Sex Differences in Pediatric Bipolar Disorder

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Objective: To explore sex differences in pediatric bipolar disorder in terms of subtype and severity of depressive and manic symptomatology.

Method: Participants were 760 youth (aged 5–17 years) and their legal guardians. Participants were part of a larger outpatient assessment protocol enriched for bipolar disorder. Youth were assessed for DSM-IV diagnoses using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version. Their presenting mood state was determined using the Young Mania Rating Scale and the Children's Depression Rating Scale-Revised. The study was conducted from January 1996 to February 2003.

Results: 387 youth (51%) met DSM-IV criteria for diagnoses of bipolar spectrum disorders. Results showed no sex differences in rates of bipolar spectrum disorders or any of the bipolar subtypes. Sex differences were found with regard to presenting mood states: boys presented with higher rates of manic mood, and girls presented with higher rates of depressed mood. Older children were also more likely than younger children to exhibit higher levels of depressed mood. There were no age differences in levels of manic mood.

Conclusion: This study highlights how bipolar disorder can manifest itself differently among girls and boys despite equivalent rates of diagnosis. It is important for clinicians to consider the full range of mood states in order to accurately diagnose and treat children. Future research is needed to assess the roles that genetics, puberty, cognitive styles, and environmental factors play in the expression of mania and depression in girls and boys over the course of their development.

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Exploring sex differences in the rates and presentation of mental disorders is an important line of research for phenomenological and clinical purposes. A substantial amount of research regarding sex differences in adults with bipolar disorder has been conducted.[1,2] In contrast, there has been less research examining sex differences in pediatric bipolar disorder. As a diagnostic entity, pediatric bipolar disorder can gain additional validity if research shows a similar pattern of sex differences among youth and adults with the disorder. Conversely, if sex differences observed among youth with bipolar disorder are markedly different from those observed among adults, then hypotheses regarding developmental processes and diagnostic dissimilarities of the adult and child subtypes may be formulated. The goal of this article is to explore these issues.

Given that a number of studies have validated pediatric bipolar disorder as a variant of the adult form,[3–8] hypotheses regarding sex differences can be derived from research on adult populations. The adult literature has elucidated sex differences in rates of diagnosis (i.e., bipolar I, bipolar II, and cyclothymia) and mood states (i.e., manic, depressed, and mixed). Epidemiologic studies suggest that the lifetime prevalence of bipolar I disorder is equivalent among men and women[9,10] and ranges from 0.7% to 1.6% in American samples.[11] This finding has been replicated in smaller samples[1,12] and cross-culturally.[13] In contrast, much of the adult literature on bipolar II disorder

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has suggested that it is more common in adult females than males.[14–17] This discrepancy may be explained by higher rates of depression among females[18] and their decreased likelihood of exhibiting purely manic episodes.[19] Sex differences in bipolar II disorder among youth may be more difficult to detect because of small sample sizes and because the diagnosis may be less developmentally stable than what is observed in adult samples.[20]

There is a paucity of literature on sex differences in cyclothymia and bipolar disorder not otherwise specified (NOS). The DSM-IV suggests that cyclothymia occurs at similar rates in adult males and females.[21] However, within a nonclinical population, Erfurth and colleagues[22] found women to be more likely to exhibit a cyclothymic temperament than men. This latter finding could be due to a number of reasons. Men and women may be socialized differently in terms of reporting on their emotions. For instance, Kilmartin[23] speculates that men are less likely to report depression because they are socialized to avoid introspection. Similarly, in Erfurth and colleagues' study, more women may have been identified with a cyclothymic temperament because they are more open to reporting their mood fluctuations. Evidence in support of a true sex difference in cyclothymia may be extrapolated from findings showing that women with bipolar disorder are more likely to exhibit mixed and rapid-cycling presentations[24]; these presentations may represent a more severe form of the mood lability observed in individuals with cyclothymia. Overall, the data regarding sex differences in cyclothymia are minimal and inconclusive.

