

CHAPTER 25

Depression in Early Childhood

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Only in the last 10 years have the mental health and developmental communities generally accepted that depression may arise in very early childhood. As early as the 1940s, clinical depression was observed and described in infants deprived of primary caregiving relationships (Spitz, 1946). However, in subsequent years, prevailing developmental theory suggested that young children are too immature to experience the core emotions of depression, thereby ruling out the possibility of clinical depression before school age (Rie, 1966). Subsequent advances in studies of early childhood emotion development provided data refuting this claim, demonstrating the previously unrecognized emotional sophistication of infants and toddlers (Denham, 1998; Shonkoff & Phillips, 2000). Despite this, empirical data to validate and describe a clinical depressive syndrome in infants and toddlers under the age of 3 years remains scarce, with some retrospective data suggesting it may arise in the toddler years (Luby & Belden, 2012).

In order to understand whether depression can arise early in life and how it might manifest, it is essential to understand the normative trajectory of early emotional development. Normative emotional development provides a framework against which alterations in early emotional experiences and expressions can be assessed. In the late 1800s, based on observation of facial expressions, Darwin (1872) theo-

rized that several core emotions are present at birth in the human infant. Subsequently, empirical studies provided support for this hypothesis (e.g., Izard, Huebner, Risser, & Dougherty, 1980). Despite these early insights, a significant body of empirical data that began to outline the trajectory of early emotion development did not become available until the late 1980s. Over the last two decades, data informing how children recognize and express discrete emotions, develop the ability to regulate emotional responses, understand the causes and consequences of emotions, as well as experience more complex emotions, have become available (for review, see Denham, 1998; Saarni, 1999). While these data have provided a broad framework illustrating that emotional competence develops earlier in life than previously recognized, many details about when and how emotional development unfolds in the infancy and preschool period remain understudied. Further investigation of this early trajectory may be key to understanding the earliest possible onset of depression and its developmental characteristics.

From a public health perspective, the identification of depression at the earliest possible point in development is an important goal because not only is relieving the suffering of young children a necessary and worthy cause, but also earlier intervention may provide a window of opportunity for greater therapeutic change and benefit.

The unique efficacy of early intervention during the preschool period has been demonstrated for several specific childhood mental disorders such as autistic spectrum disorder and some disruptive disorders (e.g., Eyberg et al., 2001; Faja & Dawson, 2006; Webster-Stratton, Reid, & Beauchaine, 2013). This may be related to greater neuroplasticity and therefore increased sensitivity to environmental inputs earlier in development (Troller-Renfree & Fox, 2016). Early intervention may be of particular importance in depressive disorders given the known chronic and relapsing course, suboptimal treatment responses, and high rates of treatment resistance in older depressed children and adolescents (Kennard et al., 2006; Weisz, McCarty, & Valeri, 2006). For these reasons, as well as the compelling accounts of clinical observation of depressive affect very early in life, depression is a disorder for which the earliest possible identification may hold promise to advance the public health; therefore, early identification is imperative and early interventions are necessary.

We explore in this chapter the empirical and theoretical literature on depression in infants, toddlers, and preschool-age children. We begin the discussion with the preschool period, which has the largest body of available empirical data. Then, we explore the relevant literature and available data pertaining to toddlers and infants. In these youngest age groups, there is a much smaller body of available empirical data on clinical symptoms or syndromes. However, we do review related literature on early alterations in emotion expression and neural functioning in high-risk groups, and discuss novel early interventions for depression that are currently being tested.

Emotion Development in Early-Onset Depression

A developmental issue of interest in the study of early-onset depression, as well as mood disorders more generally, is the question of whether early alterations in patterns of emotion development can be identified. This is important not only for the purpose of identifying developmental manifestations of early-onset mood disorders, but also, and perhaps more clinically relevant, to specify developmental targets for early intervention. Recognizing that emotional competence develops earlier than previously thought and develops rapidly during infancy and preschool years has been clearly document-

ed. This suggests that impairments or alterations in this domain are likely to be associated with early-onset mood disorders and should therefore be explored.

