Current Psychiatry Reports (2019) 21: 128
https://doi.org/10.1007/s11920-019-1102-4

CHILD AND ADOLESCENT DISORDERS (TD BENTON, SECTION EDITOR)

Preschool Depression: a Diagnostic Reality

Meghan Rose Donohue[1] · Diana J. Whalen[1] · Kirsten E. Gilbert[1] · Laura Hennefield[1] · Deanna M. Barch[1,2,3] · Joan Luby[1]

Published online: 20 November 2019

Abstract

Purpose of Review We review findings related to predictors, correlates, outcomes, and treatment of preschool depression that have been published in the last 3 years.

Recent Findings Preschool depression displays a chronic course through late adolescence and is associated with temperamental and personality traits, poorer physical health, and negative parenting practices. Preschool depression predicts deficits into adolescence, including social difficulties and blunted neural response to rewards. Depressed preschoolers can experience suicidal ideation and behaviors and display an accurate understanding of the finality of death. A treatment for preschool depression has now been validated that uses the parent-child relationship to enhance emotion development and reduce depressive symptoms.

Summary Preschool depression is homotypic with depression that occurs later in life. Future work elucidating mechanisms through which preschool depression develops and informs the sub-groups for which particular treatments may be most effective will have considerable implications for prevention and early intervention.

Keywords Preschool depression · Review · Physical health · Social functioning · Neurobiology · Suicidality

Introduction

As recently as 15 years ago, the concept of depression occurring during the preschool period was met with great resistance in clinical and scientific communities. The idea that a preschooler could be depressed conflicted with prevailing theories that young children were too developmentally immature to experience the complex negative cognitions and emotions that are central to depressive disorders. Adding to this resistance, imagining a young child experiencing such a grave disorder was quite unsettling given that early childhood is widely considered a carefree time of joy. Yet, dozens of studies published since have firmly established the validity of preschool-onset major depressive disorder (PO-MDD). Indeed, current research has moved past validating the disorder and on to illuminating its neurobiology, characterizing its correlates, and examining long-term outcomes of experiencing depression this early in life.

The first observations of depressive symptoms in young children were published in the mid-1940s when psychoanalyst Rene Spitz described cases of "anaclitic depression" in institutionalized infants. Children who had been separated from their mothers displayed excessive crying, withdrawal, flat affect, insomnia, and, despite receiving adequate nutrition, failure to thrive [1]. Although astonishing, these findings of depressed affect and physical deterioration resulting from psychosocial deprivation had little impact on child psychiatry or developmental psychopathology for decades given the prevailing notion that depression was developmentally impossible early in life [2]. When the idea of childhood depression began to gain some acceptance, mainstream clinicians maintained that children did not display typical symptoms of depression as defined in the Diagnostic and Statistical Manual (DSM) and as experienced by adults, but instead displayed "masked" symptoms such as somatization or aggression [3]. However, in the 1980s, Carlson and Cantwell

This article is part of the Topical Collection on *Child and Adolescent Disorders*

✉ Meghan Rose Donohue
rdonohue@wustl.edu

[1] Department of Psychiatry, Washington University School of Medicine, 4444 Forest Park Avenue, Suite 2500, St. Louis, MO 63110, USA

[2] Department of Psychology, Washington University, St. Louis, MO, USA

[3] Department of Radiology, Washington University, St. Louis, MO, USA

provided empirical data that children as young as 7 predominantly displayed typical symptoms of depression, refuting the idea that depression in children would primarily manifest as masked symptoms [4]. In a series of papers, Kashani and colleagues identified preschoolers from the ages of 2.5 to 6 years old who displayed concerning depressive symptoms but did not typically meet full DSM criteria for depression, leading to the suggestion that age-appropriate modifications to DSM criteria should be examined to identify preschool depression [5, 6].

In 2002, Luby and colleagues initially validated and established age-specific criteria for preschool-onset MDD (Table 1). These criteria removed the 2-week duration requirement and described age-appropriate DSM symptom manifestations in preschoolers [7]. The validity of PO-MDD has since been established in multiple independent national and international samples [7, 8•, 9–11]. PO-MDD has demonstrated familial transmission, and children with PO-MDD have greater objectively observed negative affect, self-reported depressive symptoms, and functional impairment in multiple domains compared with healthy controls [7, 12, 13]. Numerous biomarkers of PO-MDD have been identified, such as elevated cortisol reactivity to stressors similar to what is found in adult depression [14] as well as neural markers detailed below. Furthermore, PO-MDD has been shown to have content and discriminant validity and homotypic continuity with DSM 5 MDD in school-age and adolescence [13, 15, 16]. Currently, research has moved beyond validating the disorder and onto illuminating risk factors and neurobiological correlates. Moreover, novel efficacious treatments have been developed and are being tested. In this article, we describe the most recent empirical findings that advance our understanding of PO-MDD. In each section, we first briefly review previous findings before discussing in detail studies published in the last 3 years (2017–2019) and their implications for clinical practice.