The literature on sex differences in adults with bipolar disorder NOS is equally scarce. Because children rarely present with the classic, episodic pattern described in the DSM-IV, bipolar disorder NOS is a more relevant and rigorously explored research topic among pediatric samples. The recent reanalysis of the Epidemiologic Catchment Area data provides some insight into bipolar disorder NOS among adults.[25] This study explored the prevalence of subsyndromal bipolar disorder, which the authors defined as the experience of 2 or more lifetime manic symptoms. Approximately 5% of the 18,252 adults surveyed fell within this category, and the rates of males and females with subsyndromal bipolar disorder were roughly equivalent (respectively, 48% and 52%). Unlike studies conducted with pediatric bipolar samples (e.g., Birmaher et al.[26]), Judd and Akiskal's[25] study did not require subsyndromal participants to meet the elated or irritability criteria outlined by the DSM-IV.[21] Thus, it is difficult to draw conclusions regarding sex differences in pediatric bipolar disorder NOS from adult samples due to the lack of shared diagnostic requirements.

Additionally, the bipolar disorder NOS requirements across pediatric research groups often differ. For example, some research groups have implicitly created their own bipolar disorder NOS categories by waiving the durational criteria[5,27] or by altering the DSM requirements and only enrolling children who exhibit "cardinal" symptoms, such as grandiosity.[4,28] The present study defines bipolar disorder NOS in strict accordance with DSM-IV criteria. Accordingly, the bipolar NOS diagnosis was reserved for youth exhibiting bipolar symptoms not meeting sufficient durational and/or severity criteria for a specific bipolar diagnosis.

Considering that bipolar disorder is a complex and fluctuating mental illness, this study also explored sex differences in presenting mood states. Among adults with bipolar I disorder, there is evidence that males may be more likely to experience manic symptoms and episodes than females.[1,29–31] Data from the National Comorbidity Study found that males were more likely to experience unipolar mania than females.[12] Some studies (e.g., Kubacki[32]) also suggest that men may have an earlier age at onset of mania and bipolar disorder than women. Among youth with bipolar disorder, symptoms of mania are typically the most disruptive, obvious, and concerning to parents, teachers, and clinicians. Research has also shown that children who exhibit manic symptoms, regardless of their formal diagnosis, are typically more impaired.[33,34] Given that pediatric samples typically identify more boys than girls with bipolar spectrum disorder, there is reason to hypothesize that manic mood states are more common in boys. However, it should be noted that referral biases and the tendency for boys to exhibit externalizing behavior consistent with manic/hypomanic or mixed states, such as attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and conduct disorder (CD), in general, may lead to an underidentification of girls with the disorder.

In contrast to manic mood states, depressive states among adults and youth, particularly adolescents, are thought to be more common among females. Within the more dated literature, adult females with bipolar disorder have been more likely to exhibit depression than males.[12,29–31,35] More recent studies have shown less of a sex difference in depression among adults with bipolar disorder.[2,15,36,37] Better detection and decreased stigmatization of depression among men may account for this latter finding. The depressive phase of the illness among youth is less established and studied given that they typically present with manic or mixed symptomatology. It is also possible that studies of unipolar depression in youth may include children who eventually exhibit manic or hypomanic symptoms, thus moving them into a bipolar diagnosis (see, for example, Lewinsohn et al.[5]). Based on the existing research in unipolar depression, there is a strong basis for hypothesizing that depressive symptomatology is more common among girls with bipolar disorder, particularly adolescents.[38,39]

Although the research on adult sex differences in hypomanic mood states is scarce, there is some epidemiologic

Table 1. Demographic Characteristics of Sample (N = 760)[a]

Characteristic	Value
Age, mean (SD), y	11.4 (3.4)
Sex, N (%) male	469 (62)
Ethnicity, N (%)	
Hispanic or Latino	25 (3)
Not Hispanic or Latino	735 (97)
Race, N (%)	
White	602 (79)
Black or African American	108 (14)
Other[b]	50 (7)

[a]There was a nonsignificant effect of sex by race ($\chi^2 = 0.78$, df = 2, N = 760, p = .68) and ethnicity ($\chi^2 = 0.03$, df = 1, N = 760, p = .86). Females were significantly older than males by about 1 year (t = –3.81, p < .0005).
[b]American Indian or Alaskan Native (N = 2), Asian or Pacific Islander (N = 3), biracial (N = 21), and participants who did not identify their race (N = 24).

evidence suggesting that adult males and females exhibit equivalent rates of DSM-IV hypomania.[11] Substantially less research exists regarding hypomania among children. Given that transient periods of developmentally appropriate elated mood are not considered pathologic, it is difficult to identify youth who exhibit hypomania in the absence of larger clinical concerns. Thus, the present study will be more exploratory than hypothesis-driven regarding sex differences in hypomanic mood states.

