

Preschool Bipolar Disorder

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KEYWORDS

• Preschool • Bipolar • Mania

Despite significant progress over the last decade in the characterization and validation of numerous forms of preschool psychopathology, the area of bipolar disorder remains perhaps the most controversial. The difficulty of distinguishing normative extremes in mood intensity and lability known to characterize early childhood from those emotions and behaviors that cross the threshold into clinically significant psychopathology is a central issue. Further, another fundamental problem is the ongoing lack of clarity about the diagnostic criteria and validity of the diagnosis in older children, as phenotypes in older children are a key source for the downward extension of nosologies in the preschool period. Along this line, contrasting definitions of bipolar disorder in children and adolescents have been proposed and tested. This definitional debate remains a salient issue in the existing literature. Questions about the basic validity of the diagnosis in children, its temporal features, and continuity into adulthood, as well as treatment are only a few key areas debated in both the psychiatric literature and in public forums.¹

While a growing body of empirical research is available to inform these issues in older children, studies in preschoolers remain scarce. Along this line, the studies that are available in preschoolers with suspected bipolar disorder are limited predominantly to case reports and chart reviews. There is a smaller body of systematic literature, but many of these studies are limited by retrospective designs with small sample size. In 2007, for example Danielyan and colleagues² reviewed 26 outpatient charts of preschoolers referred to a psychiatric clinic and diagnosed bipolar and found high recovery and relapse rates. Similarly, Ferreira Maia and colleagues³ also retrospectively reviewed outpatient charts in a mood disorders clinic and found preschoolers to have classic symptoms of mania, but the reports were also limited by the small sample size of preschoolers who met Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), bipolar disorder criteria ($n = 8$). Classic

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features of mania such as elation, grandiosity, psychomotor agitation, and decreased need for sleep were also observed by Dilsaver and Akiskal⁴ over a 2-year period, and a family history notable for affective illness was described. Three presumptive cases of preschool bipolar disorder were also described, with subjects having classic symptoms or “cardinal features,” by Luby and colleagues,⁵ but these cases were from a specialty preschool mood disorders clinic and with potentially limited generalizability. One larger systematic study of preschoolers in a community-based sample investigated the presence of age-adjusted mania symptoms.⁶ Ironically, there is a somewhat larger body of literature on treatment in preschoolers, although this is limited to case reports and retrospective chart reviews, with only a couple of open label investigations available to date.

REVIEW OF NOSOLOGY IN OLDER CHILDREN: IMPLICATIONS FOR STUDY OF PRESCHOOLERS

Amid the ongoing debate on the appropriate criteria for diagnosis in older children, the rate of clinical diagnosis of bipolar disorder in children has increased 40-fold between 1994 and 2003.⁷ The precise source of this increase in diagnosis remain unclear. However, there is significant concern that the diagnosis may be liberally and nonspecifically applied in many cases. Multiple perspectives exist as to which primary symptoms best characterize the disorder and importantly how to distinguish it from other disruptive behavioral disorders, especially attention-deficit hyperactivity disorder (ADHD).^{8–11} Geller and colleagues¹² have provided empirical data suggesting that all DSM-IV symptom criteria, but not standard discrete episode criteria, must be met to make the diagnosis in childhood. This group has provided data suggesting that the cardinal features of mania, elation, grandiosity, hypersexuality, flight of ideas (racing thoughts), and increased energy along with decreased need for sleep are the best discriminators from ADHD. While some argue that irritability is a highly nonspecific symptom in childhood psychopathology, others suggest that “extreme irritability” is a key marker of the disorder in childhood.^{13,14} Others have suggested that the irritability is a nonspecific feature of many childhood psychiatric disorders and therefore cannot be used as a marker of childhood bipolar disorder.^{12,15} Leibenluft and colleagues¹⁶ have proposed another view, outlined below, in which a distinction between broad and narrow phenotypes is made.