Table 1 Diagnostic criteria for MDD adapted for preschool age

1. Depressed, sad, or irritable mood for a portion of the day for several days, as observed (or reported) in behavior.
2. Markedly diminished interest or pleasure in all, or almost all, activities or play for a portion of the day for several days (as indicated by either subjective account or observations made by others).
3. Significant weight loss or weight gain (not explained by normal growth) or decrease or increase in appetite nearly every day.
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (change that is observable by others).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (that may be only evident as persistent themes in play).
8. Diminished ability to concentrate on a task, or indecisiveness, for several days (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide. Suicidal or self-destructive themes may be evident only as persistent themes in play.

Note: Reprinted from the Journal of the American Academy of Child & Adolescent Psychiatry, volume 41 edition 8, Luby et al. (2002), with permission from Elsevier

Myths About Preschool Depression

Given public resistance to accepting the construct of preschool depression as a valid diagnostic entity, several widely held—but not scientifically valid—notions are common. One is that a child only becomes depressed at such an early age if they are exposed to trauma, abuse, or adversity. While these exposures do increase risk, studies have documented that children from advantaged families who do not experience these stressors may also become depressed, similar to patterns in older individuals [7, 17]. Another assumption is that a young child could only become depressed if exposed to a depressed caregiver. Again, although parental depression is a known risk factor for childhood depression, this is not a prerequisite or a known salient causal factor. In contrast to these notions, PO-MDD appears to be a familial disorder with all of the same core symptom features as depression later in life that manifests in a developmentally adjusted fashion (e.g., anhedonia is not manifested as poor libido but as decreased ability to enjoy play). Depressed young children often go clinically undetected as they tend to not be disruptive at home or preschool/daycare and symptoms are more "internal" (e.g., guilt and shame) and less often overtly expressed. Based on this, it is important for caregivers to be attuned and perceptive to these more subtle symptom manifestations in order to bring these young children to needed clinical attention.

Prevalence, Characteristics, and Course of Preschool Depression

Several large community samples and one population-based study of Norwegian children have consistently found rates of preschool depression of ~2.0% [18–20]. Similar to previous estimates, a 2018 study conducted in the United States found a rate of 1.7% in a large community sample of 3-year-olds [21]. These studies also documented high comorbidity with other psychiatric disorders, particularly anxiety disorders, oppositional defiant disorder, conduct disorder, and attention-deficit/hyperactivity disorder [19, 20, 22]. Overall, there have been few population-based studies of PO-MDD, as younger children have not been included in many large epidemiological studies.

One study by Bufferd and colleagues (2017) explored the characteristics of depression in preschoolers using a diary method in which parents reported the daily frequency and

severity of 12 different symptoms of depression over 2 weeks and examined the frequency at which each symptom was identified as severe (i.e., greater than the 95th percentile) [23]. Sadness, irritability, and tearfulness/sensitivity were more "normative" such that for the symptom of sadness to reach clinical significance, it had to occur at least 31 times over 14 days. By contrast, anhedonia, low self-worth, talking about death/suicide, appetite/weight changes, and difficulty concentrating were non-normative; for example, low self-worth had to occur only twice to be considered severe. This study was the first to identify specific frequencies at which depressive symptoms in preschoolers may shift from developmentally normative to clinically significant. These findings are consistent with earlier studies demonstrating that whereas symptoms such as guilt are highly specific to PO-MDD, sadness is a common but not specific symptom [13].

As discussed, older studies have established evidence of continuity of PO-MDD with MDD in school-age and adolescence [24], and newer studies replicate and extend this work. A study of a Norwegian community sample by Finsaas and colleagues (2018) found homotypic continuity of depression from age 4 to 10, largely due to common time-invariant familial factors such as genetics or stable parenting practices [21]. Another study found that PO-MDD was associated with greater odds of meeting full DSM-5 criteria for MDD after the onset of puberty in adolescence [24], providing the strongest evidence to date that PO-MDD displays continuity with MDD later in life. These studies underscore that PO-MDD is not developmentally transient, but rather, longitudinally continuous with MDD into adolescence. As such, PO-MDD does not simply serve as a general risk factor for later psychopathology, but instead strongly predicts later depression.

The Neurobiology of Preschool Depression

A particularly novel line of work has involved elucidating the neurobiology of PO-MDD. Pinpointing the earliest possible neural alterations associated with preschool depression is critically important to inform intervention strategies during periods of relatively greater neuroplasticity. To date, this literature has documented structural and functional neural alterations in depressed preschoolers or older children with a history of PO-MDD that are similar to those found in depressed adults. Specifically, prior work has documented cortical thinning and gray matter volume loss both globally [25] and in regions such as the hippocampus and ventromedial prefrontal cortex [26, 27], increased amygdala activity while viewing negative emotional faces [28, 29], atypical functional connectivity of the subgenual anterior cingulate cortex and the default mode network [30, 31], and altered connectivity between regions related to emotion regulation and cognitive control [32].