As previously mentioned, adult females have been found to be at a greater risk of experiencing mixed episodes than males.[1,40,41] Among youth, mixed presentations tend to be the rule rather than the exception.[42–44] Thus, one might conclude that because there are higher rates of boys identified in pediatric bipolar samples, there may be a preponderance of mixed mood states among boys. Dilsaver et al.[45] found that boys were more likely to exhibit mixed episodes. However, consistent with the adult literature,[46] the girls that did present with mixed episodes were more impaired than boys with mixed episodes. In contrast to Dilsaver and colleagues' findings, Geller et al.[28] found no sex differences in rates of children presenting with mixed mood states. The conflicting findings between and within the adult and child literatures warrant tentative hypotheses regarding pediatric sex differences in mixed mood states.

The aim of the present study was to explore sex differences in bipolar diagnoses and presenting mood states among a diagnostically diverse sample enriched for bipolar disorder. On the basis of the above review of the adult and child literature, the authors hypothesized the following about bipolar diagnoses: (1) no sex differences will be found in the overall rate of bipolar spectrum disorders; (2) more females will be identified with bipolar II disorder; and (3) sex differences among other disorders (e.g., unipolar depression, ADHD, ODD, and CD) will replicate established findings such that females will be more likely identified with unipolar depression, and boys will be overrepresented in the latter 3 diagnostic groups. With regard to presenting mood states, the authors hypothesized the following: (4) males will be overrepresented in the manic mood state category, and males on the bipolar spectrum will have higher total scores on the Young Mania Rating Scale (YMRS) than females on the bipolar spectrum; (5) females will be more likely to present with depressed and mixed mood states, and females on the bipolar spectrum will have higher total scores on the Children's Depression Rating Scale-Revised (CDRS-R) than males on the bipolar spectrum; and (6) there will be no observable sex differences in euthymic or hypomanic mood states, neither of which results in higher rates of referral for mental health services.

METHOD

Participants

The Institutional Review Board of University Hospitals Case Medical Center approved all procedures used in this study. Participants were 760 youths (62% male, 79% white) aged 5 to 17 years (mean = 11.4, SD = 3.4) and their legal guardians. Table 1 provides detailed information about age, racial, and sex distributions. There were no significant sex differences in the racial ($\chi^2 = 0.78$, df = 2, N = 760, p = .68) or ethnic ($\chi^2 = 0.03$, df = 1, N = 760, p = .86) composition of the sample. Females were significantly older than males by about 1 year (t = –3.81, p < .0005).

The study took place in an outpatient academic medical center conducting several treatment trials, most of which were pharmacologic. These trials included patients with bipolar disorder as well as youths suffering from other conditions. The sample was enriched by referrals of children whose parents were diagnosed with bipolar disorder and participating in treatment or research at an affiliated adult mood disorders clinic. Participants were also recruited via flyers and word of mouth. Families interested in participating in treatment studies were asked to complete a baseline diagnostic assessment. The information gathered from these assessments served as the data for the present study. The study was conducted from January 1996 to February 2003.

Measures

Schedule for Affective Disorders and Schizophrenia for School-Age Children. All participants and their families were administered either the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version (K-SADS-E)[47] or the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL).[48] The K-SADS-E was initially employed for approximately 17% of the sample. The K-SADS-PL was

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utilized for the remainder of the sample in order to make the visits less time-intensive for participants. Both versions of the K-SADS are semistructured diagnostic interviews designed to assess the presence or absence of previous or current psychiatric symptomatology.

Highly trained research assistants (N = 17) administered the K-SADS. Their qualifications ranged from bachelor's degrees to doctorate-level degrees. To be considered a reliable K-SADS rater, assistants needed to achieve an overall κ greater than or equal to 0.85 at the symptom severity level on 10 interviews, 5 of which they observed and 5 of which they administered. They also needed to achieve a κ of 1.0 regarding the presence or absence of diagnoses. Interrater reliability was maintained ($\kappa \geq 0.85$) by having joint assessments at approximately every tenth interview. The K-SADS was administered separately to youth and guardian(s) by the same research assistant. The research assistant used both sources of information to derive a summary score that best captured the clinical presentation of the youth. More than half the participants were independently diagnosed by a child and adolescent psychiatrist who agreed with the research assistants' diagnoses on more than 95% of the cases.

