CHAPTER 20

Depression in Children

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The goal of this chapter is to give a general overview of the characteristics and risk factors for depression in prepubertal children. At the outset, it should be noted that there is significantly less research in child populations than in adolescents and adults. In addition, research with youth samples typically combine children and adolescents, rarely examining child versus adolescent participants separately. As much as possible, the current chapter focuses on research with children specifically, and age ranges are noted when adolescents are also included in the study.

Prevalence

In the late 1970s and early 1980s, theorists and researchers still debated whether children were capable of experiencing clinical levels of depression (e.g., Lefkowitz & Burton, 1978). We now recognize that children not only do experience clinical depression, including major depressive disorder (MDD), but also that they do so at alarming rates. Results of the National Health and Nutrition Examination Survey (NHANES) indicate that the 12-month prevalence of mood disorders in children ages 8–11 years old is approximately 2.5% (MDD: 1.6%; dysthymia: 0.8%; Merikangas et al., 2010). Similar estimates have been observed in other studies suggesting that approximately 2% of 6- to 11-year-olds have a history of depressive diagnoses (for a review, see Centers for Disease Control and Prevention [CDC], 2013a). There is also growing recognition that major depression can occur even earlier in life, including in preschool-age children (Domènech-Llaberia et al., 2009; Luby et al., 2002, 2006). Although few epidemiological studies have been conducted with children this young, it is estimated that 0.5–2% of children ages 3–6 years old experience major depression (CDC, 2013a; Domènech-Llaberia et al., 2009; Egger & Angold, 2006; Wichstrøm et al., 2012). In addition, although the occurrence of documented suicide is rare in children younger than age 8, suicide is the seventh leading cause of death among 8- to 12-year-olds and the third leading cause of death when

focused specifically on 11- to 12-year-olds. This rate continues into adolescence, with suicide being the second leading cause of death among 13- to 18-year-olds (CDC, 2013b). Clearly, then, clinically significant episodes of depression not only occur during childhood, but they are also far too frequent and are sometimes fatal.

There is a well-known sex difference in rates of major depression among adolescents and adults, with the gender gap starting around age 13 and reaching the 2:1 female:male ratio observed in adults by age 18 (Hankin et al., 1998). In contrast, among children, studies have either found no evidence for gender differences in depressive symptoms or diagnoses (Domènech-Llaberia et al., 2009; Egger & Angold, 2006; Twenge & Nolen-Hoeksema, 2002) or have suggested that boys have higher rates of depression than girls (Angold, Costello, & Worthman, 1998; McGee & Williams, 1988; Wichstrøm et al., 2012).

Phenomenology

The DSM criteria for diagnosing MDD in children are identical to those used for adults, with the exception that the Criterion A symptom of sadness may be exhibited as irritability. In addition, the criteria for diagnosing dysthymia (DSM-IV)/persistent depressive disorder (DSM-5) require only 1 year of illness rather than 2 years. However, there have been questions about whether there may be other developmental differences in the expression of depression in children.

For example, some have suggested that certain cognitive symptoms, such as low self-esteem, hopelessness, and depressive guilt, may not be apparent in children with depression because of developmental differences in cognitive development (i.e., prior to the development of abstract thought; Weiss & Garber, 2003). However, findings from studies testing this hypothesis are mixed. Partially supporting theories of developmental differences in cognitive development on symptom expression, concerns about the future (e.g., hopelessness) loaded more strongly onto a depression latent variable in adolescents than in children; however, guilt loaded more strongly onto depression for children than for adolescents (Weiss & Garber, 2003). In addition, other studies have found no difference in factor structure or patterns of item-total correlations for measures of depressive symptoms in children versus adolescents (e.g., Mitchell, McCauley, Burke, & Moss, 1988; Ryan et al., 1987; Smucker, Craighead, Craighead, & Green, 1986). Currently, therefore, there is no clear evidence for developmental differences in the relevance of cognitive symptoms of depression in children versus adolescents or adults. This said, there is evidence for age-related increases in cognitive (and other) symptoms of depression (i.e., hopelessness, as well as anhedonia, hypersomnia, weight gain, decreased energy, and social withdrawal; for a review, see Weiss & Garber, 2003). However, this may speak more to developmental differences in *rates* of depression than to developmental differences in the *expression* of depression.

