Review

Adolescent depression: Description, causes, and interventions

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Abstract

Depression is one of the most prevalent of the psychiatric disorders and is common among individuals with epilepsy. Depression often begins in adolescence. The present review focuses on adolescent depression. In particular, this review first summarizes the definition, description, and classification of adolescent depression. Next, potential causes of adolescent depression are reviewed from a vulnerability–stress perspective. This part of the review focuses on the role of stressors and how stressors interact with genetic, biological, cognitive, personality, and interpersonal vulnerabilities to predict adolescent depression. Last, clinical aspects of adolescent depression are reviewed, including treatment and prevention of depression and the relation to epileptic disorders in adolescence. In sum, a substantial percentage of youth with epilepsy and seizures exhibit depression, and many are not diagnosed or treated in a timely manner. The present review shows that there are valid, empirically based assessments, treatments, and preventions for depression in adolescence that hold promise for reducing the significant burden associated with depression.

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1. Introduction

Depression is one of the most commonly occurring of the major psychiatric disorders, and it has become increasingly recognized that depression over the life span often begins in adolescence. It is a prototypical multifactorial disorder that profoundly affects individuals’ emotions, thoughts, sense of self, behaviors, interpersonal relations, physical functioning, biological processes, work productivity, and overall life satisfaction. Indeed, given the multiple effects that depression has, it has been ranked as the fourth leading cause of disability and premature death worldwide [1]. Given these factors and its typical onset during adolescence, this review focuses on three main issues: definition and description, causes, and interventions.

2. Definitions, diagnostic criteria, and classification issues in depression

According to the official psychiatric classification system (the Diagnostic and Statistical Manual, fourth edition, DSM-IV-TR) [2], an episode of major depression can be diagnosed on the basis of the same symptoms in childhood and adolescence and in adulthood (e.g., sleep changes, appetite changes, feelings of worthlessness, concentration difficulties), except that irritability can be applied as a mood symptom along with depressed, sad mood and anhedonia (loss of pleasure) in youth. DSM-IV-TR states that dysthymia in youth has the same symptom profile as in adults, but there is a minimum 1-year duration in youth compared with 2 years in adulthood. Although in some research, Major Depressive Disorder is considered separately from Dysthymia, most studies either combine them to examine clinically significant depressive disorders or focus on depressive symptoms more broadly. As such, this article reviews evidence about the causes of and interventions for depression generally, as opposed to a specific
diagnosis of Major Depressive Disorder or Dysthymia, unless otherwise noted.

While DSM-IV-TR asserts that the structure and nature of depression in youth are largely the same as in adults, researchers have investigated whether this claim is accurate. Such research suggests that the syndrome and predominant symptoms of depression may differ as a function of age and development given the cognitive, social, emotional, and biological changes that transpire over time throughout childhood and adolescence [3,4]. The specific symptoms that constitute depression and influence its phenomenological manifestation may differ developmentally because (1) younger children may not have developed the requisite cognitive, social, emotional, or biological capacities to experience certain typical adult depressive symptoms, and/or (2) the causes and/or consequences of depression may change across different developmental periods. It appears that very young children, especially preschoolers, tend not to report depressed mood or hopelessness and that younger children are more likely to describe somatic symptoms of depression [4–7]. Other symptoms, such as anhedonia and psychomotor retardation, tend to increase and become more prevalent with the transition from childhood into adolescence, whereas the symptoms of somatic complaints and the physical appearance of looking depressed tend to decrease with age. Still, these studies have not been able to determine conclusively whether the symptoms and structure of depression differ across development. More research is needed to determine whether depression is the same in children, adolescents, and adults because there may be a need for changes or age-appropriate modifications to make the diagnostic criteria for depression developmentally sensitive over the life span. Importantly, though, it is clear that children, and especially adolescents, who fit adult DSM-IV-TR criteria can be identified.

Another important issue regarding the definition and classification of depression is whether the latent structure of depression is best considered as a category or dimension. When viewed dimensionally, depression is said to differ quantitatively by degree (i.e., individuals are more or less depressed); there is no sharp boundary between individuals who are normal from those who are abnormally “depressed.” When viewed categorically, depression is said to differ in kind in a qualitatively distinct way, such that individuals either are depressed or not. For the most part, research shows that the structure of depression is dimensional in children and adolescents [8] and adults (e.g., [9,10]). In addition to these structural studies, other researchers have investigated causes of depression at differing degrees of severity (e.g., mild depressive symptoms to more severe clinical depression) and suggest that many vulnerability factors predict depression at these varying severity levels. Thus, the preponderance of extant evidence suggests that depression varies along a continuum of affective severity. This implies that there is not an obvious, discrete break in depression that “carves nature at its joints” and separates youth who are “truly” depressed from those who are only subclinically depressed with fewer than the required number of symptoms for an official diagnosis. Depression appears to be continuously, dimensionally distributed, like many medical disorders, such as essential hypertension and obesity. Importantly, though, for assessment in clinical practice and research, various artificial cut points (e.g., fewer than five of nine symptoms according to DSM-IV-TR) can be imposed on this natural dimension for practical, diagnostic, and reimbursement purposes in the same way that practical cutoffs are used to diagnose high blood pressure (systolic > 140 mm Hg, diastolic > 90 mm Hg) or obesity (BMI > 30), along with the criteria that the youth is experiencing distress or impaired functioning (e.g., in social, academic, family domains).

