M. J., Brown, K. M., & Hildebrand, T. (2002). Preschool major depressive disorder: Preliminary validation for developmentally modified DSM-IV criteria. *Journal of the American Academy of Child and Adolescent Psychiatry, 41*, 928–937.

Luby, J. L., Mrakotsky, C., Heffelfinger, A., Brown, K., Hessler, M., & Spitznagel, E. (2003). Modification of DSM-IV criteria for depressed preschool children. *American Journal of Psychiatry, 160*, 1169–1172.

Luykx, J. J., Laban, K. G., van den Heuvel, M. P., Boks, M. P., Mandl, R. C., Kahn, R. S., et al. (2012). Region and state specific glutamate downregulation in major depressive disorder: A meta-analysis of (1)H-MRS findings. *Neuroscience & Biobehavioral Reviews, 36*(1), 198–205.

MacMillan, S., Szeszko, P. R., Moore, G. J., Madden, R., Lorch, E., Ivey, J., et al. (2003). Increased amygdala: Hippocampal volume ratios associated with severity of anxiety in pediatric major depression. *Journal of Child and Adolescent Psychopharmacology, 13*(1), 65–73.

MacQueen, G., & Frodl, T. (2011). The hippocampus in major depression: Evidence for the convergence of the bench and bedside in psychiatric research? *Molecular Psychiatry, 16*(3), 252–264.

Markham, J. A., & Koenig, J. I. (2011). Prenatal stress: Role in psychotic and depressive diseases. *Development and Psychopathology, 214*(1), 89–106.

Matas, L., Arend, R. A., & Sroufe, L. A. (1978). Continuity of adaptation in the second year: The relation between quality of attachment and later competence. *Child Development, 49*, 547–556.

Mathew, S. J., Coplan, J. D., Goetz, R. R., Feder, A., Greenwald, S., Dahl, R. E., et al. (2003). Differentiating depressed adolescent 24 h cortisol secretion in light of their adult clinical outcome. *Neuropsychopharmacology, 28*(7), 1336–1343.

Mayberg, H. S. (2003). Modulating dysfunctional limbic-cortical circuits in depression: Towards development of brain-based algorithms for diagnosis and optimised treatment. *British Medical Bulletin, 65*, 193–207.

McCarty, C. A., Vander Stoep, A., & McCauley, E. (2007). Cognitive features associated with depressive symptoms in adolescence: Directionality and specificity. *Journal of Clinical Child and Adolescent Psychology, 36*, 147–158.

McEwen, B. S. (1999). Stress and hippocampal plasticity. *Annual Review of Neuroscience, 22*, 105–122.

McGinn, L. K., Cukor, D., & Sanderson, W. C. (2005). The relationship between parenting style, cognitive style, and anxiety and depression: Does increased early adversity influence symptom severity through the mediating role of cognitive style? *Cognitive Therapy and Research, 29*(2), 219–242.

McKinnon, M. C., Yucel, K., Nazarov, A., & MacQueen, G. M. (2009). A meta-analysis examining clinical predictors of hippocampal volume in patients with major depressive disorder. *Journal of Psychiatry and Neuroscience, 34*(1), 41–54.

Merikangas, K. R., He, J.-P., Brody, D., Fisher, P. W., Bourdon, K., & Koretz, D. S. (2010). Prevalence and treatment of mental disorders among U.S. children in the 2001–2004 NHANES. *Pediatrics, 125*, 75–81.

Merikangas, K. R., & Knight, E. (2009). The epidemiology of depression in adolescents. In S. Nolen-Hoeksema & L. M. Hilt (Eds.), *Handbook of depression in adolescents* (pp. 386–404). New York, NY: Taylor and Francis Group, LLC.

Mezulis, A. H., Hyde, J. S., & Abramson, L. Y. (2006). The developmental origins of cognitive vulnerability to depression: Temperament, parenting, and negative life events in childhood as contributors to negative cognitive style. *Developmental Psychology, 42*, 1012–1025.

Mitchell, A. M., & Possel, P. (2012). Frontal brain activity pattern predicts depression in adolescent boys. *Biological Psychology, 89*(2), 525–527.

