Clinical Characteristics of Bipolar vs. Unipolar Depression in Preschool Children: An Empirical Investigation

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Background: Despite retrospective reports of the onset of childhood bipolar disorder during the preschool period, few studies have investigated whether mania symptoms can be identified in preschoolers. A group of children with a cluster of mania symptoms that showed discriminant validity from other disruptive disorders was identified in a large preschool sample. These empirical data add to descriptive studies of mania in clinical preschool populations. An investigation of the characteristics of depression among putative bipolar preschoolers may inform the controversial nosologic questions that surround the diagnosis in this young age group.

Method: This study, conducted from 2002 to 2007, investigated major depressive disorder (MDD) symptoms and severity in preschoolers with a bipolar syndrome in comparison to those with unipolar MDD, identified by an age-appropriate structured psychiatric interview, the Preschool Age Psychiatric Assessment (based on DSM-IV).

Results: Twenty-one preschoolers were identified who met DSM-IV symptom criteria for bipolar I disorder and MDD and were compared to 54 preschoolers with unipolar MDD. The bipolar depressed preschoolers had significantly higher depression severity ($p < .0001$) and higher rates of comorbidity than did those with unipolar depression. The study is limited by the exploratory nature of clinical mania characteristics in preschoolers as well as reliance on parent reports of these symptoms.

Conclusions: These findings suggest that, similar to adult bipolar patients, preschoolers with a putative bipolar syndrome experience clinically significant and severe depression. Symptom characteristics and comorbidity patterns also distinguished this group from the unipolar depressed preschoolers. Our findings underscore the marked depression that characterizes this putative bipolar syndrome and suggest that further investigation of this domain may clarify the nosology of this early-onset disorder.

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A substantial body of literature validating and describing the clinical characteristics of bipolar disorder in school-aged children and adolescents has become available.[1–4] Despite ongoing high levels of controversy about the specific characteristics or behaviors that should be included in the criteria for diagnosis, there has been some consensus about the manifestations of cardinal symptoms of mania in children. While patterns of cycling remain a major point of controversy,[5] there is some convergence of findings from independent research groups suggesting that the childhood-onset form of the disorder is characterized by very rapid or ultradian cycling patterns also known in a smaller, more treatment-resistant group of bipolar adults.[1–3,6] Findings from the few follow-up longitudinal studies available to date suggest that the childhood-onset disorder has a chronic course with high rates of relapse.[7–9] In addition, retrospective parent reports from several samples of bipolar children and adolescents have suggested that in a substantial proportion of children, their first onset of the disorder occurred during the preschool period.[3,4,8] These findings taken together suggest that childhood bipolar disorder is a severe and likely chronic disorder that may have onset as early as the preschool period of development.

Obtaining data on the longitudinal follow-up of bipolar children as they enter adulthood is critical to determining whether the childhood-onset form is the same disorder as the adult form. However, on the basis of the converging evidence of a clinically severe childhood form of this mood disorder with possible early onset, the identification of childhood bipolar disorders or mania-like syndromes at the earliest possible developmental point is of paramount importance. Early intervention in mental disorders, made possible by early identification, has been demonstrated to be a window of opportunity for more effective treatment in several childhood mental disorders such as autistic

spectrum disorders and disruptive behavioral disorders.[10,11] However, given the greater developmental ambiguities and the absence of age-appropriate diagnostic measures, there has been little investigation to date of the validity and age-adjusted symptom manifestations of mania symptoms in children younger than 6 years of age. One impediment to progress in this area is that many of the cardinal symptoms of mania are thought to be more difficult to distinguish from developmental norms known in early childhood. In addition, the identification of clinical mood cycling is more ambiguous in young children for whom relative mood lability is a developmental norm. Related to these same developmental issues, until recently there have been no available age-appropriate measures designed to assess mania symptoms as they might manifest in preschool-aged children.

An exploratory study of preschool mania was conducted after developing a mania module of the Preschool Age Psychiatric Assessment (PAPA).[12] The PAPA is an age-appropriate interviewer-based psychiatric assessment with established reliability.[13] The mania module was administered to the caregivers of preschoolers from a large sample ascertained from community sites using a screening checklist (see Method section for details of sample recruitment). A subgroup of 26 preschoolers met age-adjusted DSM-IV symptom criteria for bipolar I disorder (duration criteria were set aside). This symptom constellation showed discriminant validity from a disruptive-disordered comparison group composed of preschoolers with DSM-IV attention-deficit/hyperactivity disorder, oppositional defiant disorder, and/or conduct disorder.[14] Preschoolers with this putative bipolar syndrome were previously shown to have very high levels of impairment rated by both parents and teachers.[14] These exploratory but systematic data have suggested that a bipolar syndrome can arise at this early age. Adding to this evidence, reports describing substantial groups of preschoolers with symptoms of mania presenting to clinical settings have also become available.[15–17] In addition, numerous case reports and several retrospective chart reviews have described mania symptoms and syndromes in preschool children.[18–21]