Other work examining event-related potentials (ERP) documented that blunted neural responses to rewards, a key marker of depression in adolescents and adults, also characterizes PO-MDD [33]. Three recent studies enrich our understanding of the role of altered response to pleasant stimuli, including rewards, in preschool depression. Using ERP, our research group found that compared to healthy children, children with PO-MDD exhibited reduced responding to pleasant stimuli as indexed by the late positive potential (LPP) during a passive picture-viewing task [34]. Two recent functional neuroimaging studies have focused specifically on reward responding. Gaffrey and colleagues (2018) found that amygdala hyporeactivity in response to reward mediated the relationship between increased cortisol output following a stressor and greater depression severity in preschoolers [35]. This finding suggests a pathway in which the effect of chronic stress and associated HPA axis functioning has a negative impact on the developing neural response to reward, which in turn confers risk for depression. Another study found that whereas current depression in adolescence was associated with focal hyporeactivity in the ventral striatum in response to reward anticipation, depression severity during preschool was associated with a globally blunted response across the cortico-striatal network during adolescence [36••]. This finding may indicate that global hyporeactivity across the cortico-striatal circuit is a risk factor for forms of depression that are more severe or arise earlier in development; alternatively, this global blunting may be indicative of a depression scar in which the development of the cortico-striatal circuit is disrupted in children with PO-MDD.

Overall, this literature demonstrates that PO-MDD displays the same underlying neurobiology as depression in later developmental periods, providing particularly strong evidence of the validity of PO-MDD and its homotypic continuity with depression arising at older ages. Furthermore, these structural and functional brain disruptions provide important clues regarding potential neural mechanisms that may be contributing to this very early-onset form of MDD, as well as to the mechanisms that may sustain the often chronic and relapsing course of PO-MDD.

Predictors, Correlates, and Outcomes of Preschool Depression

The bulk of studies published in the past 3 years have focused on identifying aspects of children's individual characteristics and their environments that correlate with or predict PO-MDD. The most recently published studies of child-level factors have focused on children's temperamental and personality traits and physical health characteristics. Previous literature has demonstrated that preschool depression is concurrently associated with specific temperamental traits, namely difficult

temperament, greater negative affect, and lower levels of sensory regulation, effortful control, and inhibitory control [8•, 37, 38]. A new study by Hopkins et al. (2019) found an indirect effect of negative affect on the relationship between depressive symptoms and effortful control—the trait-like ability to use "top down" or deliberate cognitive processes to self-regulate [39]. Indeed, decreased negative affect at age 5 partially explained why greater effortful control at age 4 was associated with fewer depressive symptoms at age 6 [40]. These findings reinforce the importance of enhancing effortful control in the preschool period given its relationship with negative affect and depressive symptoms. Work from our own group has extended the temperament literature via observational measures of preschool personality based on the five-factor model [41, 42]. Specifically, although none of the personality dimensions (extraversion, agreeableness, conscientiousness, openness, neuroticism) measured at preschool were associated with concurrent depressive symptoms, higher extraversion and lower conscientiousness predicted elevated depressive symptoms across childhood [43]. Although the notion of personality, rather than temperament, in preschoolers remains controversial, temperament and personality are thought to be measuring similar underlying constructs using different terminology [44]. Assessing personality in preschoolers provides consistency across the lifespan, and the above finding demonstrates that observed personality traits in preschoolers that are well-established in adolescents and adults can predict later childhood depression. Future work would benefit from further exploring how preschool personality interacts with depression across development.

Whereas existing work demonstrates that PO-MDD is associated with global physical health problems [45], newer research has explored relations between preschool depression and specific health indices—sleep and body mass index (BMI). Research by Whalen and colleagues (2017) found that parent-reported difficulty falling asleep (i.e., sleep onset latency) and children's refusal to sleep alone independently predicted children's depression from late preschool through middle childhood [46]. This work identifies two relatively common sleep problems that may be important targets for early intervention. Another study found that preschoolers with more sleep problems and parents who engaged in greater sleep reinforcement (i.e., involvement at bedtime and reinforcement of the child's problematic sleep behaviors) exhibited increases in depressive symptoms at age 6–9, whereas there was no relationship between preschool sleep problems and later depressive symptoms for children with lower sleep reinforcement scores. This work furthers that of Whalen and colleagues (2017) by highlighting the role of parent-child bedtime interactions as a potential target in interventions aimed at decreasing the lasting impact of early sleep problems.

One recent study investigated whether higher BMI is associated with depressive symptoms in preschoolers [47], an area of great public health significance given the well-documented detrimental impact of overweight status on health outcomes across the lifespan. During the first assessment (at age 2), a group of overweight children displayed more depressive symptoms than a group of children of a healthy weight. Whereas depressive symptoms increased across two subsequent assessments conducted over the course of 6 years, BMI remained fairly stable across time. Interesting sex differences also emerged with overweight females endorsing fewer depressive symptoms than overweight males at the first assessment, but significantly greater depressive symptoms than males at each subsequent assessment. Together, this work adds to an emerging evidence-based linking symptoms of depression and risk for a variety of physical health problems in the preschool period and later development.