Monroe, S. M., & Harkness, K. L. (2005). Life stress, the "kindling" hypothesis, and the recurrence of depression: Considerations from a life stress perspective. *Psychological Review, 112*, 417–445.

Monroe, S. M., Rohde, P., Seeley, J. R., & Lewinsohn, P. M. (1999). Life events and depression in adolescence: Relationship loss as a prospective risk factor for first-onset of major depressive disorder. *Journal of Abnormal Psychology, 108*, 606–614.

Monroe, S. M., & Simons, A. D. (1991). Diathesis-stress theories in the context of life stress research: Implications for the depressive disorders. *Psychological Bulletin, 110*, 406–425.

Moran, M. (2013). DSM-5 updates depressive, anxiety, and OCD criteria. *Psychiatric News, 48*(4), 22–43.

Morehouse, R. L., Kusumakar, V., Kutcher, S. P., LeBlanc, J., & Armitage, R. (2002). Temporal coherence in ultradian sleep EEG rhythms in a never-depressed, high-risk cohort of female adolescents. *Biological Psychiatry, 51*(6), 446–456.

Morris, M. C., Ciesla, J. A., & Garber, J. (2008). A prospective study of the cognitive-stress model of depressive symptoms in adolescents. *Journal of Abnormal Psychology, 117*, 719–734.

Mrug, S., Hoza, B., & Bukowski, W. M. (2004). Choosing or being chosen by aggressive-disruptive peers: Do they contribute to children's externalizing and internalizing problems? *Journal of Abnormal Child Psychology, 32*, 53–65.

Natsuaki, M. N., Ge, X., Brody, G. H., Simons, R. L., Gibbons, F. X., & Cutrona, C. E. (2007). African American children's depressive symptoms: The prospective effects of neighborhood disorder, stressful life events and parenting. *American Journal of Community Psychology, 39*, 163–176.

Nigg, J. T. (2006). Temperament and developmental psychopathology. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 47*, 395–422.

Nobile, M., Cataldo, M. G., Giorda, R., Battaglia, M., Baschirotto, C., Bellina, M., et al. (2004). A case–control and family-based association study of the 5-HTTLPR in pediatric-onset depressive disorders. *Biological Psychiatry, 56*(4), 292–295.

Nolan, S. A., Flynn, C., & Garber, J. (2003). Prospective relations between rejection and depression in young adolescents. *Journal of Personality and Social Psychology, 85*, 745–755.

Nolan, C. L., Moore, G. J., Madden, R., Farchione, T., Bartoi, M., Lorch, E., et al. (2002). Prefrontal cortical volume in childhood-onset major depression: Preliminary findings. *Archives of General Psychiatry, 59*(2), 173–179.

Nolen-Hoeksema, S., & Hilt, L. M. (2009). Gender differences in depression. In I. Gotlib & C. Hammen (Eds.), *Handbook of depression* (2nd ed., pp. 386–404). New York, NY: Guilford.

Oldehinkel, A. J., Veenstra, R., Ormel, J., de Winter, A. F., & Verhulst, F. C. (2006). Temperament, parenting, and depressive symptoms in a population sample of preadolescents. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 47*, 684–695.

Olino, T. M., Klein, D. N., Dyson, M. W., Rose, S. A., & Durbin, C. E. (2010). Temperamental emotionality in preschool-aged children and depressive disorders in parents: Associations in a large community sample. *Journal of Abnormal Psychology, 119*, 468–478.

Olvera, R. L., Caetano, S. C., Stanley, J. A., Chen, H. H., Nicoletti, M., Hatch, J. P., et al. (2010). Reduced medial prefrontal N-acetyl-aspartate levels in pediatric major depressive disorder: A multi-voxel in vivo(1)H spectroscopy study. *Psychiatry Research, 184*(2), 71–76.

Ormel, J., Oldehinkel, A. J., Ferdinand, R. F., Hartman, C. A., de Winter, A. F., & Verhulst, F. C. (2005). Internalizing and externalizing problems in adolescence: General and dimension-specific effects of familial loadings and preadolescent temperament traits. *Psychological Medicine, 35*, 1825–1835.