Many tools are available to assess depression in children and adolescents (see [11] for additional information); some of these map directly onto DSM-IV-TR’s definition and criteria for youth depression, whereas other assessment measures are moderately related to, but meaningfully different in approach from, the DSM-IV-TR conceptualization of depression. These assessment tools include brief, reliable, valid, and normed questionnaires that can be completed in a short time frame by the adolescent, e.g., the Children’s Depression Inventory [12], or the parent, e.g., Child Behavior Checklist [13]. Adolescents who score higher than a certain cut point, as based on normed national samples, can be evaluated with additional, more thorough diagnostic assessments. These include clinical rating scales or semistructured interviews, e.g., K-SADS [14], in which a trained professional interviews the adolescent and often a parent, and a diagnosis of a depressive disorder can be given based on the youth’s and parent’s responses about the child’s symptoms.

3. Epidemiology of depression

3.1. Prevalence and development of depression over the life course

The rate of prevalence of depression has been examined in many studies with different age groups and with different methods and samples. In this review, community samples are emphasized for estimating rates of prevalence of depression because samples drawn from psychiatric clinics may be biased in various ways (e.g., actively seeking treatment, exhibiting greater severity, and revealing higher comorbidity), and these biases can artificially inflate the rates of prevalence of depression.

Cross-sectional studies of adolescent self-reported depressive symptoms (i.e., less than a clinically significant depressive disorder) indicate that between 20 and 50% [15,16] of adolescents report significant, subsyndromal levels of depression. Prospective longitudinal studies of self-reported depressive symptoms show that average levels of depressive mood and symptoms rise substantially from relatively low levels in childhood to much higher levels start-
ing in middle adolescence [17–20]. It is important to note that elevated rates of depressed mood or symptoms do not merely indicate typical, benign adolescent “moodiness” or “tumult,” but rather represent a substantial risk for later, clinically significant depressive disorder [21] and impaired functioning [22].

Cross-sectional studies of diagnosed clinical levels of depression show that the rates of depression are generally low in children and increase to near-adult prevalence levels in adolescence. Preadolescent school-aged children tend to have low lifetime prevalence rates of depression (<3%) [23,24]. Rates of depression among adolescents are generally comparable to those observed among adults: the lifetime prevalence of major depression for 15- to 18-year-olds was 14%, and for minor depression, 11% [25]. Consistent with this, the lifetime prevalence of major depression for 18- to 29-year-olds was 16.6% in the most recent large-scale epidemiological study [26]. Various prospective, community-based studies [23,27–29] reveal that the rates of clinical depression are generally low in childhood (e.g., 1–3%), and then increase dramatically in middle to late adolescence, when they reach rates observed throughout adulthood (up to 17%). In sum, there is up to a sixfold increase in rates of depression from early adolescence (3% prevalence at age 15) to the end of adolescence (17% at age 18).

Finally, most individuals experience their first depression sometime during adolescence. Adult depression is typically preceded by youth depression. In a recent prospective follow-back study [30], in which an entire birth cohort of individuals was followed for 26 years, the vast majority of adults at age 26 (75%) had already had a depressive disorder in childhood or adolescence; only 25% had experienced the onset of depression in adulthood (ages 21–26). Similar results have been reported in other large-scale, prospective community studies (e.g., [31]). Yet, Kessler and colleagues [26] found that most adults with a psychiatric disorder (e.g., anxiety disorder, conduct problems) had experienced symptoms prior to age 14, but the average age at onset for depression was 30. The reasons for the discrepancy between the Kessler et al. study and the other studies with respect to age at onset for first depression are unclear, but may involve the study design and method: Kessler and colleagues [26] had adults retrospectively recall depression onset dates, whereas the studies (e.g., [30,31]) with adolescent onset prospectively followed individuals from adolescence through adulthood. This latter method with prospective follow-ups is considered more reliable and valid than retrospective recall.