Specific parenting practices, such as lower levels of warm parenting [37], as well as related family environmental factors such as stressful life events, social adversity, and parental psychopathology [17, 45] have been associated with PO-MDD. The newest literature on family environmental factors has examined moderators of the association between parenting practices and preschool depression, and psychopathology in fathers. One study focused on parental warmth and depression in 5- to 13-year-old Puerto Rican children ($N = 2491$) living in either New York or Puerto Rico [48]. Lower parental warmth was associated with 2.04 times greater odds of the child meeting diagnostic criteria for MDD across three subsequent timepoints (collected yearly). Moreover, decreased parental warmth was associated with greater odds of MDD in females and children living in Puerto Rico. These findings extend previous work by identifying groups of children for whom warm parenting might be particularly important. Studies examining parent psychopathology have historically focused on how maternal rather than paternal depression impacts children's mental health. However, Tichovolsky et al. (2018) found that changes in paternal depression significantly predicted changes in both father- and mother-reported child depressive symptoms over a 3-year period [49]. Furthermore, paternal depression when children were 3 years old predicted later depressive symptoms, but the reverse was not true—children's early symptoms did not predict later paternal symptoms. These findings suggest that paternal depressive symptoms confer risk for PO-MDD and highlight the importance of including fathers in studies examining risk for depression in young children.

Compared with work establishing predictors of preschool depression, fewer studies have focused on elucidating ways in which experiencing depression in preschool impacts later functioning. Indeed, only two recently published studies identify long-term consequences of preschool depression, and both focus on detrimental social consequences. Prior work has established bidirectional effects between PO-MDD and social deficits, such that preschool depression predicts, and

is also predicted by poorer social skills and functioning [8•, 38, 50]. A 2018 study extends this literature by demonstrating that PO-MDD prospectively predicted poorer social functioning with both peers and fathers into adolescence, even when controlling for adolescent MDD diagnoses [51•]. Past research has also documented that children with PO-MDD exhibit concurrent deficits in reparative prosocial behaviors (i.e., prosocial actions that children use after transgressions that reduce guilt, which is central to depression). Building on this work, a newer study found that PO-MDD predicted membership in a developmental trajectory of consistently low levels of reparative behaviors from preschool through adolescence [52], and this relationship was mediated through high levels of guilt. Depressed preschoolers appear to exhibit difficulty using reparative behaviors after transgressing due to maladaptive guilt, perhaps because these guilt feelings are emotionally overwhelming or include cognitions that wrongdoings are not reparable. Overall, the relationship between PO-MDD and social deficits remains understudied. Future studies are needed that elucidate mechanisms through which PO-MDD impacts later social functioning; for example, depression early in life might lead to social deficits by interfering with children's achievement of critical developmental milestones.

Suicidality in the Preschool Period

Groundbreaking findings related to preschool suicidality have emerged within the last year. Depressed preschoolers can display suicidal ideation (SI), including passive thoughts of one's own death, such as "I wish I were dead," or active expression of thoughts or plans to end one's life, such as "I'm going to jump out this window," as well as suicidal behaviors (SB), such as trying to choke oneself. Although older studies reported high rates of SI/SB in samples of hospitalized 6- to 12-year-olds [53], rates in preschoolers were relatively low, as might be expected [54]. Yet, these early forms of SI/SB displayed stability into later childhood, suggesting that attention to this phenomenon was of importance [54]. Newer work from Luby and colleagues (2019) examined depressed preschoolers participating in a treatment study (and a healthy comparison group) and found new and alarmingly high prevalence estimates of SI (19.1%) and SB (3.5%) [55•]. This study also highlighted that preschoolers with SI/SB were more likely to be male and have a history of experiencing more violent life events, and displayed greater depression severity, rates of specific depressive symptoms (e.g., neurovegetative signs of depression, recurrent thoughts of death), and impulsivity. Moreover, in an investigation of depressed preschoolers' understanding of death, a pertinent issue for which there was much skepticism, our group found that depressed preschoolers with SI/SB have a better understanding of what it means to die than either depressed preschoolers without SI or healthy peers [56••]. Furthermore, depressed preschoolers with SI were more likely to describe death as caused by violence than those without SI. These findings refute common assumptions that children who express SI/SB have a poor understanding of death and highlight the need to take preschoolers' expressions of SI/SB seriously. These findings are particularly critical given recent reports from the Centers for Disease Control and Prevention indicating that childhood suicide is at a 30-year high.