Young Mania Rating Scale. The YMRS[49] is a clinician-rated, 11-item measure that assesses the severity of manic symptoms. The item scores range from 0 to 4, with the exception of irritability, speech (rate and amount), content, and disruptive-aggressive behavior, which are given twice the weight (0 to 8). The YMRS yields a total score ranging from 0 to 60. Higher scores represent greater psychopathology. Research on using the YMRS with child and adolescent populations has found good test-retest and interrater reliability,[50] convergent validity with another measure of mania (r = .83),[51] good discriminative validity between bipolar disorder and ADHD,[52] and a strong single factor structure.[53] The internal consistency of the YMRS was excellent in the present study (α = .91). Ratings were based on the presence of symptoms over the past 2 weeks as assessed by direct interviews with the guardian and youth.

Children's Depression Rating Scale-Revised. The CDRS-R[54] is a clinician-rated, 17-item measure that assesses the presence and severity of depression. The CDRS-R yields a total score ranging from 17 to 113. Higher scores indicate more severe depression. Poznanski et al.[54] suggest that a score of 40 is a strong indicator for the presence of major depressive disorder. The CDRS-R has been used in inpatient, outpatient, and research settings, demonstrating adequate test-retest and interrater reliability[55] and good convergent validity.[56] For the present study, the internal consistency of the CDRS-R was excellent (α = .93). Ratings were based on the presence of symptoms over the past 2 weeks as assessed by direct interviews with the guardian and youth.

Procedure

Diagnostic criteria for determining diagnoses. Diagnoses of bipolar spectrum disorders (i.e., bipolar I, II, and NOS and cyclothymia) were made in strict accordance with diagnostic criteria published in the DSM-IV.[21] Failure to meet DSM-IV strict durational criteria of 7 days for a manic episode or 4 days for a hypomanic episode was the most common reason for diagnosing bipolar disorder NOS. DSM-IV criteria were also used to diagnose other disorders.

Statistical analyses. Analyses were performed using the Statistical Package for the Social Sciences for Windows (SPSS, version 13.0; SPSS, Inc.; Chicago, Ill.; 2004). The α level for statistical significance was set at $p < .05$.

Chi-square analyses tested sex differences in K-SADS diagnosis and presenting mood state on the YMRS and CDRS-R. To test for sex differences in bipolar spectrum disorders, a χ^2 analysis compared rates of boys and girls on the bipolar spectrum to those not on the bipolar spectrum. Because ADHD is a highly comorbid condition with pediatric bipolar disorder,[57] a χ^2 analysis also tested for sex differences among youth diagnosed with bipolar disorder spectrum disorders *without* comorbid ADHD. Chi-square analyses were also conducted across the 4 subtypes (bipolar I, II, and NOS and cyclothymia) given research suggesting sex differences based on subtype.

Chi-square analyses tested for sex differences in participants presenting with ADHD, ODD, CD, or unipolar depression as a primary or comorbid diagnosis. The rationale for this decision was 2-fold: (1) to replicate the established research findings on sex differences in other childhood disorders (i.e., more males present with ADHD, ODD, and CD, and more females present with unipolar depression) and (2) to validate the composition of the sample considering that it was enriched for bipolar disorder (i.e., by way of replicating established sex differences in other disorders).

To explore phenomenological differences in presenting mood states, total scores on the CDRS-R and YMRS were used to categorize participants into one of 5 categories (euthymic, manic, mixed, hypomanic, or depressed). Consistent with guidelines based on prior research,[58] scoring rules to determine presenting mood state are outlined in Table 4. Chi-square analyses evaluated sex differences at the mood presentation level. It should be noted that all participants were included in this analysis regardless of diagnosis, with most cases falling in the "euthymic" category if their behavior problems were not associated with mood disturbance. Within the bipolar sample, t tests were used to test for sex differences in total scores on the CDRS-R and YMRS. An analysis of variance (ANOVA) tested for an interaction of sex and age in terms of mood state severity (i.e., CDRS-R and YMRS total scores).