3.2. Sex differences in adolescent depression

Twice as many adult women are depressed as men. Various studies have examined the emergence of this sex difference developmentally from childhood through adolescence and into adulthood. Approximately 25–40% of adolescent girls exhibit high levels of depressed mood compared with 20–35% of adolescent boys [16]. More girls than boys report depression starting in early adolescence (around ages 12 and 13) [18–20,32,33]. Longitudinal studies investigating the emergence of the sex difference at the level of depressive disorder find the same pattern: more girls than boys begin to become clinically depressed after age 12–13 [27–29,34]. Finally, the female preponderance in depression remains at this 2:1 female: male ratio from adolescence throughout most of adulthood [35].

Pubertal development and timing have been studied relative to the sex difference in adolescent depression. Angold and colleagues [36] found that the sex difference in depression diverged at Tanner Stage III and was a better predictor than age alone. Moreover, girls who started puberty earlier than their peers were more likely to become depressed [37–39].

3.3. Continuity and recurrence of depression over the life course

Depressed mood at younger ages carries risk for development of depressive disorder later in life. For example, a prospective community study found that teachers’ reports at age 6 and children’s self-reports at age 9 of anxious/depressive symptoms predicted occurrence of Major Depressive Disorder at age 21 [40]. Compared with the continuity of depression from childhood into adulthood, there is much stronger continuity for depression from adolescence into adulthood [21,28,34,41,42]. Still, most depressed prepubertal children do not grow up to become adults with major depression [34,43]. Indeed, the fact that there is less continuity in depression from childhood into adulthood as there is from adolescence into adulthood is consistent with the notion that there are important developmental differences (e.g., symptoms and potential causes) between depression that arises during childhood and depression that develops in adolescence or adulthood [44,45].

Depression is a chronic, recurrent disorder. Approximately half of individuals with a diagnosis of depression experience a recurrence within 2 years, more than 80% within 5–7 years, and individuals who have had more than three episodes of depression are particularly likely to have another recurrence [46–48]. Moreover, for individuals with multiple recurrences, time to the next recurrence decreases with each recurrence. Approximately 40% of youth experience a depression recurrence over 3–5 years [49,50].

3.4. Comorbidity

Depression commonly occurs with other disorders, especially anxiety and disruptive behavioral disorders. Angold and colleagues [51] showed that depression is associated at greater than chance levels with anxiety disorders (median odds ratio = 8.2), conduct/oppositional defiant disorder (median odds ratio = 6.6), and attention-deficit hyperactiv-
ity disorder (ADHD, median odds ratio = 5.5). However, it has been reported that the association between depression and ADHD in youth is artificial, such that the elevated co-occurrence disappears once overlapping symptoms (e.g., irritability) are taken into account [52].

In addition, there are developmental patterns of sequential comorbidity. Children and early adolescents are more likely to have a co-occurring diagnosis of separation anxiety disorder and depression, whereas older adolescents are more likely to exhibit comorbid eating disorders and substance use problems. Elevations in symptoms of or a diagnosis of anxiety often precede the development of depressive symptoms [23,29,30,42,53,54]. Earlier externalizing behaviors tend to predict later depressive symptoms, whereas earlier depressive symptoms do not predict later externalizing behaviors [30,55].

The comorbidity of depression with other emotional and behavior symptoms and their sequential developmental unfolding over time have important implications for the diagnostic classification, the methodological study, and the clues to the etiology of depression. Methodologically, both depression and its co-occurring symptoms need to be assessed in research to examine whether hypothesized vulnerability factors and processes predict the development of depression specifically or general, comorbid problems co-occurring alongside depression. Without measuring depression and other comorbid symptoms, it is impossible to evaluate whether vulnerabilities or stressors actually predict depression or are only associated with depression because of its overlap with other symptoms and disorders. For example, the apparent overlap between ADHD and depression may be artificial because of the shared symptoms and an underlying irritable temperament [52].

4. Potential causes of the development of depression: Vulnerabilities and stress

To understand what may cause depression in youth, a vulnerability–stress framework, in which recent stressful events trigger an underlying predisposition, may be one of the most promising approaches [56]. In this section, the role of stressors is considered first, then depression vulnerabilities are reviewed. These vulnerabilities are reviewed separately, even though it is most likely that a developmentally sensitive, integrative theoretical model can and should combine these disparate depression vulnerabilities and stressors into a coherent vulnerability–stress model of depression. It is unlikely that any single etiological framework (e.g., biological, interpersonal, cognitive, emotional, personality) will provide a necessary and sufficient causal explanation for the development of depression, because depression is a prototypic multifactorial syndrome, so many processes, mechanisms, and risk factors need to be evaluated simultaneously to provide a complete understanding of the etiology of depression starting in adolescence.