Treating Preschool Depression

Consistent with treatment for most forms of preschool psychopathology, psychotherapy remains the first line of treatment for PO-MDD. However, intervention research has lagged significantly behind treatments for other preschool disorders, partially due to delayed clinical recognition. An empirically supported treatment for PO-MDD has only recently emerged [57••]. This treatment, Parent-Child Interaction Therapy Emotion Development (PCIT-ED), builds on the well-validated PCIT used to treat disruptive behavior disorders using the classic bug-in-the-ear approach to facilitate live teaching and coaching techniques. Importantly, the novel ED module focuses on teaching the caregiver to serve as the child's emotion coach and external emotion regulator, building on a theoretical model that early childhood depression is a disorder of emotional development. The ED component teaches the parent new parenting techniques that facilitate their ability to validate rather than minimize the child's emotional expression and to help the child manage, rather than ignore, the experience of intense emotions.

Compared with a waitlist control, depressed preschoolers who received PCIT-ED displayed significantly greater rates of depression remission, decrease in depression severity, and increase in adaptive functioning. PCIT-ED was also found to significantly reduce parental depression and parenting stress and improve children's emotion regulation and use of reparative prosocial skills [57••]. Importantly, the ED module improved depression over and above standard PCIT, providing evidence for the importance of a treatment specifically targeting PO-MDD [58]. Moreover, children's neural response to reward measured using ERP (RewP) increased specifically during the ED module of treatment. Furthermore, children with larger neural responses to positive stimuli (LPP) before treatment were more likely to display depression remission following treatment [58, 59]. Thus, this study pinpoints a possible neural indicator of treatment response and a neural marker of children most likely to benefit from treatment. Future studies identifying moderators of PCIT-ED treatment effects are needed to further identify children and families for whom the treatment is most likely to be effective and to compare PCIT-ED to another active treatment once available.

Use of Antidepressant Medications for Preschool Depression

Currently, there is no empirical data outside of case reports to inform the safety and efficacy of antidepressants for the treatment of depression in children under the age of 7. Based on this and findings that younger children are more vulnerable to the activating side effects of SSRI antidepressants [60], these medications should not be considered as a first or even second line of treatment. In cases where age-appropriate therapies have been given adequate trials without response and depression is severe, clinicians might consider very cautious use of an SSRI such as Fluoxetine at low doses with slow titration and close follow-up. However, this should be considered experimental and physicians should review all risks and side effects, as well as the lack of empirical data to direct treatment, with the consenting caregiver.

Clinical Implications

The last 3 years of research on PO-MDD have added significantly to our understanding of factors that clinicians should consider when assessing and treating depressed preschoolers. These studies suggest that preschool patients who present with greater early adverse life experiences, overweight BMI, and parents with low warmth and depression are at particular risk for PO-MDD and should be carefully screened. There is now evidence that specific symptoms of depression such as guilt, difficulty concentrating, appetite/weight changes, and talking about death/suicide are clinically significant in preschoolers even when displayed at very low frequencies. Moreover, some of these same symptoms were endorsed at higher rates in preschoolers with SI/SB than depressed preschoolers without SI/SB. Clinicians might take special note when these symptoms are endorsed when determining diagnosis and prognosis.

The reviewed literature has highlighted several potential targets for early interventions, including children's effortful control, sleep behaviors and BMI, and parenting factors such as parental warmth and parental depression. Moreover, studies documenting that preschoolers with depression are at-risk for chronic social problems suggest that clinicians might incorporate interventions such as social skills training into treatment. Although research on effective treatments for preschool depression is still scant, newer work points to the benefit of treatments focused on improving parent-child interactions and helping parents scaffold children's emotional expression and regulation and suggests that children with relatively more intact positive affect may be more likely to benefit from such treatments.

The newest research on suicidality has particularly important implications for clinical practice. Evidence that preschool suicidality is associated with a distinct profile of risk factors, coupled with new findings that suicidal preschoolers understand what it means to die, underscores the need to take SI/SB in preschoolers just as seriously as that expressed by older children and adolescents. Indeed, given meta-analytic evidence suggesting that talking about suicidality does not increase the risk of SI/SB [61], findings demonstrate that it is imperative to conduct suicide risk assessments as frequently and comprehensively for depressed preschoolers as for older children with depression. Although the prediction of suicide is notoriously difficult, this review also pinpoints that boys, children with greater impulsivity, and those with a history of violent life events are particularly vulnerable.

Conclusions

The most recent findings related to PO-MDD provide an increasingly fine-grained clinical description of the disorder as well as deep concurrent and predictive neurobiological validity. Despite recent advances, many gaps in the literature remain unaddressed. Future studies are needed to continue to identify pathways through which preschool depression both emerges and is associated with negative socioemotional consequences later in life, neurobiological correlates of the disorder, and effective treatments and treatment moderators. Such findings would ultimately aid in improving prevention and intervention efforts for a disorder that, when untreated, can persist and considerably impact functioning later in life.