More recently, theorists and researchers have suggested that appetite and weight symptoms of depression utilized in DSM may need to be modified for pediatric samples. According to current DSM criteria, appetite/weight disturbance can be exhibited by either an increase or a decrease from usual. However, there are normative increases in appetite and weight as children age, calling into question the utility of increases in appetite or weight as a clear feature of depression in youth. Indeed, there is growing evidence that, although decreases in appetite and weight are associated with depression in children and adolescents, increases are not (e.g., Cole et al., 2012).

Finally, there is some evidence that the duration criteria for MDD could be reduced, at least for very young children (Luby et al., 2002). As noted earlier, the duration criteria for dysthymia/persistent depressive disorder in children and adolescents is currently 1 year rather than the 2 years required for the diagnosis in adults. However, the duration criterion for MDD is 2 weeks, regardless of the age of the person. When diagnosing MDD in preschoolers, it is well to keep in mind evidence that those children who do versus do not meet the 2-week duration criteria but who meet all other diagnostic criteria both exhibit greater depression severity and functional impairment than healthy controls at a baseline assessment and 2 years later (Gaffrey, Belden, & Luby, 2011). In addition, both depression groups, regardless of whether they met the 2-week duration criteria, exhibit similar levels of depression and functional impairment, as well as risk for full MDD at 2-year follow-up (Gaffrey et al., 2011). Furthermore, preschoolers who meet all symptom and impairment criteria for MDD, whether or not they meet the duration criteria, exhibit higher levels of each of the typical MDD symptoms than children with externalizing disorders (attention-deficit/hyperactivity disorder [ADHD] and/or oppositional defiant disorder [ODD]) and nonclinical controls and greater levels of functional impairment than controls (Luby et al., 2002). Finally, the 6-month stability of MDD diagnoses is similar whether the 2-week duration criteria was met ($\phi = .81$) or not ($\phi = .71$; Luby et al., 2002). This suggests that all the hallmarks of a clinically significant major depressive episode may be present in preschool children even if the episode lasts less than 2 weeks.

Course and Outcome

Depression in childhood, as in older samples, is a chronic and recurrent disorder. Research suggests that the median episode length of MDD in childhood is 9 months, with a mean of 11 months, suggesting that a significant minority of children have episodes of MDD lasting over a year (for a review, see Kovacs, 1996). However, almost all children do achieve full remission eventually, with 99% remitting within 6 years of disorder onset (Kovacs, 1996). For dysthymia, the median duration is 4 years, with 91% of children experiencing a full remission within 9 years (Kovacs, 1996).

Childhood depression also shows substantial homotypic continuity over time. For example, preschoolers (ages 3–6 years) diagnosed with MDD were at elevated risk for MDD at 12-month and 24-month follow-up and were more likely to meet criteria for MDD than for other disorders at follow-up (Luby, Si, Belden, Tandon, & Spitznagel, 2009). Of those meeting criteria for MDD at the baseline assessment, 46% recovered and stayed depression-free at 24 months, 35% recovered but then had a recurrence of MDD, and the remaining 19% experienced chronic MDD over the follow-up. In addition, 40% of children (ages 8–13 years) who had initially recovered from MDD relapsed within 2 years (Kovacs et al., 1984). Similarly, 35% of child psychiatric inpatients with depression were rehospitalized within a year of discharge, and 45% were rehospitalized by the end of the 2nd year (Asarnow et al., 1988). Furthermore, in a sample of children recruited from the community, those exhibiting elevated depressive symptoms at age 9 continued to show these elevations at ages 11 and 13 (McGee & Williams, 1988). There is also evidence that children diagnosed with MDD are at increased risk for suicide attempts in adolescence and young adulthood compared with children with anxiety disorders or individuals with no psychiatric diagnoses in childhood, though in this study there was no difference in risk for future MDD (Weissman et al., 1999). Finally, in a study that focused on youth psychiatric inpatients and outpatients, children with a history of MDD were

more likely to meet criteria for MDD in adulthood than were psychiatric controls without depression, though there was some evidence that the reoccurrence of MDD in adulthood was more likely among youth diagnosed with MDD occurring during adolescence than during childhood (Harrington, 1996).