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Table 2. Primary Diagnostic Characteristics of Sample[a]

Diagnosis	Male, N (% within sex)	Female, N (% within sex)	Total, N (%)
Bipolar spectrum disorders[b]	246 (52)	141 (48)	387 (51)
Bipolar I	148 (32)	83 (29)	231 (30)
Bipolar II	8 (2)	10 (3)	18 (2)
Bipolar NOS	59 (13)	28 (10)	87 (11)
Cyclothymia	31 (7)	20 (7)	51 (7)
Unipolar depressive disorders	76 (16)	74 (25)	150 (20)
ADHD	94 (20)	25 (9)	119 (16)
Oppositional defiant disorder	3 (1)	4 (1)	7 (1)
Conduct disorder	9 (2)	1 (< 1)	10 (1)
Disruptive behavior disorder NOS	2 (< 1)	0 (0)	2 (< 1)
Anxiety disorders[c]	7 (1)	6 (2)	13 (2)
Substance abuse/dependence	2 (< 1)	0 (0)	2 (< 1)
Schizophrenia	1 (< 1)	0 (0)	1 (< 1)
Schizoaffective disorder	2 (< 1)	3 (1)	5 (1)
Enuresis	4 (1)	1 (< 1)	5 (1)
Adjustment disorder	1 (< 1)	0 (0)	1 (< 1)
No Axis I disorder	22 (5)	36 (12)	58 (8)

[a]Total Ns: males, N = 469 (62% of sample); females, N = 291 (38% of sample).
[b]Participants with bipolar spectrum disorders were significantly younger by about 1 year ($t = 3.57$, $p < .0005$). African American participants were less likely to be diagnosed with bipolar spectrum disorders than participants of other races ($\chi^2 = 11.51$, df = 2, N = 760, $p = .003$).
[c]Included posttraumatic stress disorder, obsessive-compulsive disorder, generalized anxiety disorder, and separation anxiety disorder.
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, NOS = not otherwise specified.

RESULTS

Diagnostic Characteristics

Three hundred eighty-seven youth met criteria for primary DSM-IV diagnoses of bipolar spectrum disorders (bipolar I, II, or NOS or cyclothymia). The remaining 373 youth met for a variety of primary DSM-IV diagnoses, including 58 youth who did not meet criteria for any Axis I disorder. The diagnostic distribution of the sample is reported in Table 2. There were significant demographic differences between participants with bipolar spectrum disorders and those without: Participants with bipolar spectrum disorders were significantly younger by about 1 year ($t = 3.57$, $p < .0005$). In addition, African American participants were less likely to be diagnosed with bipolar spectrum disorders than participants of other races ($\chi^2 = 11.51$, df = 2, N = 760, $p = .003$).

Sex Differences in Rates of Diagnosis

Consistent with hypothesis 1, no sex differences emerged when participants with bipolar spectrum disorders were compared to those without ($\chi^2 = 1.15$, df = 1, N = 760, $p = .28$). More surprisingly, this finding persisted when cases with comorbid ADHD were excluded ($\chi^2 = 0.61$, df = 1, N = 334, $p = .44$).

When the cases of bipolar spectrum disorders were broken down into 4 subtypes (bipolar I, II, and NOS and cyclothymia), no significant sex differences emerged ($\chi^2 = 3.72$, df = 3, N = 387, $p = .29$) (Table 3). This finding was inconsistent with hypothesis 2 in that no sex differences emerged in bipolar II disorder. However, this finding was limited by a small sample of 18 bipolar II cases, thereby reducing power to detect sex differences for this particular condition and for the overall comparison.

To validate the composition of the sample and to ensure that established sex differences in other disorders besides pediatric bipolar disorder were observed in the current sample, χ^2 analyses were conducted on cases presenting with unipolar depression, ADHD, ODD, and CD. Consistent with hypothesis 3, the rate of unipolar depression was higher in females (23% rate in females vs. 15% in males) ($\chi^2 = 7.07$, df = 1, N = 760, $p = .008$). In addition, more males presented with ADHD (66% rate in males vs. 40% in females) ($\chi^2 = 52.33$, df = 1, N = 760, $p < .0005$), ODD (31% rate in males vs. 17% in females) ($\chi^2 = 17.76$, df = 1, N = 760, $p < .0005$), and CD (9% rate in males vs. 5% in females) ($\chi^2 = 4.10$, df = 1, N = 760, $p < .05$).