SYMPTOM DURATION AND FREQUENCY CRITERIA IN OLDER CHILDREN

In addition to questions about the most sensitive and specific symptom criteria for diagnosis, the duration and related temporal features of these symptoms are also an area of debate. The question of whether the same duration criteria for adult bipolar disorder should be applied to children is currently unclear. Leibenluft and colleagues¹⁶ have suggested that only those children who meet full symptom criteria and who demonstrate discrete episodes of mania would be designated as “bipolar,” also referred to as the “narrow” phenotype. Alternatively, the “broad” phenotype encompasses those who have a chronic, nonepisodic illness characterized by irritability and hyperarousal but do not necessarily manifest cardinal features of mania (elation and grandiosity). In addition to the narrow and broad phenotypes, they suggested two intermediate groups: the first includes those with shorter duration criteria of 1–3 days including distinct manic episodes; the second incorporates distinct episodes of severe irritability but not “cardinal” mania symptoms of elation and grandiosity.¹⁶

Modification of duration criteria more appropriate for children has been suggested by several additional research groups who studied the disorder in school-age children.^{15,17,18} More specifically, Tillman and Geller¹⁸ have described and distinguished

between *episodes* and *cycling*. *Episodes* are used to describe the entire duration of illness, whereas *cycling* refers to fluctuations of mood within an episode. Tillman and Geller¹⁸ adapted definitions from Kramlinger and Post¹⁹ and redefined what was previously referred to as *rapid cycling* as four or more episodes in a year; *ultra-rapid* as mood fluctuations every few days to a few weeks, and fluctuation within 1 day as *ultradian cycling*. Their data suggest that children typically have a more non-episodic, chronic course than that of older adolescents and adults who often have distinct episodes of fluctuation in mood.^{15,18} This apparent developmental difference in the phenomenology of prepubertal bipolar disorder suggests that assuming that adult-based criteria can be simply extrapolated to children is unwise. Along this line, even greater caution in the generalization of adult-based phenomenology to the youngest of children is also advisable.

EMERGING LITERATURE IN PRESCHOOLERS

While there is a dearth of studies that have systematically studied mania symptoms in preschoolers as outlined above, the existing literature has begun to shed some light on this area of early psychopathology. Developmental manifestations of mania symptoms among preschool-aged children have been described in case reports of preschoolers with suspected bipolar disorder. For example, common among these case reports are observations of excessive energy, decreased need for sleep, impairing elation, as well as hypersexuality although the latter appears perhaps less common than the others. Furthermore, these preschoolers were generally described as highly impaired and challenging to treat. Historically, case histories have depicted presumptively manic, impaired preschoolers as far back as the late 1880s.^{20–24}

Between 2003 and 2007, increasing numbers of published case series describing mania manifestations during the preschool period have emerged.^{2–5,25} Tumuluru and colleagues²⁵ described mania in six hospitalized preschoolers who had irritable but not elated mood and decreased need for sleep, with significant impairment leading to hospitalization. They further noted that all met DSM criteria for ADHD at some time point as well; further, all six children were described to have a strong family history of affective illness. Similarly, family history of affective illness was also noted in an additional open case series of community mental health clinic patients with mania, but in contrast to the former study, more classical features of mania were described, including elation.⁴ Elation and other age-adjusted classical features of mania were described in a series of suspected bipolar disorder cases in several outpatient specialty mood disorders clinics;^{3,5} these studies also reported family history of affective illness in the affected preschoolers.

Conversely, aggression and irritability were the most common symptoms reported among presumptive bipolar preschoolers in a chart review of 26 outpatients.² This review contributed to the literature by noting high relapse rates defined as meeting hypomania or mania criteria along with moderate symptoms requiring intervention as rated by the Clinical Global Impression Severity-Scale (greater than or equal to five and minimally improved for at least 2 weeks) of these preschoolers with suspected bipolar disorder based on an outpatient record review.² The phenomenology of preschoolers with presumptive bipolar disorder has been detailed in a systematic investigation in 2006, outlined below.⁶