These findings characterizing mania during the preschool period add to the larger and more robust evidence base demonstrating that unipolar major depressive disorder (MDD) can arise in preschoolers.[22,23] Building on extant literature examining high-risk infants of depressed mothers[24,25] and exploratory studies in clinical populations,[26] Luby and colleagues have provided validation for a preschool-onset depressive syndrome on the basis of familial transmission, biological correlates, and observational evidence.[27–30] Despite this body of data validating preschool depression and exploratory findings suggesting that a preschool bipolar syndrome can be identified, to date, the characteristics of depression among preschoolers with a bipolar syndrome have yet to be systematically examined. This issue may be of importance for further clarifying the nosologic questions associated with putative preschool bipolar syndrome, as well as understanding its course. In addition, potential differences in the depressive symptom characteristics and their duration and frequency in bipolar vs. unipolar MDD arising during the preschool period are also of interest and have remained unexplored. To address this gap in the literature, the current study aimed to investigate whether any differences in depressive symptom manifestations and/or their temporal characteristics could be detected in the bipolar group compared to unipolar depressed preschool children. As is well established in bipolar adults, episodes of depression are expected to be an important part of the clinical presentation of bipolar disorder. Therefore, understanding the manifestations of depression, if they arise in preschoolers with a bipolar syndrome, may be important to further elucidate the nosology of preschool-onset bipolar I disorder.

METHOD

Participants and Procedure

Preschoolers between 3 and 6 years of age were recruited from multiple sites throughout the greater metropolitan St. Louis area for participation in a larger ongoing National Institute of Mental Health study examining the nosology of preschool-onset depression. The study was reviewed and approved by the Washington University School of Medicine Institutional Review Board, and consent and assent were obtained from primary caregivers and children accordingly. Recruitment was done through pediatricians' offices, primary care practices, preschools, and day care centers that were accessible to the general community. In an effort to increase the socioeconomic and ethnic diversity of the final sample, specific sites of recruitment were chosen at random using a geographically stratified method similar to random zip code selection methodologies.

To obtain a sample with a large number of children who had symptoms of depression (the primary focus of the study) and disruptive disorders (for comparison), a previously validated screening checklist, the Preschool Feelings Checklist,[31] was completed by caregivers. The aim of this sampling technique was to recruit substantial numbers of depressed and disruptive preschoolers as well as healthy children. Results from previous studies have indicated that the Preschool Feelings Checklist is a useful tool for identifying children at risk for or who have mood and/or disruptive disorders.[32] A cut-off score of ≥ 3 (or a lower score if the symptom of anhedonia was present) has been shown to maintain high sensitivity and specificity for the diagnosis of depression. In addition to identifying and including children with 3 or more symptoms of

MDD and/or disruptive disorders, children with no endorsed symptoms were also recruited to establish an adequate healthy comparison group.

Approximately 6000 checklists were distributed to sites in the St. Louis metropolitan area over a 2-year period between 2003 and 2005. In day care centers and preschool settings (from which approximately 75% of the sample was ascertained), checklists were handed out to all parents of children in the eligible age range. In primary care settings, checklists were also made available in waiting areas next to a recruitment poster describing a study of early emotional development. Completed checklists were collected by sites and returned by mail to the Early Emotional Development Program (EEDP) or were picked up by staff. By use of this method, 1474 checklists were returned to the EEDP, and individuals who met the cut-off scores as described above were contacted for possible participation. Among those who returned checklists, 335 were ineligible due to the children's ages being out of the 3- to 6-year-old range, and 240 had Preschool Feelings Checklist scores out of the inclusion range. The remaining 899 met all initial screening and other inclusion criteria and were contacted by phone for further screening. On the basis of phone screening, subjects with chronic illness, serious speech and language delays, and/or neurologic or autistic spectrum disorders were excluded. Individuals without these exclusions (N = 416) were invited for study participation, and 305 agreed to participate and presented for the assessment.

Measures

The PAPA[12] is an interviewer-based diagnostic assessment with empirically established test-retest reliability designed for use in children aged 2 through 6.[13] This interviewer-based method of assessment, which requires substantial interviewer training, is designed to be more accurate than direct coding of parent report at face value or respondent-based approaches.[33] Research assistants received 4 days of formal group training and subsequently administered audiotaped practice interviews to pilot subjects until proficiency in administration was achieved. These trained interviewers administered the PAPA, in addition to other measures of development and functioning, at baseline to parents (92% biological mothers) of study subjects. All PAPA interviews were audiotaped for later quality control and calibration. Audiotapes were reviewed weekly to maintain rater reliability on symptoms. In addition, 20% of all interviews were reviewed and, if necessary, recoded by a "master coder" in collaboration with the principal investigator/senior child psychiatrist (J.L.L.). This method of establishing reliability was deemed most appropriate for the structure of the interview by the authors of the PAPA. Notably, DSM-IV diagnoses from the PAPA were derived by application of algorithms based on standard DSM-IV criteria; therefore, clinical judgment was not involved in the final designation of diagnosis itself but only in the ratings of specific symptoms at the clinical level.