Park, I. J. K., Garber, J., Ciesla, J. A., & Ellis, B. J. (2008). Convergence among multiple methods of measuring positivity and negativity in the family environment: Relation to depression in mothers and their children. *Journal of Family Psychology, 22*, 123–134.

Park, R. J., Goodyer, I. M., & Teasdale, J. D. (2005). Self-devaluative dysphoric experience and the prediction of persistent first-episode major depressive disorder in adolescents. *Psychological Medicine, 35*, 539–548.

Phillips, B. M., Lonigan, C. J., Driscoll, K., & Hooe, E. S. (2002). Positive and negative affectivity in

children: A multitrait-multimethod investigation. *Journal of Clinical Child and Adolescent Psychology, 31*, 465–479.

Pihlakoski, L., Sourander, A., Aromaa, M., Rautava, P., Helenius, H., & Sillanpaa, M. (2006). The continuity of psychopathology from early childhood to preadolescence. *European Child and Adolescent Psychiatry, 15*, 409–417.

Pomerantz, E. M., & Rudolph, K. D. (2003). What ensues from emotional distress? Implications for competence estimation. *Child Development, 74*, 329–346.

Posner, M. I., & Rothbart, M. K. (2007). Research on attention networks as a model for the integration of psychological science. *Annual Review of Psychology, 58*, 1–23.

Post, R. M. (1992). Transduction of psychosocial stress into the neurobiology of recurrent affective disorder. *American Journal of Psychiatry, 149*, 1006.

Price, J. L., & Drevets, W. C. (2012). Neural circuits underlying the pathophysiology of mood disorders. *Trends in Cognitive Science, 16*(1), 61–71.

Prinstein, M. J., Borelli, J. L., Cheah, C. S. L., Simon, V. A., & Aikins, J. W. (2005). Adolescent girls' interpersonal vulnerability to depressive symptoms: A longitudinal examination of reassurance-seeking and peer relationships. *Journal of Abnormal Psychology, 114*, 676–688.

Rajkowska, G., & Miguel-Hidalgo, J. J. (2007). Gliogenesis and glial pathology in depression. *Current Drug Targets – CNS and Neurological Disorders, 6*(3), 219–233.

Rao, U. (2011). Sleep disturbances in pediatric depression. *Asian Journal of Psychiatry, 4*(4), 234–247.

Rao, U., & Chen, L. A. (2009). Characteristics, correlates, and outcomes of childhood and adolescent depressive disorders. *Dialogues in Clinical Neuroscience, 11*(1), 45–62.

Rao, U., Chen, L. A., Bidesi, A. S., Shad, M. U., Thomas, M. A., & Hammen, C. L. (2010). Hippocampal changes associated with early-life adversity and vulnerability to depression. *Biological Psychiatry, 67*(4), 357–364.

Rao, U., Dahl, R. E., Ryan, N. D., Birmaher, B., Williamson, D. E., Giles, D. E., et al. (1996). The relationship between longitudinal clinical course and sleep and cortisol changes in adolescent depression. *Biological Psychiatry, 40*(6), 474–484.

Rao, U., Dahl, R. E., Ryan, N. D., Birmaher, B., Williamson, D. E., Rao, R., et al. (2002). Heterogeneity in EEG sleep findings in adolescent depression: Unipolar versus bipolar clinical course. *Journal of Affective Disorders, 70*(3), 273–280.

Rao, U., Hammen, C., Ortiz, L. R., Chen, L. A., & Poland, R. E. (2008). Effects of early and recent adverse experiences on adrenal response to psychosocial stress in depressed adolescents. *Biological Psychiatry, 64*(6), 521–526.

Rao, U., Hammen, C. L., & Poland, R. E. (2009a). Ethnic differences in electroencephalographic sleep patterns in adolescents. *Asian Journal of Psychiatry, 2*(1), 17–24.

Rao, U., Hammen, C. L., & Poland, R. E. (2009b). Risk markers for depression in adolescents: Sleep and HPA measures. *Neuropsychopharmacology, 34*(8), 1936–1945.

Rao, U., Hammen, C. L., & Poland, R. E. (2010). Longitudinal course of adolescent depression: Neuroendocrine and psychosocial predictors. *Journal of the American Academy of Child and Adolescent Psychiatry, 49*, 141–151.