Luby and Belden⁶ reported on a sub-group (n = 26) of preschoolers meeting symptom criteria for bipolar disorder I from a larger community-based sample (n = 306) that was over sampled for preschoolers with mood symptoms. An age-appropriate parent informant diagnostic measure was used to assess for mania symptoms. This specific

mania module was developed in collaboration with the authors of the Preschool Age Psychiatric Assessment (PAPA)^{26,27} to ascertain DSM-IV bipolar symptoms in a developmentally appropriate manner. Favorable test-retest reliability of the mania module of the PAPA have been established and reported elsewhere.⁶ The characteristics of this group and the symptoms that distinguished them from both depressed and disruptive preschoolers were described. The study findings indicated that 5 out of 13 DSM-IV bipolar symptoms, including elation, grandiosity, hypertalkativeness, flight of ideas, and hypersexuality, could differentiate preschoolers with bipolar disorder from those with disruptive disorders (ADHD, oppositional defiant disorder [ODD], and/or conduct disorder [CD]) 92% of the time.⁶ Most notably, the bipolar group was not only found to be more impaired than healthy but, notably, also more impaired than preschoolers with other Axis I psychiatric disorders (major depressive disorder (MDD) and DSM-IV disruptive groups). This finding emerged even after controlling for comorbid disorders (important due to high rates of comorbidity found and well known in childhood disorders). This sample has been followed longitudinally more than 2 years, and longitudinal stability of the bipolar diagnosis has been demonstrated. For example, results indicated that preschoolers diagnosed with bipolar disorder at wave one were at 12 times greater risk than non-bipolar preschoolers to be diagnosed with bipolar disorder when assessed 2 years later.²⁸ Longitudinal data pertaining to symptoms, psychosocial functioning, and family history of psychiatric disorders in this population assessed at preschool age are currently being obtained at school-age in the study population.

EVIDENCE FOR ALTERATIONS IN EMOTIONAL REACTIVITY

A key issue in investigating the question of whether bipolar disorder can manifest in preschool children is whether those who manifest symptoms of the disorder also demonstrate differences in patterns of emotional reactivity. Since the disorder is characterized by a fundamental impairment in mood and affect regulation, and related to this, by periods of extremely intense emotional responses, investigating the typical emotion reactivity characteristics (in response to incentive events) of this group relative to others is of interest. Building on the emerging body of data on atypical emotion development, the idea that early onset bipolar disorder may be characterized by alterations in patterns of emotional reactivity has been previously proposed.²⁹

As a part of an ongoing National Institute of Mental Health (NIMH) funded longitudinal study focusing on preschool mood disorders (also described above), the assessment of emotional development and reactivity styles in the study population (and the mood-disordered groups in particular) was of interest. Standardized developmental measures of emotion recognition, regulation, and emotional display rules were obtained. However, to assess the child's typical pattern of emotionality, a novel parental report assessment of the intensity and duration of the child's characteristic emotional responses was developed. This measure was designed to elicit from the parent details of the timing and intensity of the child's typical emotional reactions using a narrative depicting commonly experienced evocative events. This approach was thought to capture the child's typical emotional functioning by detailing quantifiable features of emotional response rather than global ratings, which are more vulnerable to reporter bias. This measure, titled "The Emotion Reactivity Questionnaire" (ERQ) was developed based on an emotional dynamic model of mood disorders described in detail in Luby and Belden.²⁹ This model posits that the temporal and dynamic features of emotional response may be key to identifying the emotional developmental precursors and characteristics of early onset mood disorders. Observational measures of

emotional reactivity or temperament in the laboratory, which also quantify the child's emotional response to an evocative event, were obtained and will be reported elsewhere. Such objective measures, while potentially highly informative, are limited by lack of representativeness based on the cross-sectional nature of the observation.

The ERQ³⁰ is a 28-item measure that assesses the intensity of children's emotional reactions during a 24-hour period based on caregiver report. Four vignettes depicting situations that occur at the very beginning of the day and that are thought to elicit joy, sadness, guilt, or anger in young children are read to caregivers by an examiner. After hearing each vignette, caregivers are asked to rate the intensity of the emotional reactions they would expect their children to display. Caregivers are given an "emotion meter," which allows them to slide and place a red line on an exact intensity from 0 (no emotional reaction) to 100 (very intense emotional reaction). Caregivers are asked to rate their child's emotional reactions at seven time points as follows: immediately after the incentive event depicted in the narrative, 30 minutes after, 60 minutes after, at lunchtime, dinnertime, bedtime, and again the next morning when the child wakes up. Basic psychometric properties for this new measure have been tested and are described below.