The PAPA covers a broad range of psychiatric symptoms, impairment resulting from symptoms, family environment and relationships, family psychosocial functioning, and life events. Both traumatic or severe and milder and more typical stressful life events are assessed. For discrete symptom states, the PAPA assesses the intensity of each symptom (i.e., absent, normative/nonclinical, clinically significant, or clinically severe). When symptoms are present, their frequency and duration are obtained (for a portion of symptoms, context of symptom manifestation and clinical onset are also obtained). The PAPA assesses age-appropriate manifestations of all relevant DSM-IV criteria.

Examination of the psychometric properties of the newly developed PAPA mania module indicated both moderate to high α as well as high test-retest reliability coefficients (see Luby and Belden[14] for methods for test-retest study). Test-retest reliability for the expanded MDD module of the PAPA was examined in the current study using the Cohen κ. Intraclass correlation coefficients (ICC) were calculated to examine the reliability of MDD symptom sum scores. Results indicated an acceptable κ for diagnostic reliability over a 7-day period ($\kappa = 0.62$). The current κ closely approximated previous findings examining the reliability of the original MDD module of the PAPA ($\kappa = 0.61$) among the clinically referred preschoolers in a population-based sample.[13] Results examining the reliability of dimensional MDD scores over time indicated a strong correlation (ICC = 0.88). Last, results indicated a valid and coherent symptom structure in the expanded MDD module of the PAPA, with a Cronbach $\alpha = .84$, and at retest, $\alpha = .89$.

Items in both mood modules contain developmentally translated descriptions of depression and mania manifestations. Depression and mania-like manifestations at the normative level are also assessed. For example, for the assessment of grandiosity, the item makes a key distinction between a child with a fixed and false sense of elevation of powers and abilities and a child who has normative fantasy play (and pretends to be superman). Some key items, such as elation, which frequently occur normatively during the preschool period in specific contexts (such as Christmas, vacations, or special visits from loved ones), are defined by context-inappropriateness (as well as excessive frequency and duration). Therefore, a clear distinction between these behaviors at the normative versus clinical level is made in the coding of both mood modules. These modules also examine the intensity, frequency, duration, context, and onset of several MDD and bipolar symptoms. That is, in the current study, when MDD symptoms were endorsed, the frequency of the symptoms during a typical week was also obtained. In

Table 1. Demographic Characteristics of the Sample (N = 278)[a,b]

Characteristic	Healthy (n = 148)	Bipolar MDD (n = 21)	Unipolar MDD (n = 54)	Disruptive (n = 55)	χ^2 p Value
Gender					.37
Male (n = 144)	49 (71)	67 (14)	57 (31)	52 (28)	
Female (n = 131)	51 (75)	33 (7)	43 (23)	48 (26)	
Age, y					.01
3	33 (48)	14 (3)	26 (14)	44 (24)	
4	45 (66)	43 (9)	33 (18)	37 (20)	
5	22 (33)	43 (9)	41 (22)	19 (10)	
Ethnicity (child)					.18
White	59 (86)	52 (11)	50 (27)	44 (24)	
Black	33 (48)	38 (8)	33 (18)	33 (18)	
Other	8 (12)	10 (2)	17 (9)	22 (12)	
Education (parents)					.08
Some high school	8 (11)	5 (1)	7 (4)	13 (7)	
High school diploma	8 (12)	29 (6)	11 (6)	9 (5)	
Some college, or 2-year degree	31 (45)	48 (10)	46 (25)	43 (23)	
Highest level, 4-year degree	26 (38)	10 (2)	17 (9)	19 (10)	
Greater than 4-year degree	8 (11)	0 (0)	2 (1)	2 (1)	
Professional or graduate degree	20 (30)	10 (2)	17 (9)	15 (8)	
Marital status (parents)					.11
Married	66 (94)	30 (6)	49 (26)	57 (31)	
Separated	1 (2)	0 (0)	6 (3)	2 (1)	
Divorced	4 (6)	15 (3)	9 (5)	7 (4)	
Widowed	1 (1)	0 (0)	0 (0)	0 (0)	
Never married	28 (39)	55 (11)	36 (19)	33 (18)	
Income (parents), $					.47
0–20,000	23 (31)	43 (9)	30 (14)	31 (16)	
20,001–40,000	16 (22)	19 (4)	26 (12)	20 (10)	
40,001–60,000	15 (21)	14 (3)	11 (5)	14 (7)	
60,001+	46 (62)	24 (5)	34 (16)	35 (18)	

[a]All data are given as % (n).
[b]Numbers not totaling the subsample size are due to missing data.
Abbreviation: MDD = major depressive disorder.

addition, when depressive symptoms were endorsed, information about the average duration of each endorsed symptom during typical expressions was obtained.

