Sex Differences in Child and Adolescent Depression

A Developmental Psychopathological Approach

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One of the most consistent findings in the literature on depression is the sex difference in prevalence rates: Twice as many women are depressed as men, starting sometime around menarche during adolescence and lasting throughout most of adulthood (Hankin & Abramson, 1999; Mazure & Keita, 2006; Nolen-Hoeksema, 1990, 2002). Understanding why this sex differences exists, why it begins around puberty, how it unfolds over development, and how it affects normal and abnormal development are some of the most captivating and least understood phenomena in developmental psychopathology.

Given the focus of this edited volume, this chapter concentrates on sex differences in depression during childhood and adolescence and reviews what is known about sex differences in rates and manifestation of depression, its etiology, treatment, and prevention among youth. In particular, we cover five main areas. First, we review briefly the extensive literature concerning typical sex differences in normal development during childhood and adolescence. Next, we summarize the developmental epidemiological findings to explicate when the sex difference in depression emerges. Third, we consider etiological explanations for the sex difference in depression, with a particular emphasis on the few integrative, coherent developmentally sensitive conceptual theories. Fourth, we evaluate whether and how sex affects interventions (treatment and prevention) in youth depression. Finally, we suggest future directions and discuss broad issues facing the field.

We take a developmental psychopathological perspective in covering these topics (see Cicchetti, 2006; Cicchetti & Rogosch, 2002), drawing attention to a few points here
and throughout the chapter (see also Crick & Zahn-Waxler, 2003; Rutter, Caspi, & Moffitt, 2003; Zahn-Waxler, Crick, Shirecliff, & Woods, 2006). First, it is important to study and consider both normal and abnormal factors and processes together, as both are important and inform each other. Most of the writing in the area of sex differences broadly focuses on either normal (e.g., emotions, social relationships, parental socialization) or abnormal (e.g., clinical depression, conduct disorder) development. We review the literature on sex differences from both normal and abnormal development perspectives. Second, we consider theory and empirical findings pertaining to the infant, child, and adolescent periods in order to promote a developmental pathways and lifespan perspective. We do not cover adulthood, as doing so would be beyond the scope of this chapter and sex differences in adult depression are reviewed elsewhere (e.g., Hankin & Abramson, 1999; Keyes & Goodman, 2006; Kuehner, 2003; Mazure & Keita, 2006; Nolen-Hoeksema, 2002). Most of the earlier literature has focused largely on adolescence, which is sensible, given that the sex difference in depression is most pronounced during this developmental period. Yet this means that less attention has been paid to sex differences in childhood and the potential developmental precursors contributing to the emergence of the sex difference in depression (but see Crick & Zahn-Waxler, 2003; Keenan & Hipwell, 2005, for notable exceptions). Third, we examine the role of developmental pathways in the emergence of sex differences in depression. Specifically, we consider homotypic and heterotypic continuity in the manifestation of depressive symptoms in boys and girls over time. Homotypic continuity refers to stability in both the manifestation and underlying processes of depression (i.e., the presentation of depression in boys and girls is similarly stable over time, as are the latent processes contributing to the manifestation of the symptoms), whereas heterotypic continuity denotes that there is stability over time in the underlying processes or latent construct of depression, but the observable and measurable manifestation of depressive symptoms may change over time. We also consider the etiological processes contributing to the rise in depression by sex over time and discuss equifinality and multifinality. Equifinality, in which different pathways lead to the same outcome, may make boys and girls similar to each other at one developmental point. Multifinality, in which different pathways emanate from a similar starting point, may make boys and girls follow different developmental trajectories with varying risk and protective factors at later stages. Finally, we emphasize an integrative approach involving multiple levels of analysis (e.g., genetics, hormones, cognition, relationships, emotions, etc.) to understand why more girls exhibit depression starting in adolescence. To date, there is no truly integrative theory of the emergence of the sex difference in depression that aptly includes all levels of analysis, including developmental and contextual influences. The few extant integrative models (e.g., Cyranowski, Frank, Young, & Shear, 2000; Hankin & Abramson, 2001; Keenan & Hipwell, 2005; Zahn-Waxler, 2000) have emphasized and integrated certain factors and levels of analysis to the relative exclusion of other potential influences.

**TYPICAL SEX DIFFERENCES IN NORMAL DEVELOPMENT**

**Biological Factors**

At the simplest level, there are genetic differences between boys and girls that begin at birth and have developmental significance throughout life. Males have one X and one Y chromosome, whereas females have two X chromosomes. Apart from these basic genetic differences having clear functional significance (e.g., X-linked mutations like color blind-
ness), they also affect later biological factors, such as hormones, that may influence the ontogeny of the sex difference in depression (Steiner, Dunn, & Born, 2003).

Hormones regulate and influence gene expression. Androgenic hormones directly contribute to the processes that make a male's brain masculine and less feminine, depending on the amount of hormone present in utero. These neuroendocrine effects on brain and behavior are affected by later developmental events at puberty and throughout adolescence (McEwen, 1992). During puberty, testosterone levels rise dramatically for boys, and estradiol levels increase for girls (Hayward, 2003). Despite these clear changes in sex hormones, the effects they have on mood, emotion, and behavior are subtle, complex, and depend on an individual's developmental stage and other biosocial influences (McEwen & Alves, 1999; Steiner et al., 2003; Udry, 2000).

In addition, gonadal steroids can moderate the functional role of other hormones for girls, as compared with boys. The hypothalamic–pituitary–adrenal (HPA) axis, which is important for managing the body's response to stress, interacts with gonadal steroids: Testosterone suppresses and estrogen enhances HPA axis activity (Rhodes & Rubin, 1999). Thus, girls may respond more to the long-term consequences of stress. Moreover, girls' response to stress differs from boys' because oxytocin (a hormone that enhances caregiving and relaxation and reduces fearfulness and sympathetic activity) and endogenous opioids appear to be fundamental to females' response to stress, whereas vasopressin (a hormone involved in aggressive social behavior) is more indicative of males' stress response (Insel & Fernald, 2004; Rhodes & Rubin, 1999; Taylor et al., 2000). Estrogen also enhances girls' more typical social/affiliative response to stress (i.e., tend-and-befriend), whereas testosterone decreases this response (Taylor, Dickerson, & Klein, 2002).

There are also sex differences in most neurotransmitter levels and activity. For example, females respond less to serotonin (5-HT), 5-HT receptors are down-regulated more in girls than boys, 5-HT binds more in males, and there are sex differences in the way in which sex hormones regulate 5-HT (McEwen, 2001; McEwen & Alves, 1999).

**Emotional Development and Temperament**

Starting as early as infancy and toddlerhood, there are sex differences in the display of basic emotions. Boys tend to exhibit more irritability and anger, whereas girls show more fearfulness (Brody, 1999; Ruble & Martin, 1998; Ruble, Martin, & Berebaum, 2006). By age 2, girls show greater levels of empathy (Zahn-Waxler, Robinson, & Emde, 1992). Also early in life, girls are more socially aware and sensitive to others' affective states (Brody, 1985). In contrast, boys exhibit more frustration, anger, and emotional dysregulation than girls starting by preschool and persisting thereafter (Zahn-Waxler, Schmitz, Fulker, Robinson, & Emde, 1996). By adolescence, boys tend to deny their sadness and seek to hide internalizing and submissive forms of negative emotions, especially sadness and anxiety, whereas girls report higher levels and more intense degrees of sadness, shame, and guilt (Brody & Hall, 2000; Zahn-Waxler, 2000; Zeman & Shipman, 1997). It has been suggested that these differences may be due to temperamental factors or parental socialization factors, as discussed in greater detail next.

Generally consistent with these findings from individual studies of emotion, a recent meta-analysis of temperament showed sex differences in temperament (Else-Quest, Hyde, Goldsmith, & Van Hulle, 2006). Girls showed higher levels of effortful control (e.g., attentional shifting, inhibitory control, ability to control inappropriate behavior), whereas boys demonstrated greater levels of surgency/extraversion (e.g., in ratings of
has been insufficiently rigorous and has produced inconclusive results. This means that the field has not been able to rule out rigorously the possibility that the sex difference in depression is not as real and as substantial as it is believed to be and portrayed. There is reason to suspect sex differences in symptom presentation at any particular developmental stage, as well as a potential reporting bias, because girls are socialized to express more sadness and to be more comfortable talking about sadness, whereas boys are socialized to inhibit expressions of sadness.