Internal consistency for each of the four emotion subscales using Chronbach's alpha ranged from 0.87 to 0.89. The ability of the ERQ to assess emotionally specific reactions of children (versus global reactions) was evidenced by the results of a principal component analysis illustrating four predominant factors that represented each of the 4 emotions assessed in the ERQ. As described in the findings below, initial indicators are that the ERQ also has strong face validity. Additional analyses were conducted to examine convergent validity between the ERQ and the Child Behavioral Questionnaire (CBQ),³¹ a well-established measure of children's dispositional temperament. It was hypothesized that caregivers' reports on the CBQ 1 year before completing the ERQ would predict mothers' reports of children's initial scores on each of the three ERQ emotions (the CBQ does not include a guilt subscale). As hypothesized, the CBQ sadness subscale was associated with ERQ initial sadness scores 1 year later ($r = .20, p < .01$), CBQ anger subscale scores were associated with ERQ initial anger scores 1 year later ($r = .25, p < .001$), and CBQ pleasure subscale scores were correlated with ERQ initial joy scores 1 year later ($r = .14, p < .05$).

Based on these preliminary findings suggesting the ERQ is a psychometrically acceptable measure, we tested whether bipolar preschoolers' ERQ scores differed significantly from those of same-age peers in healthy and psychiatric comparison groups. Analyses were also conducted to determine whether preschoolers with bipolar disorder versus comparison groups had longer emotional reaction durations, suggesting difficulty with emotion regulation. To address this question, nonparametric Mann-Whitney *U* tests (M-W test) were conducted because of the small sample sizes in two of three comparison groups.

Compared with healthy preschoolers, preschoolers with bipolar disorder were described by their parents as expressing significantly higher levels of joy after 30 (M-W test, $Z = -2.847, P < .01$) and 60 (M-W test, $Z = -2.831, P < .01$) minutes in response to a joy-inducing incentive event (Fig. 1). Preschoolers with bipolar disorder also retained higher levels of joy by lunch time (M-W test, $Z = -2.514, P < .05$) and by dinnertime (M-W test, $Z = -2.024, P < .05$) compared with those of healthy peers. * $P < .05$ ** $P < .01$.

Bipolar preschoolers were also rated as having significantly higher levels of sadness after 30 minutes (M-W test, $Z = -2.439, P < .05$) compared with those of healthy preschoolers. Notably, in the domain of anger, bipolar preschoolers were also reported to have significantly higher initial levels of anger (M-W test, $Z = -3.400,$

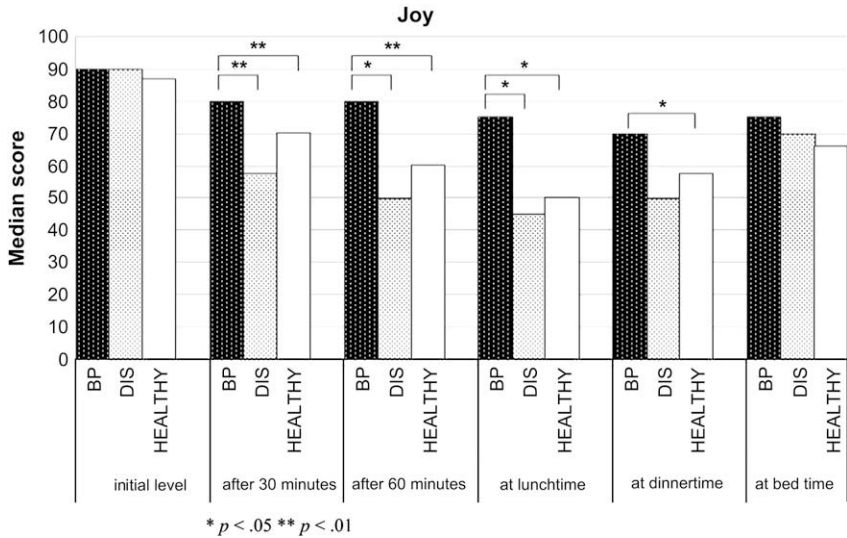


Fig. 1. Comparison of joy levels over time between healthy disruptive and bipolar preschoolers.