Charles Darwin was the first to suggest that human infants are born with the ability to express a limited repertoire of discrete emotions. Subsequently, developmental psychologist Carroll Izard and colleagues (1980) provided empirical data demonstrating that human infants displayed specific and discrete facial expressions that were consistent with incentive events designed to evoke these emotional states. Pertinent to the development of depression in infancy is the normative development of sadness and joy. Izard, Hembree, and Huebner (1987) showed that facial expressions of sadness can be clearly and reliably distinguished from other negative emotions by the age of 2 months in human infants. Furthermore, by age 6 months, sad facial expressions arise in response to or concurrent with sadness-provoking incentive events (Izard et al., 1995). Similarly, studies have also shown that human infants display discrete facial expressions of joy as early as 6–8 months of life. The greater differentiation of emotional expression in which more subtle and complex expressions are observed occurs after the first year of life (Demos, 1986). These findings that demonstrate the experiences of sadness and joy appear to arise in human infants during the first 6 months of life suggest that depressive affects also may be possible at this early stage of development. However, as outlined below, apart from compelling clinical observations, there are no empirical data to address the issue of whether depression arises in infancy.

Emotional expression of joy and sadness, as well as emotion recognition of these emotions and more complex emotions such as guilt, has received more empirical attention in older preschool children for obvious reasons. One area of interest is whether depressed preschoolers may demonstrate an earlier ability to recognize and label negative emotions compared to nondepressed preschoolers. There is some support for the notion that early experiences of depression may enhance the ability to recognize and label negative emotions, specifically sadness (Hankin, Gibb, Abela, & Flory, 2010; Lopez-Duran, Kuhlman, George, & Kovacs, 2013). Further focused investigations of clinically relevant alterations in emotion development are now needed.

An investigation of the development of more complex emotions, particularly guilt and

shame, are of special interest given the central importance of these emotions to depressive states. Kochanska, Gross, Lin, and Nichols (2002) have previously shown that children understand the experience of guilt as early as 3 years of age. In light of this finding, we hypothesized that depressed preschoolers, like older depressed individuals, would experience higher levels of guilt than nondepressed preschoolers. Two qualitatively different measures were used to assess guilt within our preschool sample. One measure, the My Child, is a parent report of the child's tendency to display guilt and actions to repair guilt (Kochanska, 1992). In addition, the MacArthur Emotion Story Stem Battery was used to tap guilt emotions (Bretherton, Oppenheim, Buchsbaum, Emde, & the MacArthur Transition Network Narrative Group, 2001). In this latter technique, preschoolers are given a story stem that sets up a conflict that may evoke guilt. Their completion of the story is coded for guilt (and other) themes and content. Luby, Belden, Pautsch, Si, and Spitznagel (2009) demonstrated that depressed children experienced higher levels of guilt on both measures than did several nondepressed comparison groups, including those with DSM-IV disruptive disorders (attention-deficit/hyperactivity disorder [ADHD], oppositional defiant disorder [ODD], and conduct disorder [CD]), anxiety disorders, and a bipolar I-like syndrome. Also notable was that depressed preschoolers had less of a tendency to take actions to repair feelings of guilt. These findings suggest that the experience of excessive guilt is a central feature of depression as early as the preschool period and therefore should be a focus of early clinical identification and intervention.

Depression in Infancy

Despite significant amounts of lay public and media attention to the issue of infant depression, there are no empirical scientific data available at this time to inform the question of whether a true depressive syndrome can arise before a child is 3 years of age. Nevertheless, the first observations of depressed affect arising in infants date back to the mid-1940s, when psychoanalyst René Spitz (1946) provided compelling reports of withdrawal, apathy, depressed mood, and failure to thrive among institutionalized infants. Spitz described this syndrome as “ana-

clitic depression,” and he speculated that it was based on the infant's reaction to separation from a primary caregiver. Underscoring the life-sustaining importance of the emotional elements of the early caregiving relationship, these infants deprived of primary caregivers displayed failure to thrive, despite adequate nutrition and physical care. Despite this compelling finding of depressed affect and physical growth retardation arising from psychosocial deprivation, Spitz's observations, although now recognized as pioneering, had little impact on enhancing the recognition of very early-onset depression in the mainstream mental health community.