First, there is evidence showing that clinically depressed males and females exhibit a different pattern of depressive symptoms. Most of this evidence is based on adult samples (e.g., Angst & Dobler-Mikola, 1984; Frank, Carpenter, & Kupfer, 1988; Kornstein et al., 2000a; Silverstein, 2002). As compared with depressed men, depressed women tend to exhibit more anxiety, somatic complaints, hypervigilance, increased appetite and weight gain, fatigue, psychomotor retardation, and concerns about body image and physical appearance, although these exact symptom differences are not always found (Khan, Gardner, Prescott, & Kendler, 2002). There is little sex difference in functional impairment (Angst & Dobler-Mikola, 1984; Kornstein et al., 2000a). Fewer sex differences in symptoms are found among clinically depressed adolescents, although most studies have limited power, owing to small sample sizes (e.g., Kovacs, 2001; Mitchell, McCauley, Burke, & Moss, 1988; Roberts, Lewinsohn, & Seeley, 1995; Sorensen, Mors, & Thomsen, 2005). The largest study to date (Bennett, Ambrosini, Kades, Metz, & Rabinovich, 2005) of clinically depressed adolescents found that adolescent girls reported more guilt, body image dissatisfaction, self-blame and disappointment, beliefs of failure, concentration difficulties, sadness/depressed mood, sleep problems, and fatigue, whereas boys reported more problems with anhedonia as well as diurnal variation (with greater levels of sadness and fatigue in the morning). Kovacs, Obrosky, and Sherrill (2003) followed their clinically referred sample of depressed children (49 girls and 38 boys) from age 10 to age 21 to examine this issue longitudinally. They found that girls were more likely to exhibit irritability during midadolescence, which then declined into adulthood, but most of the boys were consistently irritable throughout the follow-up; that girls were at greater risk for suicide in midadolescence, but boys during later adolescence; and that girls displayed more somatic symptoms than boys, and these complaints increased with age. Only negative body image and dysphoric mood displayed significant sex differences in manifestation equally across age (more typical among girls than boys).

Second, the issue of a possible reporting bias in willingness to discuss depressive symptoms has been examined indirectly. For example, the evidence that an equal proportion of adult men and women are likely to seek help or to be referred for treatment (Gater et al., 1998; Olsson, Zarin, Mittman, & McIntyre, 2001) has been inferred to mean that there is not a substantial sex difference in openness to report depression. We located no study that examined this issue among youth, so it remains an open question.

Third, males and females exhibit some differences in how they respond to assessments of depression (i.e., possibility of sex bias in measurement). The main issue is that the observed mean level sex difference found in certain symptoms or clusters of depression (e.g., anxious/somatic symptoms or concerns about body image) could be the result of a sex bias in reporting those symptoms rather than a true sex difference in depression manifestation. Data analytic methods, such as item response theory (IRT) and differential item functioning (DIF), can be used to differentiate the possible sex difference in manifestation of symptoms from the potential sex bias in measurement, yet few researchers have used them to examine this issue (Santor & Ramsay, 1998). In an examination of the Beck Depression Inventory (BDI) among depressed outpatient and nonpatient college samples,
there was little evidence of a sex bias (Santor, Ramsay, & Zuroff, 1994), although some BDI items, especially the symptom concerning distorted body image, revealed a sex bias such that women were more likely to endorse it than men. A second study of a community sample of late adolescents (Hankin, Conrad, & Wang, 2006) examined this issue with the BDI and the Mood and Anxiety Symptoms Questionnaire (MASQ; Watson et al., 1995), which assesses both general distress and anhedonic symptoms of depression. This study found that boys were less likely to endorse some BDI items (sadness, episodes of crying, and change in body image), and other items were less likely to be endorsed by girls (insomnia, loss of appetite, and loss of weight). On the MASQ, boys were less likely to respond to the items indicating affective distress (e.g., felt sad, felt like crying, felt unattractive), whereas girls were less likely to respond to more behavioral/nonaffective items (e.g., felt really bored, felt as if it took extra effort to get started) and positively worded affective items (e.g., felt cheerful, felt as though I was having a lot of fun). It is important to note, however, that the sex difference in depression remained even after removing these potentially sex-biased items. Additional research examining the psychometric properties of depression assessments and possible sex-linked biases in responding is needed to evaluate this issue.

Fourth, there may be sex differences in depression manifestation over time in terms of developmental pathways (i.e., homotypic and heterotypic continuity). In their longitudinal research, Gjerde and colleagues (Gjerde, 1995; Block, Gjerde, & Block, 1991) showed that the manifestation and developmental antecedents of depressed mood may differ for boys and girls. Dysphoric boys expressed their unhappiness directly, whereas girls hid their unhappiness through introspection, greater self-preoccupation, and lack of direct hostility. Earlier in life, these dysphoric boys were described as undercontrolled and aggressive, whereas the girls tended to be oversocialized and overcontrolled. Rowe and colleagues (Rowe, Maughan, Pickles, Costello, & Angold, 2002) found that early oppositional behavior characterized a pathway that led to conduct disorder for boys, but depression for girls.

Finally, we highlight an additional methodological and conceptual difficulty in addressing whether depressive symptoms manifest themselves the same way in boys and girls. A significant complication is the fact that the symptoms and general syndrome of depression appear to change across development from preadolescence through adolescence (Weiss & Garber, 2003; Hankin & Abela, 2005). Thus, at present, the degree of continuity (either homotypic or heterotypic) in depression is uncertain, although the best available evidence is consistent with heterotypic continuity, such that depression is believed to be the same underlying construct across development despite some changes in manifest symptoms across development (e.g., anhedonia being less common in children but more prevalent starting in adolescence). As a result, the conundrum of establishing continuity in the syndrome of depression in general makes the investigation of potential sex differences in the manifestation of depression across development all the more difficult and complicated (e.g., presentation of depression in preadolescent girls versus boys and adolescent girls versus boys).

In sum, the available evidence suggests some small but replicable sex difference in the manifestation of depressive symptoms among youth and adults. However, the relatively small size of these differences in a few symptoms suggests that although the overall sex difference in depression is a real phenomenon, further research would help to determine the degree to which the sex difference in the manifestation and measurement of these particular symptoms affects the overall strength of the sex difference in depression across age.
Emergence of Sex Differences in Depression

We selectively focus our review on relatively large, community-based samples, in contrast to smaller convenience samples or psychiatric and clinically referred samples that are less representative and exhibit greater comorbidity (Newman et al., 1996). Overall, depressed mood is fairly common during adolescence, particularly among adolescent girls, with the likelihood of depressed mood ranging between 25 and 40% for girls and between 20 and 35% for boys (Petersen et al., 1993). Prospective longitudinal studies from preadolescence to young adulthood show that girls' depressive symptoms and depressed mood increase after age 13, whereas boys' symptoms and mood remain relatively constant or increase at a lower rate than girls' (Angold, Erkanli, Silberg, Eaves, & Costello, 2002; Petersen, Sarigiani, & Kennedy, 1991; Ge, Lorenz, Conger, Elder, & Simons, 1994; Cole, Martin, Peeke, Seroczynski, & Fier, 1999; Wade, Cairney, & Pevalin, 2002). Twenge and Nolen-Hoeksema (2002), in a meta-analytic review of self-reported symptoms, found this same pattern: Girls' depressive symptoms increased starting at age 13, whereas boys' levels of depressive symptoms remained relatively stable during adolescence.

Cross-sectional studies of children and adolescents provide evidence that more girls than boys are diagnosed with clinical depression after age 13 (Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993; Silberg et al., 1999; Angold, Costello, & Worthman, 1998). Prospective community studies indicate that more girls than boys show clinical depression beginning after age 13 (Cohen, Cohen, Kasen, & Velez, 1993; Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Hankin et al., 1998; Reinherz, Giaconia, Lefkowitz, Pakiz, & Frost, 1993; Weissman, Warner, Wickramaratne, Moreau, & Offson, 1997). For example, one study (Hankin et al., 1998) showed that both boys and girls became increasingly more depressed between the ages of 15 and 18 (from 3 to 17%), and this increase was greater for girls (from 4 to 23%) than for boys (from 1 to 11%).