$P < .01$) and higher levels after 30 minutes (M-W test, $Z = -2.111$, $P < .05$) than those of healthy preschoolers. No other differences were found between bipolar and healthy preschoolers. * $P < .05$ ** $P < .01$.

Notably and in contrast to the findings above, preschoolers without bipolar disorder but who had a DSM-IV disruptive disorder were rated by parents as displaying significantly lower levels of sadness than those of healthy preschoolers after 60 minutes (M-W test, $Z = -1.997$, $P < .05$, **Fig. 2**). Preschoolers with disruptive disorder were also reported to display significantly lower levels of anger after 30 (M-W test, $Z = -2.129$, $P < .05$) and 60 (M-W test, $Z = -1.957$, $P = .05$) minutes compared with those of healthy peers (**Fig. 3**). Furthermore, in the area of guilt, they were reported to display significantly lower levels of guilt after 60 minutes (M-W test, $Z = -2.845$, $P < .01$), at lunch time (M-W test, $Z = -2.558$, $P < .05$), and at dinnertime (M-W test, $Z = -2.664$, $P < .01$) compared with those of healthy peers (**Fig. 4**). * $P < .05$ ** $P < .01$.

Comparing preschoolers with bipolar disorder to those with disruptive disorders, parents described bipolar preschoolers as expressing significantly higher levels of joy after 30 (M-W test, $Z = -2.865$, $P < .01$) and 60 (M-W test, $Z = -2.544$, $P < .05$) minutes, as well as at lunch time (M-W test, $Z = -2.510$, $P < .05$) compared with those of disruptive preschoolers. Bipolar preschoolers versus disruptive preschoolers were also reported to display significantly higher levels of sadness after 30 (M-W test, $Z = -3.090$, $P < .01$) and 60 (M-W test, $Z = -2.559$, $P < .05$) minutes as well as at bedtime (M-W test, $Z = -2.377$, $P < .05$). The bipolar group was also rated as having a significantly higher initial level of anger (M-W test, $Z = -2.177$, $P < .05$) and higher levels of anger after 30 (M-W test, $Z = -3.072$, $P < .01$) and 60 (M-W test, $Z = -2.168$, $P < .05$) minutes. Similar differences were also detected between the groups in the domain of guilt in which bipolar preschoolers had higher levels of guilt after 30 (M-W test, $Z = -2.010$, $P < .05$) and 60 (M-W test, $Z = -2.857$, $P < .01$) minutes, at lunch time (M-W test, $Z = -2.209$, $P < .05$), and at bedtime (M-W test, $Z = -2.146$, $P < .05$) compared to disruptive preschoolers.

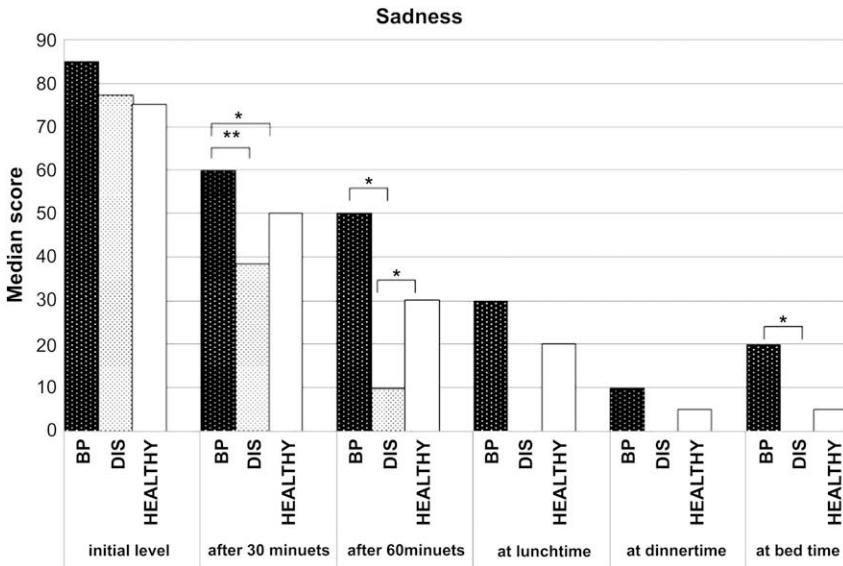
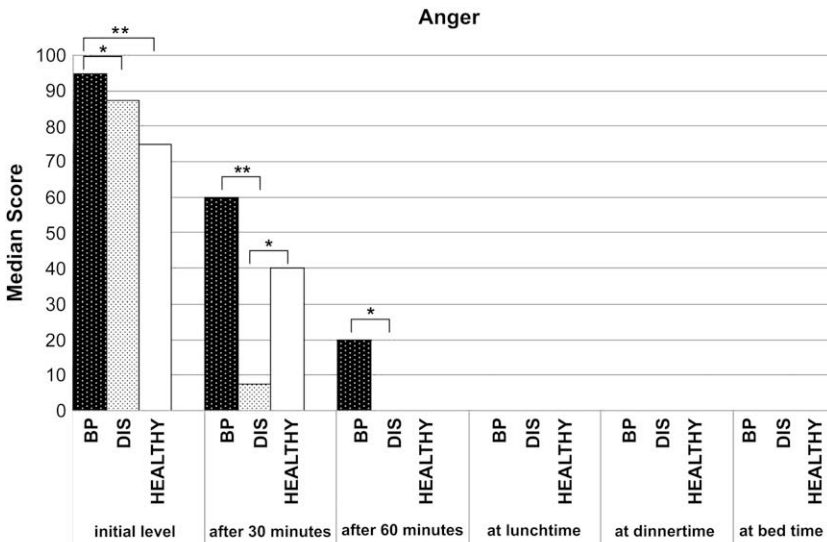