Infants of Depressed Mothers

Maternal depression (see Murray, Halligan, & Cooper, Chapter 10, this volume) is a well-known risk factor for a range of poor developmental outcomes in children (Diego et al., 2004; Murray et al., 2011; Murray, Halligan, & Cooper, 2010). Infants of depressed mothers are at high risk for depression based on both genetic and psychosocial factors (Cohn & Tronick, 1989; Field, 1984; Murray & Cooper, 1997; Murray et al., 1999). In particular, the parenting/caregiving practices of depressed mothers are often characterized as less supportive and sensitive (Downey & Coyne, 1990; Goodman & Gotlib, 1999; Lovejoy, Graczyk, O'Hare, & Neuman, 2000), which leads to a range of negative emotional developmental outcomes for infants (Field et al., 1988; Hernandez-Reif, Field, Diego, Vera, & Pickens, 2006; Murray et al., 1999). Infants of depressed mothers have been observed to be less active, more withdrawn, and to display less positive affect than infants of nondepressed mothers during face-to-face interactions with their mothers. This body of research highlights the early interpersonal and environmental factors that may have a material impact on emotion development in the infant and very young child, and may therefore be of importance in the developmental psychopathology of mood disorders.

In addition to inferring differences in infants' emotional responses based on their facial expression or bodily movements, other physiological markers of reactivity, such as brain activity, have informed our understanding of factors that impact development among the offspring of depressed mothers during the infancy and preschool period. For example, infants

of mothers with depression evidence greater relative right frontal electroencephalographic (EEG) asymmetry, a pattern often associated with increased negative affect and withdrawal-type behaviors (Jones, Field, & Almeida, 2009). Recently, Lusby, Goodman, Yeung, Bell, and Stowe (2016) found that infants of mothers with high prenatal depressive symptoms had synchronous, negative associations between negative affect and EEG asymmetry at 3 months of age, but asynchronous, positive associations between these indices at 12 months of age. The authors interpreted these findings to suggest that prenatal depression was associated with pathways of co-occurring vulnerability early in infancy, as well as additional vulnerability later in infancy. Prenatal maternal depression has also been shown to predict differences in infant brain function measured using functional magnetic resonance imaging (fMRI), specifically in the microstructure of the amygdala (Rifkin-Graboi et al., 2013), functional connectivity between the amygdala and frontal brain regions (Qiu et al., 2015), and alterations within the amygdala–prefrontal cortex circuits (Posner et al., 2016).

Diagnosing Depression in Infants and Toddlers

To date, there have been no large-scale, systematic, empirical investigations of clinical depression in infants and toddlers (under the age of 3 years). Despite this, the collective experience of clinicians and compelling case descriptions, as well as some retrospective accounts from depressed adults, strongly suggest that the syndrome can arise in infants and toddlers. Furthermore, in one prospective investigation of depressed preschoolers, Luby and Belden (2012) suggested that symptoms were evident as early as 18 months of age. Based on these observations, diagnostic criteria and symptom descriptions of depression as it applies to infants and toddlers have been outlined in an alternative developmentally sensitive diagnostic system entitled the *Diagnostic Classification of Mental Health and Developmental Disorders in Infancy and Early Childhood* (DC:0–5; Zero to Three, 2005). DSM-5 major depressive disorder (MDD) criteria may also apply to children across the age span, with no specified lower age limit (American Psychiatric Association, 2013). However, DSM-5, like DSM-IV, also does not specify any developmental modifications to

the criteria as presented in DSM-IV (American Psychiatric Association, 1994). This is in part based on empirical data suggesting that the core depressive symptoms show continuity from preschool through adulthood.

Depression in Preschool Children

The first empirical investigations of clinical symptoms of depression in preschool-age children were conducted by Kashani and colleagues in the 1980s. These researchers were interested in whether preschool-age children could manifest symptoms of depression as described in DSM-III (American Psychiatric Association, 1980), a previously empirically unexplored issue. This group provided case reports of preschoolers in clinical settings who met criteria for MDD (Kashani & Carlson, 1985). In addition, they investigated whether preschoolers in a general population sample could be identified with the disorder. They concluded, based on the finding of a number of preschoolers with concerning symptoms who did not meet full or formal criteria for DSM-III MDD, that developmental modifications to the criteria might be needed (Kashani, Holcomb, & Orvaschel, 1986; Kashani, Ray, & Carlson, 1984).