In addition to age as a developmental index, pubertal development and timing have also been studied as factors that may affect the time when more girls become depressed than boys (Angold, Worthman, & Costello, 2003; Hayward & Sanborn, 2002). Pubertal development (measured by Tanner stages) predicted the emergence of the sex difference in depression better than age: Girls reported increased rates of depressive disorders after Tanner Stage III (Angold et al., 1998). Regarding pubertal timing, most studies find that early puberty in girls, but not boys, is linked with elevated depression (e.g., Ge, Conger, & Elder, 1996; Graber, Lewinsohn, Seeley, & Brooks-Gunn, 1997; Paikoff, Brooks-Gunn, & Warren, 1991; but see Angold, et al., 1998, for contrary evidence). Stice, Presnell, and Bearman (2001) showed that body dissatisfaction, dieting, and high body mass partially explained why early puberty is linked with depression in girls. Still, it is worth noting that early pubertal timing is a complex phenomenon resulting from various biological, social, and contextual factors: Genetics and environmental influences (e.g., nutrition and exercise) affect pubertal timing (Hayward, 2003). However, Crick and Zahn-Waxler (2003) note that researchers must look beyond only a biological examination to understand the role of puberty in onset of depression. For example, maternal depression contributes to early puberty in daughters (Ellis & Garber, 2000).

Other research has examined whether ethnicity influences the unfolding of the sex difference in depression. One study (Kistner, David, & White, 2003) found that boys were more depressed than girls among African American youth (grades 3–5), whereas European American girls were more depressed than boys. Yet other studies (S克拉德利, Gotlib, & Hayward, 1999; Siegel, Aneshensel, Taub, Cantwell, & Driscoll, 1998; Twenge & Nolen-Hoeksema, 2002) found that Hispanic adolescents reported the great-
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1999) found that menarche was associated with depressed mood only among European American girls, not among Hispanic or African American girls. Thus, these few studies highlight the need for further research on how ethnicity may influence the sex difference in depression.

Sex Differences and Comorbidity of Depression with Other Psychopathologies

It is well known that depression co-occurs with other common emotional and behavioral symptoms and problems. A comprehensive review of comorbidity is beyond the scope of this chapter (see Avenevoli, Knight, Kessler, & Merikangas, Chapter 2, this volume; Angold, Costello, & Erkanli, 1999); briefly, some of the most common comorbidities occur between depression, anxiety, externalizing behaviors such as attention-deficit/hyperactivity disorder (ADHD) and conduct disorder (CD), and eating disorders. In this section we review how sex influences the co-occurrence of depression with these psychopathologies and whether there are sex-linked developmental trajectories linking these comorbid conditions.

Overall, Rutter and colleagues (2003) have argued that the sex difference in psychopathology can be roughly categorized: Early-onset psychiatric disorders, such as ADHD, CD, autism, and language disorders, are more prevalent among boys, whereas adolescent-onset emotional disorders, such as depression, eating disorders, and anxiety, are more prevalent among girls. As a general rule describing the prototypic onset of these disorders and their association with sex, this dichotomy is accurate, yet it may obscure the investigation of issues important for advancing a more complete understanding of the development of the sex difference in depression. It is important to study the early onset of problems in girls and the later onset of symptoms in boys that may not fit into the prototypic pattern. Moreover, there may be important prodromal indicators and developmental precursors of problems in both boys and girls that are less likely to be noticed because they are subsyndromal and thus not diagnosed. As we discuss in greater detail later in the chapter, there has been increasing theoretical and empirical attention to the preadolescent precursors of the sex difference in depression (e.g., Keenan & Hipwell, 2005; Zahn-Waxler, 2000), and this line of research centers on subtle and early predictors of depression well before the substantial surge of depression among adolescent girls. A focus on only when the sex difference in modal patterns of marked, diagnosable syndromes occurs may obscure the study of early signs and predictors of problems.

Comorbidity of depression and anxiety is more common among girls than boys (Lewinsohn, Rohde, & Seeley, 1995). Prospective community studies (Cohen et al., 1993; Cole et al., 1999; Lewinsohn, Gotlib, Lewinsohn, Seeley, & Allen, 1998; Reinherz et al., 1993; Pine, Cohen, Gurley, Brook, & Ma, 1998) show that more girls than boys have an anxiety disorder, and the anxiety disorder often precedes the onset of a depressive disorder. In particular, certain anxiety disorders, including generalized anxiety disorder and panic disorder, tend to precede depression, especially in early adolescence and among girls (Parker & Hadzi-Pavlovic, 2004). Moreover, co-occurrence of depression with more than one anxiety disorders tends to occur primarily among girls (Parker & Hadzi-Pavlovic, 2004). Taken together, these results suggest that there may be a developmental pathway for girls from anxiety to depression.
In contrast, more boys than girls show overt, physically aggressive, externalizing behaviors (Loeber & Keenan, 1994; Keiley, Bates, Dodge, & Pettit, 2000; Moffitt, Caspi, Rutter, & Silva, 2001; Rutter et al., 2003). The co-occurrence of depression with disruptive behavioral problems (CD and oppositional defiant disorder) was found to be more likely among clinically depressed boys than girls (Rohde, Lewinsohn, & Seeley, 1991), and this likelihood holds longitudinally over time (Kovacs, Obrosky, & Sherrill, 2003). Yet the sex difference in aggression seems to diminish when both indirect/relational and direct/physical aggression are considered (Crick et al., 1999). Starting in preschool, girls show more indirect aggressive behaviors (e.g., threatening to end a friendship unless demands are met; retaliating by socially excluding others) than boys within interpersonal relationships (Crick & Grotpeter, 1995; Crick et al., 1999).

More adolescent girls than boys have been diagnosed with lifetime histories of eating disorders (Lewinsohn et al., 1993; Steiner & Lock, 1998). There is evidence that eating disorders co-occur among clinically depressed girls more than boys (Rohde et al., 1991) and that depressed girls, but not boys, are at elevated risk for developing eating disorders as they become young adults (Kovacs et al., 2003).

ETIOLOGICAL FACTORS AND CONCEPTUAL MODELS

Evaluating Proposed Causal Explanations for the Sex Difference in Depression

Prior to reviewing the various possible explanations for the emerging sex difference in depression, it is important to note that no comprehensive theory of depression has been offered that adequately accounts for the multiple facets of depression, including when and why sex differences in depression emerge. Multiple processes (i.e., equifinality and multifinality) likely contribute to the development of sex differences in depression. This review focuses on extant research examining those factors that may explain why the sex difference in depression emerges during early adolescence. Other factors may contribute to the sex difference in depression at different points during the lifespan. For example, gender role inequality in marital relationships may explain why more adult women are depressed than men (Strazdins, Galligan, & Scannell, 1997), but this association would not account for why more girls start becoming depressed around midpuberty. Similarly, factors associated with the emergence of the sex difference in depression may be developmentally specific to adolescence and may not apply to adults.

The potential range of studies to be reviewed is immense and beyond the scope of this chapter. In theory, any factor that has been shown to predict depression could be relevant for understanding why more girls are depressed than boys. We limited our focus to those major depression vulnerabilities and stressors that have received sufficient theoretical and empirical attention and for which there is a reasonable basis to expect a potential sex difference. We organized our review around mediational and moderational models when possible. We start by reviewing what mediation and moderation mean (Baron & Kenny, 1986), specifically in reference to understanding the sex difference in youth depression.

Mediation indicates that (1) there is a sex difference in levels of depression, (2) there is a sex difference in levels of a given etiological factor, (3) the factor leads to depression, and (4) the association between sex and depression is accounted for (i.e., reduced) by the mediating variable. Manipulating the mediating variable (e.g., by lowering levels of the etiological factor through intervention) would provide further support that this mediator
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explains the sex difference in depression, because reducing the etiological factor directly would result in lowered levels of depression. Most of the research conducted to date has examined only one mediating factor, even though it is most likely that multiple mediators may be involved as part of a developmental causal chain leading to the emerging sex difference in depression. Moreover, many studies that we reviewed did not conduct the appropriate mediational analyses, so it is unknown whether hypothesized factors account for the sex difference in depression. It is recommended that future studies conduct mediational analyses to evaluate whether a hypothesized factor or mechanism truly accounts for the sex difference in depression.