Duration was set aside for mood modules because of the current ambiguity of episode durations of mood disorders in young children.[6,27] Depression sum scores, a dimensional measure of depression previously shown to be a valid and useful marker of depression severity and related subtypes, were derived by summing all PAPA depression symptoms endorsed at the clinical level. For the purpose of the subsequent analyses, preschoolers who fell into 1 of 4 diagnostic groups were included: bipolar MDD, n = 21; unipolar MDD, n = 54; DSM-IV "disruptive" (which included attention-deficit/hyperactivity disorder, oppositional defiant disorder, and/or conduct disorder), n = 55; and "healthy" (those who did not meet criteria for any DSM-IV Axis I disorder), n = 148. Of the total 26 bipolar preschoolers in the whole sample, 21 (81%) were in a mixed state, whereas 5 (19%) were in a manic-only state at the time of assessment and were therefore excluded from the analyses that follow.

Statistical Analyses

χ^2 analyses were conducted to determine whether the composition of the diagnostic groups differed in relation to socioeconomic status, gender, age, and several other categorical demographic variables. Next, a univariate analysis of variance was conducted to test for a main effect of diagnostic group status on preschoolers' depression severity scores. Post hoc tests using Bonferroni correction techniques were used to test all between-group pairwise comparisons in relation to preschoolers' depression severity scores.

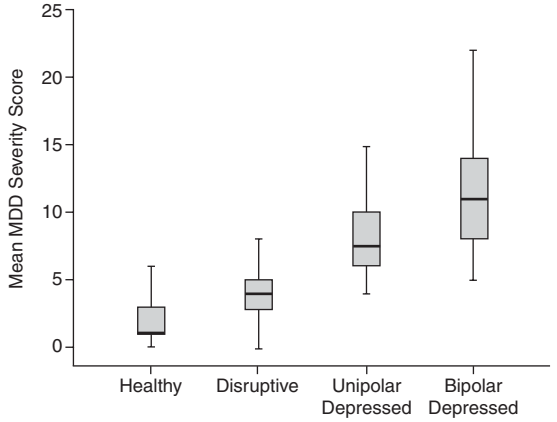
To test for the likelihood that a greater proportion of unipolar vs. bipolar preschoolers would have co-occurring Axis I psychiatric disorders, odds ratios were calculated for all additional DSM-IV Axis I diagnoses in the analyses. χ^2 analyses were conducted to determine whether the proportion of preschoolers who endorsed core DSM-IV MDD symptoms differed significantly in relation to their diagnostic group classification. Mann-Whitney U tests (i.e., the parametric equivalent of a t test) were conducted to test for diagnostic group differences in relation to the number of times children expressed MDD symptoms over a 6-month period. The same nonparametric statistical techniques were conducted to test for diagnostic group differences in relation to the total length of time (on average) preschoolers express specific MDD symptoms. Nonparametric analyses were conducted instead of more commonly used parametric analyses (i.e., t tests) because of the violation of several assumptions required for conducting parametric tests (e.g., the assumption of normal distribution).

RESULTS

As seen in Table 1, χ^2 analyses indicated a significant difference in the proportion of 3-, 4-, and 5-year-old children within each diagnostic group. That is, a significantly greater proportion of 4- and 5-year-olds were found in the depressed group than in the healthy and disruptive groups. In addition, the disruptive group had a significantly greater proportion of 3-year-olds than did the healthy and depressed groups. No other significant group differences were found in relation to demographic variables and diagnostic group distribution (see Table 1).

Before testing the proposed hypotheses for the current study, we explored the possibility that different outcomes between diagnostic groups could be influenced by the types and frequencies of deleterious environmental events often experienced by children with varying types of early-onset psychopathology. Examples of adverse environmental outcomes include caregiving neglect and/or abuse as well as psychosocial stressors and trauma. Although these constructs were measured and data is available for the current study, addressing these issues in detail was deemed to be beyond the scope of this article. However,

Figure 1. Depression Severity by Diagnostic Group (N = 278)[a]



[a]The boxes represent severity scores from the 25th to 75th percentile for each group. The black line that splits each box represents the median score for that group. The vertical line extending above the box represents scores from the 75th percentile up to the maximum value for that group. The vertical line below the box represents scores from the 25th percentile down to the minimum score for that group.
Abbreviation: MDD = major depressive disorder.

for the purpose of this report, we tested whether preschoolers in the putative bipolar group experienced significantly more types of these adversities and/or experienced life stressors more frequently than did preschoolers in each of the comparison groups. One-way analysis of variance tests followed by Scheffé post hoc tests were conducted to determine whether there were diagnostic group differences in relation to preschoolers' experiences of stressful life events. Results indicated no significant diagnostic group differences in relation to the total proportion of stressful life events experienced by preschoolers (28 total stressors were possible). In addition, analyses revealed no significant diagnostic group differences in association with the frequency at which children encountered specific life stressors. That is, preschoolers in diagnostic groups versus the healthy group, in general, did not experience more types of life stressors or experience specific life stressors more frequently in the years prior to participating in the current study.