Comorbidity

As in older samples, diagnostic comorbidity is common in children with depression, with the highest rates of comorbidity observed for anxiety and disruptive behavior disorders (Copeland, Shanahan, Costello, & Angold, 2009; Kovacs, Gatsonia, Paulauskas, & Richards, 1989; Kovacs, Paulauskas, Gatsonis, & Richards, 1988; McGee & Williams, 1988; Merikangas et al., 2010). This outcome appears to be due at least in part to shared genetic influences between depression and these other disorders (Eley & Stevenson, 1999; Rice, van den Bree, & Thapar, 2004; Subbarao et al., 2008; Thapar & McGuffin, 1997). There is some evidence of sex differences in patterns of comorbidity, with antisocial behavior more common in boys than in girls diagnosed with depression (McGee & Williams, 1988; but see Kovacs et al., 1988). With regard to temporal ordering, behavior disorders (e.g., conduct disorder) are more likely to develop subsequent to depression in children than prior to it (Kovacs et al., 1988). In contrast, anxiety disorders are more likely to precede the development of depression than to follow it (Kovacs et al., 1989) though there is also evidence of bidirectional influences, particularly for generalized anxiety disorder (GAD; Copeland et al., 2009). In terms of sequential comorbidity, there is evidence that youth with childhood-onset MDD are also at increased risk for substance abuse later in life (Weissman et al., 1999; but see also Copeland et al., 2009).

Etiology

Depression is a stress-related disorder that is often preceded by the occurrence of negative life events. However, there is also considerable individual variability in reactions to negative events, and models of depression risk focus on factors thought to increase stress reactivity, often within a vulnerability–stress or stress–diathesis framework. In this section, research on neurobiological, genetic, and cognitive models of risk is reviewed, as is research on specific types of environmental influences.

Neurobiology

Neural Circuits

Neural models of depression, developed largely from structural and functional neuroimaging studies of adults, emphasize disruption in corticolimbic circuits, with heightened activity in limbic regions such as the amygdala that is not effectively down-regulated by prefrontal cortical regions (e.g., dorsolateral prefrontal cortex; for reviews, see Cusi, Nazarov, Holshausen, MacQueen, & McKinnon, 2012; Hamilton et al., 2012). For example, a recent meta-analysis of neuroimaging data in adults with MDD showed that, compared with adults with no history of MDD, adults with MDD exhibited greater reactivity to negative stimuli (e.g., sad faces) in the amygdala, dorsal anterior cingulate, and insula and lower reactivity in the dorsolateral prefrontal cortex and dorsal striatum (Hamilton

et al., 2012). The results of this meta-analysis also suggested that individuals with depression exhibit higher resting activity than controls in the pulvinar nucleus.