Moderation signifies that the association between depression and a causal factor varies as a function of sex (e.g., the strength of the relationship between depression and an etiological factor may be stronger in girls than in boys). Moderating variables, by themselves, cannot explain why the sex difference in depression occurs, because moderation indicates that the association between depression and an explanatory factor varies by level of sex (Baron & Kenny, 1986). Several of the studies we reviewed reported how sex moderated the association between a particular factor and depression and then suggested that this statistical interaction supported an explanation for why girls are more depressed than boys. However, obtaining a significant interaction between sex and a factor does not necessarily qualify as support for an explanation of the sex difference in depression, because moderation indicates several different possible patterns between sex and the factor (could hold for one sex but not the other, or the strength of the association is stronger for boys or girls). Additional research would still be required to elucidate why (i.e., the processes, mediation) a particular association is stronger among girls than boys (the moderation effect) in order to provide an explanation for the sex difference in depression.

Complicating any etiological explanation is the timing of a hypothesized mediating or moderating factor. A complete explanation of the sex difference in depression needs to account for the developmental unfolding of causal factors over time that leads to girls becoming more depressed than boys at about age 13. A comprehensive account of the emergence of the sex difference in depression around age 13 (or Tanner Stage III) would specify whether there is a developmental rise in the mediating variable occurring prior to or at about the same time that girls become depressed. Further, a mediating or moderating variable may vary along a temporal dimension from more distal to more proximal. A distal factor can mediate the sex difference in depression, but other more proximal factors need to be incorporated to explain why girls become more depressed at a particular developmental time point (age 13). For example, demonstrating that childhood abuse mediates the sex difference in depression constitutes an important finding, but this by itself may not provide a comprehensive explanation, because childhood abuse is likely a more distal factor (especially if the abuse occurred early in childhood). Further research would still need to explicate the other more proximal mediating factors in the developmental pathway occurring closer in time to when girls begin to become more depressed.

It is important to consider how different mediating and moderating variables may fit together in a larger etiological developmental pathway from childhood into young adulthood. A mediating factor may interact with a moderating factor so that the particular mediating factor predicts increases in depression more strongly for some individuals than others. For example, stressors may mediate the sex difference in depression, but early pubertal onset may moderate the association between sex and stressors. In this example, then, a subset of girls (those going through puberty early) is at especially high risk for experiencing stressors, and these early pubertal girls may account for a substantial portion of the sex difference in depression. Unfortunately, most of the research to date has, at
best, examined only one mediating mechanism or one moderating variable in isolation to explain the sex difference in depression. Future research needs to expand beyond simple, one-factor explanations of the sex difference in depression to a more developmentally sensitive, transactional model with various mediating and moderating factors and pathways. Given the current state of knowledge, we next review the different, isolated explanatory constructs and mechanisms intended to account for the rise of depression in girls.

**Stressors**

Research suggests that stressors precede and predict depression (Grant, Compas, Thurin, McMahon, & Gipson, 2004). The association between stressors and depression can be broken down into four conceptually different models: stress exposure, reactivity, generation, and depression contagion.

**Stress Exposure**

The stress exposure hypothesis is a mediational model in which girls experience more stressors than boys, and as a result, become more depressed. Data from multiple studies support this model and show that adolescent girls report more stressors overall than boys (e.g., Allgood-Merten, Lewinsohn, & Hops, 1990; Davies & Windle, 1997; Ge et al., 1994; Graber, Brooks-Gunn, & Warren, 1995; Hankin, Mermelstein, & Roesch, 2007). Girls also report more interpersonal stressors, including peers, romantic partners, and family members, whereas boys experience more achievement and self-relevant stressors (Gore et al., 1993; Hankin et al., 2007; Larson & Ham, 1993; Leadbeater, Blatt, & Quinlan, 1995; Rudolph, 2002; Rudolph & Hammen, 1999; Shih, Eberhart, Hammen, & Brennan, 2006; Towbes, Cohen, & Glyshaw, 1989; Wagner & Compas, 1990; Windle, 1992). The sex difference in adolescent depression is mediated, at least in part, by adolescent girls' greater exposure to interpersonal peer (Liu & Kaplan, 1999; Hankin et al., 2007; Rudolph, 2002; Rudolph & Hammen, 1999; Shih et al., 2006) and family (Davies & Windle, 1999) stressors.

**Stress Reactivity**

The stress reactivity hypothesis is a moderational model in which girls are expected to exhibit greater levels of depression than boys in response to stressors. Evidence is somewhat consistent, but more mixed, with this model. Some studies find that adolescent girls respond to general stressors with greater depression than boys (Achenbach, Howell, & McConaughy, 1995; Ge et al., 1996; Hankin et al., 2007; Marcotte, Fortin, Potvin, & Papillon, 2002; Rudolph, 2002; Schraedley et al., 1999; Shih et al., 2006; see review by Grant et al., 2006), whereas others have not found a sex difference in stress reactivity (Burt, Cohen, & Bjorck, 1988; Cauce, Hannan, & Sargeant, 1992; Larson & Ham, 1993; Leadbeater, Kuperminc, Blatt, & Hertzog, 1999; Wagner & Compas, 1990). To interpersonal stressors, girls respond with higher levels of depressive symptoms, as compared with boys (Goodyer & Altham, 1991; Hankin et al., 2007; Moran & Eckenrode, 1991; Leadbeater et al., 1995; Shih et al., 2006), whereas boys react to school stressors with higher depression than girls (Sund, Larsson, & Wichstrom, 2003).

An important consideration is why girls may react to stressors with elevated depression, as compared with boys. It is likely that certain vulnerabilities, especially those risks
(e.g., genetic, cognitive, etc.) that girls have more than boys, may help account for girls’ greater stress reactivity. These vulnerabilities are reviewed later in the chapter.

**Stress Generation**

The stress generation hypothesis is a transactional model that suggests that characteristics of the individual youth (e.g., elevated depression, temperament/personality traits) precede and contribute to increases in the experience of stressors, called “dependent” stressors (Hammen, 1991). Stress generation theories suggest that interpersonal, dependent stressors are most typically experienced in adolescence, especially among girls (Hankin & Abramson, 2001; Rudolph, 2002). The few studies available show that girls experience more dependent stressors than boys (Hankin et al., 2007; Rudolph & Hammen, 1999; Rudolph, 2002), but less research has examined whether depressive symptoms are associated with future dependent stressors (see Shih et al., 2006, for evidence with young adults). Among youth, a three-wave prospective study examined the longitudinal direction of effects between depressive symptoms and contextually coded stressors in different developmentally salient domains over a 1-year follow-up (Hankin et al., 2007). Evidence for stress generation was observed: Initial depressive symptoms at baseline significantly predicted future increases in romantic stressors and overall dependent stressors. In contrast, evidence was also observed for the stress exposure model: Initial levels of independent, peer, and general interpersonal stressors predicted prospective increases in depressive symptoms over time. Taken together, these findings show that there are sex differences in different domains of stressors (e.g., peer and romantic) and stressor type (independent and dependent), but the longitudinal associations between depressive symptoms and stressors is not simple and straightforward. It is important to consider the particular stress model (e.g., generation and exposure) to understand more fully how stressors help to explain the sex difference in depression because the longitudinal direction of effects varies, depending on the stressor type and domain.

**Depression Contagion**

The depression contagion model pertains to the “contagion” of depression between adolescents and others in the context of an interpersonal relationship. Research shows a temporal synchrony between mothers’ and daughters’ depressive episodes (e.g., Hammen, Burge, & Adrian, 1991) and depressive symptoms between youth and parents longitudinally over time (e.g., Abela, Skitch, Adams, & Hankin, 2006). Other research has found that depressive symptoms among adolescents’ best friends prospectively predict adolescents’ own reported depressive symptoms (Hogue & Steinberg, 1995; Stevens & Prinstein, 2005), especially among girls (Prinstein, Borelli, Cheah, Simon, & Aikins, 2005). Depression in a parent (typically studied among mothers; see Goodman & Tully, Chapter 17, this volume) is a significant context for stressors. Girls, as compared with boys, of depressed mothers are more likely to develop anxiety and depression (Boyle & Pickles, 1997; Conger et al., 1993; Cummings, DeArth-Pendley, Du-Rocher-Schudlich, & Smith, 2001; Sheeber, Davis, & Hops, 2002). Furthermore, girls’ greater reactivity to mothers’ depression exhibits effects over time; maternal depression prospectively predicts later depression among girls but not boys (Davies & Windle, 1997; Duggal, Carlson, & Sroufe, & Egeland, 2001; Fergusson, Horwood, & Lynskey, 1995). Finally, girls react to family discord and conflict with greater depression as compared with boys (Crawford, Cohen, Midlarsky, & Brook, 2001; Essex, Klein, Cho, & Kraemer, 2003).
Child Abuse and Maltreatment as Severe Negative Events