Fig. 2. Comparison of sadness levels between healthy and bipolar preschoolers.

These findings provide evidence that preschool children who meet DSM-IV symptom criteria for bipolar disorder display more intense emotional responses in the domains of joy, sadness, and anger than those of healthy peers, as would be expected. In addition, they also display higher intensities of these emotions (as well as guilt) than those of a key psychiatric comparison group of children with disruptive disorders. The latter group is of particular importance given that the differential diagnosis between early onset bipolar



* $p < .05$ ** $p < .01$

Fig. 3. Comparison of anger levels between healthy and bipolar preschoolers.

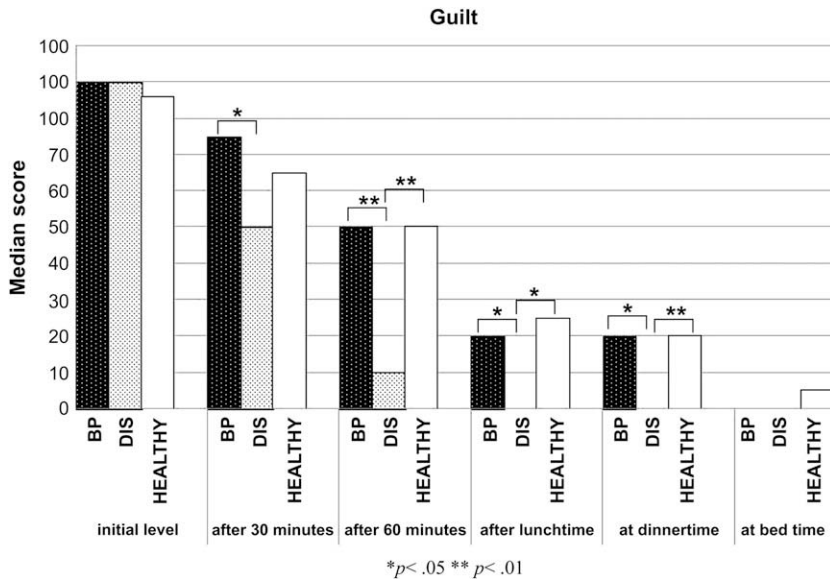


Fig. 4. Comparison of guilt levels between healthy and bipolar preschoolers.

disorder and disruptive disorders is particularly difficult clinically. Beyond elevations in intensity, these findings also provide support for the notion that bipolar preschoolers have more difficulty regulating their emotions over time. This is evidenced by sustained elevations in emotional intensity at periods several hours after the incentive event (eg, lunch and dinner) compared with healthy and disruptive peers. These findings suggest that an emotional reactivity model may be useful in the understanding and diagnosis of bipolar disorder in young children.