Findings in child samples are largely consistent with the adult literature (for a review, see Hulvershorn, Cullen, & Anand, 2011). For example, severity of MDD in preschool children is associated with greater amygdala activation when viewing sad, but not happy or neutral, faces (Gaffrey, Luby, et al., 2011). In addition, among 7- to 11-year-olds without current depression, severity of prior preschool-onset MDD (PO-MDD) was associated with increased reactivity to sad faces in various regions of the corticolimbic circuit including amygdala, hippocampus, parietal regions, and orbital frontal cortex (Barch, Gaffrey, Botteron, Belden, & Luby, 2012), which suggests that disruptions in this circuit are not simply correlates of current depression. Furthermore, these differences in reactivity were largely specific to sad faces rather than angry or happy faces. There is also evidence for a link between functional and structural differences in PO-MDD. For example, one study found that 7- to 12-year-old children with a history of PO-MDD have significantly smaller hippocampal volumes than children with no depression history (Suzuki et al., 2013). Furthermore, smaller right hippocampal volume in children with a history of PO-MDD was associated with greater putamen activation to sad faces and greater amygdala activation to negative faces generally (sad, angry, fearful), with the link between hippocampal volume and amygdala activation being significantly stronger in children with a history of PO-MDD than in controls (Suzuki et al., 2013). Finally, there is evidence for differences in functional connectivity between limbic regions and both prefrontal and striatal regions among children with a history of PO-MDD compared with children with no history of depression. For example, children with a history of PO-MDD, compared with children with no history of depression, exhibited reduced connectivity between the amygdala and regions of dorsal prefrontal and parietal cortex (Luking et al., 2011).

Hypothalamic–Pituitary–Adrenal Axis

Limbic areas directly influence activity in the hypothalamic–pituitary–adrenal (HPA) axis, the body's stress-response system, via projections to the thalamus (Guerry & Hastings, 2011; Gunnar & Quevedo, 2007). In normal functioning, a perceived stressor triggers the release of corticotropin-releasing hormone (CRH) from the hypothalamus, which causes adrenocorticotropic hormone (ACTH) to be released by the pituitary, causing glucocorticoids, including cortisol, to be synthesized and released by the adrenal cortex. HPA-axis reactivity to acute stressors is typically self-limiting, with cortisol downregulating production of CRH through a negative feedback loop. In nonclinical samples, preschool and school-age children exhibit hyporesponsiveness of the HPA axis such that they exhibit lower cortisol response to stressors than do infants, adolescents, and adults (Guerry & Hastings, 2011; Gunnar & Quevedo, 2007; Lupien, McEwen, Gunnar, & Heim, 2009). The results of one study suggest that this may be particularly true among children with depression. Specifically, one study found that preschool and prepubertal children with dysphoria exhibited significantly lower cortisol reactivity to a laboratory-based stressor (for preschoolers, exposure to a scary robot and a frustration task; for older children, the Trier Social Stress Test) than did children without dysphoria, whereas adolescents with dysphoria exhibited the expected greater cortisol reactivity compared with adolescents without dysphoria (Hankin, Badanes, Abela, & Watamura, 2010). In contrast, however, a second study of preschool-age children found that children with MDD exhibited greater cortisol increases following a stressor (separation from mothers)

than children with ADHD or ODD or children with no history of psychopathology (Luby et al., 2003), differences that appear to have been due to the inclusion of children with anhedonic depression (Luby et al., 2003; Luby, Mrakotsky, Heffelfinger, Brown, & Spitznagel, 2004).

The reasons for the differences in reactivity findings across studies are unclear. It may be due to the difference in severity of depression examined (elevated symptoms vs. diagnoses of MDD) or differences in the types of stress tasks used. Or it may be that heightened cortisol reactivity characterizes only a subset of children with depression. Consistent with this latter possibility, approximately 45% of children with depression exhibit cortisol nonsuppression following the dexamethasone suppression test (for a review, see Guerry & Hastings, 2011), suggesting the role of altered HPA-axis activity in at least a subset of children with depression. Also similar to adults, rates of nonsuppression among child inpatients were approximate those seen in outpatients (Guerry & Hastings, 2011), suggesting that rates of dexamethasone nonsuppression track severity of disease. There is also evidence from a meta-analysis that children with depression exhibit slightly, but significantly, higher basal cortisol levels than children without depression (Hankin et al., 2010; Lopez-Duran, Kovacs, & George, 2009). Similar results have been observed among infants exposed to prenatal or postnatal depression in their mothers (for a review, see Guerry & Hastings, 2011).