Comparing Depression Severity in Unipolar and Bipolar Depression

Findings from a univariate analysis of variance indicated a significant main effect of diagnostic group on preschoolers' MDD severity scores ($F = 167.39$, $df = 3,274$; $p < .001$). Post hoc analyses (using Bonferroni corrections) revealed that each of the 4 diagnostic groups differed significantly from each other in a hierarchical fashion (Figure 1). Bipolar depressed preschoolers had significantly higher depression severity scores (mean = 11.14, SD = 4.27; $p < .0001$ for each of the pairwise comparisons) than did preschoolers in the unipolar depressed (mean = 7.93, SD = 2.86), disruptive (mean = 3.82, SD = 1.98), and healthy (mean = 1.81, SD = 1.68) groups. Depressed preschoolers had significantly ($p < .0001$) higher depression severity scores than did preschoolers in the disruptive and healthy groups. Last, preschoolers in the disruptive group had significantly ($p < .0001$) higher depression severity scores than did children in the healthy group.

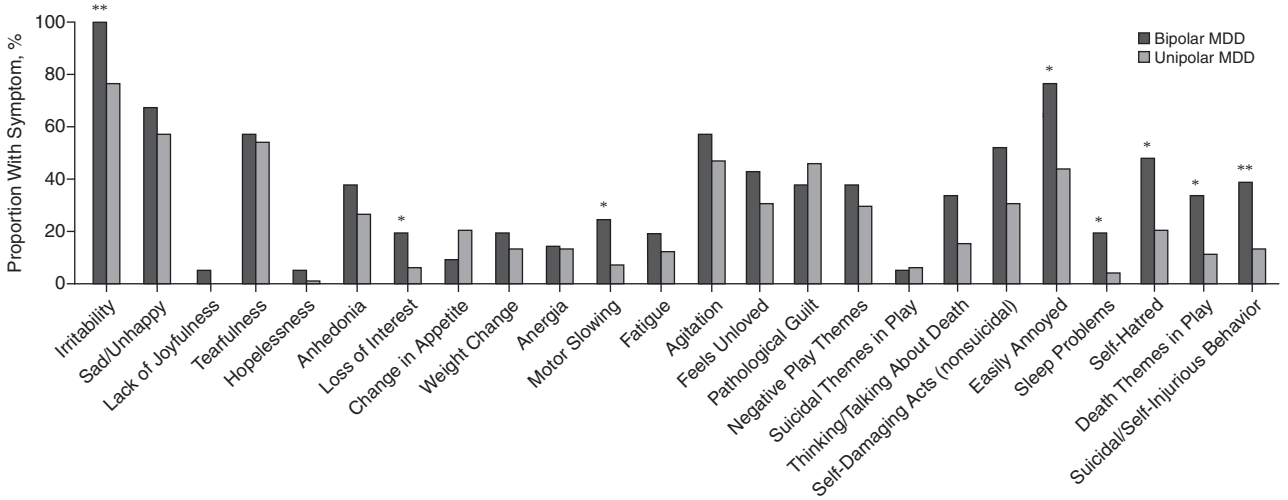
Comorbidity in Unipolar vs. Bipolar Depressed Preschoolers

Odds ratios were used to test the likelihood of unipolar vs. bipolar depressed preschoolers' having comorbid disorders. Results indicated that bipolar depressed preschoolers were significantly more likely to have attention-deficit/hyperactivity disorder (OR = 13.06, 95% CI = 3.38 to 50.40, $p < .001$), oppositional defiant disorder (OR = 4.65, 95% CI = 1.49 to 14.58, $p < .01$), conduct disorder (OR = 54.40, 95% CI = 11.69 to 253.14, $p < .001$), and/or anxiety disorders (OR = 7.60, 95% CI = 2.38 to 24.28, $p < .001$) than did preschoolers with unipolar depression.

DSM-IV MDD Symptoms in Unipolar vs. Bipolar Depressed Preschoolers

χ^2 analyses were conducted to examine whether having unipolar vs. bipolar depression increased the proportion of preschoolers who exhibited 1 or more specific DSM-IV MDD symptoms (Figure 2). Results indicated that although the endorsement of the symptom of irritability was very high in both groups, preschoolers with putative bipolar depression were significantly more likely to exhibit irritability (100% of subjects in the bipolar MDD group displayed this symptom) compared to unipolar MDD preschoolers (76% displayed this symptom) ($\chi^2 = 6.12$, $df = 1$, $p < .01$). χ^2 analyses were also conducted to examine whether the proportion of preschoolers diagnosed with unipolar MDD versus those with bipolar MDD differed significantly in relation to their irritability intensity ratings (i.e., 0 = never irritable, 1 = normative transient irritability, 2 = irritability in at least 2 activities, 3 = irritable mood present in most activities). The overall χ^2 was significant ($\chi^2 = 7.20$, $df = 2$, $p < .05$). Follow-up analyses indicated that 24% (n = 13) of unipolar MDD preschoolers routinely experienced normative and/or transient episodes of irritability compared to preschoolers with bipolar MDD, who never displayed normative and/or transient episodes of irritability. Therefore, 100% of preschoolers (n = 21) with bipolar MDD were reported to consistently manifest irritability at clinically significant levels (i.e., at a rating of 2 or higher). It is important to note that the irritability symptom is measured only once and is contained in the PAPA MDD module. Thus, the irritability symptom from the