Raynor, P., & Rudolf, M. (1996). What do we know about children who fail to thrive? *Child: Care, Health and Development, 22*(4), 241.

Resnick, M. D., Bearman, P. S., Blum, R. W., Bauman, K. E., Harris, K. M., & Udry, R. (1997). Protecting adolescents from harm: Findings from the National Longitudinal Study on Adolescent Health. *Journal of American Medical Association, 278*, 823–832.

Rice, F. (2010). Genetics of childhood and adolescent depression: Insights into etiological heterogeneity and challenges for future genomic research. *Genome Medicine, 2*(9), 68.

Rice, F., Harold, G. T., & Thapar, A. (2002). Assessing the effects of age, sex and shared environment on the genetic aetiology of depression in childhood and adolescence. *Journal of Child Psychology and Psychiatry, 43*(8), 1039–1051.

Rice, F., Harold, G. T., & Thapar, A. (2003). Negative life events as an account of age-related differences in the genetic aetiology of depression in childhood and adolescence. *Journal of Child Psychology and Psychiatry, 44*(7), 977–987.

Richey, J., Schmidt, N., Lonigan, C., Phillips, B., Catanzaro, S., & Kotov, R. (2009). The latent structure of child depression: A taxometric analysis. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 50*(9), 1147–1155.

Rizzo, C. J., Daley, S. E., & Gunderson, B. H. (2006). Interpersonal sensitivity, romantic stress, and the prediction of depression: A study of inner-city, minority adolescent girls. *Journal of Youth and Adolescence, 35*, 444–453.

Roberson-Nay, R., McClure, E. B., Monk, C. S., Nelson, E. E., Guyer, A. E., Fromm, S. J., et al. (2006). Increased amygdala activity during successful memory encoding in adolescent major depressive disorder: An FMRI study. *Biological Psychiatry, 60*, 966–973.

Robert, J. J., Hoffmann, R. F., Emslie, G. J., Hughes, C., Rintelmann, J., Moore, J., et al. (2006). Sex and age differences in sleep macroarchitecture in childhood and adolescent depression. *Sleep, 29*(3), 351–358.

Rohde, P., Lewinsohn, P. M., & Seeley, J. R. (1991). Comorbidity of unipolar depression: II. Comorbidity with other mental disorders in adolescents and adults. *Journal of Abnormal Psychology, 100*, 214–222.

Rosso, I. M., Cintron, C. M., Steingard, R. J., Renshaw, P. F., Young, A. D., & Yurgelun-Todd, D. A. (2005). Amygdala and hippocampus volumes in pediatric major depression. *Biological Psychiatry, 57*(1), 21–26.

Rothbart, M. K., & Bates, J. E. (2006). Temperament. In W. Damon, R. M. Lerner, & N. Eisenberg (Eds.),

Handbook of child psychology: Vol. 3. Social, emotional, and personality development (6th ed., pp. 99–166). New York: Wiley.

Rubio-Stipec, M., Fitzmaurice, G., Murphy, J., & Walker, A. (2003). The use of multiple informants in identifying the risk factors of depressive and disruptive disorders: Are they interchangeable? *Social Psychiatry and Psychiatric Epidemiology, 38*, 51–58.

Rudolph, K. D. (2009). The interpersonal context of adolescent depression. In S. Nolen-Hoeksema & L. Hilt (Eds.), *Handbook of depression in adolescents* (pp. 377–405). New York: Routledge.

Rudolph, K. D., & Clark, A. G. (2001). Conceptions of relationships in children with depressive and aggressive symptoms: Social-cognitive distortion or reality? *Journal of Abnormal Child Psychology, 29*, 41–56.

Rudolph, K. D., & Conley, C. S. (2005). Socioemotional costs and benefits of social-evaluative concerns: Do girls care too much? *Journal of Personality, 73*, 115–137.

Rudolph, K. D., & Flynn, M. (2007). Childhood adversity and youth depression: Influence of gender and pubertal status. *Development and Psychopathology, 19*(2), 497–521.

Rudolph, K. D., Flynn, M., & Abaied, J. L. (2008). A developmental perspective on interpersonal theories of youth depression. In J. R. Z. Abela & B. L. Hankin (Eds.), *Child and adolescent depression: Causes, treatment, and prevention*. New York: Guilford.