Findings are limited by the fact that they are based on parent report of typical emotional responses. Reporter biases, as well as the fact that diagnostic determinations were also based on parent report, are important issues to consider in the interpretation of these findings. However, this limitation may also be offset by the fact that the measure aimed to obtain an objective and quantitative estimate of the child's response through the use of an emotion meter and obtaining estimation at multiple fixed time points over a 24-hour period. Further investigation of emotional reactivity in groups of mood-disordered preschoolers using similar measures as well as observational measures is now indicated.

FAMILY HISTORY AND BIPOLAR DISORDER IN OLDER CHILDREN

Elevations in reported rates of bipolar disorder in the older offspring of bipolar parents compared with the offspring of healthy parents vary depending on study design. However, prior studies have suggested that the offspring of bipolar parents are at four to five times greater risk for any affective disorder (including bipolar disorder) compared with the offspring of parents without mental disorders.^{32,33} One source of variation might be that some meta-analyses have included both adult and child offspring. In a review of studies involving only child and adolescent offspring of parents with bipolar disorder, Delbello and Geller³⁴ found rates of mood disorders ranging from 5% to 52%. Furthermore, these offspring were also at higher risk for

disruptive and anxiety disorders than those from healthy parents.³⁴ Similarly, Chang and colleagues³⁵ reported that 51% of the offspring of bipolar parents had psychiatric disorders, including bipolar disorder. Parents with earlier onset symptomatology were more likely to have offspring with bipolar disorder.³⁵ This earlier age of symptom onset has been suggested to be a marker of heritability in a more recent study using genome-wide scanning.³⁶ In addition to the heritability of early age at onset, poor social functioning and comorbid conditions have also been suggested to be familial.³⁷

IMPLICATIONS OF BIPOLAR FAMILY HISTORY IN PRESCHOOL CHILDREN

The notion that early onset of bipolar symptoms in a parent may increase the risk of heritability of the disorder suggests that such offspring would be an ideal group in which to search for prodromes or early markers of the disorder. Findings to date in preschool populations have suggested that preschoolers with MDD and family history of bipolar disorder have distinctive symptoms of MDD suggestive of mania precursors when compared with those of preschoolers with MDD but no family history of bipolar disorder. In particular, depression in this group was characterized by increased rates of agitation and restlessness.³⁸ Extrapolating from the work of Geller and colleagues^{39,40} suggesting that prepubertal children with early onset MDD with a family history of bipolar disorder are at higher risk for later switching to mania, younger depressed children may be an important group to follow and assess for mania based on the hypothesis that they are at a particularly high risk for switching.

Unique behavioral features have been identified in studies of the young children of parents with bipolar disorder in at least one study.⁴¹ More specifically, the rate of behavioral disinhibition among offspring of bipolar parents was significantly increased compared with that of offspring of parents with both panic disorder and unipolar depression, even after controlling for parental ADHD, substance use disorders, CD, and antisocial personality disorder. Although this pilot study was limited by the small sample size of the bipolar offspring, it proposes early intervention when markers of risk such as behavioral disinhibition are observed among high-risk offspring.⁴¹ Similarly, difficulties in sharing and challenges in inhibiting aggressive impulses with peers were observed in 2-year-olds who had a bipolar parent, in a naturalistic observational study focusing on social and emotional functioning of offspring of bipolar parents. Conversely, these children were also noted to have a heightened sense of recognizing suffering in others, despite having difficulty in modulating their own emotions.^{42,43}

DIFFERENTIAL DIAGNOSIS OF BIPOLAR DISORDER IN THE PRESCHOOL PERIOD

The prevailing controversy about the nosology of bipolar disorder in older children provides an uncertain framework for studies of nosology in preschoolers as outlined above. Amid these diagnostic uncertainties, clinicians are increasingly placed in the position of evaluating preschool children for suspected bipolar disorder. As evidenced by dramatic increases in the rates of clinical diagnosis of bipolar disorder in childhood more generally as mentioned above, clinicians appear to more readily consider the diagnosis of bipolar disorder in young children presenting with intense mood lability or bouts of extreme irritability associated with functional impairment. Because further scientific clarity of the clinical characteristics of the disorder in young children is still needed, proper consideration in the differential diagnosis for other more clearly understood disruptive disorders and/or ADHD is even more critical.