Genetic Influences

There are clear genetic influences on depression risk, with heritability estimates suggesting that approximately 40% of the variance in depression risk is due to genetic factors (Eley, 1997; Sullivan, Neale, & Kendler, 2000). There are also developmental changes in the strength of genetic influences that increase as children age into adolescence (Eley & Stevenson, 1999; Rice, Harold, & Thapar, 2003; Silberg et al., 1999; Thapar & McGuffin, 1996). These changes are attributed to an increased role for gene–environment correlations, reflecting adolescents' greater control over their environments, which can lead to an increase in negative life events (Eley & Stevenson, 1999; Rice et al., 2003; Silberg et al., 1999). Twin studies have also noted clear evidence for genetic moderation of the impact of negative life events on depression risk (Silberg, Rutter, Neale, & Eaves, 2001; Wilkinson, Trzaskowski, Haworth, & Eley, 2013) in addition to gene–environment correlation effects.

Although twin and adoption studies can tell us what proportion of variance in depression risk is attributed to genetic influences, they do not tell us which specific genes or genetic pathways may be implicated. More recently, therefore, there has been increasing emphasis on examining specific genes that may increase risk for depression. Researchers have taken two approaches to identifying specific genes: genomewide association studies (GWAS) and candidate gene studies. GWAS are largely atheoretical investigations requiring extremely large sample sizes in which hundreds of thousands of single nucleotide polymorphisms (SNPs) are compared between individuals with current or past MDD versus those with no depression history. Despite the strengths of GWAS, they have revealed few replicable genetic loci for depression risk thus far (Cohen-Woods, Craig, & McGuffin, 2013; Major Depressive Disorder Working Group of the Psychiatric GWAS Consortium et al., 2013).

In contrast, candidate gene studies are theory-driven investigations and typically include much smaller sample sizes. In these studies, candidate genes are chosen because of their known or hypothesized influence on neural or physiological mechanisms underlying

depression risk. The first of these studies was conducted by Caspi and colleagues (2003) and focused on a functional polymorphism (5-HTTLPR) in the serotonin transporter gene (*SLC6A4*). In this study, adults who carried one or two copies of the 5-HTTLPR short allele, which is associated with less transcriptional efficiency of *SLC6A4* compared with the long allele, were at greater risk for developing MDD in the context of negative life events than were adults homozygous for the long allele. Intriguingly, similar results were observed when focusing on adults' histories of childhood abuse, suggesting that early life stress could increase lifelong risk for depression among carriers of specific genetic polymorphisms. In the years following the publication of this study, there has been considerable debate about the influence of 5-HTTLPR on depression risk (Karg, Burmeister, Shedden, & Sen, 2011; Risch et al., 2009). However, consistent with neural models of depression risk, there is evidence from meta-analyses that the presence of the 5-HTTLPR short allele is associated with increased amygdala activation to emotional stimuli (Munafò, Brown, & Hariri, 2008), as well as greater cortisol reactivity in youth (Dougherty, Klein, Congdon, Canli, & Hayden, 2010; Gotlib, Joormann, Minor, & Hallmayer, 2008; Mueller, Brocke, Fries, Lesch, & Kirschbaum, 2010). In addition, there is growing evidence for its role in moderating the impact of negative life events on depression risk in youth (for a review, see Dunn et al., 2011).

It is clear, however, that genetic risk for depression is not limited to any single gene, and a number of studies have focused on other candidate polymorphisms, primarily those thought to influence disruptions in corticolimbic areas (e.g., the Val158Met polymorphism in the catechol-*O*-methyl transferase [*COMT*] gene) or HPA-axis functioning (e.g., the protective TAT haplotype in the corticotropin-releasing hormone receptor 1 [*CRHR1*] gene). Although few studies have examined these polymorphisms in childhood depression, there is preliminary support for their role in moderating the impact of environmental stress (Cicchetti, Rogosch, & Oshri, 2011; Conway, Hammen, Brennan, Lind, & Najman, 2010). This said, depression risk is likely to be influenced by variation in a number of genes acting together, and future research is needed to examine aggregate levels of influence across a number of genes. In addition, research is needed that moves beyond a simple examination of genotypes to explore methylation and gene expression to gain a more detailed understanding of the actual activity of specific genes within an individual.