Sex Differences in Presenting Mood State

There were significant sex differences across the 5 presenting mood states ($\chi^2 = 13.47$, df = 4, N = 760, $p = .009$) (Table 4). Consistent with hypothesis 4, males were overrepresented in the manic group (73% of pure manic cases were male, versus 62% males in the total sample). When severity of manic mood states among the smaller bipolar sample (i.e., YMRS total scores) was analyzed, no sex differences emerged ($t = .52$, $p = .60$) (Table 5). Thus, although boys in general are more likely to be categorized as presenting in manic mood states, boys and girls on the bipolar spectrum show equivalent levels of manic mood. Because developmental changes may constitute differences in YMRS scores such that younger boys may exhibit greater levels of hyperactivity leading

Table 3. Absence of Sex Differences in Bipolar Disorder Subtypes[a,b]

	Male		Female	
Diagnosis	Actual, N (% within sex)	Expected, N	Actual, N (% within sex)	Expected, N
Bipolar I	148 (60)	147	83 (59)	84
Bipolar II	8 (3)	11	10 (7)	7
Bipolar NOS	59 (24)	55	28 (20)	32
Cyclothymia	31 (13)	32	20 (14)	19

[a]Comparing the actual observed frequency to the expected frequency provides a sense of where diagnoses are occurring at much different rates than would be expected by chance.
[b]Neither sex was significantly overrepresented nor underrepresented among the bipolar subtypes ($\chi^2 = 3.72$, df = 3, N = 387, p = .29).
Abbreviation: NOS = not otherwise specified.

Table 4. Sex Differences in Presenting Mood State[a,b]

	Male		Female	
Mood State[c]	Actual, N (% within sex)	Expected, N	Actual, N (% within sex)	Expected, N
Euthymic	140 (30)	131	73 (25)	82
Manic	86 (18)	73	32 (11)	45
Mixed	124 (26)	132	90 (31)	82
Hypomanic	20 (4)	20	12 (4)	12
Depressed	99 (21)	113	84 (29)	70

[a]Comparing the actual observed frequency to the expected frequency provides a sense of where diagnoses are occurring at much different rates than would be expected by chance.
[b]There were significant sex differences in presenting mood state ($\chi^2 = 13.47$, df = 4, N = 760, p = .009).
[c]Euthymic mood = Children's Depression Rating Scale-Revised (CDRS-R) score ≤ 28 and Young Mania Rating Scale (YMRS) score < 12, depressed mood = CDRS-R > 28 and YMRS < 12, manic mood = CDRS-R ≤ 28 and YMRS ≥ 16, hypomanic mood = CDRS-R ≤ 28 and YMRS = 12–15, mixed mood = CDRS-R > 28 and YMRS ≥ 12.

to higher scores on the YMRS, an ANOVA tested whether there was a significant age-by-sex interaction among those youth with bipolar spectrum disorders. Age was treated as a categorical variable with younger (5–10 years) and older (11–17 years) age cohorts. Interestingly, there were no significant main effects of sex (F = 0.10, df = 1, N = 383, p = .75), age (F = 0.63, df = 1, N = 383, p = .43), or an interaction of the two (F = 2.73, df = 1, N = 383, p = .10).

Hypothesis 5 was only partially supported: Females were overrepresented in the depressed group more than they were in the mixed mood state group. Females on the bipolar spectrum were also more likely than males on the bipolar spectrum to have higher total scores on the CDRS-R (t = –2.85, p = .005) (Table 5). Because of literature suggesting higher rates of depression among adolescent females,[59] an ANOVA tested whether there was a significant age-by-sex interaction in CDRS-R scores within the bipolar sample. There was a main effect of sex, with females scoring higher on the CDRS-R than males (F = 5.20, df = 1, N = 383, p < .05), and a main effect of age, with older children scoring higher on the CDRS-R than younger children (F = 15.91, df = 1, N = 383, p < .0005). Unexpectedly, there was no age-by-sex interaction (F = 0.30, df = 1, N = 383, p = .58).

Finally, neither sex was overrepresented nor underrepresented in the euthymic or hypomanic mood state categories (hypothesis 6). Overall, the most robust sex differences were among those presenting with depressed or manic mood states.