ADHD and ODD are disorders known and relatively well characterized in preschool children. ADHD has been reported to have a prevalence rate of 3.3% in preschoolers, and those with ADHD were reported to have an 8-fold greater rate of ODD.⁴⁴ Therefore,

the occurrence of one of these more common disorders is more likely and must be considered first. Further, at least one report has suggested that preschoolers who meet symptom criteria for bipolar disorder have high rates of comorbid ODD and ADHD similar to those found in school-age bipolar samples.⁶ In addition, extreme temper tantrums and irritability in young children may also be a marker of an autistic spectrum disorder (ASD), a group of disorders increasing in prevalence. Therefore, in preschool children presenting with extreme irritability, more commonly occurring diagnoses should be considered and ruled in or out before consideration of bipolar disorder.

Differentiating bipolar disorder from these more common disorders may be difficult in cases in which there is a complex comorbid and/or developmental delay clinical picture. Key features in differentiating bipolar disorder from ASD are that the latter is characterized by a core impairment in social relatedness, whereas bipolar preschoolers would be expected to have intact or often unusually high social interest. Further, stereotypes and perseverations that characterize ASDs are not a typical feature of bipolar disorder, although developmental delay and social rejection may be present.

One of the more challenging aspects of the differential diagnosis is distinguishing oppositional behaviors toward adults found in ODD from grandiosity found in bipolar disorder. It is important to determine whether the oppositional or extremely bossy behavior is generalized or relationship-specific; the latter would be associated with ODD rather than bipolar disorder. Perhaps even more important is whether this behavior is associated with a fixed and false elevated sense of powers and capabilities that is acted upon. Such behavior is an important manifestation of clinical level and delusional grandiosity, which appears to be a key feature of mania that may manifest as early as the preschool period.

TREATMENT CONSIDERATIONS

Although the diagnostic characteristics of bipolar disorder in the preschool period remain ambiguous as outlined, and much empirical work is needed, to date there has been relatively more scientific investigation of treatments for presumptive mania in this age group. Most of the available treatment literature has been descriptive and is composed of case reports and retrospective chart reviews. These reports provide some promising findings for the use of atypical antipsychotic agents and mood stabilizers, both singly and in combination.^{13,45–49} Such observations in uncontrolled clinical settings suggest that systematic open-label studies of these agents should be pursued as a next step. An open-label study of olanzapine and risperidone was conducted in a sample of preschoolers with a form of bipolar disorder that might best be classified as bipolar disorder not otherwise specified.¹³ Both medications rapidly decreased mania symptoms but residual symptoms remained. Similarly, case reports of open-label use of the mood stabilizers valproate, lithium, topiramate, and carbamazepine have described reduction in preschool mania symptoms, with atypical antipsychotics used for augmentation of residual symptoms when necessary.^{45–49} At this time, reliance on these data for treatment decisions must be approached with caution due to the small sample sizes and lack of necessary controlled investigations. Although studies of psychotherapeutic interventions for preschool bipolar disorder have not been conducted to date, an age-appropriate parent–child dyadic treatment modality has been designed and described for treatment of preschool bipolar disorder for future testing in this population.⁵⁰

SUMMARY

Although some empirical work has now been added to the larger body of case material, preschool bipolar disorder remains a highly ambiguous diagnostic area. This is notable in the context of the significant progress that has been made in many other areas of psychopathology in the preschool period. Although there is a need for well-controlled empirical investigations in this area, a small but growing body of empirical literature suggests that some form of the disorder may arise as early as age 3 years. The need for large-scale and focused studies of this issue is underscored by the high and increasing rates of prescriptions of atypical antipsychotics and other mood stabilizing agents for preschool children with presumptive clinical diagnosis of bipolar disorder or a related variant. Clarifying the nosology of preschool bipolar disorder may also be important to better understand the developmental psychopathology of the disorder during childhood. Data elucidating this developmental trajectory could then inform the design of earlier potentially preventive interventions that may have implications for the disorder across the lifespan.

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