4.1. Stressful negative life events

Grant and colleagues proposed that stress be defined as environmental events or chronic conditions that objectively threaten the physical and/or psychological health or well-being of individuals of a particular age in a particular society [57]. Life events, particularly negative events and stressors defined and assessed in this manner, play a substantial contributory role in the development of depression from childhood through adulthood [58–61]. Almost all individuals with a depressive disorder will have encountered at least one significant negative life event in the month prior to the onset of depression [59]. Additionally, longitudinal studies have discovered that experiencing stressors precedes the initial elevation, recurrence, and exacerbation of depression (e.g., [39,62]).

In addition to the perspective that stressors precede and contribute to depression, a complementary perspective suggests that the stress–depression relationship is not a static, unidirectional one, but rather a bidirectional, transactional process. The stress generation hypothesis [63] suggests that some individuals, because of personality characteristics or behaviors, such as being depressed, generate stressful circumstances and additional events for themselves, and these can then lead to further increases in depression. Cross-sectional studies show that depressive symptoms are associated with self-generated stressors (e.g., [64,65]). Longitudinal studies show that depressive symptoms are associated with subsequently occurring negative events [66–71].

More recent multiwave longitudinal studies provide the strongest support to date for the stress generation hypothesis. In a three-wave, 1-year longitudinal study of adolescents (8th and 10th graders), Hankin and colleagues [72] found that depressive symptoms at one time point predicted later increases in objectively assessed stressors at the following time point and that stressors at the same time point were concurrently associated with depressive symptoms. Similar results were obtained in a 10-wave 1-year longitudinal study of children (aged 6–14) of affectively ill parents [73]: a bidirectional relationship was found between negative events and increases in depressive symptoms.

There are developmental changes that occur in the frequency and types of stressors. There is a dramatic rise in the number of uncontrollable negative life events experienced starting after age 13, and this increasing trajectory in stressors closely parallels the rise in depressive symptom elevations throughout adolescence [18]. Thus, the fact that stressors appear to be on an increasing trajectory from late childhood into adolescence provides a potential explanation of why levels of depression rise throughout adolescence. The increasing trajectory of stressors begins around puberty, which is a transitional period in development, and transitions frequently are associated with elevated emotional distress and increases in stress [39,74,75]. Further, adolescent girls exhibit a significantly greater increase in stressors after age 13 than boys [18,76] and this developmental timeline for the sex difference in stressors
matches the emergence of the sex difference in depression. Indeed, girls’ increased experience of stressors, particularly interpersonal stressors, partly explains why girls are more depressed than boys [77].

It is clear that not everyone who experiences negative life events becomes depressed, although the majority of those individuals who are significantly depressed have experienced at least one major negative life event prior to the onset of the depression. Indeed, only 20–50% of individuals who experience severe, major negative life events develop clinically significant levels of depression (e.g., [2,78]). In sum, negative life events are neither necessary nor sufficient to cause depression without some underlying vulnerability. Various depression vulnerabilities that may enhance the risk for depression, especially in the context of stressors, are reviewed next.

4.2. Genetic vulnerability

Having a parent with a history of major depression is one of the strongest predictors of depression in youth [79]. Behavior genetic studies with children and adolescents have found depression to be moderately heritable (see [80,81] for reviews). Heritability estimates for parents’ rating of youth’s depressive symptoms are modest to high (range, 30–80%), whereas these genetic estimates are lower for youth’s own ratings of their depressive symptoms (range, 15–80%; 35% average) [82]. Evidence from twin research also suggests that depressive symptoms are heritable starting in adolescence (after age 11) and continuing throughout adulthood, whereas shared common family environment, but not genetic factors, is linked with depression in childhood (before age 11 [82]).

In addition, some of the etiological risk factors for depression are moderately heritable. The liability to experience negative events is partially heritable [83]. A longitudinal twin study [84] found that genetic liability increased the risk for depression and experiencing stressors for girls after, but not before, puberty.

Research has also revealed gene–environment interactions: some individuals are more likely to become depressed in the face of certain environmental risks because of genetic liability. The most specific evidence to date for a gene–environment interaction comes from molecular genetic studies with adults that include assessments of environmental stressors ([85–88], but see [89] for failure to replicate). These studies have found that a functional polymorphism in the promoter region of the serotonin transporter (5-HTT) interacts with the occurrence of stressors over time in adulthood to predict the onset of depression. Specifically, those individuals who had one or two copies of the short allele form of 5-HTT (the genetic vulnerability) and encountered more stressors over time experienced the greatest incidence of depression, even compared with adults who experienced equivalent stress levels but were homozygous for the long allele of the 5-HTT promoter (less genetic risk). In the only genetic × stress study to date with an adolescent sample, the short form 5-HTTLPR interacted with stressors to predict youth-rated depressive symptoms cross-sectionally among 12- to 17-year-old girls, but not boys [90].