The vast majority of studies examining abuse have utilized samples of adults who have retrospectively reported on these abusive events. There is little discernible retrospective bias in recalling abusive experiences or bias affecting reports of depression (Brewin, Andrews, & Goldblip, 1993; Maughan & Rutter, 1997). Depressed mood and depressive disorders are more likely to be reported among adults retrospectively reporting childhood abuse (see Harkness & Lumley, Chapter 19, this volume). Sex differences in child abuse also exist, especially in childhood sexual abuse (CSA) (Cutler & Nolen-Hoeksema, 1991; Levitan et al., 1998). A meta-analysis (Rind, Tromovitch, & Bauserman, 1998) of adults retrospectively recalling CSA concluded that 14% of men and 27% of women reported CSA. There is some evidence that CSA mediates the sex difference in depression (Whiffen & Clark, 1997). In this study, only childhood abuse, but not further adult victimization, was associated with depression. However, most of the studies of adults retrospectively recalling abusive experiences do not clearly consider when the abuse occurred as a potential factor. Given the importance of and interest in studying childhood maltreatment as a potential explanation of the sex difference in depression, especially its emergence in early adolescence, it will be important for future studies to indicate whether and how age influences any associations between abuse, sex, and depression, because abuse experienced early in childhood may serve as a more distal, rather than proximal, mediator.

Cognitive Vulnerabilities

There are various cognitive vulnerabilities (Abela & Hankin, Chapter 1, this volume), and some research has examined potential sex differences in these cognitive factors. The corpus of research has focused on a negative cognitive, or attributional, style (Abramson, Metalsky, & Alloy, 1989), dysfunctional attitudes (Beck, 1987), rumination (Nolen-Hoeksema, 1991), and interpersonal dependency/sociotropy (Blatt & Zuroff, 1992).

Among adult samples, women tend to score higher than men on measures of negative attributional/cognitive style (Angell et al., 1999; Nolen-Hoeksema, Larson, & Grayson, 1999), whereas men exhibit more dysfunctional attitudes than women (Angell et al., 1999; Goldblip, 1984; Haeffel et al., 2003). Women are more likely than men to ruminate in response to sad or anxious moods (Roberts, Gotlib, & Kassel, 1996; Mezulis, Abramson, & Hyde, 2002; Nolen-Hoeksema et al., 1999; Tamres, Janicki, & Helgeson, 2002). Women display higher scores than men on some measures of sociotropy (Leadbetter et al., 1995; McBride, Bacchiocchi, & Bagby, 2005; Shih et al., 2006). Among adolescents, the evidence is consistent with the adult studies. Girls exhibit more cognitive vulnerability than boys on measures assessing a negative cognitive style (Hankin & Abramson, 2002; Hankin, 2006), rumination (Broderick, 1998; Hankin, 2006; Schwartz & Koenig, 1996; Ziegert & Kistner, 2002), whereas boys display more dysfunctional attitudes than girls (Hankin, 2006). Girls are more cognitively vulnerable in interpersonal domains than boys (Bandura, Pastorelli, Barbaranelli, & Caprara, 1999; Leadbetter et al., 1995, 1999). The research with children appears to be less consistent, such that sex differences in these cognitive vulnerabilities often are not observed (Abela, 2001; Abela, Brozinia, & Haigh, 2002; Abela, Vanderbilt, & Rochon, 2004). This suggests the possibility that girls may become more cognitively vulnerable to depression than boys, starting in early adolescence, with such vulnerability lasting throughout adulthood. Indeed, a meta-analysis showed that girls exhibit a more negative attributional style than boys that starts in early adolescence and continues in adulthood (Mezulis, Abramson, Hyde, & Hankin, 2004).
Research examining mediational models shows that a negative cognitive style among adolescents (Hankin & Abramson, 2002), rumination among youth (Grant et al., 2004; Schwartz & Koenig, 1996) and adults (Nolen-Hoeksema et al., 1999), and interpersonal/social-evaluative concerns (Rudolph & Conley, 2005) partially explain why more girls are depressed than boys. Shih et al. (2006) found that female young adults with high interpersonal dependency experienced more dependent interpersonal stressors and that this stress generation effect partially mediated the association between sociotropy and depression among women. Among girls transitioning into high school, a greater interpersonal orientation was associated with increases in depressive symptoms after their experiencing interpersonal stressors (Little & Garber, 2004). Adolescent girls' negative interpretations of their peer experiences predicted future levels of depression (Prinstein & Aikins, 2004; Prinstein, Cheah, & Guyer, 2005; Quiggle, Garber, Panak, & Dodge, 1992).

Cognitive theories postulate different domains of vulnerability, and a particularly important domain for understanding the sex difference in depression is beliefs about physical attractiveness and body image (Hankin & Abramson, 2001). There is a marked sex difference in perceptions of physical appearance, and it occurs prior to the emergence of the sex difference in depression (Harter, 1999; Kostanski & Gullone, 1998). Cross-sectional (Kostanski & Gullone, 1998) and longitudinal (Cole, Martin, Peeke, Seroczynski, & Hoffman, 1998) research shows that beliefs about physical unattractiveness predicted depressed mood for girls more than boys, but mediation was not reported. Other research conducting mediational analyses demonstrates that girls' excessive body dissatisfaction partially explains the sex difference in depressive symptoms (Allgood-Merten et al., 1990; Wichstrom, 1999).

Adolescent girls have more cognitive vulnerability to depression than boys, but how do girls develop such cognitive risk factors? We note two possible mechanisms, although there are certainly others. First, adolescent girls are more likely to experience negative events, especially interpersonal stressors, than adolescent boys. Researchers have hypothesized that individuals confronted with repeated occurrences of negative life events in a wide variety of domains should develop a more stable, global attributional style for negative events over time, and hence increases in cognitive vulnerability to depression (e.g., Coyne & Whiffen, 1995; Just, Abramson, & Alloy, 2001; Rose & Abramson, 1991). Thus, girls' greater likelihood of experiencing negative events, especially during the transition from early to middle adolescence, may contribute to their greater cognitive vulnerability to depression, which may become more depressogenic around early adolescence (Mezulis et al., 2004). Second, females encode life events involving emotional memory, but not nonemotional memory, in more detail than males (Seidt & Diener, 1998; Davis, 1999). Parents discuss emotional material in more detail with their daughters than with their sons, and mothers discuss sadness in longer and more detailed conversations with daughters. Females having greater cognitive vulnerability than males may be the result, in part, of parents' sex-linked socialization practices and girls' encoding negative events in more emotional detail than boys. Girls' negative beliefs about themselves, their world and future may be more accessible and more tightly interconnected in associative cognitive networks linked with affective nodes.

**Emotion and Temperament**

An extensive literature grounded in temperament and personality research has identified three broad, innate temperamental traits that may be relevant to psychopathology: positive affectivity, negative affectivity, and disinhibition (Clark, 2005). Higher levels of nega-
tive affectivity and reduced levels of positive affectivity predict the development of depression (see, e.g., Caspi, Moffitt, Newman, & Silva, 1996; Krueger, 1999; Lonigan, Phillips, & Hooe, 2003); disinhibition has not been shown to have strong and reliable associations with depression. However, fewer studies have explicitly reported sex differences in these temperament dimensions. Some research shows age and sex differences in both negative and positive affectivity, such that adolescent girls exhibit less positive affectivity and greater negative affectivity than adolescent boys, with little sex difference during childhood (e.g., Jacques & Mash, 2004; Lonigan, Hooe, David, & Kistner, 1999), whereas other research shows sex differences in negative, but not positive, affectivity (Chorpita, Plummer, & Moffitt, 2000).