Table 5. YMRS and CDRS-R Scores in Bipolar Spectrum Subsample[a]

Scale	Male	Female
YMRS		
Mean (SD)	21.90 (9.03)	21.41 (8.38)
Range	0–42	0–46
CDRS-R[b]		
Mean (SD)	32.24 (13.93)	36.52 (14.72)
Range	17–75	17–81

[a]246 males, 141 females.
[b]Of the participants on the bipolar spectrum, girls were more likely than boys to have higher total scores on the CDRS-R (t = –2.85, p = .005).
Abbreviations: CDRS-R = Children's Depression Rating Scale-Revised, YMRS = Young Mania Rating Scale.

DISCUSSION

Sex difference research in pediatric bipolar disorder is a relatively new line of inquiry. This study explored sex differences with regard to the diagnosis of bipolar spectrum disorders and presenting mood states. Hypotheses were based on the existing adult and child literature. Consistent with expectations, this study found no sex differences in rates of bipolar spectrum disorders. Predicting the null hypothesis with regard to sex differences in

bipolar spectrum disorders was justified for 2 reasons: One, the preponderance of adult studies indicates no sex differences in the rates of bipolar disorder, with the possible exception of bipolar II disorder. Child studies typically find low rates of bipolar II disorder, as was also true in this study, suggesting that the impact of bipolar II disorder on sex distributions in pediatric bipolar disorder would be small. Two, a post hoc power analysis provided evidence that a type II error was unlikely given that the study had a power of 79% even when assuming small effects (e.g., Cohen's $w = .10$; α set at $p < .05$; $df = 1$, $N = 760$).

Sex differences were also explored among the different bipolar subtypes (bipolar I, II, and NOS and cyclothymia). On the basis of the adult literature, it was hypothesized that a sex difference would emerge among the bipolar II subtype. This hypothesis was not supported. As previously stated, the bipolar II sample may have been too small to detect a sex difference. Future studies with larger samples of bipolar II youth may reveal a similar sex difference pattern as that observed among adults (i.e., female predominance). However, identifying large numbers of bipolar II youth may be challenging given that hypomanic episodes in a child (1) may not be viewed as developmentally inappropriate or impairing and (2) may be conceptualized by parents and teachers as a "relief from depression" rather than a pathologic mood state. Thus, a subset of children currently diagnosed as suffering from unipolar depression may actually have bipolar II disorder.

It may also be that the fluctuating presentation typical of children with bipolar disorder makes it less common for them to meet the durational criteria for a major depressive episode. Thus, bipolar NOS and cyclothymia may be more common diagnoses among children and adolescents given that these diagnoses have less stringent durational criteria. Developmental factors and the progression of bipolar illness provide additional explanations for why it may be difficult to identify bipolar II youth. For example, individuals who ultimately receive a diagnosis of bipolar II disorder may initially present during childhood and adolescence as depressed and not exhibit hypomanic symptomatology until early adulthood.[60] It will be important for retrospective and prospective studies to examine developmental precursors to bipolar II disorder. Adolescent samples of females would also be a helpful population to assess given that their rates of depression increase compared to males, whose rates of depression are more stable.[59]

Because individuals with bipolar disorder have diverse clinical presentations, this study also explored sex differences in terms of presenting mood states (i.e., euthymic, manic, mixed, hypomanic, and depressed). Consistent with expectations, males were overrepresented within the manic mood state category and females were overrepresented within the depressive mood state category. Because these findings were demonstrated within the larger sample (i.e., the sample that included nonbipolar cases), they may reflect that boys, in general, are more likely to exhibit externalizing symptomatology and girls are more likely to exhibit internalizing symptomatology. When looking solely at youth with bipolar spectrum disorders, there were no sex differences in levels of manic mood. Thus, girls on the bipolar spectrum may exhibit just as severe and disruptive presentations as do boys with the disorder. This hypothesis, however, would need to be tested in a prospective study. The course of the disorder may look very different for boys versus girls despite the fact that they may be able to reach moments similar in manic severity. Additionally, referral biases may account for the present study's higher rate of male participants; it may be more socially acceptable for parents and teachers to refer boys with disruptive behavior problems of varying degrees, whereas girls may need to exhibit more severe "acting out" behavior to warrant intervention. With regard to depressive states, this study showed that girls on the bipolar spectrum exhibited more severe levels of depressive mood states than boys on the spectrum. However, both sexes on the bipolar spectrum have equivalent increases in depression during the adolescent years. Thus, the sex differences that are observed during adolescence in studies on unipolar depression (see, for example, Hankin and Abramson[59]) may be less pronounced among bipolar samples.