Despite the general consensus across these adult molecular genetic studies, there is an interesting inconsistency in results that points to an area of future research to understand how stressors interact with genetic risk. Almost all of the studies (e.g., [85]) used self-report checklists in which severe stressors and major negative life events were assessed. Adults who experienced more severe stress and had the short 5-HTT allele were the most likely to develop depression. In contrast, Kendler and colleagues [88] found that smaller stressors, or minor hassles, interacted with the genetic risk of having a short 5-HTT allele to predict depression, whereas experiencing more severe stress directly contributed to depression regardless of genetic risk. Understanding whether this genetic risk interacts with severe stressors or more minor hassles has important implications for advancing knowledge about the etiology and potential pathophysiology of depression, as well as suggesting whether future interventions might more effectively target at-risk youth experiencing everyday minor stress or occasional major stress.

4.3. Personality/temperament vulnerability

Depression has consistently been linked with personality traits subsumed under negative emotionality [91,92], and these traits are moderately heritable [93]. Neuroticism, or negative emotionality, reflects the extent to which an individual perceives and experiences the world as threatening or distressing [94]. Neuroticism serves as a vulnerability to developing depression among children and adolescents [95–97] and to experiencing more stressors [98–100]. Despite the link between neuroticism and depression, considerably less attention has focused on how personality traits, such as neuroticism, may interact with other depression vulnerabilities and/or stressors to explain how neuroticism leads to depression. Kendler and colleagues [101] found that the strongest predictors of a major depressive episode among adults were negative life events, genetic factors, a previous depressive episode, and neuroticism. Building on this, prospective research [98] with adolescents (6th–10th grades) showed that initial levels of neuroticism predicted the occurrence of additional stressors over four prospective waves of follow-ups, and these stressors explained the prospective association between baseline neuroticism and elevations in depressive symptoms over time. Thus, neuroticism, which itself is partially heritable, confers vulnerability to develop depression and may do so through stress generation.

4.4. Biological vulnerability

Numerous aspects of biological vulnerability to depression have been investigated in children, adolescents, and
adults (see [102,103] for reviews). This brief review focuses on research highlighting (1) the role of neurotransmitter and neuroendocrine dysregulation in the central nervous system in response to stressors and (2) a putative dysregulated brain circuit underlying depression.

Humans biologically respond to stressors in their environment through activation of the hypothalamic–pituitary–adrenal (HPA) axis, and dysregulation of this human stress response may be a biological vulnerability to depression [60,104]. In response to the perception or experience of stress, the hypothalamus releases peptides that act on the pituitary, which, in turn, releases hormones to control the release of cortisol from the adrenal glands. Cortisol is a stress hormone that allows the body to manage stress effectively in the short term, and growth hormone (GH) is released by the pituitary. Both hormones have been examined to determine whether HPA axis dysfunction is a biological vulnerability for depression. Corticotropin-releasing hormone (CRH) and norepinephrine (NE) are the core central regulators of the HPA axis; activation of CRH and NE increases behavior, arousal, and activity and interferes with vegetative functions (e.g., sleep and eating, which constitute depressive symptoms when impaired).

Cross-sectional comparisons of youth with clinical depression and youth with other psychiatric symptoms or normal controls show that depressed and nondepressed kids do not differ on baseline cortisol levels [105], and the findings are mixed when physiological challenges of the HPA axis system (e.g., dexamethasone suppression test) are used [106]. Developmental changes in HPA axis response may explain some of the equivocal findings to date because results with adults have been consistently stronger [103]. Studies with children (e.g., [107]) have found blunted GH secretion in response to biological challenges. Birmaher and colleagues [108] found that offspring of depressed parents, who were at high-risk for depression but had not yet experienced clinical depression, exhibited reduced GH response; these studies suggest that GH response may index a biological vulnerability for depression in youth.

In addition, a neural circuit in the brain has been implicated in vulnerability to depression [109]. The amygdala is a subcortical region of the brain that mediates fear, anxiety, and emotional memory. The mesolimbic dopamine system is involved with reward and pleasure. The prefrontal cortex helps control behavioral and affective flexibility and is involved with approach/withdrawal systems. These regions have been found to be abnormal in studies comparing depressed adults with normal persons [109]. Also, asymmetry in electrophysiological activity in resting frontal brain activity has been used to assess this neurobiological vulnerability for depression and is probably associated mostly with potential prefrontal cortex dysfunction. Relative left-frontal underactivity compared with right-frontal activity has been associated with depression in adults and may constitute a stable biological vulnerability for depression [109,110]. Research indicates that children [111] and infants [112] of depressed mothers, who are at high risk for depression but not yet depressed, have left-frontal underactivity.