In addition to these temperament dimensions, other emotion constructs have been proposed as risks for depression, some of which may exhibit a sex difference (Keenan & Hipwell, 2005). First, theoretically, excessive empathy may predispose a person to the development of depression, so that individuals who experience high levels of empathy are more likely to take on others’ problems as if they were their own, causing them to experience feelings of guilt and responsibility, placing them at risk for depression (Zahn-Waxler, 2000). Starting in early childhood, girls demonstrate higher levels of empathy and prosocial behavior than boys (Zahn-Waxler, Cole, & Barrett, 1991; Eisenberg & Fabes, 1998). Cross-sectional research shows that scores on an excessive empathy questionnaire uniquely predicted depressive symptoms (Robins & Hinkley, 1989), although no prospective longitudinal study has tested this association from childhood into adolescence. Second, girls demonstrate higher levels of compliance than boys as early as the toddler period and extending throughout childhood (see, e.g., Briggs-Gowan, Carter, Moye Skuban, & McCue Horwitz, 2001; Kochanska, Coy, & Murray, 2001; Mistry, Vanderwater, Huston, & McLoyd, 2002). Excessive compliance is associated with internalizing symptoms in children (e.g., Grant & Compas, 1995; Kochanska et al., 2001), although the evidence is predominantly indirect and there is a lack of prospective research in this area. Third, deficits in emotion regulation (i.e., over- or underregulation of emotion) may serve as distal risk factors for the development of internalizing disorders (John & Gross, 2004; Chaplin & Cole, 2005). Specifically, individuals who suppress negative emotions (e.g., sadness, anger) are at an increased risk of experiencing depressive symptoms (Zeman, Shipman, & Suveg, 2002; Penza-Clyve & Zeman, 2002), have low levels of well-being and life satisfaction, and are more pessimistic about their future (Gross & John, 2003). Research also indicates the presence of sex differences in emotion regulation. Girls demonstrate higher levels of regulation of negative emotions (e.g., anger) as compared with boys (e.g., Cole, Zahn-Waxler, & Smith, 1994; Underwood, Hurley, Johanson, & Mosley, 1999; Durbin & Shafir, Chapter 7, this volume; Chaplin & Cole, 2005).

**Biological Factors**

**Genetics**

The evidence is mixed with respect to sex differences in heritability estimates for depression. Some studies find no differences in adulthood (e.g., Lyons et al., 1998; Kendler & Prescott, 1999) or childhood/adolescence (Eaves et al., 1997; Rutter, Silberg, O’Connor, & Siminoff, 1999), whereas others have revealed mean level heritability differences (Bierut et al., 1999; Jacobson & Rowe, 1999; Kendler, Gardner, Neale, & Prescott, 2001; Tambs, Harris, & Magnus, 1995). Silberg and colleagues (Silberg et al., 1999; Silberg,
Sex Differences in Depression

Rutter, & Eaves, (2001) found that genetic influences had a larger effect on the emergence of depression among postpubertal adolescent girls who had experienced stress and that the stability of depression was more genetically mediated for these girls than for boys. All of these studies employed behavioral genetic designs, and given the limitations that accompany behavioral genetics (i.e., investigation of abstract, nonspecific, latent genetic influence; see Rutter, Moffitt, & Caspi, 2006; Lau & Eley, 2006; Chapter 6, this volume), it will be important to investigate potential sex differences in measured genes using molecular genetics techniques.

Sex Hormones

The evidence for hormonal explanations is mixed, although mostly negative. Little evidence supports the hypothesis that rising hormonal levels (e.g., progesterone, estrogen) mediate the sex difference in depression (see Bebbington, 1998, for a review). Brooks-Gunn and Warren (1989) found that the effect of estradiol was minimal as compared with the influence of social factors (negative life events) in predicting depressed mood among girls (ages 10–14). Moreover, Susman’s research (Susman, Inoff, Germain, Nottelmann, & Loriaux, 1987; Susman, Dorn, & Chrousos, 1991) found that there was no sex difference in sex hormones or cortisol levels and that estradiol was not associated with depressive affect, so these sex hormones could not mediate the sex difference in depression. Despite little support for mediation, these hormones could affect boys and girls differently (i.e., moderation). Susman and colleagues (1991) found that boys reporting higher levels of negative affect had lower testosterone and higher androstenedione levels, whereas girls with higher levels of negative affect had higher levels of testosterone and lower levels of dehydroepiandrosterone sulfate (DHEAS). Angold, Costello, Erkami, and Worthman (1999) found that testosterone and estradiol were associated with depression in an all-girls sample, but moderation could not be tested because boys were not included. Taken together, these results suggest that different gonadal and adrenal hormones may provide some limited risk for later negative affect for boys and girls, separately (Brooks-Gunn, Graber, & Paikoff, 1994).

Cortisol

Results from adult studies examining the biological stress response of the HPA axis have shown increases in the stress hormone, cortisol, among depressed individuals as compared with controls (Thase, Jindal, & Howland, 2002), yet similar research with depressed adolescents has not found HPA axis dysfunction or elevations of cortisol, as compared with controls (Dahl, Kaufman, Ryan, & Perel, 1992; Dorn, Burgess, Susman, & von Eye, 1996). Although most studies (e.g., Birmaher, Rabin, Garcia, & Jain, 1994; Goodyer et al., 1996; Susman et al., 1987, 1991) have found comparable cortisol levels for boys and girls, and thus mediation seems unlikely, other research using uncertain and challenging conditions found evidence for increased cortisol levels and higher emotional distress in girls, as compared with boys (Susman, Dorn, Inoff-Germain, Nottelmann, & Chrousos, 1997). In a longitudinal study of children, girls exhibited higher cortisol levels than boys, and elevated cortisol predicted greater depressive and anxiety symptoms 18 months later in girls only (Smidt et al., 2002). Other research showed that depressed girls exhibited a flattened diurnal rhythm, whereas normal controls and depressed youth with comorbid externalizing problems displayed the expected diurnal pattern of early morning cortisol elevations and a significant decline throughout the day (Klimes-Dougan,
Hastings, Granger, Usher, & Zahn-Waxler, 2001). Thus, the evidence for cortisol and biological stress reactivity as an explanation for sex differences in depression is intriguing but mixed.

In summary, existing studies of biological explanations have provided equivocal evidence that sex hormones or cortisol levels mediate the sex difference in depression (see Hayward & Sanborn, 2002; Seeman, 1997; Steiner et al., 2003, for other reviews). Hormonal changes, by themselves, are not likely to lead to significant alterations in mood or poor adjustment (Buchanan, Eccles, & Becker, 1992). The mixed evidence may be due to several factors. Many of the studies conducted to date have utilized small sample sizes, so the lack of statistically significant sex differences may result from a lack of statistical power. Moreover, most of the studies have considered only simple linear models in which hormonal changes directly influence depressive symptoms or negative affect (Brooks-Gunn et al., 1994), although it is unlikely that such a direct hormonal model would capture the complexity of the hormonal system. Brooks-Gunn and colleagues (1994) highlight the interdependencies among hormones and indicate that it may not be appropriate to consider independent effects of specific hormones. They recommend a transactional model involving bidirectional effects between hormonal changes, negative affect, pubertal timing, and social events to examine how hormones and other factors may influence negative affect.

**Integrated Conceptual Models of the Sex Difference in Youth Depression**

As noted earlier, there are few theoretical models that have been proposed to integrate coherently the various etiological influences contributing to the sex difference in depression in children and adolescents. In this section, we summarize the central conceptual models, review the available empirical research in support of them, and discuss each theory briefly.

_Nolen-Hoeksema and Girgus (1994)_ were the first to review systematically the literature on etiological factors underlying the emergence of the sex difference in depression. Their seminal review stimulated the field and advanced knowledge by organizing previously disparate etiological factors into three coherent and distinct conceptual models. The first model proposes that although the same factors cause depression in both boys and girls, girls experience an increase in these factors in early adolescence, whereas boys do not. The second model suggests that the causes of depression are different for boys and girls, and that in early adolescence the causes of depression in females become more prevalent than the causes of depression in males. The third model follows a vulnerability-stress framework. Girls exhibit greater risk for depression than boys in childhood, but it is not until early adolescence, when girls experience additional stressors, that their greater levels of risks for depression interact with the increase in stressors to contribute to elevated levels of depression among girls.

After reviewing evidence from various literatures, Nolen-Hoeksema and Girgus (1994) concluded that the available evidence best supported the third model, but there was little direct evidence to support this assertion. Support for this model was based on the individual effects of different etiological constructs, what the authors framed as personality characteristics, biological challenges, and social challenges. Unfortunately, at the time their article was published, the interaction of personality and biological factors with the challenges of adolescence had not been studied directly. Since then, much of the research reviewed earlier in this chapter lends support to aspects of their third model.
(e.g., sex differences in rumination, social challenges, and stressors, including sexual abuse). However, few studies exist that have sought to test any of the three models in totality (but see Seiffge-Krenke & Stemmmer, 2002, for a comprehensive test of their models); rather, the preponderance of the supporting evidence is based on individual aspects of their vulnerability–stress model. To adequately test the third model, longitudinal data using repeated measures of many vulnerabilities and stressors would be required, spanning childhood through the adolescent transition and into adulthood, when the sex difference grows.