Figure 2. DSM-IV Depression Symptoms in Bipolar vs. Unipolar Depressed Preschoolers (n = 75)



*p < .05, **p < .01.
Abbreviation: MDD = major depressive disorder.

MDD module is also used when conducting the bipolar algorithms.

Bipolar depressed preschoolers were significantly more likely to have experienced a loss of interest in activities and play they previously had enjoyed (χ^2 = 3.25, df = 1, p < .05) and to be touchy or easily annoyed (χ^2 = 6.49, df = 1, p < .05) than were preschoolers with unipolar depression. Results indicated that a significantly greater proportion of bipolar preschoolers experienced sleep problems compared to same-age peers with unipolar depression (χ^2 = 4.84, df = 1, p < .05). Bipolar preschoolers were significantly more likely to experience motor slowing compared to unipolar depressed preschoolers (χ^2 = 3.85, df = 1, p < .05). Preschoolers in the bipolar depressed group were also significantly more likely to express self-deprecation or self-hatred (48% displayed this symptom) compared to unipolar depressed preschoolers (21% displayed this symptom) (χ^2 = 5.34, df = 1, p < .05). Finally, putative bipolar depressed preschoolers were significantly more likely than unipolar depressed preschoolers to include death themes in their play (χ^2 = 5.21, df = 1, p < .05) and engage in suicidal or self-injurious behaviors (χ^2 = 5.97, df = 1, p < .01). There were no significant differences between groups in any of the other symptoms assessed in the depression module of the PAPA (see Figure 2).

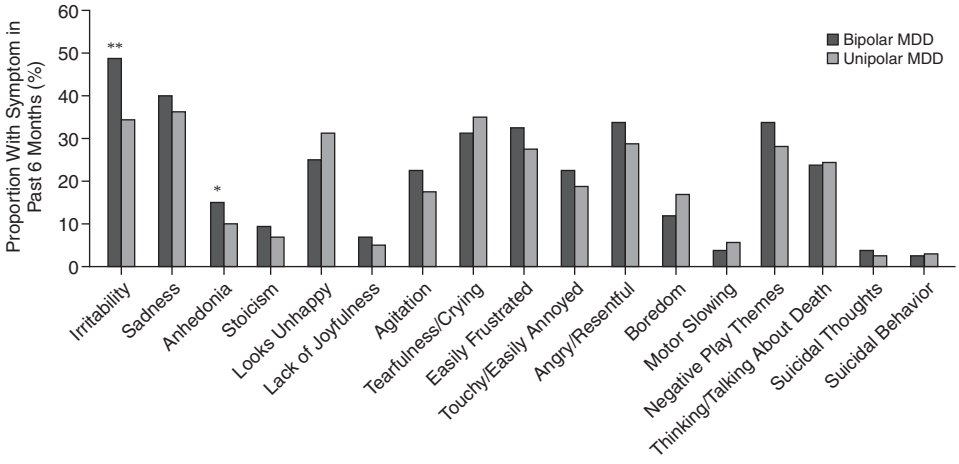
Frequencies of Depressive Symptoms in Unipolar vs. Bipolar Depressed Preschoolers

Mann-Whitney U tests, which are the nonparametric equivalent of t tests, were conducted to test for diagnostic group differences (unipolar vs. bipolar depressed preschoolers) in relation to the frequencies with which MDD symptoms occurred at clinically significant levels. As illustrated in Figure 3, bipolar MDD preschoolers expressed irritability significantly more frequently than did unipolar MDD children over the course of a 6-month period (Z = –2.59, p < .01). Bipolar MDD preschoolers also displayed anhedonia significantly more often than did unipolar MDD preschoolers during a 6-month period (Z = –1.76, p < .05). No other significant differences between diagnostic group and MDD symptom frequencies were found.