The findings of Kashani and colleagues, in addition to the finding of alterations in affect in the offspring of depressed mothers known to be at high risk for depression, led to larger-scale investigations of depression in preschoolers at the Washington University School of Medicine Early Emotion Development Program, as well as other national and international sites. The first large-scale investigation of preschool depression advanced earlier methodologies in several important ways. First, it used an age-appropriate structured diagnostic interview in which developmental translations of symptom states were assessed. An example of a developmental translation was that “anhedonia” was described as the inability to enjoy activities and play (as opposed to lack of libido, for example, as might be evident in an adult). In addition, both healthy and psychiatric comparison groups were ascertained, so that the specificity of symptoms to depression could be determined. Findings from this study provided evidence for a specific and stable depressive symptom constellation arising in preschool children ages 3–5½ years (Luby et al., 2002). In addition, based on data about

the psychiatric status of the first- and second-degree relatives of the preschool subject, the finding that depressed preschoolers came from families with greater histories of related affective disorders compared to families of healthy controls also emerged. Based on these parent-report data, these results suggested that familial transmission of depression was also evident in the preschool period, as had been previously demonstrated in older child and adult populations (e.g., Jaffee et al., 2002; Neuman, Geller, Rice, & Todd, 1997). Familial transmission, whether genetic or psychosocially transmitted, in addition to a specific and stable symptom constellation, are key elements in the validation of psychiatric disorders as described by Robins and Guze (1970).

The question of whether these very young depressed children displayed “masked” symptoms of the disorder, such as somatic complaints or regression in development, also was examined. This was of interest, since the idea that young children could not manifest the core symptoms of depression but would instead display “masked” symptoms was a widely accepted but empirically unexplored clinical adage. Notably, depressed preschoolers displayed age-appropriate manifestations of “typical” DSM symptoms of depression more frequently than masked symptoms (Luby et al., 2003a, 2003b). However, masked symptoms also occurred at higher rates in the depressed group than in the comparison groups. This finding was remarkably similar to earlier findings regarding older school-age children with depression (Carlson & Cantwell, 1980). The finding that young children display the core symptoms of depression, including vegetative signs, guilt, and anhedonia, suggests that clinicians should look for typical age-adjusted symptoms of depression as the most specific and sensitive markers of the disorder, even in preschool-age children.

Several additional markers of the validity of preschool-onset depression also emerged from this study. Evidence of impairment, which is key to determining “caseness” in the DSM system, was also detected in depressed preschoolers. The finding of unique patterns of guilt processing distinct from healthy preschoolers, those with externalizing disorders, and those with anxiety disorders also emerged (Luby, Belden, Sullivan, et al., 2009). Depressed preschoolers tend to experience high levels of guilt and engage in low guilt reparation behaviors (behaviors designed to correct the transgression).

Neurobiological Correlates of Preschool Depression

While a specific and stable symptom constellation, family history of related disorders, and evidence of social impairment are key markers of the validity of a psychiatric disorder and of preschool depression, biological evidence offers a more objective level of scientific validity. For this reason, biological measures such as neurophysiological indices and brain structure and function are of interest as key markers of the validity of preschool depression. Alterations in the physiological response to stress measured through the hypothalamic–pituitary–adrenal (HPA) axis are well established in depressed adults (Plotsky, Owens, & Nemeroff, 1998; Rubin et al., 1987). Consistent with this, Luby and colleagues (2003a) found alterations in stress cortisol reactivity in depressed preschoolers compared to those with other psychiatric disorders and healthy comparison groups. Dougherty, Klein, Olino, Dyson, and Rose (2009) examined relations between morning or evening cortisol and two prominent risk factors for depression, maternal depression and child temperament, in 166 four-year-old children participating in an ongoing longitudinal study. Prior to the onset of depression, elevated waking cortisol was found to be associated with maternal history of depression and lower positive emotionality in the children. The authors suggest that elevated waking cortisol may be one vulnerability marker for the onset of later depression.

Other work has focused on neural reactivity assessed using event-related potentials (ERPs) in preschoolers with depression (Belden et al., 2016) and as an indicator of risk for depression onset (Shankman et al., 2011). For example, 53 depressed preschoolers enrolled in a large, randomized controlled trial completed a guessing game while ERP’s were recorded. When compared to 25 healthy preschoolers, depressed preschoolers evidenced reduced reward positivity, one ERP component that measures responses to positive outcomes. These findings offer the first evidence of positive, reward-related neural alterations during the preschool period, and the findings continue to support the value of reward processing in the pathophysiology of early-onset depression.