Similar to Nolen-Hoeksema and Girgus’s (1994) third model, Cyranowski, Frank, Young, and Shear (2000) propose that females possess an interpersonally oriented vulnerability that interacts with particular negative life events to contribute to higher levels of depression. Females’ vulnerability consists of a high affiliative focus, low attachment security, high anxiety, and low instrumentality. When girls with this vulnerability encounter stressors, especially those that have interpersonal consequences, they are likely to become depressed. More distally, insecure parental attachments, anxious or inhibited temperaments, and low instrumental coping skills can lead to a more difficult transition into adolescence, especially for girls. Difficulty with this transition can produce increased anxiety, which, when combined with traditional female gender socialization and the hormonal changes of puberty (especially the increased release of oxytocin in females), can lead to an increase in affiliative need for girls (the basis of their vulnerability).

One study (Stemmmer & Peterson, 2005) tested this model using growth curve modeling and found that the risk factors, such as insecure parental attachment, low instrumental coping skills, an anxious or inhibited temperament, and early physical maturaton, differentiated the development of adolescents’ emotional tone, or level of positive/negative affect. Results of other research, reviewed earlier, such as girls (as compared with boys) encountering more interpersonal stressors, exhibiting more fearful temperament, and displaying more anxiety, are all consistent with this theory.

Another related model is Taylor et al.’s (2000) bioevolutionary theory, although it is not specifically formulated to explain the sex difference in depression. Taylor and colleagues postulate that females possess a stress response different from the traditional male response of “fight or flight.” The female stress response, as a result of biological and behavioral differences, is better characterized as “tend and befriend.” Females are more apt to “tend” to relationships and act in ways that will protect themselves and their offspring, thus improving the likelihood that these traits will be passed on to future generations. Furthermore, females are more likely to “befriend” and to create social networks that provide resources, safety, and support under conditions of stress. Like Cyranowski et al.’s (2000) model, this framework highlights the role of oxytocin as a primary mechanism underlying these biobehavioral differences. Oxytocin is related to the attachment–caregiving system that underlies the theory (Taylor et al., 2000). This model holds promise for understanding why more girls become depressed than boys, especially from an interpersonal and biobehavioral perspective, but because it was not formulated to explain the ontogeny of depression, no research has yet examined whether the hypothesized processes are associated with depression or can explain the sex difference in depression.

Hankin and Abramson (2001) proposed an elaborated cognitive vulnerability–transactional stress model. They argued that a general depression model, based on existing and empirically supported depression theories, could be elaborated and expanded to include developmentally sensitive influences that improve the understanding of why more girls become depressed than boys. They emphasized the scientific goal of parsimony—
having a general theory capable of explaining disparate research findings (e.g., the sex difference in depression), rather than postulating sex-specific theories of depression (i.e., one model for boys, another for girls).

They stated that females encounter more negative life events than males and that this increase in stressors leads to elevations in depressed mood. Females exhibit more cognitive vulnerabilities to depression (e.g., negative cognitive style, rumination, negative cognitions about perceptions of physical attractiveness) than males. Females' greater cognitive vulnerability enhances the likelihood that they will experience depression when they encounter negative events, consistent with existing cognitive vulnerability–stress theories (Abela & Hankin, Chapter 1, this volume).

In addition, they elaborated on the traditional vulnerability–stress model to incorporate developmentally sensitive factors that may explain why girls encounter more stressors and exhibit more negative cognitive vulnerabilities. Girls are hypothesized to possess more distal preexisting vulnerabilities, such as genetic influences, temperament/personality factors, and environmental adversities like childhood maltreatment, and these contribute to girls' greater proximal vulnerabilities and exposure to stressors. Moreover, the traditional vulnerability–stress model was expanded to include initial negative affect and stress generation processes in the proximal etiological chain. Most individuals are expected to experience initial elevations in general negative affect (e.g., anger, anxiety, sad mood, frustration, etc.) after experiencing stressors, but depression is hypothesized to result more specifically when individuals possess cognitive vulnerabilities. The inclusion of initial negative affect may account for the observed comorbidity of depression; exposure to stressors is a general risk factor for the development of many psychopathologies, but cognitive vulnerabilities are hypothesized to be depression-specific risks, such that they moderate the likelihood that the initial negative affect after a stressor will progress to full-blown depression, specifically. Finally, the model incorporates a transactional stress generation mechanism, consistent with interpersonal models of depression (e.g., Hammen, 1991; Joiner & Coyne, 1999). As levels of depression rise, it is hypothesized that they will contribute to the generation of additional stressors, particularly in interpersonal contexts.

Evidence reviewed earlier in the chapter is consistent with many of the tenets of this theory. Girls exhibit greater cognitive vulnerabilities (e.g., negative cognitive style, rumination, negative beliefs and perceptions of physical attractiveness) than boys. Girls encounter more stressors (overall, interpersonal, and dependent) than boys. There may be a sex difference in genetic risk, so that girls may exhibit stronger heritability to depression than boys, particularly starting in adolescence. Finally, girls experience more of the hypothesized distal risk factors (e.g., maltreatment, such as sexual abuse, and perhaps negative emotionality) than boys. However, no published research has directly tested more than one component of the model at a time, so it is uncertain how well it explains the sex difference.

Keenan and Hipwell (2005) propose a framework to identify preadolescent precursors to individual differences in risk for depression in girls. In contrast to the other conceptual models that emphasize etiological influences primarily during adolescence, their model mostly focuses on sex differences in childhood. The authors extend previous theories on sex differences in depression, specifically building on the theoretical foundation provided by Zahn-Waxler and colleagues (Zahn-Waxler et al., 1991; Zahn-Waxler, 2000), and identify three constructs that may function, either singularly or in combination, as preadolescent precursors to depression: excessive empathy, compliance, and overregulation of emotions. The authors use a vulnerability–stress perspective in which
these three factors act as the vulnerability and the psychological onset of puberty acts as a stressor in the development of depression. The results reviewed earlier in this chapter support these factors as putative vulnerabilities.

In addition to these preadolescent vulnerabilities, Keenan and Hipwell (2005) postulate two contexts, family conflict and maternal depression, that may trigger depression in girls. The evidence reviewed earlier is consistent with this aspect of their model as well. The presence of stressors may affect girls differently and at different times, and certain stressors may even be causally related to the precursors to depression.

This model is relatively new, so understandably there is no specific test of it. The theory is particularly innovative and has great potential for advancing knowledge about the preadolescent precursors that may contribute to more girls becoming depressed than boys.

**TREATMENT AND PREVENTION**

Most of the available literature on the effects of sex on interventions is based on research with adults, so we review this evidence briefly and highlight pertinent research with youth when available. Treatment studies have not found evidence for substantial sex differences in response to treatment (Garfield, 1994; Sinha & Rush, 2006; Zlotnick, Elkin, & Shea, 1998). For example, the National Institute of Mental Health’s Treatment of Depression Collaborative Research Program (Zlotnick et al., 1998) shows that the depressed patient’s sex did not affect the process or outcome of treatment (psychotherapy or pharmacotherapy). Still, most past studies were not designed to examine sex differences in treatment.

Among children and adolescents, the largest treatment outcome study to date is the Treatment for Adolescents with Depression Study (TADS) Team, 2004), and the influence of sex was not reported. As this is the largest efficacy study of depression in youth, it has the greatest power to examine sex as a potential moderator of effects (psychotherapy or pharmacotherapy). Other investigators have suggested that group-based treatment of depression that includes only girls may be more effective than mixed-sex groups, and studies have been initiated to test the efficacy of psychosocial interventions in all-girls groups (Stark et al., 2006). For example, Stark and his colleagues have evaluated the effects of group-based cognitive-behavioral therapy (CBT) for clinically depressed girls only and reported remarkable success in their efficacy trial. To our knowledge, only one study has examined all-girl groups versus coed groups (Chaplin et al., 2006), and it was found that all-girl groups were better at reducing hopelessness and increasing girls’ therapy attendance, although no differences were found between groups for reducing depressive symptoms (both types of group significantly reduced depression). Thus, the influence of sex on outcome in efficacy trials among youth and the sexual composition of group-based interventions are important areas for research.