Duration of Depressive Symptoms in Unipolar vs. Bipolar Depressed Preschoolers

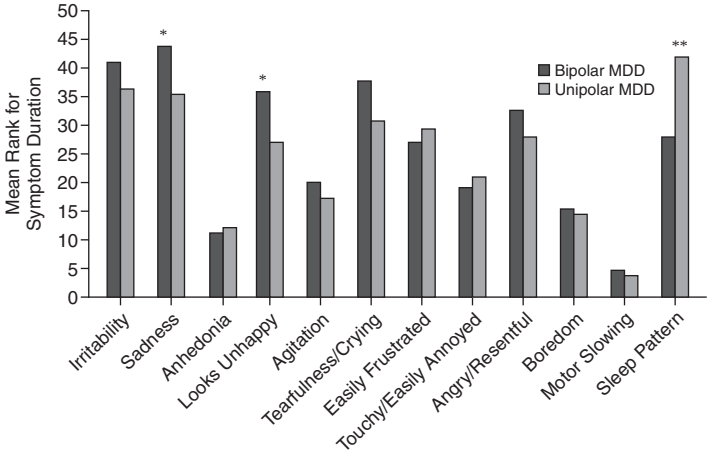
Similar to the previous analyses, Mann-Whitney U tests were conducted to examine differences between unipolar and bipolar depressed preschoolers in relation to the duration of MDD symptoms when they occurred. Results indicated that although there was no significant difference between the frequency at which bipolar and unipolar depressed preschoolers expressed sadness, when bipolar depressed preschoolers did express sadness, these episodes lasted for significantly longer periods of time in comparison with unipolar depressed children (Figure 4) (Z = –1.68, p < .05). More specifically, bipolar depressed preschoolers, on average, expressed sadness (at a clinical level) for 4 hours, whereas unipolar depressed preschoolers were reported to exhibit sadness, on average, for 26 minutes. Consistent with the previous findings, preschoolers with bipolar vs. unipolar MDD expressed the symptom of looking unhappy for significantly longer periods of time, on average (Z = –1.73, p < .05). Last, unipolar depressed preschoolers reportedly slept for significantly longer durations (mean = 10 hours, 15 minutes; SD = 1 hour, 47 minutes) compared to bipolar depressed preschoolers (mean = 9 hours, 5 minutes; SD = 1 hour, 41

Figure 3. MDD Symptom Frequencies in the Past 6 Months in Bipolar vs. Unipolar Depressed Preschoolers



*p < .05, **p < .01.
Abbreviation: MDD = major depressive disorder.

Figure 4. Duration of Depression Symptoms in the Past 6 Months in Bipolar vs. Unipolar Depressed Preschoolers



*p < .05, **p < .01.
Abbreviation: MDD = major depressive disorder.

minutes) ($Z = -2.50$, $p < .01$). There were no significant differences in the duration of unipolar vs. bipolar preschoolers' episodes of irritability.

Psychosis

Given their extreme rarity in preschool-aged children, psychotic symptoms such as hallucinations are not assessed by the PAPA. However, the mania module does assess grandiosity at the delusional level. Forty-eight percent of bipolar MDD preschoolers (10 of 21) received the highest possible rating for the grandiosity symptom. That is, almost half of the bipolar MDD group were described by caregivers as having a fixed, false, inflated self-appraisal and grandiose fantasies that they reportedly had acted on regularly (e.g., jumping off dangerously high objects because they think they "really" can fly). No preschoolers in the healthy group received this rating, and fewer than 4% of unipolar and disruptive preschoolers had grandiosity endorsed by their caregivers at this severity level.

DISCUSSION

These findings suggest that preschoolers with a putative bipolar syndrome, similar to older bipolar children and adults, also experience clinically significant and se-

vere episodes of depression. Highly notable was that the clinical characteristics of depression in the bipolar group were significantly more severe and associated with poorer prognostic indicators than in the unipolar depressed group. While this finding does not confer the validity of preschool bipolar disorder, it does suggest that preschoolers with a cluster of mania symptoms also display significant depression, underscoring further that mood disturbance is a central part of this clinical syndrome. Further, the finding that high levels of depression were not found in preschoolers with attention-deficit/hyperactivity disorder, oppositional defiant disorder, or conduct disorder suggests that depressed mood is not merely secondary to disruptive symptoms. Therefore, findings lend further support to the notion that this preschool bipolar syndrome is indeed on the mood disorder spectrum rather than a disruptive variant. In addition, the finding that preschoolers with this bipolar syndrome did not experience greater trauma or adverse life events than other groups is also of importance. While this again does not confirm that the syndrome is a bipolar disorder, it does suggest that it cannot be explained by developmental deviation secondary to trauma, as has been widely speculated. However, longitudinal follow-up data will be needed to more definitively clarify this nosologic issue.

A pattern of comorbidity that distinguished putative bipolar from unipolar depressed preschoolers was also found. This pattern of comorbidity was similar to that described in older bipolar children.[1,3] This similarity in comorbidity may suggest continuity between the preschool-aged and school-aged syndromes. However, others have argued that these high levels of comorbidity associated with childhood bipolar disorder may signal a lack of specificity of these symptoms.[34] While the less differentiated nature of psychopathology in early childhood has been described, the finding of a specific bipolar syndrome that displays discriminant validity from other disruptive disorders suggests that this mania-like symptom constellation is not general and nonspecific but instead is a specific and differentiated mood disorder.