Adding and extending these physiological data, a series of studies have investigated neural correlates of currently depressed preschoolers

(Gaffrey, Barch, Singer, Shenoy, & Luby, 2013; Gaffrey et al., 2011) and children/adolescents with a history of preschool depression (Barch, Gaffrey, Botteron, Belden, & Luby, 2012; Belden, Barch, et al., 2015; Belden, Pagliaccio, Murphy, Luby, & Barch, 2015; Gaffrey, Luby, Botteron, Repovs, & Barch, 2012; Gaffrey et al., 2010; Luby et al., 2016; Luking et al., 2011; Marrus et al., 2015; Pagliaccio et al., 2012; Suzuki et al., 2013). For example, Gaffrey and colleagues (2013) have demonstrated alterations in amygdala reactivity in response to negative faces in 23 acutely depressed preschoolers, consistent with findings in depressed adolescents and adults.

Furthermore, findings from the Preschool Depression Study (PDS) sample indicate that alterations in the function and structure of key brain regions known to be altered in depression in adults have also been found in depressed preschoolers when they were scanned at school age, even when not acutely depressed at the time of scan. For instance, children with a history of preschool-onset depression evidenced greater activation in response to sad faces in the amygdala, bilateral functional cortex, claustrum hippocampal and parahippocampal gyrus (Barch et al., 2012), as well as less activation in regions of the prefrontal cortex following a brief, sad mood induction (Pagliaccio et al., 2012). When compared to healthy children, children with a history of preschool-onset MDD exhibited significantly smaller left hippocampal volume (Suzuki et al., 2013). These individual volumetric differences were also associated with functional differences in brain responses to sad or negatively valenced faces. Greater functional connections were found between the subgenual anterior cingulate cortex and dorsomedial prefrontal brain regions among healthy children, whereas greater functional connections were between the subcortical and posterior medial parietal regions for children with a history of preschool-onset depression (Gaffrey et al., 2010). Gaffrey and colleagues (2010) suggest that the pattern of functional relations seen in the children with preschool-onset depression may be associated with decreased cognitive control and behavioral flexibility, and increased visceral—motor/self-focused operations. Even after accounting for key covariates, such as age, gender, and IQ, children with a history of preschool-onset MDD also show alterations in the default mode network connectivity (Gaffrey et al., 2012) and functional connectivity of the

amygdala (Luking et al., 2011). Taken together, these findings offer evidence for longitudinal alterations in the functioning of several brain areas as a function of preschool-onset depression, even when children were not in an acute episode of depression.

The PDS study sample has collected up to three fMRI scans on each subject, allowing researchers to model trajectories of brain development in specific regions of interest. Recently, Luby and colleagues (2016) examined the impact of preschool-onset depression on the trajectory of cortical gray-matter development across the three fMRI scans spanning several years. Children with a history of preschool-onset depression had differences in their trajectories of cortical gray-matter development, specifically cortical gray-matter volume loss and thinning over time. These results highlight the importance of assessing the same children repeatedly across time in order to more accurately capture developmental changes in brain functioning.

These findings taken together demonstrate that depressed preschoolers have changes in the structure and function of key brain regions involved in emotion processing, as has been established in adult depression, suggesting that alterations in these biological substrates known to be associated with depressive disorders are also evident early in development. The finding that these alterations in neural structure and function are also evident in early-onset depression during the preschool period and in school-age children with a history of preschool depression suggests some continuity in the underlying pathophysiology of depression across the age span. Along these lines, further evidence of this continuity could provide clues to both the developmental psychopathology of depressive disorders and more effective early intervention strategies.

Melancholic Subtype

A more severe melancholic subtype of depression characterized by the presence of anhedonia also has been identified in preschool children. Preschoolers who met all DSM-IV symptom criteria for MDD (when symptoms were translated for developmental appropriateness as described earlier) and also had the symptom of anhedonia had significantly higher depression severity scores than a depressed nonanhedonic group (Luby, Mrakotsky, Heffelfinger, Brown, & Spitznagel, 2004). In addition, melancholi-

cally depressed preschoolers had a number of features similar to melancholically depressed adults, such as lack of brightening in response to positive events, as well as higher rates of neurovegetative signs, including sleep disturbances and changes in appetite. These findings suggest that a subtype of severe depression that has clear biological correlates known in adults may also arise during the preschool period. This melancholic subgroup should be a focus of future longitudinal investigations that address outcome and course, as well as other biological markers, such as structural and functional changes in the brain. Neuroimaging of young children with a history of melancholic depression could be illuminating.