With respect to antidepressant medication, the Institute of Medicine (2001) highlighted that little is known about potential sex differences in pharmacokinetics and pharmacodynamics, both of which are highly relevant to understanding possible sex differences in treatment with antidepressant medication. The available studies show that adult women are more likely than men to be diagnosed with atypical depression, and as a result, tend to be prescribed tricyclic antidepressants, whereas men more often receive selective serotonin reuptake inhibitors (SSRIs; Yonkers, Kando, & Cole, 1992). Women
show a more potent response to sertraline than imipramine, whereas men respond better to imipramine (Kornstein, et al., 2000b). These results may be related to sex differences in the metabolism of sertraline (Ronfeld, Tremaine, & Wilner, 1997). A different study found that men and women had equal responses to fluoxetine and tricyclic antidepressants, but women responded better to monoamine oxidase (MAO) inhibitors (Quitkin, Stewart, & McGrath, 2002).

Results from two meta-analyses (Horowitz & Garber, 2006; Merry, McDowell, Hetrick, Bir, & Muller, 2004) of prevention studies of depression among youth reveal somewhat conflicting findings regarding possible sex differences. Merry and colleagues reported that boys had reduced depressive symptoms scores immediately after intervention, whereas girls did not; no sex data were reported for any follow-ups. In contrast to findings for depressive symptoms, prevention results for depressive disorder show that girls responded to intervention immediately after prevention but boys did not. Horowitz and Garber (2006) found that prevention studies with a greater percentage of girls in the samples showed larger effect sizes at immediate postintervention but no sex effect at follow-up. The reasons for this discrepancy in sex effects for depressive symptoms versus disorder are unclear. It is recommended that future research include individual difference characteristics, especially age and sex, as potential moderators of the effects of interventions, so as to improve our understanding of whether and how these affect interventions for individual youth.

SUMMARY, FUTURE DIRECTIONS, AND BROAD ISSUES CONFRONTING THE FIELD

In summary, it is clear that many robust results have been found and replicated in the field. It is now fairly well established that more girls than boys begin to become depressed starting in early adolescence (ages 12–13 or middle puberty). From an early age, there is a sex difference in social and emotional factors that is seen in both normal and abnormal development. On the average, girls tend to be more interpersonally oriented and emotionally focused than boys (see also Rose & Rudolph, 2006). This sex difference in girls' greater socioemotional orientation can be seen in many of the findings reviewed here. As compared with boys, girls experience more stressors, especially interpersonal peer events; girls ruminate and coruminate; girls exhibit more cognitive vulnerabilities to depression; girls exhibit more socially submissive emotions (e.g., fear and sadness) and are less likely to deny these affects; girls display stronger affiliative needs and have more intimate, emotional social relationships in which they are more invested; and girls exhibit higher levels of oxytocin, a hormone that enhances caregiving. Many of the etiological conceptual models highlight various aspects of this general sex difference, although each of the causal theories emphasizes different variations of girls' greater socioemotional vulnerability. Girls' relatively greater socioemotional orientation may contribute to some of the differences in manifestation of depressive symptoms (e.g., girls reporting more sadness and body image concerns).

Clearly, much has been learned in the past several decades about sex difference in normal and abnormal development, yet to advance understanding of why more girls than boys become depressed at a particular developmental point, more research is required. In this final section, we discuss some broad issues that could enhance research and present opportunities for future study.
First, in regard to methodology, we encourage all investigators to report findings (means and standard deviations) on all central variables separately by sex, even if there is no significant sex difference (see also the recommendation by the Institute of Medicine, 2001). Many published articles in the depression and normal child development literatures have statistically controlled for sex and removed any potential influence of sex on effects. This practice implies that sex is a nuisance variable to be controlled. However, we suggest that the practice is unwise for at least two reasons. First, meta-analyses of sex differences of different constructs often reveal small effect size differences that may not be statistically significant in individual studies with small to modest sample sizes (Hyde, 2005). By not reporting central findings separately by sex, the accrual of knowledge is impeded and makes a cumulative science, via meta-analysis, substantially more difficult. Second, conceptually, sex differences should not be viewed merely as a nuisance to be controlled statistically but, rather, as an opportunity for studying causal processes that can illuminate the complex etiological influences contributing to depression (Hankin & Abramson, 2001; Rutter et al., 2003). Understanding why more girls than boys become depressed can provide vital clues as to why individuals in general develop depression. Some of the sex differences in vulnerabilities and contextual developmental changes that may be relevant for explaining the sex difference in depression can provide windows that offer potentially important insights into the etiology of depression more broadly. By evaluating and reporting potential sex differences routinely in research, even when they are not the primary focus of a study, the field may unearth new and unexpected findings that can advance knowledge in this area.

Second, in regard to statistics, we recommend that investigators conduct appropriate mediational and moderational analyses to test properly and rigorously their hypotheses and theoretical models. Practically, this means conducting research with samples of both boys and girls, as opposed to a unisex sample, so that the appropriate statistical analyses can be conducted. Moreover, integrating multiple etiological factors, as opposed to single variable explanations, in combination with examination of more complex models that involve both mediation and moderation at different points along the developmental pathway, would be more informative and contribute more substantially to understanding the sex difference in depression. Testing these more complicated models can be accomplished with recent data analytic innovations (see, e.g., Collins & Sayer, 2001; Curran & Willoughby, 2003) as well as conceptual and statistical advancements in developmental pathways (Pickles & Hill, 2006).

Third, with respect to theory, we believe there are areas of research that to date have received less attention, but may provide important advances in understanding the developmental pathways leading to the sex difference in depression. First, developmental psychopathological research and theory suggest that the causes of depression may be different in children versus adolescents and adults irrespective of sex (e.g., Duggal et al., 2001; Jaffee, Moffitt, & Caspi, 2002; Hankin & Abela, 2005). Moreover, as reviewed earlier in this chapter, there is a switch in the sex difference in depression such that more boys are depressed than girls in childhood, and then more girls become depressed than boys starting in early adolescence. These findings suggest that the etiological influences in prepubertal-onset depression (predominantly more boys) versus postpubertal-onset depression (preponderance of girls) may be different. Existing theories do not address these potentially different pathways very well. The fact that the direction of the sex difference in depression switches at about the same time (i.e., early adolescence) that the some of the general causal factors contributing to depression are...
changing is suggestive and potentially informative. Second, the apparent sex-linked developmental unfolding of patterns of sequential comorbidity of depression, especially girls showing increased levels of anxiety in childhood and anxiety preceding and predicting later depression, is another area ripe for future research. What accounts for this sex-linked developmental pathway of comorbid patterns in depression? Is the likely heterotypic continuity from anxiety to depression stronger for girls than boys? Third, an emphasis on developmental pathways should include investigation of both the manifest symptomatic presentation of depression as well as the underlying causal processes contributing to depression over time. Taking the possible developmental pathway from anxiety to depression as an example, it is unknown whether the apparent pathway is the result of (1) an overlapping symptom manifestation (e.g., broad negative affect is common to both anxiety and depression; Clark & Watson, 1991), (2) similar etiological influences (e.g., shared genetic liability to experience broad negative affects of anxiety and depression [Thapar & McGuffin, 1997] or exposure to stressors contributing to emotional distress [Hankin & Abramson, 2001]), or (3) both manifest symptom and latent etiological influences. As noted earlier, there is some sex difference in the manifestation of depressive symptoms, and addressing this issue from a developmental pathways perspective could shed needed light on the reasons. Finally, it is important to integrate the many potential explanatory influences into a coherent developmental psychopathological model of the sex difference in youth depression. Some have postulated a sex-specific model (e.g., Keenan & Hipwell, 2005; Zahn-Waxler, 2000), whereas others have argued for a general depression model that posits factors that highlight sex differences (e.g., Hankin & Abramson, 2001). It will be interesting and informative for future research to evaluate these theories' hypotheses to ascertain whether sex-specific or general depression models more accurately explain why more girls become depressed in adolescence. It may be the case that both approaches are correct at different points along development trajectories. Perhaps the sex-specific preadolescent precursors to depression predominate in childhood and the general depression etiologic influences prevail in adolescence and beyond. We look forward to future conceptual and empirical advancements in the study of sex differences in depression that address the normal and abnormal development of such differences.

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