Rudolph, K. D., & Hammen, C. (1999). Age and gender determinants of stress exposure, generation, and reactions in youngsters: A transactional perspective. *Child Development, 70*, 660–677.

Rudolph, K. D., Hammen, C., & Burge, D. (1997). A cognitive-interpersonal approach to depressive symptoms in preadolescent children. *Journal of Abnormal Child Psychology, 25*, 33–45.

Rudolph, K. D., Hammen, C., Burge, D., Lindberg, N., Herzberg, D., & Daley, S. (2000). Toward an interpersonal life-stress model of depression: The developmental context of stress generation. *Development and Psychopathology, 12*, 215–234.

Rudolph, K. D., Kurlakowsky, K. D., & Conley, C. S. (2001). Developmental and social-contextual origins of depressive control-related beliefs and behavior. *Cognitive Therapy and Research, 25*, 447–475.

Rudolph, K. D., Troop-Gordon, W., & Llewellyn, N. (2013). Interactive contributions of self-regulation deficits and social motivation to psychopathology: Unraveling divergent pathways to aggressive behavior and depressive symptoms. *Development and Psychopathology, 25*(2), 407–418.

Rueter, M. A., Scaramella, L., Wallace, L. E., & Conger, R. D. (1999). First onset of depressive or anxiety disorders predicted by the longitudinal course of internalizing symptoms and parent-adolescent disagreements. *Archives of General Psychiatry, 56*, 726–732.

Rutter, M., & Sroufe, L. A. (2000). Developmental psychopathology: Concepts and challenges. *Development and Psychopathology, 12*(3), 265–296.

Ryan, N. D., Puig-Antich, J., Ambrosini, P., Rabinovich, H., Robinson, D., Nelson, B., et al. (1987). The clinical picture of major depression in children and adolescents. *Archives of General Psychiatry, 44*(10), 854–861.

Sandstrom, M. J., Cillessen, A. H. N., & Eisenhower, A. (2003). Children's appraisal of peer rejection experiences: Impact on social and emotional adjustment. *Social Development, 12*, 530–550.

Sapolsky, R. M. (2003). Stress and plasticity in the limbic system. *Neurochemical Research, 28*(11), 1735–1742.

Schneider, M. L., Moore, C. F., & Kraemer, G. W. (2003). On the relevance of prenatal stress to developmental psychopathology: A primate model. In D. Cicchetti & E. Walker (Eds.), *Neurodevelopmental mechanisms in psychopathology* (pp. 155–186). New York, NY: Cambridge University Press.

Schrepferman, L. M., Eby, J., Snyder, J., & Stropes, J. (2006). Early affiliation and social engagement with peers: Prospective risk and protective factors for childhood depressive behaviors. *Journal of Emotional and Behavioral Disorders, 14*, 50–61.

Scourfield, J., Rice, F., Thapar, A., Harold, G. T., Martin, N., & McGuffin, P. (2003). Depressive symptoms in children and adolescents: Changing aetiological influences with development. *Journal of Child Psychology and Psychiatry, 44*(7), 968–976.

Shad, M. U., Bidesi, A. P., Chen, L. A., Ernst, M., & Rao, U. (2011). Neurobiology of decision making in depressed adolescents: A functional magnetic resonance imaging study. *Journal of American Academy of Child and Adolescent Psychiatry, 50*(6), 612–621.

Shad, M. U., Muddasani, S., & Rao, U. (2012). Gray matter differences between healthy and depressed adolescents: A voxel-based morphometry study. *Journal of Child and Adolescent Psychopharmacology, 22*(3), 190–197.

Sheeber, L., Hops, H., Alpert, A., Davis, B., & Andrews, J. A. (1997). Family support and conflict: Prospective relations to adolescent depression. *Journal of Abnormal Child Psychology, 25*, 333–344.

Sheeber, L., Hops, H., & Davis, B. (2001). Family processes in adolescent depression. *Clinical Child and Family Psychology Review, 4*, 19–35.