Suicidal Ideations and Expression in Preschool Children

Surprisingly little work has focused on thoughts of death and suicidal ideation (SI) in preschool-onset depression (Connolly, 1999; Pfeffer & Trad, 1988; Rosenthal & Rosenthal, 1984; Rosenthal, Rosenthal, Doherty, & Santora, 1986; Whalen, Belden, Luby, Barch, & Dixon-Gordon, 2016; Whalen, Dixon-Gordon, Belden, Barch, & Luby, 2015; Zeanah & Gleason, 2015). Whalen and colleagues (2015) evaluated suicidality in a sample of 306 children between ages 3 and 7, enrolled in a longitudinal investigation of preschool depression. SI was present in approximately 11% ($N = 34$) of young children in this sample, and 75% ($N = 25/34$) of these youth continued to endorse SI at the school-age follow-up assessment. Preschool SI was concurrently associated with several forms of psychopathology, including depression, anxiety disorders, ADHD, ODD, and CD. Preschool SI predicted later school-age SI, even when researchers controlled for psychiatric disorders, and other relevant covariates at both time points (Whalen et al., 2015). Study findings are consistent with and extend extant research on later childhood SI, suggesting that this clinical phenomenon may be equally valid in younger children.

Epidemiological Evidence for Preschool Depression

Findings from several independent samples have replicated and extended the previously discussed findings about preschool depression. Using a screening checklist in a large ascertained sample from the St. Louis metropolitan

area, every age-adjusted DSM-IV symptom of depression, with the exception of irritability, occurred significantly more frequently in preschoolers meeting criteria for depression compared to those who met DSM-IV criteria for disruptive behavior disorders and those from a healthy control group. Furthermore, symptoms of depression also differentiated depressed preschoolers from those with anxiety disorders, providing the first discriminant validity to our knowledge between depression and another internalizing affective disorder (Luby, Belden, Pautsch, et al., 2009). Several epidemiological studies have also detected depression in preschool children (Bufferd, Dougherty, Carlson, Rose, & Klein, 2012; Egger & Angold, 2006; Wichstrøm et al., 2012). These findings demonstrate that a specific depressive syndrome can be identified in preschool children in community samples and have a prevalence rate similar to that known in prepubertal children (Egger & Angold, 2006).

Clinical Assessment of Preschool Depression

The identification of a depressed preschooler in the clinical setting is not always obvious despite this empirical information informing the clinical picture. Some of the key symptoms are often discounted by parents or go unnoticed. Key features that clinicians should inquire about carefully in the clinical interview with caregivers are the presence of a pattern of excessive levels of guilt, low self-esteem or persistent expression of negative self-appraisals, as well as the expression of self-harming behaviors displayed during emotional distress, such as self-hitting, head banging or scratching. The clinical interview with the caregiver is key given that many symptoms may not be expressed in the clinical setting. However, observation of play is also essential to establish and verify the presence of sad or irritable mood and negative themes in play, and to ascertain features of self-perception and rule out other potential causes for the symptom presentation.

Longitudinal Course of Preschool Depression

One of the key validators that underscores the importance of early identification of depression during the preschool period is the finding of homotypic continuity across development (Luby, Si, Belden, Tandon, & Spitznagel, 2009); that is, longitudinal data suggests that children do not

simply grow out of the depression, nor does it evolve into another disorder as young depressed children grow and develop. Rather, these data suggest that preschool depression appears to be an early form of the well-known later childhood and early adolescent disorder. Longitudinal data on a study sample ascertained during the preschool period for high symptoms of depression and followed into school age and adolescence has demonstrated that preschool depression has a chronic, remitting, and relapsing course into later childhood. Findings from the same dataset have shown that children with the preschool depressive syndrome have a high risk of meeting full DSM-5 criteria for depression later in childhood (Luby, Gaffrey, Tillman, April, & Belden, 2014). This finding underscores the need for early identification and early intervention. As we mentioned earlier, another key finding that suggests the importance of early identification is that alterations in cortical gray-matter development across school age and early adolescence were found in relation to preschool depression (Luby et al., 2016). This latter finding suggests that the experience of early-onset depression may alter the later trajectory of brain development. Consistent with homotypic continuity, preschool depression predicts MDD later in childhood and adolescence (Reinfjell, Karstad, Berg-Nielsen, Luby, & Wichstrøm, 2015; Whelan, Leibenluft, Stringaris, & Barker, 2015). However, evidence also suggests that preschool depression can predict anxiety disorders and ADHD in later childhood (Bufferd et al., 2012).