Acknowledgments Meghan Rose Donohue's work was supported by NIH Grant T32 MH100019 awarded to Joan Luby and Deanna Barch. Diana Whalen's work was supported by NIH grant K23 MH118426. Kirsten Gilbert's work was supported by NIH grant K23 MH115074. Laura Hennefield's work was supported by NIH training grant F32 HD093273. Deanna Barch's work was supported by NIH grants MH 090786 and 1R01MH117436. Joan Luby's work was supported by NIH grant R01 MH064769-06A1.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Spitz RA, Wolf KM. Anaclitic depression. Psychoanal Study Child. 1946;2:313–42.

2. Rie HE. Depression in childhood: a survey of some pertinent contributions. J Am Acad Child Adolesc Psychiatry. 1966;15:653–85.
3. Cytryn L, McKnew D. Factors influencing the changing clinical expression of the depressive process in children. Am J Psychiatr. 1974;131:879–81.
4. Carlson GA, Cantwell DP. Unmasking masked depression in children and adolescents. Am J Psychiatr. 1980;137:445–9.
5. Kashani JH, Carlson GA. Major depressive disorder in a preschooler. J Am Acad Child Psychiatry. 1985;24:490–4.
6. Kashani JH, Ray JS. Depressive related symptoms among preschool-age children. Child Psychiatry Hum Dev. 1983;13:233–8.
7. Luby JL, Heffelfinger AK, Mrakotsky C, Hessler MJ, Brown KM, Hildebrand T. Preschool major depressive disorder: preliminary validation for developmentally modified DSM-IV criteria. J Am Acad Child Adolesc Psychiatry. 2002;41:928–37.
8.• Bufferd SJ, Dougherty LR, Olino TM, Dyson MW, Laptook RS, Carlson GA, et al. Predictors of the onset of depression in young children: a multi-method, multi-informant longitudinal study from ages 3 to 6. J Child Psychol Psychiatry. 2014;55:1279–87. **This study is the first to demonstrate frequency at which depressive symptoms in preschoolers are normative or severe.**
9. Fuhrmann P, Equit M, Schmidt K, von Gontard A. Prevalence of depressive symptoms and associated developmental disorders in preschool children: a population-based study. Eur Child Adolesc Psychiatry. 2014;23:219–24.
10. Wichstrøm L, Berg-Nielsen TS. Psychiatric disorders in preschoolers: the structure of DSM-IV symptoms and profiles of comorbidity. Eur Child Adolesc Psychiatry. 2014;23:551–62.
11. Gaffrey MS, Belden AC, Luby JL. The 2-week duration criterion and severity and course of early childhood depression: implications for nosology. J Affect Disord. 2011;133:537–45.
12. Luby JL, Heffelfinger AK, Mrakotsky C, Brown KM, Hessler MJ, Wallis JM, et al. The clinical picture of depression in preschool children. J Am Acad Child Adolesc Psychiatry. 2003;9.
13. Luby JL, Belden AC, Pautsch J, Si X, Spitznagel E. The clinical significance of preschool depression: impairment in functioning and clinical markers of the disorder. J Affect Disord. 2009;112:111–9.
14. Luby JL, Heffelfinger A, Mrakotsky C, Brown K, Hessler M, Spitznagel E. Alterations in stress cortisol reactivity in depressed preschoolers relative to psychiatric and no-disorder comparison groups. Arch Gen Psychiatry. 2003;60:1248.
15. Luby JL, Si X, Belden AC, Tandon M, Spitznagel E. Preschool depression: homotypic continuity and course over 24 months. Arch Gen Psychiatry. 2009;66:897–905.
16. Luby JL, Gaffrey MS, Tillman R, April LM, Belden AC. Trajectories of preschool disorders to full DSM depression at school age and early adolescence: continuity of preschool depression. Am J Psychiatr. 2014;171:768–76.
17. Luby JL, Belden AC, Spitznagel E. Risk factors for preschool depression: the mediating role of early stressful life events. J Child Psychol Psychiatry. 2006. https://doi.org/10.1111/j.1469-7610.2006.01672.x.
18. Egger HL, Erkanli A, Keeler G, Potts E, Walter BK, Angold A. Test-retest reliability of the preschool age psychiatric assessment (PAPA). J Am Acad Child Adolesc Psychiatry. 2006;45:538–49.
19. Lavigne JV, LeBailly SA, Hopkins J, Gouze KR, Binns HJ. The prevalence of ADHD, ODD, depression, and anxiety in a community sample of 4-year-olds. J Clin Child Adolesc Psychol. 2009;38:315–28.