Shih, J. H., Eberhart, N. K., Hammen, C. L., & Brennan, P. A. (2006). Differential exposure and reactivity to interpersonal stress predict sex differences in adolescent depression. *Journal of Clinical Child and Adolescent Psychology, 35*, 103–115.

Shiner, R. L., & Masten, A. S. (2012). Childhood personality as a harbinger of competence and resilience in adulthood. *Development and Psychopathology, 24*(2), 507–528.

Silberg, J., Pickles, A., Rutter, M., Hewitt, J., Simonoff, E., Maes, H., et al. (1999). The influence of genetic factors and life stress on depression among adolescent girls. *Archives of General Psychiatry, 56*(3), 225–232.

Silk, J. S., Shaw, D. S., Forbes, E. E., Lane, T. L., & Kovacs, M. (2006). Maternal depression and child

internalizing: The moderating role of child emotion regulation. *Journal of Clinical Child and Adolescent Psychology, 35*, 116–126.

Solomon, A., Ruscio, J., Seeley, J. R., & Lewinsohn, P. M. (2006). A taxometric investigation of unipolar depression in a large community sample. *Psychological Medicine, 36*, 973–985.

Sorensen, M. J., Nissen, J. B., Mors, O., & Thomsen, P. H. (2005). Age and gender differences in depressive symptomatology and comorbidity: An incident sample of psychiatrically admitted children. *Journal of Affective Disorders, 84*, 85–91.

Stein, D., Williamson, D. E., Birmaher, B., Brent, D. A., Kaufman, J., Dahl, R. E., et al. (2000). Parent–child bonding and family functioning in depressed children and children at high risk and low risk for future depression. *Journal of the American Academy of Child and Adolescent Psychiatry, 39*, 1387–1395.

Steingard, R. J., Renshaw, P. F., Hennen, J., Lenox, M., Cintron, C. B., Young, A. D., et al. (2002). Smaller frontal lobe white matter volumes in depressed adolescents. *Biological Psychiatry, 52*(5), 413–417.

Steinhausen, H. C., & Winkler, M. C. (2003). Prevalence of affective disorders in children and adolescents: Findings from the Zurich epidemiological studies. *Acta Psychiatrica Scandinavica, 108*, 20–23.

Stice, E., Hayward, C., Cameron, R. P., Killen, J. D., & Taylor, C. B. (2000). Body-image and eating disturbances predict onset of depression among female adolescents: A longitudinal study. *Journal of Abnormal Psychology, 109*, 438–444.

Strauman, T. J., Costanzo, P. R., & Garber, J. (Eds.). (2011). *Depression in adolescent girls: Science and prevention*. New York: Guilford.

Sugimura, N., & Rudolph, K. (2012). Temperamental differences in children's reactions to peer victimization. *Journal of Clinical Child and Adolescent Psychology, 41*(3), 314–328.

Sullivan, P. F., Neale, M. C., & Kendler, K. S. (2000). Genetic epidemiology of major depression: Review and meta-analysis. *American Journal of Psychiatry, 157*(10), 1552–1562.

Tackett, J. L. (2006). Evaluating models of the personality-psychopathology relationship in children and adolescents. *Clinical Psychology Review, 26*, 584–599.

Taylor, L., & Ingram, R. E. (1999). Cognitive reactivity and depressotypic information processing in children of depressed mothers. *Journal of Abnormal Psychology, 108*, 202–210.

Teasdale, J. D. (1983). Negative thinking in depression: Cause, effect or reciprocal relationship? *Advances in Behavior Research and Therapy, 5*, 3–25.

Teasdale, J. D. (1988). Cognitive vulnerability to persistent depression. *Cognition and Emotion, 2*, 247–274.

Teunissen, H. A., Adelman, C. B., Prinstein, M. J., Spijkerman, R., Poelen, E. A. P., Engels, R. C. M. E., et al. (2011). The interaction between pubertal timing and peer popularity for boys and girls: An integration of biological and interpersonal perspectives on adolescent depression. *Journal of Abnormal Child Psychology, 39*, 413–423.

Thomas, A., & Chess, S. (1977). *Temperament and development*. Oxford, UK: Brunner/Mazel.

Thomson, R. A. (1994). Emotion regulation: A theme in search of definition. *Monographs of the Society for Research in Child Development, 59*, 25–52.