Treatment of Preschool Depression

As preschool depression has only recently become widely recognized, there have been no systematic treatment studies conducted to date. The literature contains case reports, as well as descriptions of treatments of various types. Luby and colleagues have recently adapted parent-child interaction therapy (PCIT) for the treatment of preschool depression by adding an emotion development (ED) component. PCIT is a parent-child psychotherapy originally designed and proven effective for the treatment of preschool disruptive disorders (Eyberg, 1974). PCIT-ED has an additional component that specifically addresses emotion regulation and an emotional repertoire designed to address the absence of joy and excess of guilt and sadness experienced by the depressed preschooler. As in the original form of PCIT, the focus on

strengthening the parent-child relationship and using the parent as the “arm of the therapist” is central to the treatment. A large-scale randomized controlled trial of PCIT-ED is currently under way. The launch of this treatment study was based on promising findings from a small trial of this parent-child therapy showing efficacy (Lenze, Pautsch, & Luby, 2011; Luby, Lenze, & Tillman, 2012).

In younger and more vulnerable populations, greater uncertainties about safety and more immature nervous systems make psychotherapeutic interventions preferred treatments over psychopharmacological options. Psychotherapeutic approaches, including cognitive-behavioral and interpersonal psychotherapies, have demonstrated efficacy for the treatment of depression in older children and adolescents. Numerous dyadic psychotherapeutic strategies have been developed, and several have been tested for the treatment of a variety of disorders arising in the preschool period. Related to the risk for early-onset depression, treatment for depressed mothers designed to ameliorate negative effects on infants and toddlers has also been developed and tested (Cicchetti, Rogosch, & Toth, 2000). These investigators have shown that declines in cognitive development that are apparent in the infants of depressed mothers can be prevented when depressed mothers undergo preventive toddler-parent psychotherapeutic (TPP) interventions. However, to date, no age-appropriate psychotherapies designed for the treatment of preschool depression have been tested.

Questions often arise about the use of pharmacological agents, in particular antidepressants, for the treatment of preschool depression. It is important to note that no available studies inform the safety or efficacy of antidepressants for preschool depression. Concerns about activating side effects of selective serotonin reuptake inhibitor (SSRI) antidepressants that may occur at higher rates in younger children, as well as unresolved reports of possible increases in suicidality, make this treatment option more complicated and unfeasible for use in preschool-age children at this time (Zuckerman et al., 2007).

Future Research: Next Steps

Further replication and extension of the findings reported here by independent research groups in other geographical sites, as well as cross-culturally, would be an important next

step in the further validation and clarification of the clinical features of preschool depression. Furthermore, ongoing longitudinal follow-up of preschool children with a depressive syndrome into early adolescence and early adulthood is also critical to determine whether there is continuity of the early-onset form with later life forms, and such a study is currently under way. If longitudinal continuity in depressive disorders from the preschool period to later life periods could be shown, it would further support the need for early interventions. Heterotypic continuity also needs to be explored given the relatively less differentiated nature of psychopathology in younger individuals. The search for biological correlates that might give clues to the developmental pathophysiology of childhood depression is also critical to understanding, preventing, and treating this disorder.

Conclusions

Numerous studies in independent samples both nationally and internationally are now available, providing validation of clinical depression in children as young as age 3 years. The clinical characteristics of the disorder are the same as those described in older children, adolescents, and adults, but clinicians must be alert to developmentally adjusted symptom manifestations (e.g., anhedonia evident as decreased ability to enjoy activities and play rather than decreased libido) and increased guilt. Neurobiological correlates, including alterations in response to negative stimuli and brain response to reward, are evident during an acute episode of depression in preschool children. Furthermore, alterations in the structure and function of brain regions and circuits that subserve emotion function have also been demonstrated at school age and early adolescence in children who were depressed as preschoolers. Early PCIT that focus on enhancing emotion development appear promising and are now undergoing rigorous testing. Based on this, the identification of clinical depressive disorders in children as young as age 3 should now become the clinical standard of care. Despite these advances for preschool-age children, currently there are no data to inform whether a valid clinical depressive syndrome can arise earlier than age 3 during the infancy and toddler period, although compelling clinical experience suggests the syndrome does arise at this early

stage. Future studies should now focus on this younger age group, so that the earliest identification and intervention in depressive disorders can become possible.

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