Still, despite the exciting potential of biological vulnerabilities, it is important to note that most of the research to date has focused on adults and has employed cross-sectional designs. Retrospective, cross-sectional studies cannot disentangle biological factors as a cause, correlate, or consequence of depression, nor can they clearly establish whether putative biological indices (e.g., HPA axis dysregulation) constitute a relatively stable vulnerability for the development of depression. Developmentally sensitive, prospective studies are needed.

4.5. Cognitive vulnerability

Cognitive theories of depression are concerned primarily with the relationship between human mental activity (e.g., perception, recognition, judgment, attitudes, reasoning, memory) and the experience of depression. Four cognitive vulnerability factors have received the most attention: (1) negative inferential styles about causes, consequences, and the self [113], (2) dysfunctional attitudes [114], (3) the tendency to ruminate in response to depressed mood [115], and (4) self-criticism [116]. A person with a negative inferential style is likely to attribute negative events to global and stable causes, to catastrophize the consequences of negative events, and to view himself or herself as flawed or deficient following negative events. An individual with dysfunctional attitudes is likely to think his or her self-worth hinges on being perfect or receiving approval from others. For example, the dysfunctional attitude characterized by the statement “I’m worthless unless I’m perfect” may be activated if an individual does not excel in class. Rumination describes the cognitive process in which initially mildly dysphoric individuals focus on the meanings and implications of their depressed mood and, as a result, develop enduring and severe depressive symptoms. Finally, individuals high in self-criticism are preoccupied with issues pertaining to self-definition, competence, and worth. Such individuals are prone to view themselves as a failure as well as feel guilty and experience decreases in self-esteem when not meeting expectations or goals.

Several studies have examined the hypothesis that cognitive factors confer vulnerability to depression among adults, adolescents, and children [117–121]. Prospective research with adolescents shows that a depressogenic attributional style interacts with subsequently occurring negative events to predict increases in depressive symptoms [122,123], dysfunctional attitudes interact with stress to predict clinical depression [124], and rumination is associated with increases in depressive symptoms [125]. Recently, Hankin and colleagues demonstrated that these cognitive vulnerabilities interact with prospectively measured stressors to predict prospective depressive symptom trajectories in adolescence (6th–10th graders) in a multiwave study [126]. Last, a prospective study following offspring of
depressed parents showed that there was a temporal association between the parents’ and child’s levels of depression, such that as parents experienced more depression, their child was more likely to exhibit increases in depression. Of interest, this temporal association was magnified by the child’s negative inferential style: more pessimistic children experienced greater increases in depression following their parents depressive symptoms compared with optimistic youth [127].

Some researchers have argued that cognitive vulnerability to depression emerges only during the transition from late childhood to early adolescence when children acquire the ability to engage in abstract reasoning and formal operational thought [128–130]; see [119,121] for discussion. According to this “developmental hypothesis,” children lack the cognitive capacities to think abstractly about their self and future, but once stable individual differences in personality traits, styles of thinking, and self-views emerge in adolescence, these negative cognitions can interact with environmental stressors to contribute to depression. However, contrary to this “developmental hypothesis,” numerous studies have now examined a wide array of cognitive vulnerabilities, including depressogenic inferential styles [131–133], dysfunctional attitudes, self-criticism [134], and a ruminative response style [135]. These cognitive vulnerabilities interacted with the occurrence of negative events to predict increases in depressive symptoms in both children (aged 6–9) and early adolescents (aged 10–14).

Another developmental hypothesis that has garnered initial support is that some cognitive vulnerabilities in childhood exist and can be measured reliably and validly, but these cognitive risks have not yet consolidated into stable, traitlike negative thinking patterns. In other words, abstract reasoning and formal operational thought may not be necessary for cognitive vulnerabilities to function as risks for depression, but these cognitive vulnerabilities would be expected to be more variable earlier in childhood than in adolescence and adulthood. Starting sometime in adolescence and remaining in adulthood, these cognitive vulnerabilities emerge and coalesce into stable, traitlike cognitive risks for depression. Prospective, multiwave research with youth in early, middle, and late adolescence [8,136] lends initial support to this hypothesis. Youth’s negative thinking patterns, specifically negative inferential styles and dysfunctional attitudes, were not very stable in middle adolescence (6th–8th grades), but exhibited relative stability consistent with personality traits starting in middle adolescence (9th and 10th grades) through late adolescence. If correct, this developmental hypothesis may help to explain some of the inconsistent findings concerning cognitive vulnerabilities to depression in children and adolescents [119,121]. Also, this developmental hypothesis may have important implications for treatment and prevention of depression: If, prior to middle adolescence, youth have not yet developed stable, traitlike ways of viewing their selves and worlds in negative, depressogenic ways, then it may be sensible to implement cognitive-behavioral treatment and prevention approaches to reduce depression before these negative thinking patterns become ingrained, stable, individual risks for depression. Additional research is needed to test this and other developmental hypotheses prior to beginning any large-scale, developmentally sensitive depression prevention trials.