Information-Processing Biases

Cognitive models of depression focus on biases in the processing of information. Specifically, biases in attention to, interpretation of, and memory for depression-relevant information are thought to contribute to the development and maintenance of depression. These information-processing biases are driven by altered neural reactivity in the same regions reviewed earlier as underlying depression risk (i.e., corticolimbic circuits and hypothalamus; Disner, Beevers, Haigh, & Beck, 2011). The biases are hypothesized to develop during childhood and then stabilize during adolescence, increasing risk for depression across the lifespan.

The majority of research on cognitive vulnerability to depression in children has focused on cognitive vulnerability as defined in the reformulated theory of learned helplessness (Abramson, Seligman, & Teasdale, 1978) or the hopelessness theory of depression (Abramson, Metalsky, & Alloy, 1989). In the reformulated theory of learned helplessness, cognitive vulnerability is defined as the tendency to attribute the occurrence of negative events to internal, stable, and global causes. In revising the theory as the

hopelessness theory, the internality dimension of causal attributions was deemphasized, and the authors added two new domains of inferences—the tendency to infer negative consequences and the tendency to infer negative self-characteristics following the occurrence of negative events. Consistent with a vulnerability–stress model of risk, negative attributional or inferential styles are hypothesized to increase risk for depression in the presence, but not absence, of negative life events. There is consistent evidence for the impact of children's attributional and inferential styles on prospective increases in depression, as well as growing evidence that these styles moderate the impact of negative life events on future depression (Abela & Hankin, 2008; Cohen, Young, & Abela, 2012).

There is also growing support for the role of rumination in contributing to the development of depression in children. According to the response-styles theory (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008), the tendency to ruminate, or passively reflect on one's thoughts and feelings of sadness, contributes to the development and maintenance of depression. Although the response-styles theory was originally developed to help explain the gender difference in depression, with studies of adults consistently showing that women exhibit higher levels of rumination than men (Nolen-Hoeksema et al., 2008), there is little evidence for a gender difference in rumination in children (for a review, see Abela & Hankin, 2008). This said, a number of studies have now shown that rumination, perhaps specifically brooding rumination, contributes to prospective changes in depressive symptoms and to the development of depressive disorders in both girls and boys (Abela & Hankin, 2008; Gibb, Grassia, Stone, Uhrlass, & McGeary, 2012; Rood, Roelofs, Bögels, Nolen-Hoeksema, & Schouten, 2009).

In contrast to hopelessness theory and response-styles theory, which were developed in adults and later extended to explain depression risk in children, Cole's (1991) competency-based model of depression was developed specifically for children. According to this theory, children's levels of self-perceived competence in various domains (e.g., scholastic competence or social acceptance) increase risk for depression. A number of studies have now found that children's levels of self-perceived competence (particularly perceived levels of academic competence and social acceptance) increase risk for depression, though it remains unclear whether self-perceived competence mediates or moderates the influence of negative events on children's levels of depressive symptoms, nor whether there is a transition from mediation to moderation as children age into adolescence (Cole et al., 2011; Jacquez, Cole, & Searle, 2004; Uhrlass, Crossett, & Gibb, 2008).

Despite the strengths of each of these studies, the majority focus on children's self-report of their cognitions, which may be subject to response bias and may inflate relations with children's self-reported depressive symptoms. More recently, therefore, researchers have focused on computer-based assessments of information-processing biases in children. For example, there is growing evidence that children with depression or at risk for depression due to a positive family history of MDD exhibit attentional biases for depression-relevant stimuli (i.e., sad face) and, consistent with cognitive models' specificity hypothesis, these biases appear to be specific sad, rather than angry or happy, faces (e.g., Gibb, Benas, Grassia, & McGeary, 2009; Joormann, Talbot, & Gotlib, 2007; Kujawa et al., 2011; but see Johnson & Gibb, 2014). In addition, attentional biases for sad faces predict prospective increases in children's depressive symptoms (Gibb et al., 2009). However, although there is clear evidence for the presence of attentional biases to sad faces, evidence is mixed with regard to the direction of the bias, with some studies finding evidence for preferential attention to sad faces (Joormann et al., 2007; Kujawa et al., 2011) and others finding evidence for attentional avoidance (Gibb et al., 2009; Johnson & Gibb, 2014). Future research is needed to clarify this discrepancy in findings.