20. Bufferd SJ, Dougherty LR, Carlson GA, Klein DN. Parent-reported mental health in preschoolers: findings using a diagnostic interview. Compr Psychiatry. 2011;52:359–69.
21. Finsaas MC, Bufferd SJ, Dougherty LR, Carlson GA, Klein DN. Preschool psychiatric disorders: homotypic and heterotypic continuity through middle childhood and early adolescence. Psychol Med. 2018;48:2159–68.
22. Wichstrøm L, Berg-Nielsen TS, Angold A, Egger HL, Solheim E, Sveen TH. Prevalence of psychiatric disorders in preschoolers: psychiatric disorders in preschoolers. J Child Psychol Psychiatry. 2012;53:695–705.
23. Bufferd SJ, Dougherty LR, Olino TM. Mapping the frequency and severity of depressive behaviors in preschool-aged children. Child Psychiatry Hum Dev. 2017;48:934–43.
24. Gaffrey MS, TIllman R, Barch DM, Luby JL. Continuity and stability of preschool depression from childhood through adolescence and following the onset of puberty. Compr Psychiatry. in press.
25. Luby JL, Belden AC, Jackson JJ, Lessov-Schlaggar CN, Harms MP, Tillman R, et al. Early childhood depression and alterations in the trajectory of gray matter maturation in middle childhood and early adolescence. JAMA Psychiatry. 2016;73:31–8.
26. Marrus N, Belden A, Nishino T, Handler T, Ratnanather JT, Miller M, et al. Ventromedial prefrontal cortex thinning in preschool-onset depression. J Affect Disord. 2015;180:79–86.
27. Suzuki H, Botteron KN, Luby JL, Belden AC, Gaffrey MS, Babb CM, et al. Structural-functional correlations between hippocampal volume and cortico-limbic emotional responses in depressed children. Cogn Affect Behav Neurosci. 2013;13:135–51.
28. Barch D, Pagliaccio D, Belden A, Harms MP, Gaffrey M, Sylvester CM, et al. Effect of hippocampal and amygdala connectivity on the relationship between preschool poverty and school-age depression. Am J Psychiatr. 2016;173:625–34.
29. Gaffrey MS, Barch DM, Singer J, Shenoy R, Luby JL. Disrupted amygdala reactivity in depressed 4- to 6-year-old children. J Am Acad Child Adolesc Psychiatry. 2013;52:737–46.
30. Gaffrey MS, Luby JL, Repovš G, Belden AC, Botteron KN, Luking KR, et al. Subgenual cingulate connectivity in children with a history of preschool-depression. NeuroReport. 2010;21:1182–8.
31. Gaffrey MS, Luby JL, Botteron K, Repovš G, Barch DM. Default mode network connectivity in children with a history of preschool onset depression: default mode network connectivity in preschool depression. J Child Psychol Psychiatry. 2012;53:964–72.
32. Luking KR, Repovs G, Belden AC, Gaffrey MS, Botteron KN, Luby JL, et al. Functional connectivity of the amygdala in early-childhood-onset depression. J Am Acad Child Adolesc Psychiatry. 2011;50:1027–1041.e3.
33. Belden AC, Irvin K, Hajcak G, Kappenman ES, Kelly D, Karlow S, et al. Neural correlates of reward processing in depressed and healthy preschool-age children. J Am Acad Child Adolesc Psychiatry. 2016;55:1081–9.
34. Whalen DJ, Gilbert KE, Kelly D, Hajcak G, Kappenman ES, Luby JL, et al. Early childhood onset major depressive disorder is characterized by electrocortical deficits in processing pleasant emotional pictures. J Abnorm Child Psychol. in press.
35. Gaffrey MS, Barch DM, Bogdan R, Farris K, Petersen SE, Luby JL. Amygdala reward reactivity mediates the association between preschool stress response and depression severity. Biol Psychiatry. 2018;83:128–36.
36.•• Rappaport BI, Kandala S, Luby J, Barch DM. Brain reward system dysfunction in adolescence: current, cumulative, and developmental periods of depression. Am J Psychiatry. under review. **This study implicates preschool depression in predicting globally blunted response to rewards across the cortico-striatal network during adolescence**.
37. Hopkins J, Lavigne JV, Gouze KR, LeBailly SA, Bryant FB. Multidomain models of risk factors for depression and anxiety symptoms in preschoolers: evidence for common and specific factors. J Abnorm Child Psychol. 2013;41:705–22.
38. Reinfjell T, Kårstad SB, Berg-Nielsen TS, Luby JL, Wichstrøm L. Predictors of change in depressive symptoms from preschool to first grade. Dev Psychopathol. 2016;28:1517–30.