Unexpectedly, this study did not show evidence for a sex difference in mixed mood states. It was thought that girls might be more prone to exhibit mixed mood states given relatively consistent findings in the adult literature.[1,40,41] However, because fluctuating presentations are often the rule rather than the exception in pediatric bipolar disorder,[44] it may be less common for a sex difference to emerge in mixed states during childhood. As girls enter adulthood, they may be less likely than boys to develop an episodic presentation. This is supported by research showing women to be more likely to exhibit a rapid-cycling course (i.e., 4 or more mood episodes per year).[24] Biological changes (e.g., menarche, pregnancy, and menopause) may also contribute to a course that is more fluctuating over a female's lifespan.

The above findings regarding mood presentation have important clinical implications. The manic mood states that boys are more likely to present with may be mistaken for ADHD, which could result in potentially iatrogenic pharmacologic remedies (i.e., stimulants). Conversely, because it may be more common for girls to present with a depressed mood state, an underlying bipolar condition may be overlooked and lead to the prescription of antidepressants, which may instigate mania.[61] Overall, the findings of the present study emphasize the importance of completing a thorough psychological examination when children present with mood or behavioral disturbances

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and recognizing that boys and girls may present differently. It is hoped that future research will help to elucidate the roles that genetics, puberty, cognitive styles, and environmental factors have in the expression of mania and depression in girls and boys over the course of development.

Although this study focused on sex differences in pediatric bipolar disorder, an interesting finding regarding race deserves mention: African American youth in this study were less likely than white youth to be diagnosed with bipolar disorder. Research on racial differences in diagnosis has shown that youth belonging to a racial minority may be more likely to be misdiagnosed with conduct disorder and schizophrenia.[62] Additionally, African American youth may be more likely than white youth to be prescribed antipsychotic medications.[63] These findings raise concern about potential racial biases in diagnostic decision-making or in the way that families present and describe symptoms. Thus, additional research is needed to elucidate factors contributing to race effects.

Limitations

Although the present study provides important findings regarding sex differences in pediatric bipolar disorder, it is important to make note of the study's limitations. First and foremost, this study was not an epidemiologic study. Although the sample size was large, national estimates of the prevalence of pediatric bipolar disorder suggest that the disorder is relatively rare. The present study may not be representative of bipolar youths in general but rather more descriptive of a group of profoundly disturbed outpatient youths with bipolar spectrum disorders.

Another limitation of the present study is its cross-sectional design. It is unknown whether the youth in this study who were diagnosed with bipolar spectrum disorders continued to meet criteria for bipolar spectrum disorders as they aged. Prospective studies of pediatric bipolar disorder are sorely needed given that these will be the studies that confirm or disconfirm the longitudinal validity of pediatric bipolar disorder. Preliminary data suggest that bipolar spectrum disorders do, in fact, persist over time and in some cases become progressively more severe.[26]

The measures used in this study also have some disadvantages. In particular, although the YMRS has been validated for use among child and adolescent populations,[51] it is important to recognize that the scale itself was designed for use in adult inpatient settings. Similarly, although the CDRS-R was designed for use in children and adolescents, it was not specifically intended for pediatric bipolar disorder. Thus, there is a great need for assessment measures that are created for and validated among pediatric bipolar disorder samples, which some researchers have begun doing.[64]

Despite these limitations, it is hoped that the present study will encourage researchers to explore how factors related to sex impact the expression, assessment, and development of mental illness, in particular pediatric bipolar disorder. The developmental period is a particularly crucial time period to study given that there are many biological, emotional, and cognitive changes taking place. It is important for research to inform clinical practice such that clinicians are aware of how mental illness exhibits itself differently among males and females. Because pediatric bipolar disorder is a particularly severe disorder that affects multiple systems (family, school, peer, etc.),[65] it will be important for studies to assess how various patient characteristics can affect the course and treatment of the illness. The present study addressed only one of these characteristics (i.e., sex), in the hopes that the findings will advance the delivery of high-quality health care to a clinical population that is sorely in need of it.

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