4.6. Interpersonal vulnerabilities

The majority of research examining the relationship between interpersonal vulnerability factors and depressive symptoms has been cross-sectional in nature. This makes it difficult to draw conclusions about whether such factors play a role in the onset of depressive symptoms or whether they are simply a correlate or consequence of such symptoms. This review focuses attention on interpersonal vulnerabilities to depression that can be characterized as manifesting themselves within the individual, including excessive reassurance seeking [137], dependency [116], social support, and insecure attachment [138].

Excessive reassurance seeking is defined as “a relatively stable tendency to excessively and persistently seek assurances from others that one is loveable and worthy, regardless of whether such assurance has already been provided” [137, p. 270]. Cross-sectional studies show that higher levels of reassurance seeking are associated with higher levels of depressive symptoms in both children and early adolescents [127,139]. Similarly, youth psychiatric inpatients with a primary diagnosis of a depressive disorder have been found to exhibit higher levels of reassurance seeking than those with a primary diagnosis of an externalizing and/or anxiety disorder [140]. Last, high levels of reassurance seeking predicted a past history of clinically significant depressive episodes in children and early adolescents exhibiting an insecure attachment style to their parents, even after controlling for current depressive symptoms [127].

Results from a recent prospective study suggest that reassurance seeking may serve as a vulnerability to depression only starting in early adolescence. In a 1-year study with a multiwave longitudinal design of a sample of children of affectively ill parents (aged 6–14), excessive reassurance seeking was associated with increases in depressive symptoms following increases in either hassles or parental depressive symptoms in older but not younger children [141]. It may be that reassurance seeking tendencies are normative and even adaptive in children, but reassurance seeking emerges as a vulnerability to depression only in early adolescence, when lower levels of reassurance seeking become normative.

Interpersonal dependency is an exaggerated need for relatedness and a desire to be in direct, immediate contact with close others (e.g., parents, peers). Cross-sectional studies show that higher levels of dependency are associated with higher levels of depressive symptoms in adolescents but not children [134,142–144]. However, prospective stud-
ies have failed to find a relationship between dependency and increases in depressive symptoms over time [134,142]. High levels of dependency may be normative and even adaptive in younger populations, such that dependency may emerge as a vulnerability to depression only in adolescence, when low levels of dependency and high levels of autonomy become normative.

Social support is a multidimensional concept that is defined as the availability of a network of people on whom a person can rely in times of need. There are different types of social support (e.g., emotional, financial, informational, or enacted support), and a social support network might include family members, friends, significant others, as well as colleagues. Kashani and colleagues reported that compared with anxious children, depressed children had lower levels of satisfaction with their social networks; conversely, higher-functioning and more competent children reported greater social support [145]. Adolescent depression is linked to lower levels of family support [146–148] and lower levels of social support from friends [149], with some evidence for sex effects of social support on depression [150]. Stice and colleagues showed that adolescents’ perceptions of low parental support predicted future depression, whereas initial depression predicted decreased peer support, so it is clearly important to consider who provides the support.

Regarding attachment as an interpersonal vulnerability to depression, Bowlby [138] highlighted that early attachment patterns between children and their caregivers play a vital role in both normal and abnormal development. Attachment patterns are thought to derive primarily from the quality and the quantity of contact a child has with his or her caregivers [151]. Parents who are sensitive in their caregiving, who are alert to their infant’s needs, and who react quickly and appropriately to such needs are likely to have infants who develop a secure attachment [152]. Not all children, however, develop a secure attachment to their caregivers. When normal developmental processes go awry, insecure attachment patterns have been hypothesized to result. Insecure attachment patterns have been posited to serve as vulnerability to a diversity of psychological problems including depression [153].

Several cross-sectional studies have demonstrated that attachment insecurity is associated with depressive symptoms in adolescent samples (e.g., [152,154,155]). In one of the few prospective studies, Hammen and colleagues [156] reported that attachment insecurity was associated with increases in depressive symptoms over a 1-year longitudinal follow-up among female high school seniors. In addition, adolescent females who exhibited attachment insecurity reported increases in depressive symptoms when experiencing high but not low levels of interpersonal stress. More recently, results from a multiwave longitudinal study [127] showed that children who exhibited high levels of negative attachment patterns reported greater elevations in depressive symptoms following elevations in their parents’ level of depressive symptoms.