Finally, there is evidence for memory biases in children with depression, particularly overgeneral autobiographical memory biases. For example, children with a lifetime history of depressive disorders report fewer specific autobiographical memories than children with other forms of psychopathology (e.g., anxiety or behavior disorders) or nonclinical controls (Vrielynck, Deplus, & Philippot, 2007). Similar results have been observed in nonclinical samples of children, with higher levels of depressive symptoms associated with less specific autobiographical memories (Drummond, Dritschel, Astell, O'Carroll, & Dalgleish, 2006; Raes, Verstraeten, Bijttebier, Vasey, & Dalgleish, 2010). Despite the strengths of these studies, longitudinal research is needed to determine whether memory biases are simply a correlate or a consequence of depression in children or whether they predict the onset of depressive disorders.

Environmental Influences

As noted earlier, depression is considered a stress-related disorder, and the majority of episodes are preceded by some type of negative life event. As also noted earlier, there is considerable individual variability in reactivity to environmental stressors based on neurobiological, cognitive, and genetic influences. In this section, specific types of environmental influences are reviewed with a focus on those that are most strongly linked to depression risk in children.

Parents and Parenting

One of the strongest risk factors for depression in childhood is having a parent with depression (for reviews, see Goodman, 2007; Gotlib & Colich, Chapter 13, this volume). This risk is conveyed by both genetic and environmental influences. There is evidence that specific parenting styles and behaviors, even in the absence of parental depression, increase risk for depression in children. For example, parenting styles that are characterized by low levels of warmth and high levels of psychological control, referred to as "affectionless control," are associated with depression risk in children (Alloy, Abramson, Smith, Gibb, & Neeren, 2006). In terms of specific parenting behavior, one of the strongest risk factors identified for childhood depression is maternal criticism. Mothers of children with depression are rated as more critical than are mothers of children without depression (Asarnow, Tompson, Woo, & Cantwell, 2001; Silk et al., 2009). In addition, children exposed to heightened levels of maternal criticism over time are at increased risk for developing depressive disorders in the future (Burkhouse, Uhrlass, Stone, Knopik, & Gibb, 2012). There is evidence that maternal criticism mediates the link between maternal and child depression and also that it contributes to the development of cognitive vulnerabilities to depression in children (Goodman, 2007; Gotlib & Colich, Chapter 13, this volume).

Peer Influences

In addition to parents, peers also have a strong influence on a child's functioning. Of the various forms of peer influences, the one most consistently linked to risk for depression is peer victimization. Researchers have focused on two forms of peer victimization—overt victimization and relational victimization. Overt victimization includes behaviors designed to directly hurt someone (e.g., hitting, pushing, or kicking), whereas relational victimization is more indirect and includes behaviors designed to reduce someone's

standing within a social group (e.g., spreading rumors, purposefully excluding someone; Crick, Casas, & Nelson, 2002). Although there are consistent gender differences in overt victimization, with boys reporting higher levels than girls, research suggests that girls and boys experience equivalent amounts of relational victimization (Crick et al., 2002). Both forms of victimization are associated with prospective increases in levels of depression among both boys and girls (for a meta-analytic review, see Reijntjes, Kamphuis, Prinzie, & Telch, 2010). As with criticism from parents, there is growing evidence that peer victimization also contributes to the development of various cognitive vulnerabilities to depression in children (Gibb, Stone, & Crossett, 2012; Sinclair et al., 2012).