The extant literature offers surprisingly little information on the distinction between bipolar and unipolar depression in school-aged children and adolescents. However, at least 1 investigation has shown that bipolar depression among school-aged children who also had attention-deficit/hyperactivity disorder appeared to be more severe overall and associated with higher rates of hospitalization in comparison with unipolar peers.[35] An increased likelihood of comorbid conduct disorder and anxiety disorders has also been described in the same sample of bipolar children and was postulated as a possible contributor to the more severe clinical picture overall.[36] These findings demonstrating very high rates of depression severity and a pattern of serious comorbid disorders among preschoolers with a bipolar-like syndrome, consistent with what has been reported in older bipolar children, point to the need for further investigation of this currently understudied clinical syndrome.

Also of interest was the finding that the clinical characteristics of depression associated with the bipolar-like syndrome differed from unipolar depression in several key domains (i.e., type of symptoms, frequency, and duration). The symptoms of irritability and being easily annoyed were found more frequently in the bipolar-like group in comparison with unipolar depressed preschoolers, although they occurred at high rates in both groups as would be expected. It was notable that bipolar depressed preschoolers displayed more intense irritability than did those in the unipolar group, similar to findings in older bipolar children.[37] In addition, other symptoms often associated with high depression severity in older children and adults, including sleep problems, motor slowing, preoccupation with death (evident in play themes), and suicidality or self-injurious behaviors, were also found more frequently in the putative bipolar vs. unipolar depressed preschoolers. A similar constellation of severe and neurovegetative depressive symptoms has been reported in adult bipolar depression in several studies comparing unipolar and bipolar depressed adults.[35,38,39] This pattern of clinical characteristics further suggests similarities between the bipolar syndrome identified in this preschool group and the disorder arising in older children and adults.

Further, even when the intensity of specific depressive symptoms did not differ between groups, the frequency and duration with which several key DSM-IV MDD symptoms occurred did differ between groups. Depression within the bipolar-like group was characterized by significantly higher frequencies of irritability and anhedonia than those found in the unipolar depressed group. Notably, high rates of anger and irritability have also been reported in some studies of bipolar depression in adults.[39,40] These findings, demonstrating a more severe and agitated form of depression in preschoolers with a bipolar-like syndrome disorder, are also similar to findings in bipolar adults from large multicenter trials.[41] Interestingly, the duration of sadness episodes was significantly longer among the bipolar-like group in comparison to unipolar depressed preschoolers. This finding would be consistent with the phenomenon of mixed manic states in which depression and mania manifest simultaneously and over a longer period, similar to those described in older bipolar child samples.[1] The finding that unipolar depression was characterized by longer sleep durations was not surprising given that hypersomnolence is well known in adult unipolar depression, as well as the fact that decreased need for sleep is a core symptom of mania across the age span. The findings of these temporal differences provide further support for the hypothesis that an important clinical distinction can be made between the bipolar-

like and unipolar depressed groups even as early as the preschool-aged period.

Findings demonstrate that a unique clinical syndrome characterized by emotion dysregulation with mood disturbances similar to those found in older subjects with a bipolar disorder can be identified. The interpretation that this symptom constellation represents a severe mood dysregulation variant that is genetically and biologically distinct from classic bipolar disorder in adults cannot be ruled out. Longitudinal follow-up studies as well as investigations of neurobiological and genetic markers are needed to further clarify whether this early-onset bipolar syndrome is the same disorder as that identified in older children and adults. However, the distinctive clinical features demonstrated in this investigation that bear similarity to those described in older bipolar children in numerous domains, suggesting the possibility that an early preschool form of bipolar disorder can arise, is worthy of further investigation.

An important limitation of the current study is that early-onset depression, characterized in this article as "unipolar" depression, is an established precursor to later-onset bipolar disorder.[42] Therefore, as the study sample is followed longitudinally, some subjects currently classified as unipolar are likely to switch to display a bipolar diathesis. Findings should be interpreted with this possible change in diagnostic status in mind. Ongoing longitudinal follow-up diagnostic assessments in the study sample, currently underway, will provide greater clarity to these distinctions. Study findings are also limited by small sample sizes within diagnostic groups and by ascertainment from a single geographic site (St. Louis metropolitan area). Findings are also limited by sole reliance on parent report of symptom states, frequencies, and durations. Notably, and particularly important in a preschool sample, observations of the child and assessment of child behavior across contexts is critical to establish clinical diagnoses. Study findings should be replicated in larger and independent samples before clear clinical application of the data can be made.

CONCLUSIONS

Findings point to the importance of the assessment of depressive symptoms in young children presenting with mania-like symptoms and emotion dysregulation. There is a high risk that depressive symptoms would be missed in this clinical group given the greater salience and disruptive quality of the co-occurring mania-like symptoms that are likely to overshadow the more subtle internalizing symptoms of depression when present. Findings suggest that investigators as well as clinicians should be attentive to underlying depressive symptoms when assessing preschoolers who present with these symptoms. Given the high depression severity detected, study findings also suggest that depression should become a primary focus of future investigations of this bipolar syndrome.

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