39. Nigg JT. Annual research review: on the relations among self-regulation, self-control, executive functioning, effortful control, cognitive control, impulsivity, risk-taking, and inhibition for developmental psychopathology. J Child Psychol Psychiatry. 2017;58:361–83.
40. Hopkins J, Gouze KR, Lavigne JV, Bryant FB. Multidomain risk factors in early childhood and depression symptoms in 6-year-olds: a longitudinal pathway model. Dev Psychopathol. 2019:1–15.
41. Costa PT, McCrae RR. Professional manual: revised NEO personality inventory (NEO-PI-R) and NEO five-factor inventory (NEO-FFI), vol. 61. Odessa: Psychological Assessment Resources; 1992.
42. Whalen DJ, Gilbert KE, Jackson JJ, Barch DM, Luby, Joan L. (under review) Using a thin slice approach to assess preschool personality dimensions.
43. Gilbert KE, Whalen DJ, TIllman R, Barch DM, Luby JL. Observed personality in preschool: associations with current and longitudinal symptoms. J Abnorm Child Psychol. in press. https://doi.org/10.1007/s10802-019-00567-w.
44. Grist CL, McCord DM. Individual differences in preschool children: temperament or personality? Infant Child Dev. 2010; n/a-n/a.
45. Whalen DJ, Belden AC, Tillman R, Barch DM, Luby JL. Early adversity, psychopathology, and latent class profiles of global physical health from preschool through early adolescence. Psychosom Med. 2016;78:1008–18.
46. Whalen DJ, Gilbert KE, Barch DM, Luby JL, Belden AC. Variation in common preschool sleep problems as an early predictor for depression and anxiety symptom severity across time. J Child Psychol Psychiatry. 2017;58:151–9.
47. Cerniglia L, Cimino S, Erriu M, Jezek S, Almenara CA, Tambelli R. Trajectories of aggressive and depressive symptoms in male and female overweight children: do they share a common path or do they follow different routes? PLoS One. 2018;13:e0190731.
48. Santesteban-Echarri O, Ramos-Olazagasti MA, Eisenberg RE, Wei C, Bird HR, Canino G, et al. Parental warmth and psychiatric disorders among Puerto Rican children in two different socio-cultural contexts. J Psychiatr Res. 2017;87:30–6.
49. Tichovolsky MH, Griffith SF, Rolon-Arroyo B, Arnold DH, Harvey EA. A longitudinal study of fathers' and young children's depressive symptoms. J Clin Child Adolesc Psychol. 2018;47:S190–204.
50. Belden AC, Gaffrey MS, Luby JL. Relational aggression in children with preschool-onset psychiatric disorders. J Am Acad Child Adolesc Psychiatry. 2012;51:889–901.
51.• Finsaas MC, Kessel EM, Dougherty LR, Bufferd SJ, Danzig AP, Davila J, et al. Early childhood psychopathology prospectively predicts social functioning in early adolescence. J Clin Child Adolesc Psychol. 2018:1–12. **This study is one of the first to document the impact of preschool depression on social functioning much later in life, during early adolescence.**
52. Donohue MR, Tillman R, Luby JL. Early socioemotional competence, psychopathology, and latent class profiles of reparative prosocial behaviors from preschool through early adolescence. Dev Psychopathol. in press.
53. Pfeffer CR, Conte HR, Plutchik R, Jerrett I. Suicidal behavior in latency-age children: an empirical study. J Am Acad Child Psychiatry. 1979;18:679–92.
54. Whalen DJ, Dixon-Gordon K, Belden AC, Barch D, Luby JL. Correlates and consequences of suicidal cognitions and behaviors in children ages 3 to 7 years. J Am Acad Child Adolesc Psychiatry. 2015;54:926–937.e2.
55.• Luby JL, Whalen D, Tillman R, Barch DM. Clinical and psychosocial characteristics of young children with suicidal ideation, behaviors, and nonsuicidal self-injurious behaviors. J Am Acad Child Adolesc Psychiatry. 2019;58:117–27. **This study is the first to demonstrate that preschool suicidality is associated with a distinct pattern of psychosocial characteristics and risk factors.**
56.•• Hennefield L, Whalen DJ, Wood G, Chavarria MC, Luby JL. Changing conceptions of death as a function of depression status, suicidal ideation, and media exposure in early childhood. J Am Acad Child Adolesc Psychiatry. in press. **This study dispels ideas that preschoolers who express suicidality do not understand the meaning of their thoughts and behaviors.**
57.•• Luby JL, Barch DM, Whalen D, Tillman R, Freedland KE. A randomized controlled trial of parent-child psychotherapy targeting emotion development for early childhood depression. Am J Psychiatr. 2018. https://doi.org/10.1176/appi.ajp.2018.18030321. **This is the validation article for the first empirically supported treatment for preschool depression.**
58. Luby JL, Gilbert KE, Whalen DJ, TIllman R, Barch DM. The differential contribution of the components of parent child interaction emotion development for treatment of preschool depression. J Am Acad Child Psychiatry. in press.
59. Barch DM, Whalen D, Gilbert K, Kelly D, Kappenman ES, Hajcak G, et al. Neural indicators of anhedonia: predictors and mechanisms of treatment change in a randomized clinical trial in early childhood depression. Biol Psychiatry. 2019;85:863–71.
60. Safer DJ, Zito JM. Treatment-emergent adverse events from selective serotonin reuptake inhibitors by age group: children versus adolescents. J Child Adolesc Psychopharmacol. 2006;16:159–69.
61. DeCou CR, Schumann ME. On the iatrogenic risk of assessing suicidality: a meta-analysis. Suicide Life Threat Behav. 2018;48:531–43.