4.7. Summary

Based on this brief review of selected vulnerabilities to depression and the role of stressors as contributory causes of the development of depression in adolescence, it is clear that environmental stressors precede and contribute to prospective increases in adolescent depression, and further, that many vulnerabilities can enhance this association such that vulnerable adolescents are more likely to become depressed in the face of stress compared with nonvulnerable youth. Only a few of the many potential vulnerabilities (i.e., genetic, biological, cognitive, and interpersonal) are reviewed here; other vulnerabilities to depression that are theoretically interesting and empirically supported, such as emotional vulnerability (see [157] for review), are not reviewed here for space considerations. In sum, a complete causal understanding of the development of depression across the life span will likely involve a multifaceted, integrative, developmentally sensitive vulnerability-stress approach in which vulnerabilities need to be integrated in a conceptually coherent fashion to elucidate the multiple pathways and mechanisms that lead to the development of depression starting in adolescence (for examples, see [59,118,158,159]).

5. Interventions for adolescent depression

Broadly considered, intervention includes treatment of youth diagnosed with depression, as well as prevention prior to onset of depression. Many studies have investigated various treatments (e.g., see [160–162] for reviews) and preventions (e.g., see [161] for reviews) for adolescent depression. This review briefly considers the findings from the largest randomized clinical trial to date on treatment of adolescent depression, the Treatment of Adolescent Depression Study [163], and a meta-analysis of prevention studies for adolescent depression [164]. Also, research examining the link between adolescent depression and epilepsy, given the focus of this Journal, is reviewed.

Many individual, moderately sized treatment studies have shown that depression in adolescents can be ameliorated through individual psychotherapies, such as cognitive-behavioral therapy (CBT) and interpersonal psychotherapy, and antidepressants [161]. Consistent with these smaller studies, the recently completed TADS trial [163] showed that moderate to severe clinical depression in adolescence can be treated most efficaciously by the combination of antidepressants (fluoxetine in TADS) and CBT (71% response rate vs 34.8% response for placebo). This combination was also the most efficacious in reducing suicidality. No suicides occurred in the TADS trial, which was completed prior to the FDA’s warning in 2004 on the use of antidepressant medications in youth. The combination of fluoxetine with CBT was better than use of fluoxetine alone (71% response rate vs 60.6% response rate), whereas CBT alone was not significantly different than pill placebo (43.2% response rate vs 34.8% response rate). Tak-
ing both risk and benefit into account, it presently appears that the combination of fluoxetine with CBT is the superior short-term treatment for adolescent clinical depression.

Likewise, many moderately sized prevention trials have been completed, and the results have been mixed. Most of the prevention studies have used CBT-based approaches to attempt to reduce the onset of depression in youth. A recent meta-analysis of studies with youth (aged 5–19) showed that psychological preventions were effective when aimed at targeted, or at-risk, youth, whereas universal prevention programs were not effective.

Recent research shows that adolescents with epilepsy are more likely to experience depression, as well as anxiety and suicidal ideation, compared with normal youth [165]. Specifically, 71 youth (aged 5–16) with childhood absence epilepsy (CAE) and 100 youth with complex partial seizures (CPSs) had a higher rate of depressive and anxiety disorder (33%) and suicidal ideation (20%) compared with normal youth. Another study [166] showed that among youth (aged 4–18) with epilepsy (partial epilepsy, 76.4%; symptomatic, 60%; cryptogenic, 27.3%; idiopathic, 12.7%), depression was the most common psychiatric diagnosis: 36.4% of the patients received a diagnosis of depression according to DSM-IV-TR criteria. Depression in this sample was found to be untreated and undiagnosed for 4 years after the actual depressive disorder onset. Finally, consistent with these quantitative studies, a qualitative study [167] interviewing 49 youth (aged 7–18) with medically refractory seizures showed that many of the youth had emotional distress that was heightened by the seizures, felt socially isolated, perceived academic difficulties, and felt physically fatigued; these youth perceived that their seizures impaired their ability to function in a normal manner socially and emotionally. Given the higher rate of depression and its impairing effects, it is important that youth with seizures be screened and evaluated for depression, anxiety, and suicidal ideation and receive effective interventions to reduce their mental health burden.

6. Conclusion

Depression in adolescence is a prevalent mental illness with significant burden and costs in terms of social, educational, interpersonal, economic, and impaired future developmental outcomes. Adolescent depression can be identified and evaluated reliably and validly in various ways, and this is important for diagnosis and eventual treatment or prevention. Many vulnerability factors increase the risk of adolescents experiencing depression, especially when in the face of stressful life events. As youth with epilepsy and related disorders are at higher risk for depression and anxiety, it is important that appropriate evaluation, especially for those youth with elevated risk factors or high levels of stress, be conducted so that efficacious, empirically based treatments can be used to help those who are clinically depressed, and prevention efforts can be applied to those identified as at-risk.

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