Timbremont, B., & Braet, C. (2004). Cognitive vulnerability in remitted depressed children and adolescents. *Behaviour Research and Therapy, 42*, 423–437.

Tomarken, A. J., Dichter, G. S., Garber, J., & Simien, C. (2004). Resting frontal brain activity: Linkages to maternal depression and socio-economic status among adolescents. *Biological Psychology, 67*(1–2), 77–102.

Twenge, J. M., & Nolen-Hoeksema, S. (2002). Age, gender, race, socioeconomic status, and birth cohort differences on the Children's Depression Inventory: A meta-analysis. *Journal of Abnormal Psychology, 111*(4), 578–588.

Uhrlass, D. J., & Gibb, B. E. (2007). Childhood emotional maltreatment and the stress generation model of depression. *Journal of Social and Clinical Psychology, 26*, 119–130.

van Leeuwen, K. G., Mervielde, I., De Clercq, B. J., & De Fruyt, F. (2007). Extending the spectrum idea: Child personality, parenting and psychopathology. *European Journal of Personality, 21*, 63–89.

Wagner, K. D. (2003). Major depression in children and adolescents. *Psychiatric Annals, 33*, 266–270.

Waller, N. G., & Meehl, P. E. (1998). *Multivariate taxometric procedures: Distinguishing types from continua*. Thousand Oaks, CA: Sage.

Weinstock, M. (2005). The potential influence of maternal stress hormones on development and mental health of the offspring. *Brain, Behavior, and Immunity, 19*, 296–308.

Weir, J. M., Zakama, A., & Rao, U. (2012). Developmental risk I: Depression and the developing brain. *Child and Adolescent Psychiatric Clinics of North America, 21*(2), 237–259.

Weiss, B., & Garber, J. (2003). Developmental differences in the phenomenology of depression. *Development and Psychopathology, 15*, 403–430.

Weissman, M. M., & Olfson, M. (1995). Depression in women: Implications for health care research. *Science, 269*, 799–801.

Weissman, M. M., Wolk, S., Goldstein, R. B., Moreau, D., Adams, P., Greenwald, S., et al. (1999). Depressed adolescents grown up. *Journal of American Medical Association, 281*, 1707–1713.

Weisz, J. R., Southam-Gerow, M. A., & McCarty, C. A. (2001). Control-related beliefs and depressive symptoms in clinic-referred children and adolescents: Developmental differences and model specificity. *Journal of Abnormal Psychology, 110*, 97–109.

Wetter, E. K., & Hankin, B. L. (2009). Mediational pathways through which positive and negative emotionality contribute to anhedonic symptoms of depression: A prospective study of adolescents. *Journal of Abnormal Child Psychology, 37*, 507–520.

Wigg, K., Feng, Y., Gomez, L., Kiss, E., Kapornai, K., Tamás, Z., et al. (2009). Genome scan in sibling pairs with juvenile-onset mood disorders: Evidence for linkage to 13q and Xq. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 150*(5), 638–646.

Williamson, D. E., Birmaher, B., Dahl, R. E., al-Shabbout, M., & Ryan, N. D. (1996). Stressful life events influence nocturnal growth hormone secretion in depressed children. *Biological Psychiatry, 40*(11), 1176–1180.

World Health Organization. (2008). *The global burden of disease: 2004 Update*. Geneva, Switzerland: World Health Organization Press.

Yildiz-Yesiloglu, A., & Ankerst, D. P. (2006). Review of 1H magnetic resonance spectroscopy findings in major depressive disorder: A meta-analysis. *Psychiatry Research, 147*(1), 1–25.

Yorbik, O., Birmaher, B., Axelson, D., Williamson, D. E., & Ryan, N. D. (2004). Clinical characteristics of depressive symptoms in children and adolescents with major depressive disorder. *Journal of Clinical Psychiatry, 65*, 1654–1659.

Zalsman, G., Oquendo, M. A., Greenhill, L., Goldberg, P. H., Kamali, M., Martin, A., et al. (2006). Neurobiology of depression in children and adolescents. *Child and Adolescent Psychiatric Clinics of North America, 15*(4), 843–868.