Stress Generation

In addition to the well-known impact of negative life events on depression, there is growing evidence that individuals with depression contribute to the generation of additional negative events in their lives (Hammen, 2006). Although the stress-generation model was originally developed to explain the cyclic nature of depression risk in adults, there has been growing support for stress-generation models in children (Cole, Nolen-Hoeksema, Girgus, & Paul, 2006; Gibb & Alloy, 2006; Gibb & Hanley, 2010). These studies help to explain one mechanism by which early experiences with depression may lead to additional stressors in the child's life, setting in motion a vicious cycle of risk.

Conclusions and Future Directions

Research on childhood depression has come quite a long way since the early 1980s. No longer questioning whether children can experience clinically significant episodes of depression, we now have reliable estimates of its prevalence in children and a better understanding of its presentation and course. Significant strides have also been made in understanding the neural and physiological underpinnings of depression in children, as well as cognitive, genetic, and environmental risk factors.

A key direction for future research, which is already beginning to happen, is to develop more integrated models of depression risk at multiple levels of analysis to understand how these various factors operate together to increase risk for depression in children. For example, researchers are now seeking to integrate cognitive and genetic models of risk (cf. Gibb, Beevers, & McGeary, 2013) by examining whether the information-processing biases featured in cognitive theories of depression may represent endophenotypes for specific genetic influences. One promising aspect of this approach is that genetic effects (main effects or genetic moderation of environmental influences) should be stronger for more basic processes, such as attentional biases, than for heterogeneous constructs such as MDD. A number of studies have now supported the link between specific candidate genes and various information-processing biases in children, adolescents, and adults (for a review, see Gibb et al., 2013). Another way in which these models may be integrated is by examining the combined impact of cognitive and genetic factors that increase reactivity to environmental influences within a gene × cognition × environment model of risk. These models also have garnered initial support. For example, in one study, the relation between mothers' and children's depressive symptom levels over time was strongest among children carrying the 5-HTTLR short or L_G allele who also exhibited attentional avoidance of sad faces (Gibb et al., 2009). In another study, children with negative inferential styles were at increased risk for depression in response to maternal

criticism, but again only if they also carried at least one copy of the 5-HTTLR short or L_G allele (Gibb, Uhrlass, Grassia, Benas, & McGeary, 2009).

A related area for future research is to gain a better understanding of factors underlying diagnostic comorbidity in children. For example, results from twin studies suggest that depression and anxiety share common genetic influences (Eley & Stevenson, 1999; Rice et al., 2004; Subbarao et al., 2008). Also, the neural circuitry underlying depression and anxiety are similar (disruption in corticolimbic pathways), suggesting shared influence. In addition, cognitive models of psychopathology suggest that both disorders are characterized by the same types of information-processing biases—biases in attention, interpretation, and memory—and differ only in the content or focus of these biases (loss and threat for depression and anxiety, respectively; for a review, see Gibb & Coles, 2005). Recognizing the need to better understand the core mechanisms underlying disorders that may contribute to comorbidity using current diagnostic systems, the National Institute of Mental Health has begun its Research Domain Criteria (RDoC) initiative, the specific focus of which is to define mechanisms that cut across current diagnostic categories and to describe those mechanisms at the levels of genes, molecules, cells, neural circuits, physiology, and behavior (see *www.nimh.nih.gov/research-priorities/rdoc/index.shtml*). Explicit in this initiative is also gaining a better understanding of environmental influences, as well as the developmental context in which these processes occur.

Advances in both of these areas will help to integrate previously separate lines of research and will contribute to a fuller, more detailed understanding of depression risk in children. It is hoped that these advances will also pave the way for the development of novel intervention and prevention programs (cf. Hamilton, Glover, Hsu, Johnson, & Gotlib, 2011; Rozenman, Weersing, & Amir, 2011) that can alter the developmental trajectory of depressed and at-risk youth so that they can escape the vicious cycle of risk that often accompanies childhood depression.

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